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SYNTHETIC STUDIES ON (+)-HYDANTOCIDIN (2): ALDOL ADDITION APPROACHES TOWARD THE STEREOISOMERS OF (+)-HYDANTOCIDIN

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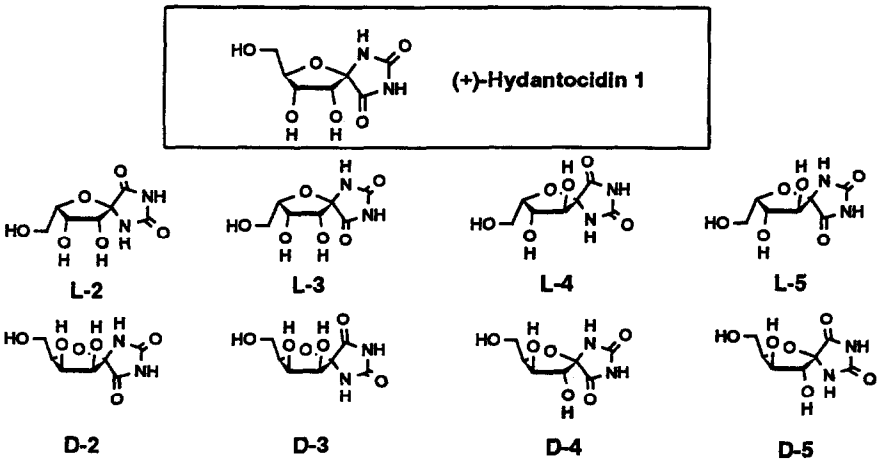
Abstract: The spiro-hydantoin ring at the anomeric position of D-and L-furanose was constructed by using aldol addition followed by acid promoted cyclization and the synthesis of thestereoisomers of (+)-hydantocidin, L- and D-series of spiro-furanose **2, 3, 4 and 5.**

The herbicidal natural product, (+)-hydantocidin **1**[1], has unique structural features, that is, a spiro-hydantoin ring at the anomeric position of D-ribofuranose[2]. The heterocyclic moiety, corresponding to the basic moiety of nucleoside antibiotics, is located in the lateral direction of the ribofuranose ring. This type of structure has never been found in the field of nucleoside antibiotics[3]. Hydantocidin has four contiguous asymmetric carbons affording sixteen stereoisomers. These structural feature aroused our interest in the recognition of the molecule at the active site of herbicidal action in the plant. Therefore, we planned to prepare the stereoisomers to



Stereoisomers of (+)-Hydantocidin

Figure 1

elucidate the herbicidal structure-activity-relationship. In this paper, we describe the synthesis of the eight stereoisomers, L- and D-series of spiro-furanose derivatives **2**, **3**, **4** and **5** (**Figure 1**).

In the preceding paper[4], we reported an aldol condensation-cyclization method for the total synthesis of **1**, which method required oxidation of the spiro-dihydrofurane systemes. In order to develop a more direct approach toward the spiro-furanoses, we employed the successive aldol addition-cyclization method (**Figure 2**): The aldol addition[5] of a highly substituted enolate **A** with an aldehyde **B** will afford an intermediate **C** in which the new chiral centers at C-1 and C-2 are introduced. The adduct **C** is to be cyclized into a spiro-isomer which can then be deprotected to a desired product **D**. In this sequence the stereochemistry at C-4 in cyclic system **D** is refrected the C-2 stereochemistry in acyclic system **C**.

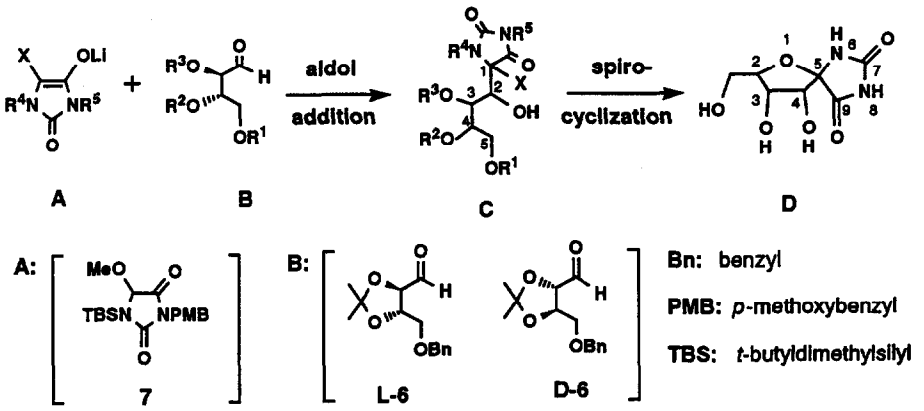


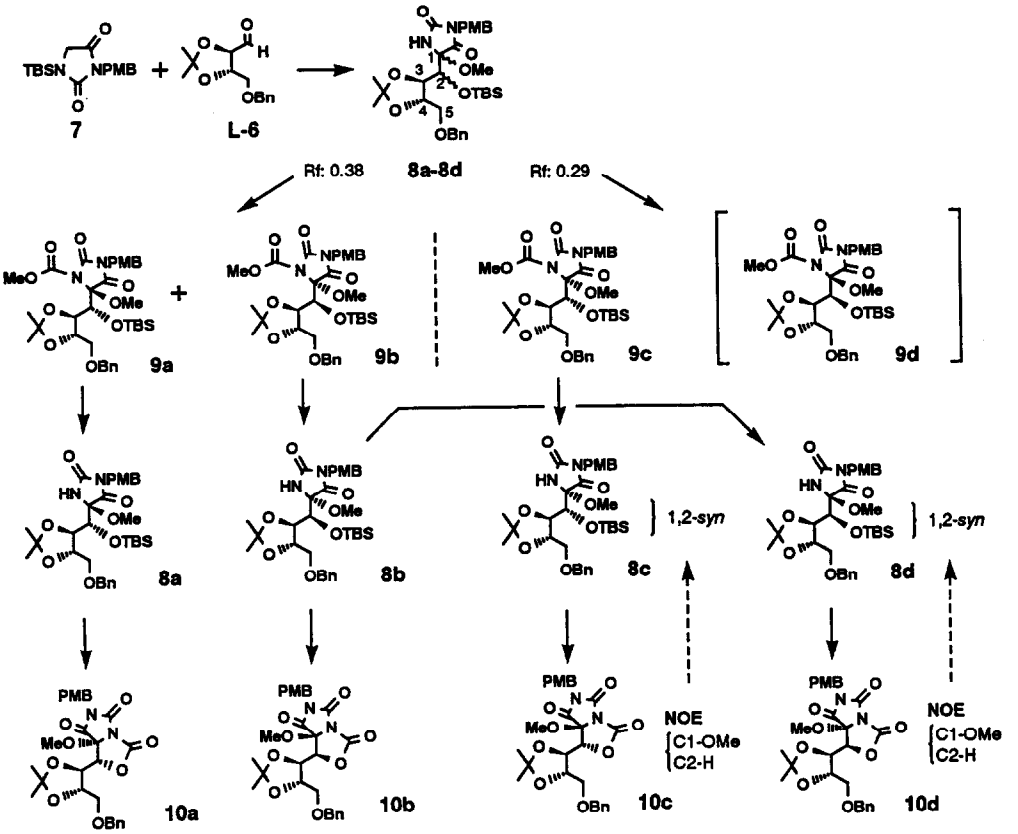
Figure 2

The synthesis was initiated by preparing the substituted hydantoin **7**. The bromination of 1-*N*-*tert*-butyldimethylsilyl-3-*N*-(4-methoxybenzyl)hydantoin[4] with *N*-bromosuccinimide followed by the substitution of the resulting bromo group with methanol *in situ* afforded **7** in 65% yield.

