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# SYNTHESIS OF KETOSYL *SPIRO*-ISOXAZOLIDINE BY 1,3-DIPOLAR CYCLOADDITION OF 1-METHYLENE-SUGARS WITH NITRONES —A NEW ACCESS TO *C*-GLYCOSYL AMINO ACIDS[#]

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**Abstract** - The 1,3-dipolar cycloaddition reactions of 1-methylenesugars (**1a~c**) with nitrones (**2** and **5**) were carried out diastereoselectively under the catalysis of $BF_3 \cdot Et_2O$ at low temperature and afforded the α-stereoselective spiro ketosyl isoxazolidines in good to excellent yields. The reductive isoxazolidine ring-opening of the spiro moiety with the treatment of zinc and acetic acid resulted in a new kind of *C*-glycosyl amino acid possessing a ketose form, providing an access to *C*-glycosyl amino acids. The structures of the synthesized compounds were confirmed by the spectroscopic analyses.

## INTRODUCTION

Spiro-glycoside ring substructures, such as spiro-nucleoside, spiro-orthoesters, and spiro-ketal have been found in many biologically active natural products.[1-3] The strong biological activity of these compounds have triggered great interest in building such substructures.[4-6] Of the conventional method, cyclo-glycosidation reactions were used for the syntheses of the spiro-glycosides, especially for that of spiro-ketal. However, recent studies revealed that the rigid spiro system of a spiro-ketodisaccharide made the stereoselectivity of cyclo-ketosylation different from that of linear ketosylation.[5e,6,7] While the ketosylations of ketopyranoses could provide the thermodynamic stable α-ketodisaccharides exclusively,[6b,6c,7] the cyclo-ketosylation of forming the spiro-ketodisaccharide preferred the α,β-stereoselectivity to the α,α-selectivity in the two spiro anomeric carbons, affording the mixture of α,α- and α,β-isomers.[6b,6d] The stereoselective and efficient formation of a spiro-anomeric center is still a great challenge.

[#]*Dedicated to Professor Yuichi Kanaoka on the occasion of his 75th birthday.*

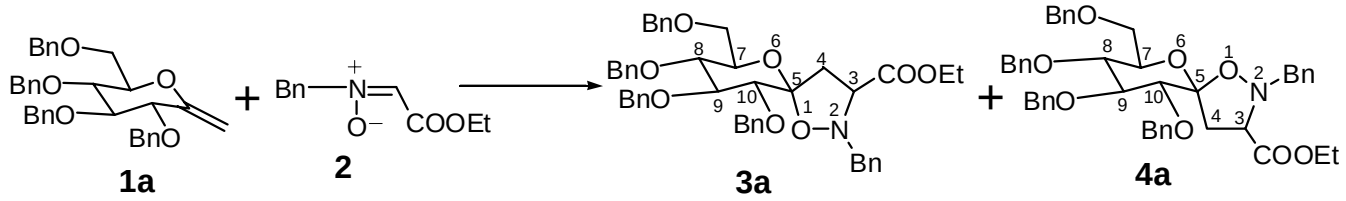
1,3-Dipolar cycloadditions of nitrones with alkenes, as one of the most important methods of cyclization reactions, have been widely used in organic synthesis.[8] With this reaction up to three new contiguous chiral centers could be created in one step. A stereoselective cycloaddition could be achieved by choosing an appropriate nitrone or alkene which contains either an electron-donating or electron-withdrawing substituent. Moreover, the use of Lewis acid could also control the stereoselectivity by forming metallic complexes with the nitrones or alkenes.[8c,8d,8g,9]

Although the utility of the 1,3-dipolar cycloaddition in the synthesis of carbohydrate derivatives has been recently reported,[8e~h,10] very few of the application of this methodology in the formation of spiro-glycoside has been briefly studied so far.[11] As an extension of our recent work on the syntheses of ketosyl glycosides and spiro-ketodisaccharides using 1-methylenesugars as the precursor,[6b,7d,7e] we describe in this article the stereoselective synthesis of glycosyl spiro-isoxazolidine by the 1,3-dipolar cycloaddition of nitrone to 1-methylenesugar and the further exploration of converting the spiro isoxazolidine to new *C*-glycosyl amino acids.

## RESULTS AND DISCUSSION

Most of nitrones are relatively stable and easily accessible compounds and they have been successfully used in organic synthesis.[8,12] The nitrones (**2**) and (**5**) were readily prepared according to the Dondoni's procedure[13] by the reaction of ethyl glyoxalate with the corresponding *N*-benzylhydroxylamine and *N*-methylhydroxylamine, respectively.

Considering the achievements of the stereoselective 1,3-dipolar cycloadditions of nitrones to alkenes[8,9] and the stereoselective glycosidations of 1-methylenesugars **(1)** [6b,7d,7e] catalysed by Lewis acids, we firstly examined the cycloaddition of the 1-methylenesugar (**1a**) with the nitrone (**2**) under various conditions (Scheme 1). The results are listed in Table 1.




Scheme 1

It should be noted that the 1,3-dipolar cycloaddition of **1a** with **2** proceeded diastereoselectively and gave only two anomeric isomers (**3a**) and (**4a**) possessing R-configuration on C-3, although the 1,3-dipolar cycloadditions of the 1-methylenesugars (**1a**) with the nitrones (**2**) should be supposed to afford four diastereomers, that is, two anomeric isomers having R-configuration on C-3 (**3a** and **4a**) and their diastereomers with S-configuration on C-3 (**3s** and **4s**) (as shown in Figure 2). The reaction did not

produce the other two anomeric isomers (**3s**) and (**4s**).

Table 1 1,3-Dipolar cycloaddition of the methylenesugar (**1a**) with nitrone (**2**)[a]

| Entry | Conditions | **3a** (%) (α-isomer) | **4a** (%) (β-isomer) | α : β |
|---|---|---|---|---|
| 1 | $BF_3 \cdot OEt_2$ (0.3 eq.), $CH_2Cl_2$, -78°C, 4 h | 33.2 | 2.2 | 15.1 : 1.0 |
| 2 | $BF_3 \cdot OEt_2$ (1.3 eq.), $CH_2Cl_2$, -78°C, 4 h | 56.8 | 3.8 | 14.9 : 1.0 |
| 3 | $BF_3 \cdot OEt_2$ (0.5 eq.), $CH_2Cl_2$, rt, 3 h | 57.2 | 11.2 | 5.1 : 1.0 |
| 4 | ***$BF_3 \cdot OEt_2$ (1.3 eq.), $CH_2Cl_2$, -78°C, 4 h→0°C*** | 71.9 | 6.4 | 11.3 : 1.0 |
| 5[b] | $BF_3 \cdot OEt_2$ (1.3 eq.), $CH_2Cl_2$, -78°C, 4 h→0°C | 87.5 | 8.0 | 10.9 : 1.0 |
| 6 | $BF_3 \cdot OEt_2$ (1.5 eq.), $Et_2O$, -78°C, 4 h→rt | 67.8 | 5.6 | 12.1 : 1.0 |
| 7 | $ZnBr_2$ (1.5 eq.), $CH_2Cl_2$, rt, 24 h | 28.1 | 35.9 | 1.0 : 1.3 |
| 8 | $ZnBr_2$ (1.5 eq.), $Et_2O$, rt, 24 h | 18.2 | 13.2 | 1.5 : 1.0 |
| 9 | $ZnCl_2$ (1.5 eq.), $CH_2Cl_2$, rt, 24 h | 18.4 | 29.5 | 1.0 : 1.6 |
| 10 | $Et_2AlCl$ (1.5 eq.), $CH_2Cl_2$, rt, 4 h | 22.1 | 18.4 | 1.2 : 1.0 |
| 11 | $AlCl_3$ (1.5 eq.), $CH_2Cl_2$, rt, 4 h | 16.3 | 14.8 | 1.1 : 1.0 |
| 12 | $TiCl_4$ (1.0 eq.), $CH_2Cl_2$, rt, 4 h | 12.7 | 10.5 | 1.2 : 1.0 |
| 13 | ***benzene, reflux, 24 h*** | 43.4 | 52.3 | 1.0 : 1.2 |

a: **1a** (0.2 mmol) and **2** (0.25 mmol) were used.

b: 2.0 equiv. of **2** was used.

As shown in Table 1, the cycloaddition reaction of the 1-methylenesugar (**1a**) with the nitrone (**2**) under the catalysis of $BF_3 \cdot Et_2O$ provided a mixture of the α- and β-anomeric isomers, ketosyl spiro-isoxazolidines (**3a**) and **(4a**) with the α-isomer (**3a**) as the predominant (Entries 1~6). In the presence of a catalytic amount of $BF_3 \cdot Et_2O$ (0.3 equiv.), the reaction of **1a** with **2** (1.25 equiv.) at -78°C gave the adducts (**3a**) and (**4a**) in low yield (35.4%) and in a α,β-stereoselective ratio of 15.1 : 1 with the nearly 58% recovery of the starting material (**1a**) (Entry 1), indicating that the stoichiometric amounts of the Lewis acid might be necessary for the reaction. In fact, the use of $BF_3 \cdot Et_2O$ in 1.3 equiv. afforded the products (**3a**) and (**4a**) in the overall yield of 60.6% without the remarkable change of the α-stereoselectivity (Entry 2). Moreover, increasing the reaction temperature up to 0°C after reacting at -78°C for 4 h resulted in a good yield (78.3%) of the adducts (**3a**) and (**4a**) with a satisfying α-stereoselectivity (Entry 4, this condition is called as **Procedure A**). Under this condition, an excessive use of the nitrone (**2**) (2.0 equiv.) provided an excellent yield (95.5%) of the products with a similar stereoselectivity (Entry 5).

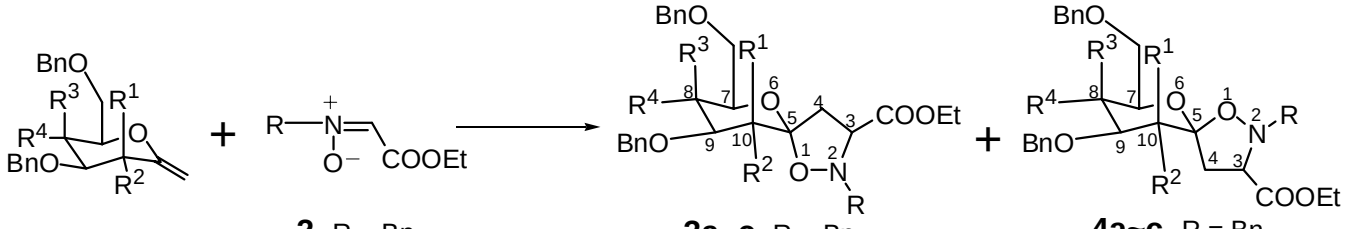
However, other Lewis acids, such as $ZnBr_2$, $ZnCl_2$, $Et_2AlCl$, $AlCl_3$, and $TiCl_4$, were found not to be efficient to this reaction and gave a poor stereoselectivity (Entries 7~12), although it has been recently

observed that the Lewis acids, such as $ZnBr_2$ and $Et_2AlCl$ could induce the 1,3-dipolar cycloaddition of some nitrone and enolic compounds to proceed in contrary stereoselective way.[9]

Further experiments showed that the reaction temperature could remarkably influence the reaction stereoselectivity and reactivity (Entries 2, 3, 4, and 13). A considerable decrease of the stereoselectivity was observed when the reaction was performed at room temperature with 0.5 equiv. of $BF_3 \cdot Et_2O$ catalyst (Entry 3). Moreover, while the cycloaddition could not complete at -78°C in the presence of 1.3 equiv. of $BF_3 \cdot Et_2O$ (Entry 2), the reaction could efficiently proceed in benzene at reflux to afford the mixture of **3a** and **4a** in excellent overall yield of 95.7% without using any Lewis acid catalyst (Entry 13, this condition is called as **Procedure B**). Unfortunately, the stereoselectivity of the reaction was not satisfied. The reaction stereoselectivities observed above were identical with those in the cycloglycosylations of forming spiro-ketodisaccharides.[6b]

The reaction stereoselectivity was slightly affected by the nature of the solvent due to the anomeric effects.[14] For example, the use of $Et_2O$ instead of $CH_2Cl_2$ was of benefit to the α-stereoselectivity in the reaction (Entries 6, 8).

The 1,3-dipolar cycloaddition reactions of **1b~c** to **2** and **1a~c** to **5** were also carried out according to **Procedure A** and **Procedure B**, respectively (Scheme 2), and the similar stereoselectivity as in the reaction of **1a** to **2** was obtained. The results are summarized in Table 2. In the case of mannose derivative (**1c**) possessing an axial 2-benzyloxy group, the reaction exhibited an increase of β-stereoselectivity under each condition of **Procedure A** and **B** in comparison with the cases of glucose derivative (**1a**) and galactose derivative (**1b**).