In following parts, we mainly described the L-series of isomers starting from the aldehyde **L-6**[5], while the same series of reaction sequences were performed in the D-series. The lithium enolate of the hydantoin, prepared by acting lithium bis(trimethylsilyl)amide in THF at -60°C, was treated with **L-6** at -60°C for 10min, and -20°C for 2h (**Scheme 1**). The adducts were obtained in 83% yield containing four diastereomers which exhibited two spots on analytical TLC (Rf=0.38 and 0.29, ethyl acetate-hexane 1:5). Since it was difficult to separate chromatographically the two isomers in each spots, we tried to isolate each isomer through derivatization. The pair of *N*-methoxycarbonylated products, (**9a** and **9b**) and (**9c** and **9d**), from each spot were easily separated by chromatography, affording **9a**, **9b** and **9c**. But **9d** was not isolated because of the small quantity. The hydrolysis (aq.K_2CO_3/MeOH, r.t.) of their methoxycarbonyl groups recovered the pure **8a-8c**, respectively. The miner isomer **8d** was obtained by the epimerization (NaOMe/MeOH, 60°C) of **8d** and they are easily separated each other.

In order to elucidate the relative stereochemistry between C-1 and C-2, **8a-d** were converted to the tricyclic compounds **10a-d** by desilylation followed by carbonylation, independently. The NOE in ^{1}H-NMR was

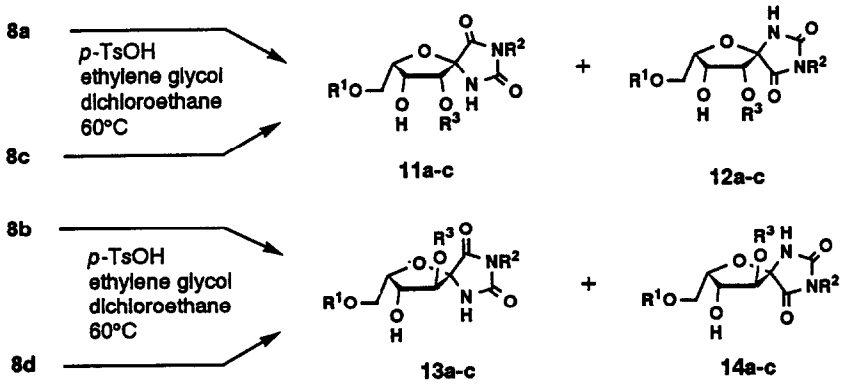
observed between the C-1 methoxy group and the C-2 proton in **10c** and **10d**, indicating a *cis*-relationship between the two groups. Therefore, it was confirmed that **8a** and **8b** exhibits *anti*-stereochemistry and **8c** and **8d** exhibits *syn*-stereochemistry at the C-1 and C-2 position. At this stage, it was difficult to elucidate the stereochemistry at C-2 and C-3 in the acyclic system, we therefore tried to investigate the cyclization condition of each isomer.



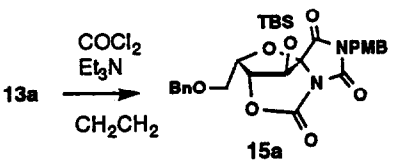
Scheme 1

The transketalization condition[7] (*p*-TsOH·H_2O, ethylene glycol, dichloroethane, 60°C) was employed to remove the isopropylidene group in **8a-d**. Under the same conditions, the expected cyclization occurred spontaneously. It turned out that both **8a** and **8c** were transformed into the same pair of two cyclized isomers **11a** and **12a** (*ca.* 5:1), and **8b** and **8d** transformed into the pair, **13a** and **14a** (*ca.* 3:1), respectively. These ratios were found to be attributed to the stereochemistry at the anomeric position based on the analysis of ^{1}H-NMR and other spectral data. X-ray diffraction analysis was performed in D-series of **11a** (**Figure 3**). The result indicated the *cis*-relationship between the substituents at C-3 and C-4, *trans*-relationship between the hydroxy group at C-3 and the carbonyl group at C-5 in **11a**, and *cis* for the former and *cis* for the later in **12a**. On the other hand, the other pair of **13a** and **14a** were found to have a *trans*-relationship between the substituents at C-3 and C-4. The remaining problem of stereochemistry at C-5 in **13a** and **14a** was resolved by converting **13a** to

a tricyclic derivative **15a** by treatment of phosgene. It is obvious that **13a** has a *cis*-relationship between the hydroxy group at C-3 and NH-group at C-5. In this manner, the structure of the cyclic isomers **11a-14a** were determined as shown in Scheme 2.



11-14	R^1	R^2	R^3
a	Bn	PMB	TBS
b	Bn	PMB	H
c	Bn	H	H
2-5	H	H	H



Scheme 2

Figure 3

Perspective view of **D-11a** in the crystallographic analysis.

We then turned our attention back to the acyclic derivatives **8a-d**. The *cis*-relationship at C-3 and C-4 substituents in cyclic isomer **11a** and **12a** corresponds to the 2,3-*anti*-relationship in acyclic systems **8a** and **8c**. On the other hand, **8b** and **8d** has a 2,3-*syn*-relationship on the basis of the stereochemistry of **13a** and **14a**. Since the four aldol-adducts **8a-d** were identified, we then focused on the stereoselectivity of the aldol-addition.

The ratio of isomers (**8a:8b:8c:8d**) was estimated to be 22:6:18:1 by the intensity of 270MHz ^{1}H-NMR signals utilizing the differences in chemical shift of C-1 methoxy groups. This result indicates that the 2,3-*anti*-selectivity was predominant to the 2,3-*syn*-selectivity in the ratio of 5.7:1, which could be explained by the Felkin-Ahn's model[8] preferring the transition state E (**Figure 4**). On the other hand, the 1,2-stereoselectivity was found to be low (*anti:syn*=1.5:1) because of similar degree of non-bonded interaction of the substituents in each transition state G and H.

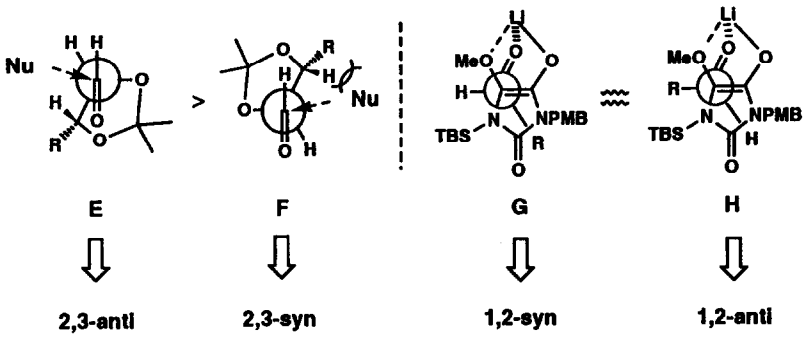


Figure 4

Interestingly, the migration of the *N*-silyl group to the resulting hydroxy group during the aldol-addition to give the C-2 silyloxy adducts. This process would prevent the retro-aldol reaction. Furthermore, the silyloxy group, which was bulky substituent, would play an important role in the distribution of spiro-isomers by restricting the conformation of the transition state during the cyclization process.

After characterizing all the stereoisomers, we next cyclized the mixture of aldol-adducts directly under the acidic conditions. The products ratio (**11a:13a:12a+14a**) was analyzed by HPLC to be 74:11:15. The major isomer **11a** was easily isolated in 51% yield after crystallization.

Now that the four cyclized stereoisomers were in hand, a sequence of deprotection was carried out, independently (**Scheme 2**). The desilylation at C-3 was performed with tetra-*n*-butylammonium fluoride, and then the resulting diols **11b-14b** were treated with celic ammonium nitrate (CAN)[9] to provide the de-*N*-(4-methoxybenzyl) derivatives **11c-14c**. Finally, the *O*-benzyl group was hydrogenated in the presence of Pd-C to afford L-series of **2**, **3**, **4** and **5**, respectively. Similarly, we carried out a series of reactions started from the D-threose derivative **D-6**, and completed the synthesis of **D-2**, **D-3**, **D-4** and **D-5**, which are enantiomers of the corresponding L-isomers.

In conclusion, we developed the general method for constructing the spiro-hydantoin ring at the anomeric position of furanose derivativesemploying the aldol addition-cyclization method. It can be applied to the synthesis of (+)-hydantocidin itself and other stereoisomers and the results will be reported elsewhere.

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Experimental

All melting points were determined on a Yanaco micro melting point apparatus and were uncorrected. ^{1}H-NMR spectra were recorded on JOEL GX-400, JOEL GX-270 and Varian EM 360A spectrometers. Infrared spectra were recorded on a Jasco A-102 spectrometer. Mass spectra were recorded on a JOEL JMS-D300 spectrometer. Optical rotations were measured on a Jasco DIP-360 polarimeter. Merck Kieselgel 60 Art. 9385 was used for SiO_2 column chromatography.

Crystal Data of (D-11a): $C_{28}H_{38}N_2O_7Si$, *Mw*=542.7, orthorhombic, $P2_12_12_1$, *a*=22.314(4), *b*=11.439(2)), *c*=11.728(2)Å, *U*=2993.6Å^3, *Z*=4, *Dc*=1.21gm^{-3}, μ(Cukα=1.5418Å)=11cm^{-1}, *F*(000)=1160, *T*=297K, Intensity data were obtained on a Rigaku AFC-5R diffractometer with graphite-monochromatized Cukα radiation using the θ-2θ scan technique (2θ<128°). Among 2828 independent reflections measured, 2514 were considered as observed on the basis of the criterion $Fo>2\sigma(Fo)$. All intensities were corrected for Lorents and polarization effects but not for absorption. Structure was solved by MULTAN84[10] and refined by block-diagonal least-squares methods. Positions of the hydrogen atoms were estimated from standard geometry. The final refinements with anisotropic temperature factors for the non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms lowered *R* value to 0.099(Rw=0.074, $w=1/\sigma^2(Fo)$). Fractional atomic coordinates, tables of bond lengths and angles and isotropic thermal parameters have been deposited with the Cambridge Crystallographic Data Centre.

1-*t*-Butyldimetylsilyl-5-methoxy-3-(4-methoxybenzyl)hydantoin (7). A mixture of 1-*t*-butyldimethylsilyl-3-(4-methoxybenzyl)-hydantoin (9.50g, 28.4mmol) and *N*-bromosuccunimide (5.20g, 29.2mmol) in CCl_4 (100ml) was refluxed for 1h. After cooling in an ice bath, methanol (40ml) and Et_3N (3.16g, 43.0mmol) were added to the reaction mixture, and the solution was stirred at 0°C for 1h. The mixture was diluted with ether and the organic layer was washed with water, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on silica gel (EtOAc-hexane 1:3) and distilled by Kugelrohr apparatus (175°C, 1mmHg) to give **7** (8.83g, 85%) as an colourless oil; IR ($CHCl_3$) 1780, 1715, 1615, 1180cm^{-1}; NMR (60MHz, $CDCl_3$) δ 7.34(2H, d, J=9Hz), 6.83(2H, d, J=9Hz), 4.87(1H, s), 4.54(2H, s), 3.74(3H, s), 3.31(3H, s), 0.96(9H, s), 0.29(6H, s); MS *m/z* 364(M^+), 307, 121; Anal. found: C, 59.19; H, 7.78; N, 7.63. Calcd. for $C_{18}H_{28}N_2O_4Si$: C, 59.31; H ,7.74; N , 7.68%.

Aldol addition of (7) and 4-*O*-benzyl-2,3-*O*-isopropylidene-L-threose (L-6).

[*5R,1'R,2'R,3'S*]-5-(1'-*t*-Butyldimethylsilyloxy-2',3'-*O*-isopropylidenedioxy-4'-benzyloxy)butyl-5-methoxy-3-(4-methoxy-benzyl)hydantoin (8a), [*5S,1'S,2'R,3'S*]-isomer (8b), [*5S,1'R,2'R,3'S*]-isomer (8c) and [*5R,1'S,2'R,3'S*]-isomer (8d). To a stirring solution of **7** (11.94g, 32.75mmol) at -78°C in THF (400ml) were added $LiN(TMS)_2$ (1.0M in THF, 36.5ml, 36.5mmol) and after 30min, a solution of **L-6** (8.12g, 32.4mmol) in THF (8ml). After being stirred at -20°C for 70min, the reaction mixture was poured into sat. NH_4Cl and extracted with ether (x3). The combined extract was washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue indicated two spots on analytical TLC plate (Rf=0.38 and 0.29, EtOAc-hexane 1:5), which were separated by silica gel chromatography (EtOAc-hexane 1:5) to give the upper fraction (8.11g, 41% containing **8a** and **8b**) and the lower fraction (7.03g, 35% containing **8c** and **8d**) as a colourless syrup. Since the pure each isomer was not isolated at this stage, the following derivatization was carried out to separate the each isomer.

[*5R,1'R,2'R,3'S*]-5-(1'-*t*-Butyldimethylsilyloxy-2',3'-*O*-isopropylidenedioxy-4'-benzyloxy)butyl-5-methoxy-3-(4-methoxy-benzyl)-1-*N*-methoxycarbonylhydantoin (9a) and [*5S,1'S,2'R,3'S*]-isomer (9b). To a solution of **8a** and **8b** (1.23g, 2.00mmol) in THF (40ml) were added *t*-BuOK (0.28g, 2.4mmol) and methyl chloroformate (1.7ml, 2.2mmol) at 0°C. After 30min, the reaction mixture was pored into sat. NH_4Cl and extracted with ether (x3). The combined organic layer was washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure. The resulting residue was chromatographed on silica gel (EtOAc-hexane 1:3) to

give **9a** (0.93g, 69%) as a colourless syrup and **9b** (0.24g, 18%) as a colourless syrup. **Data of 9a:** $[\alpha]_D^{27}$ +27.0° (c=1.35, $CHCl_3$); IR ($CHCl_3$) 3950, 1825, 1810, 1750, 1620, 1520, 1470cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.36-7.27(7H, m), 6.76(2H, d, J=8.8Hz), 4.68(1H, d, J=10.3Hz), 4.68(2H, s), 4.51(2H, ABq, 12.1Hz), 4.09(1H, dt, J=1.8, 10.3Hz), 3.24(1H, dd, J=7.3, 10.3Hz), 3.16(3H, s), 1.22(3H, s), 1.06(3H, s), 0.89(9H, s), 0.18(3H, s), 0.07(3H, s); MS *m/z* 657(M^+-15), 615, 557, 453, 395, 363, 221, 121, 91; Anal. found: C, 60.50; H, 7.28; N, 4.17. Calcd. for $C_{34}H_{48}N_2O_{10}Si$: C, 60.69; H , 7.19; N , 4.16%. **Data of 9b:** $[\alpha]_D^{27}$ -26.2° (c=1.25, $CHCl_3$); IR ($CHCl_3$) 1820, 1805, 1750, 1615, 1590, 1515cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.40-7.27(7H, m), 6.28(2H, d, J=8.8Hz), 4.71(1H, d, J=2.2Hz), 4.56(2H, ABq, J=12.3Hz), 4.34(1H, dt, J=7.7, 5.3Hz), 3.83(1H, dd, J=2.2, 7.7Hz), 3.80(3H, s), 3.77(3H, s), 3.58(1H, dd, J=5.3, 9.7Hz), 3.07(3H, s), 1.24(3H, s), 1.13(3H, s), 0.95(9H, s), 0.16(3H, s), 0.07(3H, s); MS *m/z* 657(M^+-15), 615, 583, 453, 412, 395, 363, 221, 121, 91; Anal. found: C, 60.89; H, 7.31; N, 4.13. Calcd. for $C_{34}H_{48}N_2O_{10}Si$: C, 60.69; H , 7.19; N , 4.16%.