**1a~c**

**2** R = Bn
**5** R = Me

**3a~c** R = Bn
**6a~c** R = Me
**(α-isomer)**

**4a~c** R = Bn
**7a~c** R = Me
**(β-isomer)**

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **a (Glc)** | H | BnO | H | BnO |
| **b (Gal)** | H | BnO | BnO | H |
| **c (Man)** | BnO | H | H | BnO |

Scheme 2

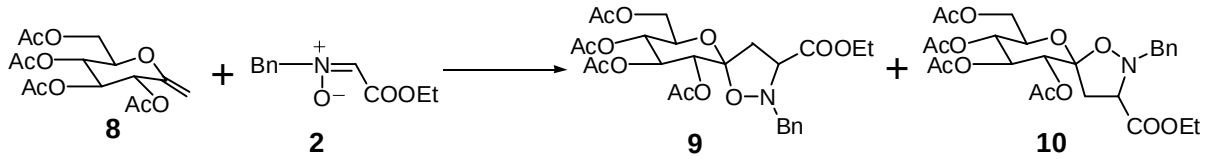
Table 2 1,3-Dipolar cycloadditions of the methylenesugar (**1a~c**) with nitrones (**2**) and (**5**)

| Entry | **1** | Nitrones | Conditions (**Procedure**) | Products (Yield %) | | α : β |
|---|---|---|---|---|---|---|
| 1 | **1a** | **2** | **A** | **3a** (71.9) | **4a** (6.4) | 11.3 : 1.0 |
| 2 | **1b** | **2** | **A** | **3b** (72.6) | **4b** (4.9) | 14.8 : 1.0 |
| 3 | **1c** | **2** | **A** | **3c** (58.0) | **4c** (10.8) | 5.4 : 1.0 |
| 4 | **1a** | **2** | **B** | **3a** (43.4) | **4a** (52.3) | 1.0 : 1.2 |
| 5 | **1b** | **2** | **B** | **3b** (31.0) | **4b** (31.5) | 1.0 : 1.0 |
| 6 | **1c** | **2** | **B** | **3c** (23.4) | **4c** (42.1) | 1.0 : 1.8 |
| 7 | **1a** | **5** | **A** | **6a** (70.1) | **7a** (7.7) | 9.1 : 1.0 |
| 8 | **1b** | **5** | **A** | **6b** (68.6) | **7b** (7.8) | 8.8 : 1.0 |
| 9 | **1c** | **5** | **A** | **6c** (53.7) | **7c** (28.6) | 1.9 : 1.0 |
| 10 | **1a** | **5** | **B** | **6a** (41.0) | **7a** (41.4) | 1.0 : 1.0 |
| 11 | **1b** | **5** | **B** | **6b** (37.5) | **7b** (41.3) | 1.0 : 1.1 |
| 12 | **1c** | **5** | **B** | **6c** (12.3) | **7c** (38.2) | 1.0 : 3.1 |

**Procedure A:** 1-Methylenesugar (0.2 mmol), nitrone (0.25 mmol), $BF_3$•$OEt_2$ (1.3 eq.), $CH_2Cl_2$, -78°C, 4 h→0°C.

**Procedure B**: 1-Methylenesugar (0.2 mmol), nitrone (0.25 mmol), benzene, reflux, 24 h.

In order to study the effect of the protecting groups on the reaction stereoselectivity, the 1,3-dipolar cycloaddition of the acetyl-protected 1-methylenesugar (**8**) with the nitrone (**2**) was examined under the similar conditions as in the **Procedure A** using 1.5 equiv. of $BF_3$•$OEt_2$ (Scheme 3), and a similar result, except a decreased reactivity, was obtained as shown in the Table 3. Interestingly, a substantial decrease of the α-stereoselectivity was not observed, although the existence of the equatorial 2-*O*-acetyl group usually caused a remarkable increase of the β-stereoselectivity in a common glycosylation reaction due to its neighboring group participation effect.[14]

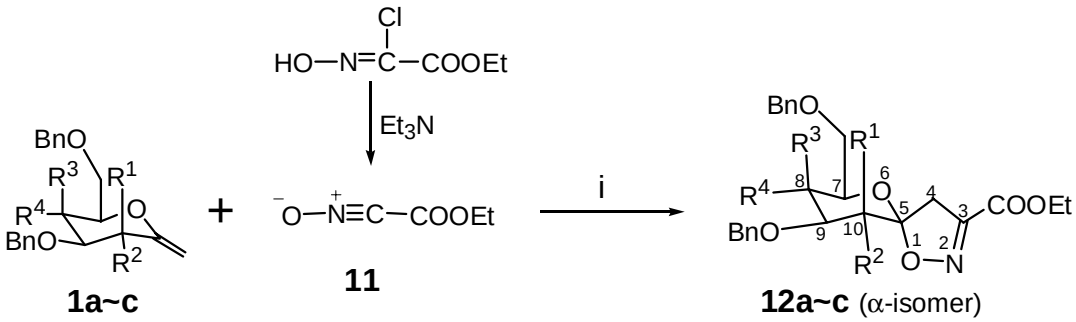



Scheme 3

Table 3 1,3-Dipolar cycloaddition of the 2,3,4,5-tetra-*O*-acetyl-1-methylenesugar (**8**) with nitrone (**2**)

| Entry | Conditions | **9** (α) | **10** (β) | α : β |
|---|---|---|---|---|
| 1 | $BF_3$•$OEt_2$ (1.5 eq.), $CH_2Cl_2$, -78°C, 1 h | No reaction | | |
| 2 | $BF_3$•$OEt_2$ (1.5 eq.), $CH_2Cl_2$, -78°C, 1 h→rt, 4 h | 72.6% | 7.3% | 9.9 : 1.0 |

The 1,3-dipolar cycloaddition reactions of **1a~c** with the nitrile oxide (**11**) which was generated *in situ* from the corresponding ethyl chlorooximidoacetate under a basic condition were also studied. The reaction proceeded stereospecifically at room temperature and provided the ketosyl spiro-isoxazoline (**12**) as the sole product (Scheme 4). This stereospecific result was consistent with the RajanBau's observation.[15]




**1a~c** **11** **12a~c** (α-isomer)

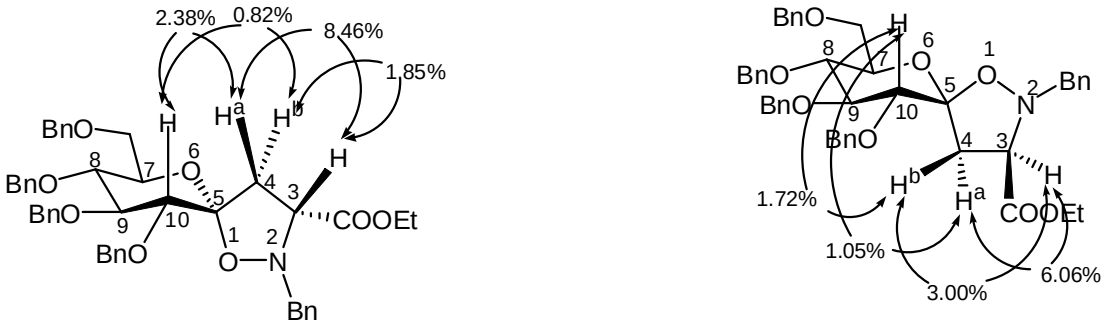
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | **12** (%) |
|---|---|---|---|---|---|
| **a (Glc)** | H | BnO | H | BnO | 55.2 |
| **b (Gal)** | H | BnO | BnO | H | 66.2 |
| **c (Man)** | BnO | H | H | BnO | 70.0 |

Scheme 4 *Reaction conditions*: (i) $CH_2Cl_2$, rt

The structures and configurations of the synthesized spiro-isoxazolidines and spiro-isoxazolines were determined by the analyses of their spectral data of $^1$H NMR, $^{13}$C NMR and 2D-COSY, and by the NOESY experiments. It has been shown that in the $^{13}$C NMR spectra of *C*-glycosides[16] and ketosyl spiro-disaccharides[6b] the signals of the anomeric carbon in the α-isomers appeared in higher field than those in the β-isomers. From this point of view, the anomeric configurations of the products were assigned by the comparison of the anomeric $^{13}$C NMR spectral data between each two anomeric isomers. Careful examination of vicinal proton-coupling constants unambiguously suggested a chair conformation for the six membered sugar rings (See the **EXPERIMENTAL** for the proton assignments). Accordingly, the configuration of the anomeric carbon and the relative orientation of the isoxazolidine ring substituents were further established from the NOE observations between $H^3$ and $H^4$, $H^4$ and $H^{10}$ as exemplified by the analyses of compounds (**3a**) and (**4a**) in Figure 1 (Also see Table 4).

The respective irradiations of $H^{4a}$ and $H^{4b}$ in **3a** resulted in the enhancements of the signals for $H^{10}$ and $H^3$. The enhancements on $H^{10}$ and $H^3$ caused by $H^{4a}$ were bigger than those resulted from $H^{4b}$. When $H^{10}$ was irradiated, the similar results that the interaction between $H^{4a}$ and $H^{10}$ was stronger than $H^{4b}$ and $H^{10}$ were observed, indicating that $H^{10}$ to $H^{4a}$ and $H^{4a}$ to $H^3$ should be in *cis*-orientation as shown in Figure 1. Comparatively, in compound (**4a**) stronger effects of $H^{4b}$ to $H^3$and $H^{10}$were observed, supporting the

conformation shown in Figure 1.




**3a** **4a**

Figure 1 NOE analyses of compounds (**3a**) and (**4a**)

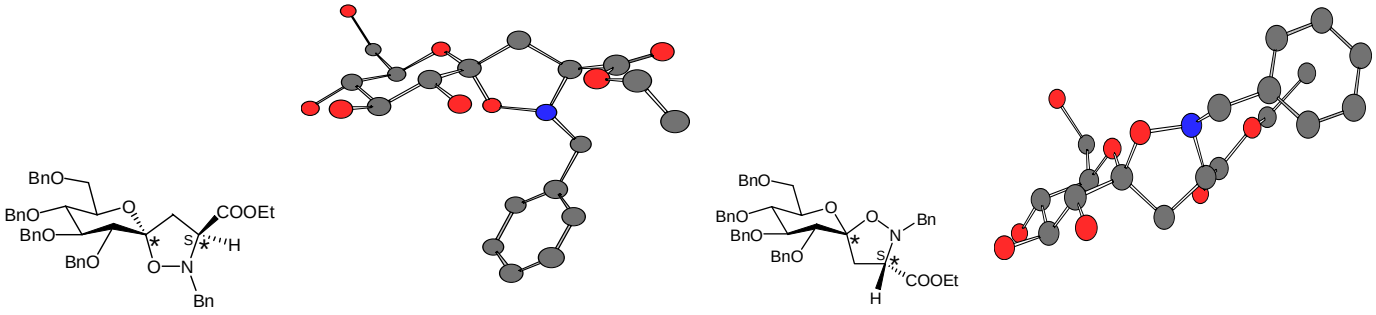
Table 4 Selected NOE data of the ketosyl spiro-isoxazolidines **3a~c**, **4a~c**, **9** and **10**

| | **3a** (%) | **4a** (%) | **4b** (%) | **3c** (%) | **4c** (%) | **9** (%) | **10** (%) |
|---|---|---|---|---|---|---|---|
| $H^{4a}\rightarrow H^{10}$ | 2.38 | 1.05 | 1.85 | 1.51 | 1.71 | 5.59 | 0.86 |
| $H^{4a}\rightarrow H^{4b}$ | 13.71 | 19.17 | 12.66 | 6.52 | 15.07 | 26.82 | 17.82 |
| $H^{4a}\rightarrow H^{3}$ | 8.46 | 6.06 | 7.01 | 2.73 | 5.83 | 9.46 | 6.87 |
| $H^{4b}\rightarrow H^{10}$ | 0.82 | 1.72 | 4.12 | 0 | 5.11 | 0.95 | 4.96 |
| $H^{4b}\rightarrow H^{4a}$ | 7.57 | 15.20 | 13.21 | 2.87 | 16.27 | 18.05 | 16.76 |
| $H^{4b}\rightarrow H^{3}$ | 1.85 | 3.00 | 1.69 | 2.62 | 1.87 | 2.62 | 2.02 |
| $H^{10}\rightarrow H^{4a}$ | 2.31 | 0.70 | - | - | - | - | - |
| $H^{10}\rightarrow H^{4b}$ | 0.70 | 1.00 | - | - | - | - | - |

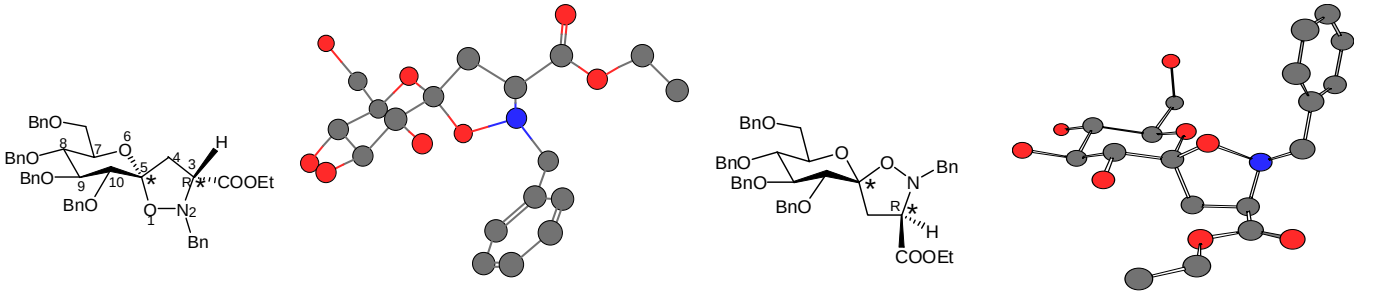
Similarly, the configurations of the other isooxazolidine compounds except **3b** were established on the basis of their NOE experiments (See Table 4). As for the compound (**3b**), since the signals of the $H^{4a}$ and $H^{4b}$ were overlapped, it was difficult to distinguish the NOE effects resulted from $H^{4a}$ or $H^{4b}$. The structure was deduced by the comparison of the signals of the anomeric carbons with its diastereomer (**4b**) whose configuration were assigned by NOE experiment. In addition, the configurations obtained from the NOE experiments as above were also supported by the molecular modeling calculation results using MacroModel program[17] as shown in Figure 2.

The conformations and their corresponding energies ($\Delta E$) of the compounds (**3a**) and (**4a**), and their diastereomers (**3s**) and (**4s**) were calculated[17] using MacroModel 6.0 with the MM2* force field[18] with LOMD (Low Mode) conformational search technique.[19] The most stable conformations of the diastereomers and the corresponding minimized energies are shown in Figure 2. It was found that in all

cases the pyranoid rings took the energetically favoured chair form. In the cases of **3a** and **4a** being anomeric isomers with the *R*-configuration on C-3, the stable conformers from the most stable one to the 20th were in the almost same conformations, but in the cases of **3s** and **4s** having *S*-configuration on C-3, there were a variety of conformations among the stable conformers from the first one to the 20th. Moreover, the calculated energies corresponding the most stable conformers of **3a** and **4a** were much lower than those of **3s** and **4s**, that is, the R-diastereomer (C-3) of **3a** and **4a** were more thermodynamically stable than the S-diastereomer (C-3) of **3s** and **4s**. With the calculation results it was reasonable to understand the reaction stereoselectivity that the 1,3-dipolar cycloadditions of 1-methylenesugars (**1a~c**) with nitrones (**2**) and (**5**) afforded only two of the four diastereomers in each case.




**3s(S)(α)** (Δ*E* = -10.70 kcal) **4s(S) (β)** (Δ*E* = -5.30 kcal)




**3a(R) (α)** (Δ*E* = -46.08 kcal) **4a(R) (β)** (Δ*E* = -40.51 kcal)

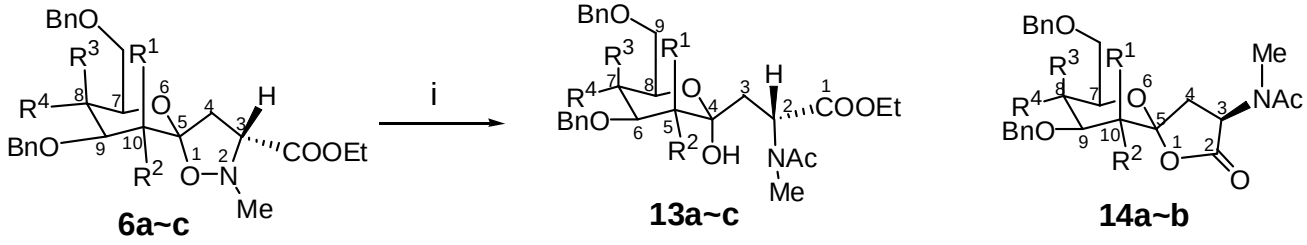
$\Delta\Delta E = \Delta E_{3a} - \Delta E_{3s}$ = -46.08 – (-10.70) = -29.38 kcal $\Delta\Delta E = \Delta E_{4a} - \Delta E_{4s}$ = -40.51 – (-5.30) = -35.21 kcal

Figure 2 Energy minimized conformations of **3a** and **4a** and their two diastereomers (**3s**) and (**4s**)
(The benzyls on pyranoid rings and all protons were omitted after minimization for clarity)

It has been revealed that the carbohydrate-protein interaction played very important roles in carbohydrate biology,[20] and great attentions have recently been attracted on the syntheses of glycopeptides and glycosyl amino acids, and their analogues.[21,22] With the convenient preparation of the ketosyl spiro-isoxazolidine in hands, we extended our study by approaching a new access to *C*-glycosyl amino acids from the ketosyl spiro-isoxazolidines in virtue of the reductive cleavage of the N-O bond.