[*5R,1'R,2'R,3'S*]-5-(1'-*t*-Butyldimethylsilyloxy-2',3'-*O*-isopropylidenedioxy-4'-benzyloxy)butyl-5-methoxy-3-(4-methoxybenzyl)-1-*N*-methoxycarbonylhydantoin (9c). A mixture of **8c** and **8d** (2.03g, 3.03mmol) was methoxycarbonylated by the same manner as described above to afford **9c** (1.43g, 64%) as a colourless syrup; $[\alpha]_D^{26}$ -19.7° (c=1.47, $CHCl_3$); IR ($CHCl_3$) 1820, 1800, 1745, 1610, 1590, 1510cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.40-7.25(7H, m), 6.82(2H, d, J=8.8Hz), 4.75-4.74(1H, m), 4.63(2H, ABq, J=12.1Hz), 4.31-4.29(2H, m), 3.90(3H, s), 3.81-3.78(1H, m), 3.78(3H, s), 3.58-3.52(1H, m), 2.98(3H, s), 1.37(3H, s), 1.34(3H, s), 0.78(9H, s), 0.13(3H, s), -0..02(3H, s); MS *m/z* 672(M^+), 657, 615, 557, 453, 394, 221, 121, 91; Anal. found: C, 60.43; H, 7.31; N, 4.18. Calcd. for $C_{34}H_{48}N_2O_{10}Si$: C, 60.69; H , 7.19; N , 4.16%.

Conversion of (9a-c) to (8a-c).

From 9a: To a solution of **9a** (0.66g, 0.86mmol) in MeOH (20ml) was added aq. K_2CO_3 (0.5M, 4.0ml, 2.0mmol) at r.t.. After 80min, the reaction mixture was poured into sat. NH_4Cl and extracted with ether(x3). The combined extract was washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on silica gel (EtOAc-hexane 1:3) to give **8a** (472.3mg, 78%) as a colourless syrup and **8c** (110mg, 18%) as a colourless syrup. **Data of 8a:** $[\alpha]_D^{26}$ -82.0° (c=1.19, $CHCl_3$); IR ($CHCl_3$) 3400, 1785, 1730, 1610, 1510, 1440cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.35-7.28(7H, m), 6.80(1H. br, s), 6.28(2H, d, J=8.8Hz), 4.58(2H, s), 4.56(2H, ABq, J=14.3Hz), 4.49(1H, ddd, J=4.6, 5.9, 8.8Hz), 4.28(1H, s), 4.14(1H, d, J=8.8Hz), 3.77(3H, s), 3.64(1H, dd, J=4.6, 10.1Hz), 3.56(1H, dd, J=5.9, 10.1Hz), 3.02(3H, s), 1.40(3H, S), 1.34(3H, s), 0.79(9H, s), 0.02(3H, s), -0.10(3H, s); MS *m/z* 557(M^+-57), 449, 211, 121, 91; Anal. found: C, 62.29 H, 7.59; N, 4.60. Calcd. for $C_{32}H_{46}N_2O_8Si$: C, 62.52; H, 7.54; N , 4.56%. **Data of 8c:** $[\alpha]_D^{26.5}$ +21.8° (c=1.58, $CHCl_3$); IR ($CHCl_3$) 3450, 1790, 1730, 1615cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.36-7.29(7H, m), 6.81(2H, d, J=8.8Hz), 5.59(1H, br.s), 4.61-4.49(4H, m), 4.21(1H, ddd, J=2.6, 6.6, 6.8Hz), 4.07(1H, d, J=8.4Hz), 3.77(3H, s), 3.59(1H, dd, J=6.8, 10.3Hz), 3.49(1H, dd, J=6.6, 8.4Hz), 3.43(1H, dd, J=6.8, 10.3Hz), 3.06(3H, s), 1.26(3H, s), 1.18(3H, s), 0.89(9H, s), 0.07(6H, s); MS *m/z* 599(M^+-15), 557, 525, 449, 337, 211, 121, 91; Anal. found: C, 62.43 H, 7.31; N, 4.52. Calcd. for $C_{32}H_{46}N_2O_8Si$: C, 62.52; H , 7.54; N , 4.56%.

From 9b: The same hydrolysis procedure as described above was carried out for **9b** (500mg, 0.743mmol) to give **8b** (400mg, 80%) as a colourless syrup; $[\alpha]_D^{26}$ +43.0° (c=0.93, $CHCl_3$); IR ($CHCl_3$) 3400, 1785, 1725, 1610cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.37-7.29(7H, m), 6.82(2H, d, J=8.8Hz), 6.37(1H, br. s), 4.60(2H, ABq, J=12.7Hz), 4.54(2H, ABq, 12.9Hz), 4.21(1H, dd, J=1.5, 8.8Hz), 4.17(1H, ddd, J=4.4, 5.4, 8.8Hz), 4.08(1H, d, J=1.5Hz), 3.78(3H, s), 3.58(1H, dd, 5.4, 9.8Hz), 3.47(1H, dd, J=4.4, 9.8Hz), 3.01(3H, s), 1.42(3H, s), 1.37(3H, s), 0.84(9H, s), 0.04(3H, s), -0.09(3H, s); MS *m/z* 599(M^+-15), 557, 525, 499, 211, 121, 91; Anal. found: C, 62.44 H, 7.35; N, 4.58. Calcd. for $C_{32}H_{46}N_2O_8Si$: C, 62.52; H , 7.54; N , 4.56%.

From 9c: The same procedure as described above was carried out for **9c** (810mg, 1.20mmol) to give **8c** (650mg, 88%) and **8a** (90mg, 12%).

Epimerization of (8b) to (8d). To a stirring solution of **8b** (135.8mg, 0.221mmol) in MeOH (2.6ml) was added aq. K_2CO_3 (0.5M, 0.6ml, 0.3mmol) at 60°C. After 8h, the reaction mixture was poured into sat. NH_4Cl and extracted with ether(x3). The combined extract was washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on silica gel (EtOAc-hexane 1:3) to give **8d** (59.1mg, 44%) as a colourless syrup and **8b** (51.4mg, 38%). **Data of 8d:** $[\alpha]_D^{27}$ -8.2° (c=0.89, $CHCl_3$); IR ($CHCl_3$) 3450, 1785, 1715, 1610cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.34-7.25(7H, m), 6.74(2H, d, J=8.8Hz), 5.50(1H, br. s), 4.54(2H, s), 4.49(2H, ABq, J=12.2Hz), 4.14(1H, dt, J=8.3, 5.4Hz), 4.01(1H, d, J=1.6Hz), 3.71(3H, s), 3.54(1H, dd, J=1.6, 8.3Hz), 3.48(1H, dd, J=5.4, 9.8Hz), 3.34(1H, dd, J=5.4, 9.8Hz), 3.07(3H, s), 1.27(3H, s), 0.98(3H, s), 0.85(9H, s), 0.01(6H, s),; MS *m/z* 615(M^++1), 599, 557, 525, 211, 121, 91; HRMS. found: 599.2770. Calcd for $C_{31}H_{43}N_2O_8Si$ (M-15, Me):599.2772.