A variety of the reductive isoxazolidine ring–opening methods which generated β-amino alcohol have been developed.[8a,8b] For example, the catalytic hydrogenation with palladium or Raney nickel and the

treatment of the isoxazolidine with zinc and acid were commonly used. The hydrogenation catalyzed by $Pd(OH)_2/C$ (20%) of the spiro-isoxazolidine (**6a**) was firstly tried in hope that the cleavage of the O-N bond and debenzylation would be finished by using this one step reaction. However, the reaction was found not to proceed efficiently and produced an inseparable mixture most likely due to the inactivation of the catalyst by the generated amino group. After careful examination, the best result of reductively cleaving the N-O bond was obtained. The treatment of ketosyl spiro-isoxazolidines (**6a~c**) with activated zinc powder in $AcOH/Ac_2O$ solution at room temperature afforded the ring-opened products (**13a~c**) (*C*-glycosyl amino acids) and the recyclized products (**14a~b**) (Scheme 5)




| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | **13** | **14** |
|---|---|---|---|---|---|---|
| **a (Glc)** | H | BnO | H | BnO | 45.8% | 39.6% |
| **b (Gal)** | H | BnO | BnO | H | 40.2% | 46.1% |
| **c (Man)** | BnO | H | H | BnO | 42.9% | - |

Scheme 5 *Reaction conditions*: (i) Zn, AcOH, $Ac_2O$, rt

In the reaction, the chiral carbons in the products (**13a~c**) (C*-2) and (**14a~b**) (C*-3) conserved the configurations on the corresponding chiral carbons (C*-3) in compounds (**6a~c**). The *R*-configuration on this carbon was further confirmed by the analyses of NOE experiments with **14a~b** as shown in Figure 3.

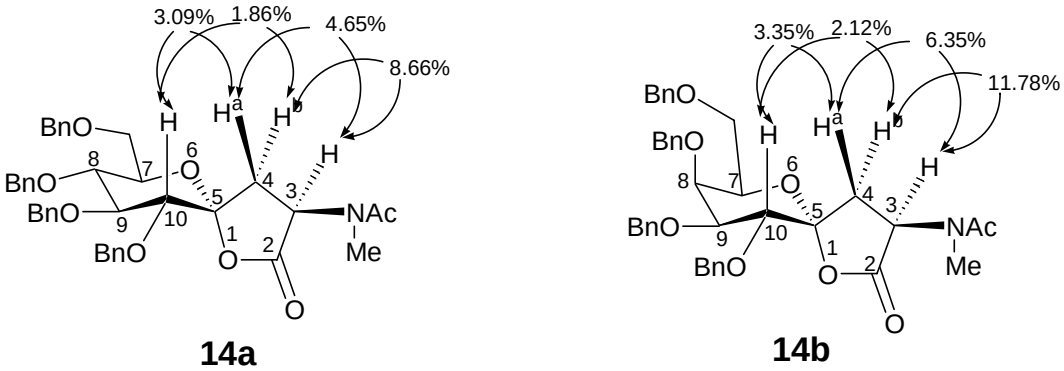
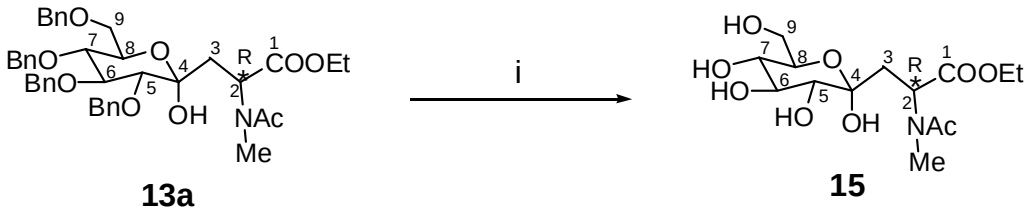



Figure 3 The NOE analyses of compounds (**14a**) and (**14b**)

Finally, the debenzylation of the *C*-glycosyl amino acid (**13a**) was completed by the catalytic hydrogenation on $Pd(OH)_2/C$ and afforded the corresponding *C*-glycosyl amino acid (**15**) as shown in Scheme 6. The spectral properties of **15** were identical with the structure shown.




**13a** **15**

Scheme 6 *Reaction conditions*: (i) $Pd(OH)_2/C$, $H_2$, MeOH.

In summary, stereoselective formation of glycosyl spiro-isoxazolidine was achieved by the 1,3-dipolar cycloaddition of 1-methylenesugar with nitrone and provided two anomeric isomers. While the reaction showed low stereoselectivity under thermodynamic conditions (**Procedure B**), the cycloaddition promoted by $BF_3 \cdot Et_2O$ at -78°C (**Procedure A**) gave the α-isomer predominantly. The stereoselectivity was similar to that in the cycloketosylation in our previous report.[6b] The treatment of the spiro-isoxazolidine (**6a**) with Zn in AcOH and $Ac_2O$ solution resulted in the reductive cleavage of O-N bond with the retention of the configuration at the chiral carbon (C*-3), and followed by debenzylation using the catalytic hydrogenation the *C*-glycosyl amino acid with a ketose-like structure was obtained, providing a new access to the *C*-glycosyl amino acids.

## EXPERIMENTAL

**General methods**. — Melting points were measured on a YANACO Micro Melting Point Apparatus and were uncorrected. IR spectra were recorded on a Jasco FT/IR-800 Fourier-transform infrared spectrophotometer. $^1$HNMR, $^{13}$CNMR and COSY spectra were measured on a JEOL ECP 600 (600 MHz) NMR spectrometers using tetramethylsilane ($Me_4Si$) as an internal standard. MS spectra and HRMS spectra were carried out on a JEOL JMS-SX102A mass spectrometer with FAB (Fast Atomic Bombardment) using 3-Nitrobenzyl alcohol (NBA) as the matrix. Optical rotations were measured with a Jasco DIP-370 digital polarimeter. TLC was performed on precoated plates (Merck TLC aluminum sheets silica 60 $F_{254}$) with detection by UV light or with phosphomolybdic acid in $EtOH/H_2O$ followed by heating. Column chromatography was performed using $SiO_2$ (Wakogel C-200, Wako).

**Calculations.** — Low-mode searches (LOMD)[19] for compounds (**3a**) and (**4a**), and their diastereomers (**3s**) and (**4s**) were performed using MacroModel ver. 6.0[18] with the MM2* derivative of MM2 force field on a Silicon Graphics IRIS-Indigo workstation. LOMD for each compound was continued until around 5,000 conformers were generated.

**General procedure of 1,3-dipolar cycloadditions of the 1-methylenesugars (1) with nitrones (2).**

**Procedure A: Under the catalysis of a Lewis acid:** — To a solution of **1a** (107 mg, 0.2 mmol), **2** (52 mg, 0.25 mmol) and Molecular sieves 4A (MS 4A, 300 mg) in 4 mL of $CH_2Cl_2$ was added $BF_3$•$Et_2O$ (32 μL, 0.25 mmol, 1.3 equiv.) under Argon atmosphere at –78°C. The solution was stirred at the same temperature for 4 h, then the reaction temperature was gradually increased up to 0°C, then, triethylamine (0.1 mL) was added to quench the reaction. The solvent was removed under reduced pressure, and the residue was applied on silica gel column chromatography using AcOEt : Hexane (1 : 5) as the eluent to afford 107.6 mg (71.9%) of **3a** and 9.5 mg (6.4%) of **4a**. With the same procedure, different conditions with various Lewis acids were examined and the results are summarized in Table 1.

**Procedure B: In the absence of Lewis acid**: — A solution of **1a** (107 mg, 0.2 mmol) and **2** (52 mg, 0.25 mmol) in 5 mL of benzene was refluxed under Argon for 24 h. The reaction was monitored by TLC (AcOEt : Hexane = 1 : 2). After the completion of the reaction, the solvent was removed under reduced pressure. The residue was submitted to silica gel column chromatography using AcOEt : Hexane (1 : 5) as the eluent to afford **3a** (64.5 mg, 43.4%) and **4a** (77.8 mg, 52.3%).

Following the procedures of **A** and **B**, the 1,3-dipolar cycloadditions of **1b**, **1c** with **2**, and **1a~c** with **5** were carried out and afforded the corresponding products. Similarly, the reaction of **8** with **2** under the conditions in **Procedure A** provided the products (**9**) and (**10**). The results are listed in Table 2 and Table 3, respectively.

**Ethyl (3*R*,5*R*,8*R*,9*S*,10*R*)-2-benzyl-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (3a)**

Colorless syrup, $[\alpha]^{25}_D$: +68.80° (*c* 1.0, $CHCl_3$); IR (neat) 3063.33, 3030.54, 2907.80, 2866.57, 1954.13, 1871.18, 1811.38, 1743.86, 1604.97, 1541.31, 1496.94, 1450.50, 1363.84, 1288.61, 1209.51, 1157.43, 1072.55, 906.65, 871.93, 736.90, 698.32 $cm^{-1}$; $^1$HNMR ($CDCl_3$): δ (ppm) 1.23 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.49 (dd, 1H, *J* = 13.20 Hz, *J* = 8.25 Hz, 4-H), 2.59 (dd, 1H, *J* = 12.65 Hz, *J* = 7.15 Hz, 4-H), 3.57 (d, 1H, *J* = 9.90 Hz, 10-H), 3.60 (t, 1H, *J* = 7.70 Hz, 3-H), 3.65 (dd, 1H, *J* = 10.99 Hz, *J* = 2.20 Hz, 7-$CH_2$), 3.76 (dd, 1H, *J* = 11.00 Hz, *J* = 2.65 Hz, 7-$CH_2$), 3.78 (t, 1H, *J* = 9.35 Hz, 8-H), 3.88 (br d, 1H, *J* = 8.80 Hz, 7-H), 3.89 (t, 1H, *J* = 9.35 Hz, 9-H), 4.06~4.18 (m, 3H, two $OCH_2$- and one $NCH_2Ph$), 4.19 (d, 1H, *J* = 13.75 Hz, one $NCH_2Ph$), 4.49 (d, 1H, *J* = 12.09 Hz, $CH_2Ph$), 4.58 (d, 1H, *J* = 10.45 Hz, $CH_2Ph$), 4.62 (d, 1H, *J* = 12.05 Hz, $CH_2Ph$), 4.70 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.82 (d, 1H, *J* = 10.44 Hz, $CH_2Ph$), 4.88 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.90 (d, 1H, *J* = 10.99 Hz, $CH_2Ph$), 5.03 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 7.17~7.18 (m, 2H, ArH), 7.25~7.39 (m, 23H, ArH); $^{13}$CNMR ($CDCl_3$): δ (ppm) 14.07 ($CH_3$), 41.24 (4-C), 61.13 ($OCH_2$), 61.38 ($NCH_2Ph$), 65.65 (3-C), 68.22 (7-$CH_2$), 72.19 (7-C), 73.42 ($CH_2Ph$), 74.83 ($CH_2Ph$), 75.40 ($CH_2Ph$), 75.45 ($CH_2Ph$), 78.03 (8-C), 79.57 (10-C), 83.90 (9-C), 105.41 (5-C), 127.35 (Ar), 127.56 (Ar), 127.59 (Ar), 127.71 (Ar), 127.77 (Ar), 127.78 (Ar), 127.81 (Ar), 127.91 (Ar), 128.18 (Ar), 128.30

(Ar), 128.31 (Ar), 128.38 (Ar), 128.46 (Ar), 129.36 (Ar), 136.21 (Ar), 138.07 (Ar), 138.12 (Ar), 138.27 (Ar), 138.51 (Ar), 169.59 (C=O); HRMS (FAB) calcd for $C_{46}H_{49}NO_8Na$ 766.3356, Found: 766.3353.

**Ethyl (3*R*,5*S*,8*R*,9*S*,10*R*)-2-benzyl-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (4a)**

White solid, mp 104~105°C; $[\alpha]^{25}_D$: +22.40° (*c* 1.0, $CHCl_3$); IR (KBr): 3088.41, 3063.33, 3030.54, 2976.52, 2916.72, 2870.43, 1954.13, 1880.82, 1817.17, 1740.00, 1604.97, 1496.94, 1454.50, 1394.70, 1358.05, 1188.30, 1172.86, 1078.34, 1062.91, 1030.11, 995.39, 891.22, 752.33, 698.32; $^1$HNMR ($CDCl_3$): δ (ppm) 1.10 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.51 (dd, 1H, *J* = 12.65 Hz, *J* = 8.25 Hz, 4-H), 2.83 (dd, 1H, *J* = 13.19 Hz, *J* = 8.24 Hz, 4-H), 3.57 (d, 1H, *J* = 9.90 Hz, 10-H), 3.65 (t, 1H, *J* = 9.90 Hz, 8-H), 3.67 (dd, 1H, *J* = 10.99 Hz, *J* = 1.65 Hz, 7-$CH_2$), 3.73 (dd, 1H, *J* = 10.99 Hz, *J* = 4.40 Hz, 7-$CH_2$), 3.86 (t, 1H, *J* = 8.24 Hz, 3-H), 3.91 (qd, 2H, *J* = 7.15 Hz, *J* = 1.10 Hz, $OCH_2$-), 3.98 (t, 1H, *J* = 9.35 Hz, 9-H), 3.99~4.01 (m, 1H, 7-H, overlapped with 9-H), 4.16 (d, 1H, *J* = 12.65 Hz, $NCH_2Ph$), 4.49 (d, 1H, *J* = 12.64 Hz, $NCH_2Ph$), 4.53 (d, 1H, *J* = 12.65 Hz, $CH_2Ph$), 4.54 (d, 1H, *J* = 9.90 Hz, $CH_2Ph$), 4.63 (d, 1H, *J* = 12.09 Hz, $CH_2Ph$), 4.71 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.84 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.85 (d, 1H, *J* = 11.45 Hz, $CH_2Ph$), 4.88 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.96 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 7.17~7.18 (m, 2H, ArH), 7.25~7.38 (m, 23H, ArH); $^{13}$CNMR ($CDCl_3$): δ (ppm) 13.95 ($CH_3$), 41.18 (4-C), 61.08 ($OCH_2$), 64.80 ($NCH_2Ph$), 65.52 (3-C), 68.77 (7-$CH_2$), 72.09 (7-C), 73.47 ($CH_2Ph$), 74.98 ($CH_2Ph$), 75.19 ($CH_2Ph$), 75.53 ($CH_2Ph$), 78.25 (8-C), 78.37 (10-C), 83.81 (9-C), 107.96 (5-C), 127.50 (Ar), 127.59 (Ar), 127.67 (Ar), 127.73 (Ar), 127.79 (Ar), 127.83 (Ar), 127.84 (Ar), 127.85 (Ar), 128.23 (Ar), 128.25 (Ar), 128.30 (Ar), 128.38 (Ar), 129.28 (Ar), 136.29 (Ar), 137.73 (Ar), 137.97 (Ar), 138.04 (Ar), 138.41 (Ar), 170.64 (C=O); HRMS (FAB) calcd for $C_{46}H_{49}NO_8Na$ 766.3356, Found: 766.3359.