Conversion of (8a-d) to (10a-d).

***[4R,5R,1'R,2'R]*-4-(3-Benzyloxy-1',2'-*O*-isopropylidenedioxy)propyl-5-methoxy-7-*N*-(4-methoxybenzyl)-1,7-diaza-3-oxabicyclo-[3.3.0]octane-2,6,8-trione(10a), *[4S,5S,1'R,2'S]*-isomer (10b), *[4R,5S,1'R,2'S]*-isomer (10c) and *[4S,5R,1'R,2'S]*-isomer (10d).**

From 8a: To a stirring solution of **8a** (360mg, 0.585mmol) in THF (12ml) was added *n*-Bu_4NF (1.0M in THF, 0.90ml, 0.90mmol) at 0°C. After 40min, the reaction mixture was poured into sat. NH_4Cl and extracted with ether (x3). The combined extract was washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on silica gel (EtOAc-hexane 1:1) to give ***[5R,1'R,2'S,3'S]*-5-(4'-benzyloxy-2',3'-*O*-isopropylidenedioxy-1'-hydroxy)butyl-5-methoxy-3-*N*-(4-methoxybenzyl)hydantoin** (210.3mg, 72%); $[\alpha]_D^{27}$ -19.2° (c=0.88, $CHCl_3$); IR ($CHCl_3$) 3320, 3260, 1785, 1720, 1610, 1510cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.36-7.26(7H, m), 7.29(2H, d, J=8.4Hz), 6.90(1H, br. s), 6.88(2H, d, J=8.4Hz), 4.59(2H, s), 4.58(2H, ABq, J=11.7Hz), 4.44(1H, ddd, J=4.4, 7.0, 8.1Hz), 4.23(1H, d, J=2.2Hz), 4.19(1H, dd, J=2.2, 7.0Hz), 3.76(3H, s), 3.73(1H, dd, J=4.4, 9.2Hz), 3.55(1H, dd, J=8.1, 9.2Hz), 2.96(3H, s), 2.3(1H, br. s), 1.38(3H, s), 1.38(3H, s); MS *m/z* 500(M^+), 485, 468, 421, 221, 121; Anal. found: C, 62.15; H, 6.64; N, 5.48. Calcd. for $C_{26}H_{32}N_2O_8$: C, 62.39; H , 6.44; N , 5.60%. To a stirring solution of the above hydantoin (140.3mg, 0.266mmol) in CH_2Cl_2 (8ml) were added Et_3N (0.59ml, 4.2mmol) and $COCl_2$ (1.3M in toluene, 2.8ml, 3.6mmol) at 0°C. After 5min, the reaction mixture was diluted with water and the aqueous layer was extracted with EtOAc (x3). The combined extract was washed with dil. HCl, water and brine and dried (Na_2SO_4). Evaporation of the solvent and chromatography of the residue (EtOAc-hexane 1:3) gave **10a** (138.6mg, 94%) as colourless prisms; m.p. 129.0-129.5°C; $[\alpha]_D^{25}$ +11.7° (c=0.98, CH_3OH); IR (KBr) 1840, 1775, 1740, 1610, 1585cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.36-7.27(7H, m), 6.84(2H, d, J=8.8Hz), 4.66(2H, s), 4.53(1H, d, J=7.3Hz), 4.42(1H, dd, J=5.9, 7.3Hz), 4.31(1H, dt, J=2.9, 5.9Hz), 3.79(3H, s), 3.67(1H, dd, J=2.9, 10.6Hz), 3.56(1H, dd, J=5.9, 10.6Hz), 3.09(3H, s), 1.49(3H, s), 1.40(3H, s), MS *m/z* 526(M^+), 511, 486, 405, 163, 121, 91; Anal. found: C, 61.52; H, 5.63; N, 5.29. Calcd. for $C_{27}H_{30}N_2O_9$: C, 61.59; H , 5.47; N , 5.32%.

From 8b: Treatment of **8b** (190mg, 0.31mmol) with *n*-Bu_4NF in the same manner as described above gave ***[5S,1'S,2'S,3'S]*-5-(4'-benzyloxy-2',3'-*O*-isopropylidenedioxy-1'-hydroxy)butyl-5-methoxy-3-(4-methoxybenzyl)hydantoin** (108.2mg, 70%) as a colourless syrup; $[\alpha]_D^{27}$ -11.0° (c=2.14, $CHCl_3$); IR ($CHCl_3$) 3550, 3420, 1785, 1725, 1610, 1515cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.34-7.28(7H, m), 6.83(2H, d, J=8.8Hz), 5.84(1H, br. s), 4.63(2H, s), 4.57(2H, s), 4.27(1H, d, J=8.8Hz), 4.19(1H, dt, J=4.4, 8.8Hz), 4.00(1H, br. s), 3.77(3H, s), 3.64(1H, dd, J=4.4, 10.3Hz), 3.56(1H, dd,J=4.4, 10.3Hz), 3.17(3H, s), 1.64(1H, br. s), 1.42(6H, s); MS *m/z* 500(M^+), 485, 468, 279, 250, 149, 121, 91; Anal. found: C, 62.01; H, 6.70 N, 5.34. Calcd. for $C_{26}H_{32}N_2O_8$: C, 62.39; H , 6.44; N, 5.60%. The resulting hydantoin (62.1mg, 0.124mmol) was carbonylated in the same manner as described in the above case to give **10b** (55.3mg, 85%) as a colourless syrup; $[\alpha]_D^{25}$ -32.5° (c=1.46, CH_3OH); IR ($CHCl_3$) 1850, 1785, 1740, 1610cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.37-7.27(7H, m), 6.86(2H, d, J=8.8Hz), 4.65(2H, s), 4.62(2H, s), 4.52(1H, d, J=7.3Hz), 4.45(1H, t, J=7.3Hz), 4.40(1H, ddd, J=2.9, 5.1, 7.3Hz), 3.80(3H, s), 3.74(1H, dd, J=2.9, 10.6Hz), 3.64(1H, dd, J=5.1, 10.6Hz), 2.92(3H, s), 1.47(3H, s), 1.41(3H, s); MS *m/z* 526(M^+), 511, 468, 405, 362, 211, 121, 91; Anal. found: C, 61.42; H, 5.60; N, 5.15. Calcd. for $C_{27}H_{30}N_2O_9$: C, 61.59; H , 5.47; N , 5.32%.