**Ethyl (3*R*,5*R*,8*S*,9*S*,10*R*)-2-benzyl-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (3b)**

Colorless syrup, $[\alpha]_D^{25}$ = +66.00° (*c* 1.0, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2912.87, 2870.43, 1741.93, 1496.94, 1454.50, 1367.70, 1273.17, 1207.59, 1103.42, 1060.98, 736.90, 698.32 $cm^{-1}$; $^1$H NMR ($CDCl_3$): δ 1.20 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.56 (d, 2H, *J* = 7.70 Hz, 4-H), 3.51 (dd, 1H, *J* = 8.80 Hz, *J* = 4.95 Hz, 7-$CH_2$), 3.61 (br t, 2H, *J* = 8.80 Hz, 3-H and 7-$CH_2$), 3.87 (dd, 1H, *J* = 9.89 Hz, *J* = 2.75 Hz, 9-H), 4.05~4.11 (m, 6H, 7-H, 10-H, 8-H, two H of $OCH_2$ and one H of $NCH_2Ph$), 4.17 (d, 1H, *J* = 13.75 Hz, $NCH_2Ph$), 4.42 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.46 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.63 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.69 (d, 1H, *J* = 12.09 Hz, $CH_2Ph$), 4.71 (d, 1H, *J* = 12.65 Hz, $CH_2Ph$), 4.74 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.93 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 5.07 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 7.26~7.37 (m, 25H, ArH); $^{13}$C NMR ($CDCl_3$): δ 14.06 ($CH_3$), 41.07 (4-C), 61.15 ($NCH_2Ph$), 61.44($OCH_2$), 65.73 (3-C), 67.97 (7-$CH_2$), 70.76 (7-C), 72.27 ($CH_2Ph$), 73.27 ($CH_2Ph$), 74.28 (10-C), 74.80 ($CH_2Ph$), 75.46 ($CH_2Ph$), 76.06 (8-C), 81.21 (9-C), 106.20 (5-C), 127.49 (Ar), 127.54 (Ar), 127.65 (Ar), 127.70 (Ar), 127.91 (Ar), 128.09 (Ar), 128.14 (Ar), 128.16 (Ar), 128.18 (Ar), 128.36 (Ar), 128.40 (Ar), 129.32 (Ar), 136.46 (Ar),

138.07 (Ar), 138.36 (Ar), 138.77 (Ar), 169.69 (C=O); HRMS (FAB) calcd for $C_{46}H_{49}NO_8Na$ 766.3356, Found: 766.3365.

**Ethyl (3*R*,5*S*,8*S*,9*S*,10*R*)-2-benzyl-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (4b)**

Colorless syrup, $[\alpha]_D^{25}$ = +36.50° (*c* 1.0, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2932.80, 2880.52, 1742.02, 1604.97, 1496.94, 1454.50, 1365.51, 1278.22, 1208.60, 1110.02, 1061.58, 906.28, 736.90, 698.32 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.12 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.55 (dd, 1H, *J* = 12.65 Hz, *J* = 8.80 Hz, 4-H), 2.88 (dd, 1H, *J* = 12.65 Hz, *J* = 7.15 Hz, 4-H), 3.52 (dd, 1H, *J* = 9.35 Hz, *J* = 7.15 Hz, 7-$CH_2$), 3.56 (dd, 1H, *J* = 9.35 Hz, *J* = 6.60 Hz, 7-$CH_2$), 3.83 (t, 1H, *J* = 7.70 Hz, 3-H), 3.92 (q, 2H, *J* = 7.15 Hz, $OCH_2$), 3.93 (dd, 1H, *J* = 9.90 Hz, *J* = 2.75 Hz, 9-H), 3.96 (dd, 1H, *J* = 2.75 Hz, *J* = 1.65 Hz, 8-H), 4.03~4.09 (m, 2H, 7-H and 10-H), 4.16 (d, 1H, *J* = 13.75 Hz, $NCH_2Ph$), 4.46 (d, 1H, *J* = 13.75 Hz, $NCH_2Ph$, overlapped), 4.46 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$, overlapped), 4.51 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.62 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.69~4.74 (m, 3H, $CH_2Ph$), 4.97 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.97 (d, 1H, *J* = 10.99 Hz, $CH_2Ph$), 7.23~7.36 (m, 25H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 13.98 ($CH_3$), 41.07 (4-C), 61.11 ($NCH_2Ph$), 61.45($OCH_2$), 65.61 (3-C), 68.14 (7-$CH_2$), 71.22 (7-C), 72.14 ($CH_2Ph$), 72.88 ($CH_2Ph$), 73.28 (10-C), 73.51 ($CH_2Ph$), 74.65 ($CH_2Ph$), 74.99 (8-C), 81.23 (9-C), 108.91 (5-C), 127.31 (Ar), 127.36 (Ar), 127.58 (Ar), 127.68 (Ar), 127.72 (Ar), 127.74 (Ar), 128.14 (Ar), 128.18 (Ar), 128.25 (Ar), 128.29 (Ar), 128.33 (Ar), 128.38 (Ar), 128.78 (Ar), 129.17 (Ar), 136.69 (Ar), 137.96 (Ar), 138.32 (Ar), 138.55 (Ar), 169.68 (C=O); HRMS (FAB) calcd for $C_{46}H_{49}NO_8Na$ 766.3358, Found: 766.3349.

**Ethyl (3*R*,5*R*,8*R*,9*S*,10*S*)-2-benzyl-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (3c)**

Colorless syrup, $[\alpha]_D^{25}$ = +71.60° (*c* 1.0, $CHCl_3$); IR (neat) ν 3063.33, 3030.54, 2903.22, 2866.57, 1741.93, 1496.94, 1450.50, 1367.70, 1207.59, 1095.70, 1028.18, 912.44, 736.90, 698.32 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.21 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.41 (br s, 1H, 4-H), 2.69 (dd, 1H, *J* = 13.47 Hz, *J* = 6.87 Hz, 4-H), 3.48 (br t, 1H, *J* = 7.15 Hz, 3-H), 3.63 (br s, 1H, 10-H), 3.68 (dd, 1H, *J* = 11.27 Hz, *J* = 1.65 Hz, 7-$CH_2$), 3.79 (dd, 1H, *J* = 11.28 Hz, *J* = 3.85 Hz, 7-$CH_2$), 3.83~3.86 (m, 2H, 9-H and 8-H), 4.04 (br d, 1H, *J* = 13.47 Hz, $NCH_2Ph$), 4.06~4.15 (m, 4H, 7-H, $OCH_2$ and one of $NCH_2Ph$), 4.48 (d, 1H, *J* = 11.82 Hz, $CH_2Ph$), 4.55 (br d, 1H, *J* = 10.99 Hz, $CH_2Ph$), 4.64 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.68 (d, 1H, *J* = 11.82 Hz, $CH_2Ph$), 4.72 (d, 1H, *J* = 11.82 Hz, $CH_2Ph$), 4.77 (d, 2H, *J* = 11.82 Hz, $CH_2Ph$), 4.99 (br d, 1H, *J* = 10.73 Hz, $CH_2Ph$), 7.17~7.19 (m, 2H, ArH), 7.23~7.39 (m, 23H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 14.05 ($CH_3$), 42.21 (4-C), 61.30 ($NCH_2Ph$), 61.43 ($OCH_2$), 64.94 (3-C), 68.84 (7-$CH_2$), 72.99 ($CH_2Ph$), 73.31 ($CH_2Ph$), 73.71 (8-C), 74.32 ($CH_2Ph$), 74.73 (7-C), 74.82 ($CH_2Ph$), 77.45 (10-C), 81.42 (9-C), 105.86 (5-C), 126.96 (Ar), 127.30 (Ar), 127.52 (Ar), 127.62 (Ar), 127.66 (Ar), 127.68 (Ar), 127.70 (Ar), 127.93 (Ar), 127.95 (Ar), 128.07 (Ar), 128.17 (Ar), 128.26 (Ar), 128.30 (Ar), 128.31 (Ar), 128.43 (Ar), 128.54 (Ar), 129.60 (Ar), 138.25 (Ar), 138.44 (two C, Ar), 138.63 (Ar), 169.17 (C=O); HRMS (FAB) calcd for $C_{46}H_{49}NO_8Na$

766.3356, Found: 766.3360.

**Ethyl (3*R*,5*S*,8*R*,9*S*,10*S*)-2-benzyl-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (4c)**

Colorless syrup, $[\alpha]_D^{25}$ = +19.40° (*c* 1.0, $CHCl_3$); IR (neat) ν 3063.33, 3030.54, 2909.01, 2868.50, 1740.00, 1496.94, 1450.50, 1369.63, 1205.66, 1095.70, 1028.18, 912.44, 736.90, 698.32 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.14 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.52 (dd, 1H, *J* = 12.65 Hz, *J* = 9.34 Hz, 4-H), 2.78 (dd, 1H, *J* = 13.20 Hz, *J* = 7.42 Hz, 4-H), 3.72~3.77 (m, 2H, 7-$CH_2$), 3.85 (dd, 1H, *J* = 9.07 Hz, *J* = 2.75 Hz, 9-H), 3.91~3.94 (m, 3H, 10-H, 8-H and 3-H), 3.98 (ddd, 1H, *J* = 9.90 Hz, *J* = 5.50 Hz, *J* = 2.47 Hz, 7-H), 4.03 (q, 2H, *J* = 7.15 Hz, $OCH_2$), 4.17 (d, 1H, *J* = 12.92 Hz, $NCH_2Ph$), 4.43 (d, 1H, *J* = 12.92 Hz, $NCH_2Ph$), 4.53 (d, 1H, *J* = 10.72 Hz, $CH_2Ph$), 4.56 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.64 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.68 (d, 1H, *J* = 11.27 Hz, $CH_2Ph$), 4.71 (d, 2H, *J* = 11.27 Hz, $CH_2Ph$), 4.85 (d, 1H, *J* = 10.73 Hz, $CH_2Ph$), 4.97 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 7.17~7.19 (m, 2H, ArH), 7.24~7.36 (m, 23H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 13.98 ($CH_3$), 43.30 (4-C), 61.40($OCH_2$), 65.07 ($NCH_2Ph$), 66.00 (3-C), 69.59 (7-$CH_2$), 72.62 ($CH_2Ph$), 73.38 ($CH_2Ph$), 73.44 (7-C), 74.58 ($CH_2Ph$), 74.83 (8-C), 75.08 ($CH_2Ph$), 77.22 (10-C), 82.06 (9-C), 108.23 (5-C), 126.95 (Ar), 127.47 (Ar), 127.53 (Ar), 127.61 (Ar), 127.62 (Ar), 127.65 (Ar), 127.67 (Ar), 127.70 (Ar), 128.08 (Ar), 128.13 (Ar), 128.27 (Ar), 128.30 (Ar), 128.33 (Ar), 128.36 (Ar), 128.41 (Ar), 128.54 (Ar), 129.31 (Ar), 135.94 (Ar), 138.19 (Ar), 138.22 (Ar), 138.28 (Ar), 138.41 (Ar), 170.48 (C=O); HRMS (FAB) calcd for $C_{46}H_{49}NO_8Na$ 766.3356, Found: 766.3352.

**Ethyl (3*R*,5*R*,8*R*,9*S*,10*R*)-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-2-methyl-1,6-dioxa-2-aza-spiro[4.5]decane-3-carboxylate (6a)**

Colorless syrup, $[\alpha]_D^{25}$ = +43.70° (*c* 1.0, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2897.43, 2870.43, 1952.20, 1869.25, 1745.79, 1496.94, 1454.50, 1363.84, 1294.39, 1209.51, 1070.62, 1028.18, 902.80, 736.90, 698.32 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.26 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.45 (dd, 1H, *J* = 13.20 Hz, *J* = 8.25 Hz, 4-H), 2.54 (dd, 1H, *J* = 13.20 Hz, *J*= 8.25 Hz, 4-H), 2.82 (s, 3H, $NCH_3$), 3.34 (br t, 1H, *J* = 8.30 Hz, 3-H), 3.54 (d, 1H, *J* = 9.89 Hz, 10-H), 3.68 (dd, 1H, *J* = 11.00 Hz, *J* = 1.65 Hz, 7-$CH_2$), 3.78 (dd, 1H, *J* = 11.00 Hz, *J* = 2.75 Hz, 7-$CH_2$), 3.80 (t, 1H, *J* = 9.90 Hz, 9-H), 3.90 (t, 1H, *J* = 9.35 Hz, 8-H), 3.96 (dt, 1H, *J* = 9.90 Hz, *J* = 2.20 Hz, 7-H), 4.15~4.20 (m, 2H, $OCH_2$), 4.48 (d, 1H, *J* = 12.64 Hz, $CH_2Ph$), 4.57 (d, 1H, *J* = 10.45 Hz, $CH_2Ph$), 4.61 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.69 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.81 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.87 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.89 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 5.00 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 7.15~7.16 (m, 2H, ArH), 7.23~7.36 (m, 18H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 12.75 ($CH_3$), 40.94 (4-C), 43.81 ($NCH_3$), 60.01 ($OCH_2$), 66.90 (7-$CH_2$), 68.14 (3-C), 70.89 (7-C), 72.17 ($CH_2Ph$), 73.54 ($CH_2Ph$), 74.04 ($CH_2Ph$), 74.16 ($CH_2Ph$), 76.66 (9-C), 78.07 (10-C), 82.63 (8-C), 103.78 (5-C), 126.26 (Ar), 126.28 (Ar), 126.40 (Ar), 126.43 (Ar), 126.45 (Ar), 126.58 (Ar), 126.60 (Ar), 126.71 (Ar), 126.98 (Ar), 127.01 (Ar), 127.04 (Ar), 127.07 (Ar), 127.17 (Ar), 136.68 (Ar), 136.77 (Ar), 136.96 (Ar), 137.21 (Ar), 167.88 (C=O); HRMS (FAB) calcd for $C_{40}H_{45}NO_8Na$ 690.3043, Found: 690.3040.