From 8c: Treatment of **8c** (490mg, 0.80mmol) with *n*-Bu_4NF in the same manner as described above gave **[5S,1'R,2'S,3'S]-5-(4'-benzyloxy-2',3'-*O*-isopropylidenedioxy-1'-hydroxy)butyl-5-methoxy-3-(4-methoxybenzyl)hydantoin** (311.5mg, 78%) as a colourless syrup; $[\alpha]_D^{26}$ +14.7° (c=1.06, $CHCl_3$); IR ($CHCl_3$) 3400, 1780, 1725, 1610, 1510cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.37-7.27(7H, m), 6.83(2H, d, J=8.8), 6.12(1H, br. s), 4.64-4.52(4H, m), 4.17(1H, m), 3.84(1H, s), 3.78(3H, s), 3.68(1H, dd, J=4.0, 10.3Hz), 3.60(1H, dd, J=5.5, 10.3Hz), 3.34(1H, br. d), 3.16(3H, s), 1.67(1H, br. s), 1.28(3H, s), 1.27(3H, s); MS *m/z* 500(M^+), 485, 468, 279, 250, 149, 121, 91; Anal. found: C, 62.57; H, 6.24; N, 5.49. Calcd. for $C_{26}H_{32}N_2O_8$: C, 62.39; H , 6.44; N , 5.60%. The resulting hydantoin (172.4mg, 0.348mmol) was carbonylated in the same manner as described in the above case to give **10c** (166.0mg, 92%) as a colourless syrup; $[\alpha]_D^{25}$ +32.8° (c=1.02, CH_3OH); IR ($CHCl_3$) 1845, 1780, 1740, 1610, 1510cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.39-7.28(7H, m), 6.83(2H, d, J=8.8Hz), 4.88(1H, d, J=1.1Hz), 4.64(2H, ABq, J=14.3Hz), 4.56(2H, s), 4.35(1H, ddd, J=4.0, 7.0, 9.5Hz), 4.21(1H, dd, J=1.1, 9.5Hz), 3.78(3H, s), 3.71(1H, dd, J=4.0, 9.5Hz), 3.50(1H, dd, J=7.0, 9.5Hz), 3.03(3H, s), 1.28(6H, s); MS *m/z* 526(M^+), 511, 435, 418, 362, 211, 162,121, 91; Anal. found: C, 61.33; H, 5.65; N, 5.19. Calcd. for $C_{27}H_{30}N_2O_9$: C, 61.59; H, 5.47; N , 5.32%.

From 8d: Treatment of **8d** (51.4mg, 0.084mmol) with *n*-Bu_4NF in the same manner as described above gave **[5S,1'R,2'S,3'S]-5-(4'-benzyloxy-2',3'-*O*-isopropylidenedioxy-1'-hydroxy)butyl-5-methoxy-3-*N*-(4-methoxybenzyl)hydantoin** (37.9mg, 90%) which was carbonylated directly in the same manner as described in the previous case to afford **10d** (29.9mg, 75%) as a colourless syrup; $[\alpha]_D^{21.5}$ -9.8° (c=0.64, $CHCl_3$); IR ($CHCl_3$) 1850, 1790, 1740, 1615, 1515cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.39-7.27(7H, m), 6.84(2H, d, J=8.8Hz), 4.68(1H, d, J=0.7Hz), 4.62(2H, ABq, J=14Hz), 4.55(2H, ABq, J=12Hz), 4.27-4.18(1H, m), 4.04(1H, dd, J=0.7, 8.1Hz), 3.78(3H, s), 3.69(1H, dd, J=4.8, 9.5Hz), 3.48(1H, dd, J=7.0, 9.5Hz), 3.24(3H, s), 1.19(3H, s), 0.95(3H, s); MS *m/z* 526(M^+), 511, 435, 362, 211, 162, 121, 91; HRMS. found: 526.1963. Calcd. for $C_{27}H_{30}N_2O_9$:526.1964.

[2S,3R,4R,5R]-2-Benzyloxymethyl-4-*t*-butyldimethylsilyloxy-3-hydroxy-8-(4-methoxybenzyl)-6,8-diaza-1-oxaspiro[4.4]nonane-7,9-dione (11a) and [2S,3R,4R,5S]-isomer (12a).

From 8a: To a stirring solution of **9a** (100.0mg, 0.163mmol) in dichloroethane (5ml) were added ethylene glycol (0.10ml, 1.8mmol) and *p*-TsOH·H_2O (20mg) and the mixture was stirred at 60°C for 4h. The reaction mixture was diluted with water and the aqueous layer was extracted with dichloromethane (x3). The combined extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and chromatography of the residue (EtOAc-hexane 1:3) gave **11a** (62.6mg, 71%) as white needles and **12a** (12.5mg, 14%) as a colourless syrup. **Data of 11a:** m.p. 127-130°C; $[\alpha]_D^{23.5}$ -16.6° (c=1.37, $CHCl_3$); IR (KBr) 3510, 3320, 1785, 1720, 1610, 1580, 1510cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.37-7.28(7H, m), 6.81(2H, d, J=8.8Hz), 6.07(1H, br. s), 4.63-4.52(4H, m), 4.49(1H, d, J=4.0Hz), 4.33(1H, dt, J=3.3, 5.9Hz), 4.22(1H, dd, J=3.3, 4.0Hz), 3.81(1H, dd, J=5.9, 10.3Hz), 3.77(3H, s), 3.68(1H, dd, J=5.9, 10.3Hz), 2.65(1H, br. s), 0.79(9H, s), -0.02(3H, s), -0.18(3H, s); MS *m/z* 542(M^+), 485, 395, 211, 91; Anal. found: C, 62.17; H, 6.90; N, 5.36. Calcd. for $C_{28}H_{38}N_2O_7Si$: C, 61.97; H , 7.06; N ,5.16%. **Data of 12a:** $[\alpha]_D^{26}$ -10.5° (c=1.22, $CHCl_3$); IR (KBr) 3450, 1790, 1720, 1610, 1515cm^{-1}; NMR (400MHz, $CDCl_3$) δ 7.33-7.27(7H, m), 6.28(2H, d, J=8.8Hz), 6.06(1H, br. s), 4.70(1H, d, J=11.7Hz), 4.57(2H, ABq, J=12.2Hz), 4.55(2H, s), 4.41(1H, dt, J=7.3, 3.4Hz), 4.29(1H, d, J=4.9Hz), 4.04(1H, ddd, J=3.4, 4.9, 11.7Hz), 3.84(1H, dd, J=3.4, 10.7Hz), 3.78(3H, s), 3.75(1H, dd, J=7.3, 10.7Hz), 0.73(9H, s), 0.05(3H, s), -0.05(3H, s); MS *m/z* 543(M^++1), 485, 395, 362, 339, 305, 211, 121, 91; Anal. found: C, 61.79; H, 6.96; N, 5.16. Calcd. for $C_{28}H_{38}N_2O_7Si$: C, 61.97; H , 7.06; N ,5.16%.

From 8c: The hydantoin **8c** (34.2mg, 0.0556mmol) was subjected to the cyclization reaction to give **11a** (22.3mg, 74%) and **12a** (4.5mg, 15%) in the same manner as described above.

[2R,3R,4S,5R]-2-Benzyloxymethyl-4-*t*-butyldimethylsilyloxy-3-hydroxy-8-(4-methoxybenzyl)-6,8-diaza-1-oxaspiro[4.4]nonane-7,9-dione (13a) and [2S,3R,4S,5R]-isomer (14a).