**Ethyl (3*R*,5*S*,8*R*,9*S*,10*R*)-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-2-methyl-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (7a)**

Colorless syrup, $[\alpha]_D^{25}$ = +22.38° (*c* 1.0, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2918.22, 2887.80, 1951.70, 1866.89, 1744.98, 1496.94, 1454.50, 1394.66, 1359.88, 1210.56, 1076.26, 1028.38, 743.88, 698.32 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.23 (t, 3H, *J* = 7.08 Hz, $CH_3$), 2.42 (dd, 1H, *J* = 13.18 Hz, *J* = 7.81 Hz, 4-H), 2.82 (dd, 1H, *J* = 13.18 Hz, *J*= 8.24 Hz, 4-H), 2.94 (s, 3H, $NCH_3$), 3.53 (d, 1H, *J* = 9.77 Hz, 10-H), 3.62 (dd, 1H, *J* = 10.50 Hz, *J* = 1.46 Hz, 7-$CH_2$), 3.67 (t, 1H, *J* = 8.90 Hz, 3-H), 3.71 (t, 1H, *J* = 9.52 Hz, 8-H), 3.73 (dd, 1H, *J* = 10.50 Hz, *J* = 3.47 Hz, 7-$CH_2$), 3.92~4.01 (m, 2H, 9-H and 7-H), 4.06~4.15 (m, 2H, $OCH_2$), 4.49 (d, 1H, *J* = 12.21 Hz, $CH_2Ph$), 4.52 (d, 1H, *J* = 11.96 Hz, $CH_2Ph$), 4.60 (d, 1H, *J* = 12.45 Hz, $CH_2Ph$), 4.68 (d, 1H, *J* = 11.48 Hz, $CH_2Ph$), 4.83 (d, 2H, *J* = 10.74 Hz, $CH_2Ph$), 4.80 (d, 1H, *J* = 10.98 Hz, $CH_2Ph$), 4.93 (d, 1H, *J* = 11.72 Hz, $CH_2Ph$), 7.14~7.17 (m, 2H, ArH), 7.26~7.36 (m, 18H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 14.23 ($CH_3$), 40.92 (4-C), 45.24 ($NCH_3$), 61.33 ($OCH_2$), 67.90 (3-C), 68.60 (7-$CH_2$), 71.73 (7-C), 73.43 ($CH_2Ph$), 74.95 ($CH_2Ph$), 74.15 ($CH_2Ph$), 75.52 ($CH_2Ph$), 78.15 (10-C), 78.24 (9-C), 83.76 (8-C), 107.18 (5-C), 127.52 (Ar), 127.55 (Ar), 127.61 (Ar), 127.63 (Ar), 127.70 (Ar), 127.75 (Ar), 127.77 (Ar), 127.88 (Ar), 128.09 (Ar), 128.13 (Ar), 128.18 (Ar), 128.21 (Ar), 128.24 (Ar), 137.58 (Ar), 137.80 (Ar), 137.95 (Ar), 138.26 (Ar), 169.84 (C=O); HRMS (FAB) calcd for $C_{40}H_{45}NO_8Na$ 690.3043, Found: 690.3040.

**Ethyl (3*R*,5*R*,8*S*,9*S*,10*R*)-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-2-methyl-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (6b)**

Colorless syrup, $[\alpha]_D^{25}$ = +46.30° (*c* 1.0, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2914.80, 2872.36, 1745.79, 1496.94, 1454.50, 1209.51, 1136.21, 1101.49, 1059.05, 736.90, 698.32 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.23 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.51 (dd, 2H, *J* = 8.24 Hz, *J* = 4.40 Hz, 4-H), 2.81 (s, 3H, $NCH_3$), 3.34 (br t, 1H, *J* = 7.70 Hz, 3-H), 3.54 (dd, 1H, *J* = 8.52 Hz, *J* = 4.95 Hz, 7-$CH_2$), 3.62 (t, 1H, *J* = 8.80 Hz, 7-$CH_2$), 3.88 (dd, 1H, *J* = 10.18 Hz, *J* = 2.75 Hz, 9-H), 4.03 (d, 1H, *J* = 10.17 Hz, 10-H), 4.08 (dd, 1H, *J* = 2.75 Hz, *J* = 1.38 Hz, 8-H), 4.12~4.16 (m, 3H, 7-H and $OCH_2$), 4.10 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.45 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.60 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.67~4.73 (m, 3H, $CH_2Ph$), 4.91 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 5.03 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 7.25~7.35 (m, 20H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 14.02 ($CH_3$), 42.30 (4-C), 45.18 ($NCH_3$), 61.20 ($OCH_2$), 67.81 (7-$CH_2$), 69.33 (3-C), 70.67 (8-C), 72.25 ($CH_2Ph$), 73.33 ($CH_2Ph$), 74.18 (7-C), 74.80 ($CH_2Ph$), 75.31 ($CH_2Ph$), 75.92 (10-C), 81.33 (9-C), 105.62 (5-C), 127.36 (Ar), 127.46 (Ar), 127.51 (Ar), 127.57 (Ar), 127.59 (Ar), 127.64 (Ar), 127.66 (Ar), 127.91 (Ar), 128.04 (Ar), 128.07 (Ar), 128.10 (Ar), 128.13 (Ar), 128.14 (Ar), 128.17 (Ar), 128.26 (Ar), 128.30 (Ar), 128.32 (Ar), 128.33 (Ar), 137.90 (Ar), 138.20 (Ar), 138.31 (Ar), 138.72 (Ar), 169.35 (C=O); HRMS (FAB) calcd for $C_{40}H_{45}NO_8Na$ 690.3043, Found: 690.3038.

**Ethyl (3*R*,5*S*,8*S*,9*S*,10*R*)-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-2-methyl-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (7b)**

Colorless syrup, $[\alpha]_D^{25}$ = +35.15° (*c* 1.0, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2910.84, 2891.64, 2870.32, 1745.79, 1604.97, 1496.94, 1454.50, 1359.86, 1210.68, 1098.35, 1039.80, 743.50, 698.32 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.20 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.45 (dd, 1H, *J* = 12.65 Hz, *J* = 7.70 Hz, 4-H), 2.84 (dd, 1H, *J* = 12.65 Hz, *J* = 8.80 Hz, 4-H), 2.93 (s, 3H, $NCH_3$), 3.50 (dd, 1H, *J* = 8.45 Hz, *J* = 6.90 Hz, 7-$CH_2$), 3.51 (t, 1H, *J* = 8.45 Hz, 7-$CH_2$), 3.68 (br t, 1H, *J* = 7.70 Hz, 3-H), 3.92 (dd, 1H, *J* = 10.17 Hz, *J* = 2.75 Hz, 9-H), 3.97 (dd, 1H, *J* = 2.75 Hz, *J* = 1.35 Hz 8-H), 4.03 (d, 1H, *J* = 10.17 Hz, 10-H), 4.11~4.15 (m, 3H, 7-H and $OCH_2$), 4.42 (d, 1H, *J* = 11.82 Hz, $CH_2Ph$), 4.47 (d, 1H, *J* = 11.82 Hz, $CH_2Ph$), 4.59 (d, 1H, *J* = 11.27 Hz, $CH_2Ph$), 4.68~4.73 (m, 3H, $CH_2Ph$), 4.94 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.95 (d, 1H, *J* = 11.28 Hz, CH $_2$Ph), 7.24~7.36 (m, 20H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 14.20 ($CH_3$), 40.91 (4-C), 48.50 ($NCH_3$), 60.29 ($OCH_2$), 67.92 (7-$CH_2$), 68.84 (3-C), 70.62 (8-C), 72.71 ($CH_2Ph$), 73.38 ($CH_2Ph$), 74.64 (7-C), 74.84 ($CH_2Ph$), 74.86 (10-C), 74.99 ($CH_2Ph$), 81.10 (9-C), 108.08 (5-C), 127.46 (Ar), 127.51 (Ar), 127.57 (Ar), 127.59 (Ar), 127.66 (Ar), 127.91 (Ar), 128.10 (Ar), 128.12 (Ar), 128.15 (Ar), 128.16 (Ar), 128.27 (Ar), 128.29 (Ar), 128.31 (Ar), 137.87 (Ar), 138.00 (Ar), 138.30 (Ar), 138.54 (Ar), 170.30 (C=O); HRMS (FAB) calcd for $C_{40}H_{45}NO_8Na$ 690.3043, Found: 690.3038.

**Ethyl (3*R*,5*R*,8*R*,9*S*,10*S*)-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-2-methyl-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (6c)**

Colorless syrup, $[\alpha]_D^{25}$ = +80.80° (*c* 1.0, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2903.22, 2868.50, 1745.79, 1496.94, 1450.50, 1367.70, 1207.59, 1095.70, 1028.18, 968.38, 736.90, 698.32 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.28 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.60~2.65 (m, 1H, 4-H), 2.73 (dd, 1H, *J* = 13.75 Hz, *J*= 8.25 Hz, 4-H), 2.77 (s, 3H, $NCH_3$), 3.24 (br t, 1H, *J* = 8.25 Hz, 3-H), 3.73 (d, 1H, *J* = 2.48 Hz, 10-H), 3.75 (dd, 1H, *J* = 11.28 Hz, *J* = 1.93 Hz, 7-$CH_2$), 3.86 (dd, 1H, *J* = 11.27 Hz, *J* = 3.57 Hz, 7-$CH_2$), 3.93 (dd, 1H, *J* = 9.08 Hz, *J* = 2.48 Hz, 9-H), 3.94~3.97 (m, 1H, 7-H), 4.19 (t, 1H, *J* = 9.62 Hz, 8-H), 4.20 (q, 2H, *J* = 7.15 Hz, $OCH_2$), 4.52 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.60 (d, 1H, *J* = 10.72 Hz, $CH_2Ph$), 4.73 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.75 (d, 1H, *J* = 12.37 Hz, $CH_2Ph$), 4.79 (d, 1H, *J* = 11.74 Hz, $CH_2Ph$), 4.82 (d, 1H, *J* = 11.83 Hz, $CH_2Ph$), 4.84 (d, 1H, *J* = 11.72 Hz, $CH_2Ph$), 5.09 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 7.20~7.22 (m, 2H, ArH), 7.26~7.42 (m, 18H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 14.06 ($CH_3$), 43.12 (4-C), 45.31 ($NCH_3$), 61.36 ($OCH_2$), 68.80 (7-$CH_2$), 69.03 (3-C), 72.95 ($CH_2Ph$), 73.38 ($CH_2Ph$), 73.53 (7-C), 74.31 ($CH_2Ph$), 74.69 ($CH_2Ph$), 74.80 (8-C), 77.54 (10-C), 81.64 (9-C), 105.26 (5-C), 127.27 (Ar), 127.46 (Ar), 127.53 (Ar), 127.58 (Ar), 127.59 (Ar), 127.87 (Ar), 127.90 (Ar), 127.93 (Ar), 128.14 (Ar), 128.20 (Ar), 128.26 (Ar), 128.37 (Ar), 138.31 (Ar), 138.46 (Ar), 138.50 (Ar), 138.59 (Ar), 169.15 (C=O); HRMS (FAB) calcd for $C_{40}H_{45}NO_8Na$ 690.3043, Found: 690.3041.

**Ethyl (3*R*,5*S*,8*R*,9*S*,10*S*)-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-2-methyl-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (7c)**

Colorless syrup, $[\alpha]_D^{25}$ = +35.00° (*c* 1.0, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2905.15, 2866.57, 1741.93, 1496.94, 1450.50, 1369.63, 1205.66, 1093.77, 1028.18, 910.51, 736.90, 698.32 $cm^{-1}$; $^1H$ NMR

($CDCl_3$): δ 1.29 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.50 (dd, 1H, *J* = 12.92 Hz, *J* = 9.07 Hz, 4-H), 2.79 (dd, 1H, *J* = 12.92 Hz, *J*= 7.43 Hz, 4-H), 2.97 (s, 3H, $NCH_3$), 3.73 (br d, 1H, *J* = 10.45 Hz, 7-$CH_2$), 3.76~3.79 (m, 2H, 3-H and 7-$CH_2$), 3.88 (d, 1H, *J* = 2.48 Hz, 10-H), 3.91~3.93 (m, 1H, 9-H), 3.98~4.00 (m, 2H, 8-H and 7-H), 4.17~4.22 (m, 2H, $OCH_2$), 4.54 (d, 1H, *J* = 12.37 Hz, $CH_2Ph$), 4.55 (d, 1H, *J* = 10.72 Hz, $CH_2Ph$), 4.66 (d, 1H, *J* = 12.06 Hz, $CH_2Ph$), 4.71~4.76 (m, 3H, $CH_2Ph$), 4.89 (d, 1H, *J* = 10.73 Hz, $CH_2Ph$), 5.01 (d, 1H, *J* = 11.82 Hz, $CH_2Ph$), 7.19~7.20 (m, 2H, ArH), 7.27~7.39 (m, 18H, ArH); $^{13}$C NMR ($CDCl_3$): δ 14.06 ($CH_3$), 43.42 (4-C), 48.74 ($NCH_3$), 61.42 ($OCH_2$), 68.11 (3-C), 69.32 (7-$CH_2$), 72.57 ($CH_2Ph$), 73.03 (7-C), 73.24 ($CH_2Ph$), 74.41 ($CH_2Ph$), 74.77 (8-C), 75.01 ($CH_2Ph$), 76.71 (10-C), 81.96 (9-C), 107.73 (5-C), 127.40 (Ar), 127.54 (Ar), 127.56 (Ar), 127.59 (Ar), 127.63 (Ar), 127.92 (Ar), 128.22 (Ar), 128.26 (Ar), 128.39 (Ar), 138.23 (Ar), 138.26 (two C, Ar), 138.36 (Ar), 170.43 (C=O); HRMS (FAB) calcd for $C_{40}H_{45}NO_8Na$ 690.3043, Found: 690.3045.