From 8b: The hydantoin **8b** (119.1mg, 0.194mmol) was subjected to the cyclization reaction in the same manner as described above to give **13a** (64.7mg, 61%) as a white solid and **14a** (19.1mg, 18%) as a white solid. **Data of 13a:** $[\alpha]_D^{27}$ -34.8° (c=0.73, $CHCl_3$); IR ($CHCl_3$) 3350, 1790, 1720, 1610, 1510, 1440cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.38-7.29(7H, m), 6.80(2H, d, J=8.8Hz), 5.67(1H, br. s), 4.65-4.50(6H, m), 4.18(1H, d, J=5.9Hz), 3.85-3.75(2H, m), 3.77(3H, s), 2.99(1H, d, J=7.3Hz), 0.75(9H, s), 0.00(3H, s), -0.11(3H, s); MS *m/z* 485(M^+-57), 362, 305, 211, 121, 91; HRMS. found: 485.1739. Calcd for $C_{24}H_{29}N_2O_7Si$ (M^+-57, *t*-Bu)): 485.1740. **Data of 14a:** $[\alpha]_D^{26.5}$ +30.0° (c=1.12, $CHCl_3$); IR ($CHCl_3$)3350, 1790, 1720, 1610, 1510, 1440cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.35-7.27(7H, m), 6.85(2H, d, J=8.8Hz), 5.70(1H, br. s), 4.85-4.48(6H, m), 4.07(1H, d, J=1.5Hz), 4.03(1H, dd, J=1.5, 9.2Hz), 3.79(3H, s), 3.79(1H, dd, J=4.4, 10.6Hz), 3.70(1H, dd, J=7.3, 10.6Hz), 0.88(H, s), 0.09(3H, s), 0.05(3H, s); MS *m/z* 542(M^+), 527, 485, 395, 279, 211, 121, 91; Anal. found: C, 62.25; H, 7.07; N, 6.22 Calcd. for $C_{28}H_{38}N_2O_7Si$: C, 61.97; H ,7.06; N , 6.16%.

From 8d: The hydantoin **8d** (9.1mg, 0.015mmol) was cyclized into **13a** (3.5mg, 46%) and **14a** (1.2mg, 16%) in the same manner as described above.

***[2R,3R,4R,5R]*-2-Benzyloxymethyl-3,4-dihydroxy-8-(4-methoxybenzyl)-6,8-diaza-1-oxaspiro[4.4]nonane-7,9-dione (11b) and *[2S,3S,4R,5S]*-isomer (12b), *[2S,3S,4S,5R]*-isomer (13b) and *[2S,3S,4S,5S]*-isomer (14b).**

From 11a: To a stirring solution of **11a** (2.64g, 4.87mmol) in THF (90ml) was added *n*-Bu_4NF (1.0M in THF, 7.4ml, 7.4mmol) at 0°C. After 15min, the reaction mixture was diluted with water and then the aqueous layer was extracted with ether (x3). The combined extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and chromatography of the residue (EtOAc-hexane 3:1) gave **11a**(1.77g, 85%) as white needles; m.p. 122.0-122.5°C; $[\alpha]_D^{26.5}$ -23.5° (c=1.59, CH_3OH); IR ($CHCl_3$) 3440, 1790, 1730, 1610, 1510, 1440, 1410cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.33-7.22(7H, m), 6.84(2H, d, J=8.8Hz), 4.64-4.50(4H, m), 4.39(1H, d, J=4.0Hz), 4.30-4.21(2H, m), 3.79(1H, dd, J=4.8, 10.6Hz), 3.75(3H, s), 3.64(1H, dd, J=4.8, 10.6Hz); MS *m/z* 428 (M^+), 248, 234, 220, 162, 121, 91; Anal. found: C, 61.61; H, 5.47; N, 6.61. Calcd. for $C_{22}H_{24}N_2O_7$: C, 61.68; H , 5.65; N , 6.54%.

From 12a: The hydantoin **12a** (500mg, 0.92mmol) was converted to **12b** (297.6mg, 75%) in the same manner as described above; $[\alpha]_D^{26}$ -3.4° (c=1.10, CH_3OH); IR ($CHCl_3$) 3250, 1785, 1710, 1610, 1510cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.32-7.23(7H, m), 6.84(2H, d, J=8.8Hz), 4.56(2H, ABq, J=12.3Hz), 4.44(1H, d, J=4.8Hz), 4.40(1H, ddd, J=3.3, 4.4, 7.3Hz), 4.12(1H, dd, J=3.3, 4.8Hz), 3.83(1H, dd, J=4.4, 10.6Hz), 3.68(1H, dd, J=7.3, 10.6Hz); MS *m/z* 428 (M^+), 248, 220, 162, 121, 91; Anal. found: C, 61.45; H, 5.79; N, 6.34. Calcd. for $C_{22}H_{24}N_2O_7$: C, 61.68; H , 5.65; N , 6.54%.

From 13a: The hydantoin **13a** (10.8mg, 0.0199mmol) was converted to **13b** (4.3mg, 57%) in the same manner as described above; $[\alpha]_D^{25}$ +3.5° (c=0.21, CH_3OH); IR ($CHCl_3$) 3450, 1790, 1725, 1245cm^{-1}; NMR (270MHz,CD_3OD) δ 7.38-7.27(5H, m), 7.24(2H, d, J=8.8Hz), 6.84(2H, d, J=8.8Hz), 4.67(1H, t, J=7.3Hz), 4.56(2H, ABq, J=12.1Hz), 4,54(2H, s), 4.45(1H, ddd, J=3.3, 5.9, 7.3Hz), 4.19(1H, d, 7.3Hz), 3.75(3H, s), 3.70(1H, dd, J=3.3, 10.6Hz), 3.59(1H, dd, J=5.9, 10.6Hz); MS *m/z* 428 (M^+), 262, 248, 220, 162, 121, 91; Anal. found: C, 61.89; H, 5.52; N, 6.67 Calcd. for $C_{22}H_{24}N_2O_7$: C, 61.68; H , 5.64; N , 6.54%.

From 14a: The hydantoin **14a** (9.4mg, 0.017mmol) was converted to **14b** (4.1mg, 55%) in the same manner as described above; m.p. 129-133°C; $[\alpha]_D^{25}$ -37.9° (c=0.21, CH_3OH); IR ($CHCl_3$) 3450, 1790, 1720, 1245cm^{-1}; NMR (270MHz,CD_3OD) δ 7.36-7.24(7H, m), 6.85(2H, d, J=8.8Hz), 4.58-4.55(4H, m), 4.37(1H, m), 4.24-4.18(2H, m), 3.77(1H, dd, J=3.7, 10.6Hz), 3.75(3H, s), 3.66(1H, dd, J=7.0, 10.6Hz); MS *m/z* 428 (M^+), 350, 248, 220, 162, 121, 91; Anal. found: C, 61.41; H, 5.70; N, 6.33 Calcd. for $C_{22}H_{24}N_2O_7$: C, 61.67; H , 5.64; N , 6.54%.

***[2S,3S,4R,5R]*-3,4-Dihydroxy-2-hydroxymethy-6,8-diaza-1-oxaspiro[4.4]nonane-7,9-dione (*L*-2).** To a stirring solution of ceric ammonium nitrate (9.08g, 16.6mmol) in water (16.6ml) was added a solution of **11b** (710mg, 1.66mmol) in CH_3CN (33ml) at room temperature. After 20 min, the reaction mixture was diluted with brine (20ml) and the aqueous layer was extracted with EtOAc (x4). The combined extract was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on silica gel