**Ethyl (3*R*,5*R*,8*R*,9*S*,10*R*)-8,9,10-tris(acetyloxy)-7-(acetyloxymethyl)-2-benzyl-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (9)**

Colorless syrup, $[\alpha]_D^{25}$ = + 115.09° (*c* 1.0, $CHCl_3$); IR (neat): ν 2958.12, 2879.65, 1755.51, 1605.28, 1496.94, 1450.50, 1371.35, 1221.18, 1090.56, 978.20 $cm^{-1}$; $^1$HNMR ($CDCl_3$) δ (ppm): 1.25 (t, 3H, *J* = 7.15 Hz, $CH_3$), 1.99 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 2.01 (s, 3H, $COCH_3$), 2.09 (s, 3H, $COCH_3$), 2.51 (dd, 1H, *J* = 13.75 Hz, *J* = 8.80 Hz, 4-H), 2.74 (dd, 1H, *J* = 13.75 Hz, *J* = 7.70 Hz, 4-H), 3.51 (t, 1H, *J* = 8.25 Hz, 3-H), 4.05 (dd, 1H, *J* = 12.65 Hz, *J* = 2.20 Hz, 7-$CH_2$), 4.10~4.17 (m, 3H, 7-H and $OCH_2$), 4.17 (d, 1H, *J* = 13.75 Hz, $NCH_2Ph$), 4.22 (d, 1H, *J* = 13.75 Hz, $NCH_2Ph$), 4.28 (dd, 1H, *J* = 12.65 Hz, *J* = 3.85 Hz, 7-$CH_2$), 5.11 (t, 1H, *J* = 9.90 Hz, 8-H), 5.17 (d, 1H, *J* = 10.44 Hz, 10-H), 5.30 (t, 1H, *J* = 9.89 Hz, 9-H), 7.31 (br d, 1H, *J* = 7.15 Hz, ArH), 7.35 (t, 2H, *J* = 7.15 Hz, ArH), 7.41 (d, 2H, *J* = 7.15 Hz, ArH); $^{13}$CNMR ($CDCl_3$) δ (ppm): 14.06 ($CH_3$), 20.59 ($CH_3$), 20.61 (two C, $CH_3$), 20.74 ($CH_3$), 41.19 (4-C), 60.98 ($NCH_2Ph$), 61.52 (7-$CH_2$ and $OCH_2$), 64.67 (3-C), 67.97 (8-C), 69.16 (7-C), 69.76 (10-C), 71.70 (9-C), 103.69 (5-C), 127.73 (Ar), 128.30 (two C, Ar), 129.81 (two C, Ar), 135.08 (Ar), 168.74 (C=O), 169.53 (C=O), 169.92 (C=O), 170.01 (C=O), 170.71 (C=O); HRMS (FAB) calcd for $C_{26}H_{33}NO_{12}Na$ 534.1901, Found: 534.1905.

**Ethyl (3*R*,5*S*,8*R*,9*S*,10*R*)-8,9,10-tris(acetyloxy)-7-[acetyloxymethyl]-2-benzyl-1,6-dioxa-2-azaspiro-[4.5]decane-3-carboxylate (10)**

Colorless syrup, $[\alpha]_D^{25}$ = + 57.20° (*c* 1.0, $CHCl_3$); IR (neat): ν 2960.10, 2877.58, 1749.85, 1602.88, 1496.94, 1450.50, 1369.89, 1093.16, 978.09, 798.62 $cm^{-1}$; $^1$HNMR ($CDCl_3$) δ (ppm): 1.20 (t, 3H, *J* = 7.15 Hz, $CH_3$), 1.99 (s, 3H, $COCH_3$), 2.04 (s, 6H, $COCH_3$), 2.13 (s, 3H, $COCH_3$), 2.80 (dd, 1H, *J* = 13.20 Hz, *J* = 8.25 Hz, 4-H), 2.74 (dd, 1H, *J* = 13.20 Hz, *J* = 7.15 Hz, 4-H), 3.79 (ddd, 1H, *J* = 9.90 Hz, *J* = 5.50 Hz, *J* = 2.75 Hz, 7-H), 3.90 (t, 1H, *J* = 7.70 Hz, 3-H), 4.09~4.23 (m, 4H, $NCH_2Ph$ and $OCH_2$ overlapped), 4.46 (d, 1H, *J* = 12.65 Hz, 7-$CH_2$), 5.07 (t, 1H, *J* = 9.35 Hz, 8-H), 5.11~5.16 (m, 2H, 7-$CH_2$ and 9-H), 5.25 (d, 1H, *J* = 9.35 Hz, 10-H), 7.29~7.37 (m, 5H, ArH); $^{13}$CNMR ($CDCl_3$) δ (ppm): 14.03 ($CH_3$), 20.55 ($CH_3$),

20.58 ($CH_3$), 20.63 ($CH_3$), 20.81 ($CH_3$), 36.95 (4-C), 61.49 ($NCH_2Ph$), 61.78 ($OCH_2$), 62.50 (7-$CH_2$), 65.42 (3-C), 68.36 (8-C), 68.46 (7-C), 71.30 (10-C), 72.51 (9-C), 108.17 (5-C), 128.25 (Ar), 128.36 (two C, Ar), 129.53 (two C, Ar), 135.80 (Ar), 168.68 (C=O), 168.82 (C=O), 169.30 (C=O), 169.72 (C=O), 170.16 (C=O); HRMS (FAB) calcd for $C_{26}H_{33}NO_{12}Na$ 534.1901, Found: 534.1909.

**1,3-Dipolar cycloadditions of the 1-methylenesugars (1a~c) with the nitrile oxide (11)**: — 107 mg (0.2 mmol) of **1a** and 38 mg (0.25 mmol) of ethyl chlorooximidoacetate were dissolved in 2 mL of dry $Et_2O$ under Argon atmosphere. To the solution was added 20 μL (0.14 mmol) of $Et_3N$ at rt. After stirring for 10 min, other 15 μL (0.11 mmol) of $Et_3N$ was added. The forming suspension was stirred at rt for 3 h. The reaction mixture was diluted by $Et_2O$ and washed with $H_2O$. The organic solution was dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue was applied on silica gel column chromatography eluted by AcOEt : Hexane (1 : 8 and then 1 : 5) to afford the adduct (**12a**) (72 mg, yield 55.2 %) and the reactant (**1a**) (35 mg, 32.7 %). The reactions of **1b~c** with ethyl chlorooximidoacetate were carried out with the same procedure and the results are shown in Scheme 4.

**Ethyl (5*R*,8*R*,9*S*,10*R*)-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-1,6-dioxa-2-azaspiro[4.5]dec-2-ene-3-carboxylate (12a)**

Colorless syrup, $[\alpha]^{25}_D$: +9.40° (*c* 1.0, $CHCl_3$); IR (neat) 3063.33, 3030.54, 2982.31, 2924.44, 2868.50, 1956.06, 1875.04, 1811.38, 1722.64, 1593.40, 1496.94, 1450.50, 1408.21, 1363.84, 1278.96, 1219.16, 1122.71, 1089.91, 1028.18, 912.44, 856.50, 829.49, 738.83, 698.32 $cm^{-1}$; $^1$HNMR ($CDCl_3$): δ (ppm) 1.35 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.97 (d, 1H, *J* = 18.14 Hz, 4-H), 3.04 (d, 1H, *J* = 18.14 Hz, 4-H ), 3.58 (br d, 1H, *J* = 11.00 Hz, 7-$CH_2$), 3.68 (d, 1H, *J* = 9.90 Hz, 10-H), 3.76 (dd, 1H, *J* = 11.00 Hz, *J* = 2.75 Hz, 7-$CH_2$), 3.82 (t, 1H, *J* = 9.89 Hz, 8-H), 4.03 (br d, 1H, *J* = 10.45 Hz, 7-H), 4.11 (t, 1H, *J* = 9.35 Hz, 9-H), 4.31 (q, 2H, *J* = 7.15 Hz, $OCH_2$), 4.45 (d, 1H, *J* = 12.15 Hz, $CH_2Ph$), 4.56 (d, 1H, *J* = 10.45 Hz, $CH_2Ph$), 4.57 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.68 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.84 (d, 1H, *J* = 10.45 Hz, $CH_2Ph$), 4.89 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.93 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.97 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 7.16~7.17 (m, 2H, ArH), 7.25~7.33 (m, 18H, ArH); $^{13}$CNMR ($CDCl_3$): δ (ppm) 14.05 ($CH_3$), 41.62 (4-C), 62.06 ($OCH_2$), 67.94 (7-$CH_2$), 72.86 (7-C), 73.46 ($CH_2Ph$), 74.88 ($CH_2Ph$), 74.97 ($CH_2Ph$), 75.65 ($CH_2Ph$), 77.48 (8-C), 78.39 (10-C), 83.64 (9-C), 110.90 (5-C), 127.70 (Ar), 127.74 (Ar), 127.78 (Ar), 127.82 (Ar), 127.90 (Ar), 127.97 (Ar), 128.01 (Ar), 128.37 (Ar), 128.43 (Ar), 128.52 (Ar), 137.55 (Ar), 137.76 (Ar), 138.01 (Ar), 138.23 (Ar), 152.50 (3-C), 160.09 (C=O); HRMS (FAB) calcd for $C_{39}H_{41}NO_8Na$ 674.2730, Found: 674.2736.

**Ethyl (5*R*,8*S*,9*S*,10*R*)-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-1,6-dioxa-2-azaspiro[4.5]dec-2-ene-3-carboxylate (12b)**

Colorless syrup, $[\alpha]^{25}_D$: +11.60° (*c* 1.0, $CHCl_3$); IR (neat) ν 3063.33, 3030.54, 2982.31, 2912.87, 2872.36, 1956.06, 1880.82, 1811.38, 1720.71, 1593.40, 1496.94, 1450.50, 1408.21, 1371.55, 1286.68, 1265.46,

1205.66, 1101.49, 1059.05, 1028.18, 914.37, 862.29, 740.76, 698.32 $cm^{-1}$; $^{1}$HNMR ($CDCl_3$) δ (ppm): 1.34 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.93 (d, 1H, *J* = 18.15 Hz, 4-C), 3.08 (d, 1H, *J* = 18.15 Hz, 4-C), 3.46 (dd, 1H, *J* = 8.79 Hz, *J* = 5.50 Hz, 7-$CH_2$), 3.55 (dd, 1H, *J* = 9.35 Hz, *J* = 7.70 Hz, 7-$CH_2$), 4.09~4.11 (m, 2H, 9-H and 8-H), 4.17 (d, 1H, *J* = 9.90 Hz, 10-H), 4.22 (br d, 1H, *J* = 7.60 Hz, 7-H), 4.31 (qd, 2H, *J* = 7.15 Hz, *J* = 1.10 Hz, $OCH_2$), 4.41 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.44 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.61 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.71 (d, 1H, *J* = 12.00 Hz, $CH_2Ph$), 4.73 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.77 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.94 (d, 1H, *J* = 11.45 Hz, $CH_2Ph$), 5.00 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 7.24~7.37 (m, 20H, ArH); $^{13}$CNMR ($CDCl_3$) δ (ppm): 13.98 ($CH_3$), 41.64 (4-C), 61.90 ($OCH_2$), 67.89 (7-$CH_2$), 71.59 (7-C), 72.51 ($CH_2Ph$), 73.28 (9- or 8-C), 74.17 ($CH_2Ph$), 74.80 ($CH_2Ph$), 74.86 ($CH_2Ph$), 75.08 (10-C), 80.93 (8- or 9-C), 111.55 (5-C), 127.50 (Ar), 127.65 (Ar), 127.70 (Ar), 127.76 (Ar), 127.99 (Ar), 128.07 (Ar), 128.21 (Ar), 128.33 (Ar), 128.35 (Ar), 128.38 (Ar), 137.69 (Ar), 137.75 (Ar), 137.97 (Ar), 138.38 (Ar), 152.28 (3-C), 160.10 (C=O); HRMS (FAB) calcd for $C_{39}H_{41}NO_8Na$ 674.2730, Found: 674.2733.

**Ethyl (5*R*,8*R*,9*S*,10*S*)-8,9,10-tris(benzyloxy)-7-[benzyloxymethyl]-1,6-dioxa-2-azaspiro[4.5]dec-2-ene-3-carboxylate (12c)**

White solid, mp 96~97°C; $[\alpha]^{25}_{D}$: +63.10° (*c* 1.0, $CHCl_3$); IR (KBr) ν 3063.33, 3030.54, 2905.15, 2868.50, 1956.06, 1869.25, 1811.38, 1722.64, 1593.40, 1496.94, 1450.50, 1371.55, 1315.61, 1230.73, 1099.56, 1026.25, 912.44, 864.21, 740.76, 698.32 $cm^{-1}$; $^{1}$HNMR ($CDCl_3$) δ (ppm): 1.34 (t, 3H, *J* = 7.15 Hz, $CH_3$), 3.04 (br d, 1H, *J* = 17.59 Hz, 4-C), 3.18 (d, 1H, *J* = 18.69 Hz, 4-C), 3.63 (dd, 1H, *J* = 11.55 Hz, *J* = 1.65 Hz, 7-$CH_2$), 3.76 (dd, 1H, *J* = 11.55 Hz, *J* = 4.40 Hz, 7-$CH_2$), 3.91 (d, 1H, *J* = 2.20 Hz, 10-H), 3.98 (ddd, 1H, *J* = 9.90 Hz, *J* = 4.40 Hz, *J* = 2.20 Hz, 7-H), 4.03 (dd, 1H, *J* = 8.80 Hz, *J* = 2.20 Hz, 8-H), 4.10 (br t, 1H, *J* = 9.35 Hz, 9-H), 4.31 (qd, 2H, *J* = 7.15 Hz, *J* = 4.40 Hz, $OCH_2$), 4.47 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.53 (br d, 1H, *J* = 10.45 Hz, $CH_2Ph$), 4.63 (d, 1H, *J* = 12.09 Hz, $CH_2Ph$), 4.68 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.76 (d, 1H, *J* = 12.09 Hz, $CH_2Ph$), 4.80 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.81 (br d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 5.01 (br d, 1H, *J* = 11.51 Hz, $CH_2Ph$), 7.16~7.17 (m, 2H, ArH), 7.25~7.34 (m, 18H, ArH); $^{13}$CNMR ($CDCl_3$) δ (ppm): 14.05 ($CH_3$), 43.48 (4-C), 62.14 ($OCH_2$), 68.69 (7-$CH_2$), 73.20 ($CH_2Ph$), 73.32 ($CH_2Ph$), 73.98 ($CH_2Ph$), 74.31 (7-C), 74.36 ($CH_2Ph$), 74.76 (8-C), 76.09 (10-C), 80.92 (9-C), 111.35 (5-C), 127.49 (Ar), 127.65 (Ar), 127.78 (Ar), 127.82 (Ar), 127.89 (Ar), 127.93 (Ar), 128.14 (Ar), 128.26 (Ar), 128.31 (Ar), 128.43 (Ar), 128.49 (Ar), 137.81 (Ar), 138.14 (Ar), 138.23 (Ar), 153.15 (3-C), 160.05 (C=O); HRMS (FAB) calcd for $C_{39}H_{41}NO_8Na$ 674.2730, Found: 674.2729.

**Reductive cleavage of the O-N bond**: — Activated zinc powder (230 mg, 4.0 mmol) was added to the solution of **6a** (67 mg, 0.1 mmol) in 2 mL of AcOH and 1.5 mL of $Ac_2O$. The solution was stirred under argon atmosphere at rt for 24 h, and the reaction was monitored by TLC (AcOEt : Hexane = 1:1). After completion of the reaction, 30 mL of AcOEt were added. The solution was washed with $H_2O$ and saturated aq. $NaHCO_3$, and dried over $MgSO_4$. After removing the solvent under reduced pressure, the residue was applied on silica gel column chromatography (AcOEt : Hexane = 1 : 2.5) to afforded products

(**13a**) (32.6 mg, 45.8%) and (**14a**) (25.6 mg, 39.6%). Compounds (**6b**) and (**6c**) were treated following the same procedure and the results are shown in Scheme 5.

**Ethyl 2-[acetyl(methyl)amino]-5,6,7,9-tetra-*O*-benzyl-2,3-dideoxy-D-*glycero*-α-D-*gulo*-non-4-ulo-pyranosonate (13a)**

Colorless syrup, $[\alpha]_D^{25}$ = -7.62° (*c* 0.42, $CHCl_3$); IR (neat): ν 3267.81, 3063.33, 3030.54, 2930.23, 2866.57, 1738.07, 1651.27, 1620.40, 1495.01, 1454.50, 1406.28, 1365.77, 1209.51, 1143.93, 1070.62, 1028.18, 738.83, 700.25 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.24 (t, 3H, *J* = 7.15 Hz, $CH_3$), 1.73 (dd, 1H, *J* = 14.29 Hz, *J* = 11.00 Hz, 3-H), 1.84 (s, 3H, $COCH_3$), 2.47 (dd, 1H, *J* = 14.29 Hz, *J*= 3.85 Hz, 3-H), 2.77 (s, 3H, $NCH_3$), 3.26 (d, 1H, *J* = 9.35 Hz, 5-H), 3.39 (dd, 1H, *J* = 10.44 Hz, *J* = 2.20 Hz, 9-H), 3.36 (t, 1H, *J* = 9.35 Hz, 6-H), 3.59 (dd, 1H, *J* = 10.44 Hz, *J* = 4.39 Hz, 9-H), 3.85 (ddd, 1H, *J* = 9.90 Hz, *J* = 4.40 Hz, *J* = 2.20 Hz, 8-H), 4.11~4.20 (m, 3H, $OCH_2$ and 7-H), 4.38 (d, 1H, *J* = 12.65 Hz, $CH_2Ph$), 4.51 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.57 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.69 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.84 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.89 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.92 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.96 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 5.35 (dd, 1H, *J* = 11.00 Hz, *J* = 3.85 Hz, 2-H), 7.19~7.21 (m, 2H, ArH), 7.26~7.35 (m, 18H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 14.11 ($CH_3$), 21.42 ($COCH_3$), 32.95 ($NCH_3$), 34.92 (3-C), 52.64 (2-C), 61.53 ($OCH_2$), 68.87 (9-C), 70.54 (8-C), 73.29 ($CH_2Ph$), 74.70 ($CH_2Ph$), 75.50 ($CH_2Ph$), 75.53 ($CH_2Ph$), 78.52 (6-C), 82.23 (5-C), 83.46 (7-C), 97.56 (4-C), 127.53 (Ar), 127.59 (Ar), 127.72 (Ar), 127.81 (Ar), 127.85 (Ar), 128.22 (Ar), 128.31 (Ar), 128.33 (Ar), 128.38 (Ar), 128.62 (Ar), 137.83 (Ar), 137.92 (Ar), 138.39 (Ar), 138.70 (Ar), 170.83 (C=O), 173.33 (C=O); HRMS (FAB) calcd for $C_{42}H_{49}NO_9Na$ 734.3305, Found: 734.3300.

**(3*R*,5*R*,8*R*,9*S*,10*R*)-3-(*N*-Methylacetylamido)-8,9,10-tris(benzyloxy)-7-(benzyloxymethyl)-1,6-dioxaspiro[4.5]decane-2-one (14a)**

Colorless syrup, $[\alpha]_D^{25}$ = +56.15° (*c* 0.80, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2945.57, 2903.26, 1754.22, 1654.62, 1603.30, 1495.05, 1454.50, 1385.60, 1213.58, 1068.66, 738.85 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 2.09 (s, 3H, $COCH_3$), 2.22 (d, 2H, *J* = 10.45 Hz, 4-H), 2.68 (s, 3H, $NCH_3$), 3.53 (d, 1H, *J* = 10.34 Hz, 10-H), 3.61 (br d, 1H, *J* = 11.00 Hz, 7-$CH_2$), 3.77 (dd, 1H, *J* = 11.00 Hz, *J* = 1.85 Hz, 7-$CH_2$), 3.82~3.86 (m, 2H, 8-H and 9-H), 4.05~4.08 (m, 1H, 7-H), 4.47 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.59 (d, 1H, *J* = 10.45 Hz, $CH_2Ph$), 4.60 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.64 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.84 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.87 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 4.92 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 5.02 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 5.74 (t, 1H, *J* = 10.45 Hz, 3-H), 7.16~7.18 (m, 2H, ArH), 7.26~7.33 (m, 18H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 21.50 ($COCH_3$), 31.89 ($NCH_3$), 32.08 (4-C), 52.47 (3-C), 67.80 (7-$CH_2$), 73.53 ($CH_2Ph$), 73.66 (7-C), 74.87 ($CH_2Ph$), 75.65 ($CH_2Ph$), 75.67 ($CH_2Ph$), 77.28 (8-C), 82.23 (10-C), 83.46 (9-C), 105.64 (5-C), 127.57 (Ar), 127.68 (Ar), 127.72 (Ar), 127.77 (Ar), 127.88 (Ar), 127.91 (Ar), 128.12 (Ar), 128.35 (Ar), 128.41 (Ar), 128.43 (Ar), 128.52 (Ar), 137.51 (Ar), 137.71 (Ar), 138.03 (Ar), 138.15 (Ar), 171.33 (C=O), 172.80 (C=O); HRMS (FAB) calcd for $C_{40}H_{43}NO_8Na$ 668.2887, Found: 688.2881.

**Ethyl 2-[acetyl(methyl)amino]-5,6,7,9-tetra-*O*-benzyl-2,3-dideoxy-D-*glycero*-β-L-*manno*-non-4-ulo-pyranosonate (13b)**

Colorless syrup, $[\alpha]_D^{25}$ = -4.20° (*c* 1.0, $CHCl_3$); IR (neat): ν 3258.80, 3063.33, 3030.54, 2926.65, 2898.08, 1729.11, 1653.28, 1615.10, 1494.97, 1454.50, 1398.89, 1368.12, 1219.28, 1069.20, 1009.86, 743.24 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.24 (t, 3H, *J* = 7.15 Hz, $CH_3$), 1.80 (dd, 1H, *J* = 14.57 Hz, *J* = 11.00 Hz, 3-H), 1.91 (s, 3H, $COCH_3$), 2.62 (dd, 1H, *J* = 14.58 Hz, *J*= 4.85 Hz, 3-H), 2.79 (s, 3H, $NCH_3$), 3.34 (dd, 1H, *J* = 9.08 Hz, *J* = 6.05 Hz, 9-H), 3.41 (dd, 1H, *J* = 9.35 Hz, *J* = 6.88 Hz, 9-H), 3.74 (d, 1H, *J* = 9.89 Hz, 5-H), 3.93~3.94 (m, 1H, 7-H), 4.00 (td, 1H, *J* = 6.46 Hz, *J* = 1.37 Hz, 8-H), 4.09 (dd, 1H, *J* = 9.63 Hz, *J* = 2.75 Hz, 6-H), 4.11~4.20 (m, 2H, $OCH_2$), 4.37 (d, 1H, *J* = 11.82 Hz, $CH_2Ph$), 4.42 (d, 1H, *J* = 12.10 Hz, $CH_2Ph$), 4.59 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.71 (d, 1H, *J* = 11.27 Hz, $CH_2Ph$), 4.76 (s, 2H, $CH_2Ph$), 4.94 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 4.98 (d, 1H, *J* = 11.27 Hz, $CH_2Ph$), 5.33 (dd, 1H, *J* = 11.00 Hz, *J* = 3.85 Hz, 2-H), 7.26~7.38 (m, 20H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 14.11 ($CH_3$), 21.48 ($COCH_3$), 33.21 ($NCH_3$), 35.03 (3-C), 52.81 (2-C), 61.46 ($OCH_2$), 69.22 (9-C), 69.37 (8-C), 72.64 ($CH_2Ph$), 73.23 ($CH_2Ph$), 74.59 ($CH_2Ph$), 75.02 (7-C), 75.54 ($CH_2Ph$), 78.53 (5-C), 80.67 (6-C), 98.02 (4-C), 127.52 (Ar), 127.55 (Ar), 127.57 (Ar), 127.61 (Ar), 127.75 (Ar), 127.81 (Ar), 127.90 (Ar), 128.19 (Ar), 128.20 (Ar), 128.22 (Ar), 128.38 (Ar), 128.77 (Ar), 137.80 (Ar), 138.17 (Ar), 138.57 (Ar), 138.86 (Ar), 170.92 (C=O), 173.30 (C=O); HRMS (FAB) calcd for $C_{42}H_{49}NO_9Na$ 734.3305, Found: 734.3302.

**(3*R*,5*S*,8*S*,9*S*,10*R*)-8,9,10-Tris(benzyloxy)-7-(benzyloxymethyl)-3-(methylacetylamido)-1,6-dioxa-spiro[4.5]decane-2-one (14b)**

Colorless syrup, $[\alpha]_D^{25}$ = +34.00° (*c* 0.6, $CHCl_3$); IR (neat): ν 3063.33, 3030.54, 2936.80, 2988.61, 1758.16, 1653.90, 1606.02, 1495.03, 1454.50, 1381.75, 1210.56, 1039.81, 978.22, 739.57 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 2.08 (s, 3H, $COCH_3$), 2.21 (dd, 1H, *J* = 12.92 Hz, *J* = 9.34 Hz, 4-H), 2.26 (dd, 1H, *J* = 12.92 Hz, *J* = 10.72 Hz, 4-H), 2.66 (s, 3H, $NCH_3$), 3.48 (dd, 1H, *J* = 9.08 Hz, *J* = 5.50 Hz, 7-$CH_2$), 3.59 (dd, 1H, *J* = 9.07 Hz, *J* = 8.25 Hz, 7-$CH_2$), 3.75~3.80 (m, 2H, 8-H and 9-H), 3.91~3.94 (m, 1H, 7-H), 4.00 (d, 1H, *J* = 9.89 Hz, 10-H), 4.43 (d, 1H, *J* = 11.82 Hz, $CH_2Ph$), 4.47 (d, 1H, *J* = 11.82 Hz, $CH_2Ph$), 4.61 (d, 1H, *J* = 11.28 Hz, $CH_2Ph$), 4.65 (d, 1H, *J* = 11.55 Hz, $CH_2Ph$), 4.70 (d, 1H, *J* = 11.45 Hz, $CH_2Ph$), 4.75 (d, 1H, *J* = 11.45 Hz, $CH_2Ph$), 4.93 (d, 1H, *J* = 11.00 Hz, $CH_2Ph$), 5.06 (d, 1H, *J* = 11.54 Hz, $CH_2Ph$), 5.72 (dd, 1H, *J* = 10.73 Hz, *J* = 9.62 Hz, 3-H), 7.27~7.37 (m, 20H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 21.50 ($COCH_3$), 31.97 ($NCH_3$), 32.00 (4-C), 52.46 (3-C), 67.72 (7-$CH_2$), 72.32 (6-C), 72.57 ($CH_2Ph$), 73.48 ($CH_2Ph$), 74.05 (8-C), 74.96 ($CH_2Ph$), 75.69 ($CH_2Ph$), 76.58 (10-C), 80.46 (9-C), 106.41 (5-C), 127.59 (Ar), 127.62 (Ar), 127.75 (Ar), 127.78 (Ar), 127.85 (Ar), 127.88 (Ar), 127.94 (Ar), 128.14 (Ar), 128.31 (Ar), 128.43 (Ar), 128.45 (Ar), 128.49 (Ar), 137.64 (Ar), 137.79 (Ar), 137.93 (Ar), 138.40 (Ar), 171.31 (C=O), 173.13 (C=O); HRMS (FAB) calcd for $C_{40}H_{43}NO_8Na$ 668.2887, Found: 688.2885.

**Ethyl (2*R*)-2-[acetyl(methyl)amino]-5,6,7,9-tetra-*O*-benzyl-2,3-dideoxy-D-*glycero*-α-D-*galacto*-non-**

**4-ulopyranosonate (13c)**

Colorless syrup, $[\alpha]_D^{25}$ = -6.58° (*c* 1.0, $CHCl_3$); IR (neat): ν 3280.10, 3063.33, 3030.54, 2918.83, 2890.26, 1736.84, 1653.08, 1621.12, 1494.90, 1454.50, 1381.28, 1212.67, 1143.93, 1075.10, 986.20, 736.86, 698.32 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 1.25 (t, 3H, *J* = 7.15 Hz, $CH_3$), 1.90 (dd, 1H, *J* = 14.50 Hz, *J* = 3.42 Hz, 3-H), 1.88 (s, 3H, $COCH_3$), 2.41 (dd, 1H, *J* = 14.50 Hz, *J*= 11.96 Hz, 3-H), 2.74 (s, 3H, $NCH_3$), 3.49 (br d, 1H, *J* = 10.50 Hz, 9-H), 3.59 (dd, 1H, *J* = 10.74 Hz, *J* = 4.88 Hz, 9-H), 3.69 (d, 1H, *J* = 2.44 Hz, 5-H), 3.82 (dd, 1H, *J* = 9.15 Hz, *J* = 2.44 Hz, 6-H), 3.90 (t, 1H, *J* = 9.13 Hz, 7-H), 4.11~4.21 (m, 3H, 8-H and $OCH_2$), 4.54 (d, 1H, *J* = 10.98 Hz, $CH_2Ph$), 4.56 (d, 1H, *J* = 10.75 Hz, $CH_2Ph$), 4.68~4.74 (m, 3H, $CH_2Ph$), 4.87 (d, 1H, *J* = 11.23 Hz, $CH_2Ph$), 4.99 (d, 1H, *J* = 11.48 Hz, $CH_2Ph$), 5.05 (d, 1H, *J* = 11.64 Hz, $CH_2Ph$), 5.34 (dd, 1H, *J* = 11.96 Hz, *J* = 3.42 Hz, 2-H), 7.17~7.39 (m, 20H, ArH); $^{13}C$ NMR ($CDCl_3$): δ 14.33 ($CH_3$), 21.58 ($COCH_3$), 33.06 ($NCH_3$), 35.45 (3-C), 52.42 (2-C), 61.46 ($OCH_2$), 68.87 (9-C), 69.96 (8-C), 72.80 ($CH_2Ph$), 73.58 ($CH_2Ph$), 74.37 ($CH_2Ph$), 74.74 ($CH_2Ph$), 75.19 (8-C), 77.59 (5-C), 79.17 (6-C), 97.61 (4-C), 127.42 (Ar), 127.45 (Ar), 127.48 (Ar), 127.51 (Ar), 127.75 (Ar), 127.78 (Ar), 127.81 (Ar), 127.85 (Ar), 128.05 (Ar), 128.11 (Ar), 128.17 (Ar), 128.28 (Ar), 137.90 (Ar), 138.27 (Ar), 138.41 (Ar), 138.49 (Ar), 170.62 (C=O), 173.85 (C=O); HRMS (FAB) calcd for $C_{42}H_{49}NO_9Na$ 734.3305, Found: 734.3308.