(EtOAc) to give **[2*S*,3*S*,4*R*,5*R*]-2-benzyloxymethyl-3,4-dihydroxy-6,8-diaza-1-oxaspiro[4.4]nonane-7,9-dione (11c)** (437.0mg, 85%) as a colourless syrup; $[\alpha]_D^{27}$ -17.7° (c=1.14, CH_3OH); IR (Nujol) 3300, 1785, 1730, 1460, 1375cm^{-1}; NMR (270MHz, CD_3OD) δ 7.34-7.22(5H, m), 4.56(2H, ABq, J=12.1Hz), 4.37(1H, d, J=4.0Hz), 4.29-4.21(2H, m), 3.80(1H, dd, J=4.8, 10.6Hz), 3.65(1H, dd, J=6.6, 10.6Hz); MS *m/z* 308(M^+), 228, 217, 202, 142, 108, 91; Anal. found: C, 54.32; H, 5.38; N, 8.84. Calcd. for $C_{14}H_{16}N_2O_6$: C, 54.54; H , 5.23; N , 9.09%. The stirring mixture of **11c** (400mg, 1.3mmol) and Pd-C (5%, 0.40g) in methanol (200ml) was heated at 55°C under hydrogen atmosphere (3kg/cm^2) for 7h. After filtration of the mixture through Cerlite, the filtrate was concentrated under reduced pressure. Chromatography of the residue on Diaion CHP 20P (water) and lyophilization gave **L-2** (171.9mg, 61%) as a white amorphous solid; $[\alpha]_D^{26.5}$ -23.7° (c=0.97, CH_3OH); IR (KBr) 3300, 1780, 1720, 1400, 1310, 1150cm^{-1}; NMR (270MHz,CD_3OD) δ 4.36(1H, d, J=4.4Hz), 4.25(1H, dd, J=3.3, 4.4Hz), 4.11(1H, ddd, 3.3, 5.1, 6.6Hz), 3.82(1H, dd, J=5.1, 11.7Hz), 3.73(1H, dd, J=6.6, 11.7Hz); Anal. found: C, 37.22; H, 4.72; N, 12.35. Calcd. for $C_7H_{10}N_2O_6 \cdot 1/2H_2O$: C, 37.01; H ,4.85; N, 12.34%

[2*S*,3*S*,4*R*,5*S*]-3,4-Dihydroxy-2-hydroxymethy-6,8-diaza-1-oxaspiro[4.4]nonane-7,9-dione (L-3). 4-Methoxybenzyl group of **12b** (241.0mg, 0.562mmol) was eliminated in the same manner as described above to give the corresponding product **12c** (135.3mg. 78%), which was debenzylated under hydrogenation condition as described above to afford **L-3** (73.7mg, 77%) as a white solid; $[\alpha]_D^{25}$ -7.9° (c=0.64, CH_3OH); IR (KBr) 3600-3100, 1720cm^{-1}; NMR (270MHz, CD_3OD) δ 4.41(1H, d, J=4.8Hz), 4.25(1H, ddd, J=3.3, 5.1, 7.0Hz), 4.12(1H, dd, J=3.3, 4.5Hz), 3.85(1H, dd, J=5.1, 11.7Hz), 3.74(1H, dd, J=7.0, 11.7Hz); MS *m/z* 219(M^++1), 171, 141, 129, 100, 75; Anal. found: C, 37.05; H, 4.60; N, 12.49. Calcd. for $C_7H_{10}N_2O_6 \cdot 1/2H_2O$: C, 37.01; H ,4.85; N , 12.34%.

[2*S*,3*S*,4*S*,5*R*]-3,4-Dihydroxy-2-hydroxymethy-6,8-diaza-1-oxaspiro[4.4]nonane-7,9-dione (L-4). 4-Methoxybenzyl group of **13b** (125.6mg, 0.293mmol) was eliminated in the same manner as described above to give the corresponding product **13c** (74.1mg. 82%), which was debenzylated under the hydrogenation conditions as described above to afford **L-4** (42.5mg, 81%) as a white amorphous solid; $[\alpha]_D^{25}$ -42.0° (c=0.60, CH_3OH); IR (KBr) 3500, 3400, 3250, 1750cm^{-1}; NMR (270MHz, CD_3OD) δ 4.65(1H, t, J=7.7Hz), 4.30(1H, ddd, J=3.7, 7.7, 12.5Hz), 4.17(1H, d, J=7.7Hz), 3.74(1H, dd, J=3.7, 12.5Hz), 3.68(1H, dd, J=12.5HZ); MS *m/z* 218(M^++1), 200, 187, 170, 141, 129, 116, 100, 86; Anal. found: C, 38.21; H, 4.48; N, 12.59. Calcd. for $C_7H_{10}N_2O_6$: C, 38.53; H ,4.62; N , 12.84%.

[2*S*,3*S*,4*S*,5*S*]-3,4-Dihydroxy-2-hydroxymethy-6,8-diaza-1-oxaspiro[4.4]nonane-7,9-dione (L-5). 4-Methoxybenzyl group of **14b** (101.1mg, 0.236mmol) was eliminated in the same manner as described above to give the corresponding product **14c** (72.7mg. 86%), which was debenzylated under hydrogenation condition as described above to afford **L-5** (37.0mg, 72%) as a white amorphous solid; $[\alpha]_D^{25}$ -19.4° (c=0.31, CH_3OH); IR (KBr) 3350, 3400, 3300, 1750, 1715cm^{-1}; NMR (270MHz, D_2O) δ 4.25(1H, t, J=5.9Hz), 4.22(1H, ddd, J=3.7, 5.9, 5.5Hz), 3.79(1H, dd, J=3.7, 12.1Hz), 3.71(1H, dd, J=5.9, 12.1Hz); Anal. found: C, 38.24; H, 4.58; N, 12.61. Calcd. for $C_7H_{10}N_2O_6$: C, 38.53; H ,4.62; N , 12.84%.

[1*R*,5*R*,6*S*,8*S*]-6-Benzyloxymethyl-8-*t*-butyldimethylsilyloxy-10-(4-methoxybenzyl)-2,10-diaza-4,7-dioxatricyclo[3.2.1.3^{1,2}]-undecane-3,9,11-trione (15a). To a stirring solution of **13a** (5.7mg, 0.011mmol) in CH_2Cl_2 (1.0ml) were added Et_3N (0.022ml, 0.16mmol) and $COCl_2$ (1.3M in toluene, 0.10ml, 0.13mmol) at 0°C. After 10min, the reaction mixture was poured into sat. NH_4Cl and then the aqueous layer was extracted with ether (x3). The combined extract was washed with brine, dried (Na_2SO_4) and evaporated. Chromatography of the residue (EtOAc-hexane 1:3) gave **15a** (4.8mg, 80%) as a white amorphous solid; $[\alpha]_D^{21.5}$ +35.7° (c=0.93, $CHCl_3$); IR (KBr) 3340, 1830, 1770, 1725, 1610, 1585, 1510cm^{-1}; NMR (270MHz, $CDCl_3$) δ 7.36-7.28(7H, m), 6.38(2H, d, J=8.8Hz), 4.84(1H, dt, J=2.6, 6.2Hz), 4.66-4.54(6H, m), 3.78(3H, s), 3.78-3.68(2H, m), 0.90(9H, s), 0.09(3H, s), 0.03(3H, s), MS *m/z*

511(M^+-57, *t*-Bu), 485, 211, 121, 91; Anal. found: C, 61.11; H, 6.49; N, 4.42. Calcd. for $C_{29}H_{36}N_2O_8Si$: C, 61.25; H , 6.38; N,4.29%.

[2*R*,3*R*4*R*,5*S*]-3,4-Dihydroxy-2-hydroxymethy-6,8-diaza-1-oxaspiro[4.4]nonane-7,9-dione (D-2), [2*R*,3*R*,4*S*,5*R*]-isomer (D-3), [2*R*,3*R*,4*R*,5*S*]-isomer (D-4) and [2*R*,3*R*,4*R*,5*R*]-isomer (D-5).

D-Series of the title compounds were prepared according to the same procedure used in the L-series. $[\alpha]_D^{25}$ of D-2, D-3, D-4 and D-5 in methanol are +25.4°(c=1.06), +8.9°(c=1.01), +42.9°(c=0.60) and +18.5° (c=0.54), respectively.

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