**Ethyl 2-[acetyl(methyl)amino]-2,3-dideoxy-D-*glycero*-α-D-*gulo*-non-4-ulopyranosonate (15)**

**13a** (71.1 mg, 0.1 mmol) was dissolved in 2 mL of methanol. To the solution was added 20 mg of $Pd(OH)_2/C$ (20 wt%), and the mixture was stirred vigorously under $H_2$ atmosphere at rt for 12 h. After the reaction completed, the catalyst was removed by filtration through a Celite pad and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (AcOEt : MeOH : $H_2O$ = 4 : 2 :1) to afford 23.1 mg (65.8%) of the debenzylated product (**15**). Colorless amorphous solid, $[\alpha]_D^{25}$ = +69.11° (*c* 1.58, $CH_3OH$); $^1H$ NMR ($CD_3OD$): δ 1.25 (t, 3H, *J* = 7.15 Hz, $CH_3$), 2.11 (s 3H, $COCH_3$), 2.15 (dd, 1H, *J* = 14.85 Hz, *J* = 9.35 Hz, 3-H), 2.59 (dd, 1H, *J* = 14.85 Hz, *J* = 4.12 Hz, 3-H), 3.03 (s, 3H, $NCH_3$), 3.08 (d, 1H, *J* = 9.35 Hz, 5-H), 3.27 (t, 1H, *J* = 9.34 Hz, 7-H), 3.61~3.76 (m, 4H, 6-H, 8-H and two 9-H), 4.15~4.22 (m, 2H, $OCH_2$), 5.20 (dd, 1H, *J* = 9.34 Hz, *J* = 3.85 Hz, 2-H); $^{13}C$ NMR ($CDCl_3$): δ 14.44 ($CH_3$), 21.86 ($COCH_3$), 31.88 ($NCH_3$), 37.16 (3-C), 55.59 (2-C), 62.66 ($OCH_2$), 62.78 (9-C), 71.62 (7-C), 74.11 (8-C), 75.75 (6-C), 76.15 (5-C), 98.27 (4-C), 172.90 (C=O), 174.64 (C=O); HRMS (FAB) calcd for $C_{14}H_{25}NO_9Na$ 374.1427, Found: 374.1425.

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## REFERENCES


1 (a) H. Haruyama, T. Takayama, T. Kinoshita, M. Kondo, M. Nakajima, and T. Haneishi, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1637; (b) M. Nakajima, K. Itoi, Y. Takamatsu, T. Kinoshita, T. Okazaki, K. Kawakobu, M. Shindo, T. Honna, M. Tohjigamori, and T. Haneishi, *J. Antibiot.*, 1991, **44**, 293.

2 (a) W. D. Ollis, C. Smith, and D. E. Wright, *Tetrahedron*, 1979, **35**, 105; (b) D. E. Wright, *Tetrahedron*, 1979, **35**, 1207; (c) A. K. Ganguly, 'Oligosaccharides Antibiotics,' In *Topics in Antibiotic Chemistry*, Vol. 2, ed. by P. G. Sammes, Ellis Horwood Ltd., Chichester, 1978, part B, pp. 59~98.

3 (a) P. Traxler, J. Gruner, and J. A. L. Augden, *J. Antibiot.*, 1977, **30**, 289; (b) P. Traxler, H. Fritz, H. Fuhrer, and W. J. Richter, *J. Antibiot.*, 1980, **33**, 967.

4 For the recent syntheses of spiro-orthoesters, see: (a) H. Ohtake, X. Li, H. Takahashi, and S. Ikegami, *J. Synth. Org. Chem., Japan*, 2002, **60**, 206 and the cited therein; (b) H. Ohtake, N. Ichiba, M. Shiro, and S. Ikegami, *J. Org. Chem.*, 2000, **65**, 8164; (c) K. C. Nicolaou, K. C. Fylaktakidou, H. J. Mitchell,F. L. van Delft, R. M. Rodriguez, S. R. Conley, and Z. Jin, *Chem. Eur. J.*, 2000, **6**, 3166.

5 For the recent syntheses of spiro-nucleoside analogues, see: (a) C. J. F. Bichard, E. P. Mitchell, M. R. Wormald, K. A. Watson, L. N. Johnson, S. E. Zographos, D. D. Koutra, N. G. Oikonomakos, and G. W. J. Fleet, *Tetrahedron Lett.*, 1995, **36**, 2145; (b) T. W. Brandtetter, Y. Kim, J. C. Son, H. M. Taylor, P. M. de Q. Lilley, D. J. Watkin, L. N. Johnson, N. G. Oikonomakos, and G. W. J. Fleet, *Tetrahedron Lett.*, 1995, **36**, 2149; (c) L. Somsak, L. Kovacs, M. toth, E. Osz, L. Szilagyi, Z. Gyorgydeak, Z. Dinya, T. Docsa, B. Toth, and P. Gergely, *J. Med. Chem.*, 2001, **44**, 2843; (d) C. Gasch, M. A. Pradera, B. A. B. Salameh, J. L. Molina, and J. Fuentes, *Tetrahedron: Asymmetry*, 2001, **12**, 1267 and cited therein; (e) A. Dondoni and A. Marra, *Chem. Rev.*, 2000, **100**, 4395.

6 For the recent syntheses of spiro-ketals, see: (a) A. Dondoni, A. Marra, M.-C. Scherrmann, and V. Bertolasi, *Chem. Eur. J.*, 2001, **7**, 1371; (b) X. Li, H. Takahashi, H. Ohtake, M. Shiro, and S. Ikegami, *Tetrahedron*, 2001, **57**, 8053; (c) J. M. Benito, M. Gomez-Garcia, C. O. Mellet, J. M. G. Fernandez, and J. Defaye, *Org. Lett.*, 2001, **3**, 549 and the cited therein; (d) R. Caputo, A. Guaragna, G. Palumbo, S. Pedatella, and F. Solla, *Eur. J. Org. Chem.*, 2002, 534; (e) C. Hamdouchi, C. Jaramillo, J. Lopez-Prados, and A. Rubio, *Tetrahedron Lett.*, 2002, **43**, 3875; (f) M. Manley-Harris and G. N. Richards, Dihexulose Dianhydrides, in *Adv. Carbohydr. Chem. Biochem.*, Vol. 52, ed. by D. Horton, Academic Press, San Diego, 1997, pp. 207~266.

7 (a) A. Dondoni, A. Marra, I. Rojo, and M.-C. Scherrmann, *Tetrahedron*, 1996, **52**, 3057; (b) A. Dondoni, S. Daninos, A. Marra, and P. Formaglio, *Tetrahedron*, 1998, **54**, 9859; (c) A. Dondoni and A. Marra, *Chem. Commun.*, 1999, 2133; (d) X. Li, H. Ohtake, H. Takahashi, and S. Ikegami, *Tetrahedron*,

2001, **57**, 4283; (e) X. Li, H. Ohtake, H. Takahashi, and S. Ikegami, *Tetrahedron*, 2001, **57**, 4297.

8 (a) A. Padwa, ed., *1,3-Dipolar Cycloaddition Chemistry*, Wiley, New York, 1984; (b) K. B. G. Torssell, *Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis*, VCH, Weinheim, 1988; (c) K. V. Gothelf and K. A. Jorgensen, *Chem. Rev*., 1998, **98**, 863; (d) K. V. Gothelf and K. A. Jorgensen, *Chem. Commun*., 2000, 1449; (e) M. Lombardo and C. Trombini, *Synthesis*, 2000, 759; (f) P. Merino, S. Franco, F. L. Merchan, and T. Tejero, *Synlett*, 2000, 442; (g) M. Frederickson, *Tetrahedron*, 1997, **53**, 403; (h) A. M. G. Silva, A. C. Tome, M. G. P. M. S. Neves, A. M. S. Silva, J. A. S. Cavaleiro, D. Perrone, and A. Dondoni, *Tetrahedron Lett*., 2002, **43**, 603.

9 (a) P. Merino, S. Frabco, N. Graces, F. L. Merchan, and T. Tejero, *Chem. Commun*., 1998, 493; (b) P. Merino, S. Franco, F. L. Merchan, and T. Tejero, *Tetrahedron: Asymmetry*, 1997, **8**, 3489; (c) P. Merino, E. Castillo, S. Franco, F. L. Merchan, and T. Tejero, *J. Org. Chem.*, 1998, **63**, 2371; (d) P. Merino, E. Castillo, S. Franco, F. L. Merchan, and T. Tejero, *Tetrahedron: Asymmetry*, 1998, **9**, 1759; (e) P. Merino, E. Castillo, S. Franco, F. L. Merchan, and T. Tejero, *Tetrahedron*, 1998, **54**, 12301; (f) P. Merino, E. M. del Alamo, S. Franco, F. L. Merchan, A. Simon, and T. Tejero, *Tetrahedron: Asymmetry*, 2000, **11**, 1534.

10 (a) S. Pan, N. M. Amankulor, K. Zhao, *Tetrahedron*, 1998, **54**, 6587; (b) A. Vasella and R. Voeffray, *J. Chem. Soc., Chem. Comm*., 1981, 97; (c) A. Vasella and R. Voeffray, *Helv. Chim. Acta*, 1982, **65**, 1134; (d) N. P. Peet, E. W. Huber, and R. A. Farr, *Tetrahedron*, 1991, **47**, 7537; (e) F. J. Duff, V. Vivien, and R. H. Wightman, *Chem Commn*., 2000, 2127; (f) P. Merino, S. Franco, F. L. Merchan, and T. Tejero, *J. Org. Chem*., 2000, **65**, 5575; (g) F. G. Calvo-Flores, J. Isac-Garcia, F. Hernandez-Mateo, F. Perez-Balderas, J. A. Calvo-Asin, E. Sanchez-Vaquero, and F. Santoyo-Gonzalez, *Org. Lett*., 2000, **2**, 2499; (h) K. W. J. Baker, A. Gibb, A. R. March, and R. M. Paton, *Tetrahedron Lett*., 2001, **42**, 4065; (i) A. M. G. Silva, A. C. Tome, M. G. P. M. S. Neves, A. M. S. Silva, J. A. S. Cavaleiro, D. Perrone, and A. Dondoni, *Tetrahedron Lett*., 2002, **43**, 603; (j) R. Fischer, A. Druckova, A. Rybar, C. Hametner, and M. Cyranski, *Synlett*, 2002, 1113.

11 A. Bartolozzi, G. Capozzi, C. Falciani, S. Menichetti, C. Nativi, and A. P. Bacialli, *J. Org. Chem*., 1999, **64**, 6490.

12 Besides the 1,3-dipolar cycloadditions, the neucleophilic additions to nitrones have been also widely used in organic synthesis. See recent reviews: (a) P. Merino, S. Franco, F. L. Merchan, and T. Tejero, *Synlett*, 2000, 442; (b) M. Lombardo and C. Trombini, *Synthesis*, 2000, 759.

13 A. Dondoni, S. Franco, F. Junquera, P. Merino, and T. Tejero, *Synthetic Commun*., 1994, **24**, 2537.

14 G. H. Veeneman, “Chemical Synthesis of *O*-Glycosides”, in *Carbohydrate Chemistry*, ed. by G.-J. Boons, Blackie Academic and Proffesional, London, 1998, pp. 99~174.

15 To the best of our knowledge, only one example was reported on the 1,3-dipolar cycloaddition reaction

of 1-methylsugar with a nitrile oxide to give a single spiro isooxazoline in the α-stereospecific way. See: T. V. RajanBabu and G. S. Reddy, *J. Org. Chem*., 1986, **51**, 5458.

16 F. Nicotra, G. Russo, F. Ronchetti, and L. Toma, *Carbohydr. Res*., 1983, **124**, C5.

17 LOMD for each compound of **3a** and **4a**, and their diastereomers (**3s**) and (**4s**) was continued until around 5,000 conformers were generated. Although the steps in LOMD were not enough for the determination of the molecule conformations, the energies among the first twenty lowest energy conformers of compounds (**3a**) and (**4a**) were almost same for each molecule.

18 F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendricson, and W. C. Still, *J. Comput. Chem*., 1990, **11**, 440.

19 (a) I. Kolossary and W. C. Guida, *J. Am. Chem. Soc*. 1996, **118**, 5011; (b) G. Cheng, W. C. Guida, and W. C. Still, *J. Am. Chem. Soc*., 1989, **111**, 4379.

20 (a) N. F. Burkhalter, S. M. Dimick, and E. J. Toone, "Protein-Carbohydrate Interaction: Fundamental Considerations", in *Carbohydrates in Chemistry and Biology, Part I: Chemistry of Saccharides*, Vol. 2, ed. by B. Ernst, G. E. Hart, and P. Sina, WILEY-VCH, Weinheim, 2000, pp. 863~914; (b) M. Aubery, *Glycan in Cell Interaction and Recognition*, Harwood Academic Publishers, Singapore, 2001.

21 For the recent reviews on the synthesis of glycosyl amino acids, *see*: (a) H. P. Wessel, "Saccharide-Peptide Hybrids", in *Carbohydrates in Chemistry and Biology, Part I: Chemistry of Saccharides*, Vol. 1, ed. by B. Ernst, G. E. Hart, and P. Sina, WILEY-VCH, Weinheim, 2000, p. 565; (b) A. Dondoni and A. Marra, *Chem. Rev*., 2000, **100**, 4395; (c) C. M. Taylor, *Tetrahedron*, 1998, **54**, 11317; (d) F. Schweizer, *Angew. Chem., Int. Ed*., 2002, **41**, 230; (e) S. A. W. Gruner, E. Locardi, E. Lohof, and H. Kessler, *Chem. Rev*., 2002, **102**, 491; (f) T. K. Chakraborty, S. Ghosh, and S. Jayaprakash, *Curr. Med. Chem.*, 2002, **9**, 421.

22 The recent reports on the synthesis of *C*-glycosyl amino acids, *see*: (a) H. Kessler, V. Wittmann, M. Kock, and M. Kottenhahn, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 902; (b) F. Schweizer, A. Lohse, A. Otter, and O. Hindsgaul, *Synlett*, 2001, 1434; (c) A. Dondoni, P. P. Giovannini, and A. Marra, *J. Chem. Soc., Perkin Trans. 1*, 2001, 2380; (d) C. Grison, F. Coutrot, and P. Coutrot, *Tetrahedron*, 2001, **57**, 6215; (e) A. Wernicke and D. Sinou, *J. Carbohydr. Chem.*, 2001, **20**, 181; (f) T. Nishikawa, M. Ishikawa, K. Wada, and M. Isobe, *Synlett*, 2001, 945; (g) C. H. Röhrig, M. Takhi, and R. R. Schmidt, *Synlett*, 2001, 1170; (h) J. J. Turner, D. V. Filippov, M. Overhand, G. A. van der Marel, and J. H. van Boom, *Tetrahedron Lett.*, 2001, **42**, 5763; (i) J. L. Koviach, M. D. Chappell, and R. L. Halcomb, *J. Org. Chem*., 2001, **66**, 2318; (j) F. Schweizer and T. Inazu, *Org. Lett*., 2001, **3**, 4115; (k) D. E. Paterson, F. K. Griffin, M.-L. Alcaraz, and R. J. K. Taylor, *Eur. J. Org. Chem*., 2002, 1323.