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# Stereocontrolled Synthesis of Spirodihydrouracil Nucleoside

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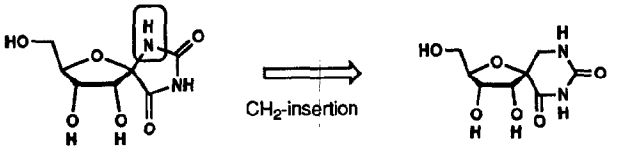
**Abstract:** Synthesis of the spiro-dihydrouracil derivative of (+)-hydantocidin (2) is described. The pivotal step is a Lewis acid-mediated *C*-glycosidation of the protected D-psicose **3** with trimethylsilyl cyanide, which proceeded in good yield and β-selectivity. Synthesis of **2** was accomplished in 27% overall yield from **3**.

The discovery of (+)-hydantocidin **1**,[1] a naturally occurring spironucleoside with herbicidal activity, has paved the way for new variations of chemical structure in the field of nucleoside chemistry.[2] The heterocyclic moiety, the hydantoin part in the natural product, is fixed directly at the anomeric center in a vertical direction relative to the furanose ring, a structural feature distinct from that of nucleosides known so far.[3]

Among considerable synthetic work carried out on (+)-hydantocidin[4] and its derivatives,[5] our previous investigation[6] on the sugar part revealed that all three hydroxy groups on the D-ribofuranose were required for the plant growth regulatory activity. One of our main points of interest has moved to the hydantoin part, which is capable of hydrogen-bonding interaction toward an undiscovered target site in plants. Herein, we designed the spirodihydrouracil derivative **2**, with a methylene group inserted at the anomeric position of (+)-hydantocidin, to examine the significance of the hydrogen bonding direction. This ring enlargement shifts the CONH groups compared with the parent compound (**Figure 1**).




**1**
**(+)-hydantocidin**

**2**

**Figure 1**

Our synthetic plan is shown in **Figure 2**. Oxidation of the hydroxymethyl group in a D-psicofuranose derivative **B**, followed by cyclization, is to provide the spiro-dihydrouracil skeleton **C**. The key to our plan is the stereocontrolled introduction of an aminomethylene unit at the anomeric position of a protected psicose **A**. As the aminomethylene unit, we employed trimethylsilyl cyanide (TMSCN), which we considered would serve as the precursor for the methylamino unit in the desired compound **2**.

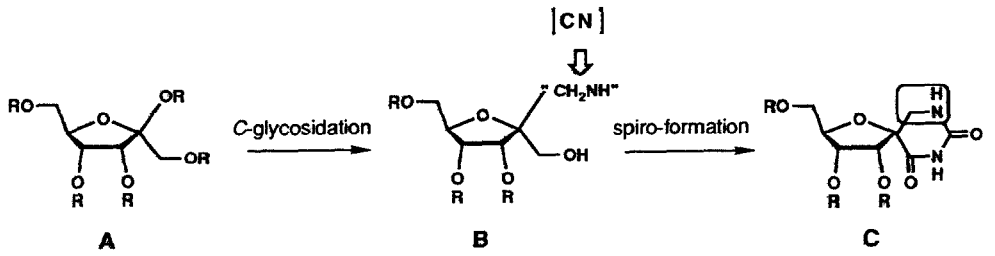
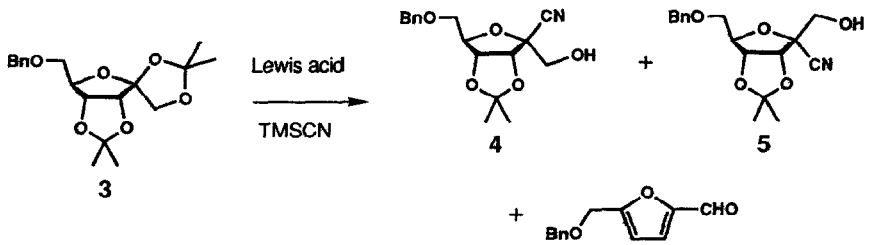


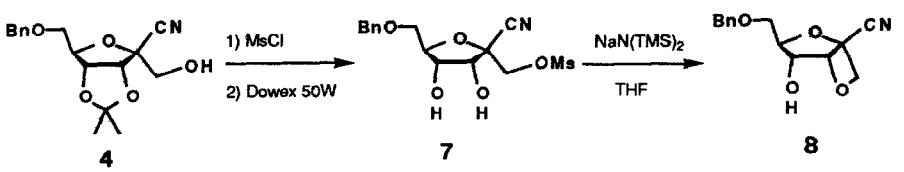

**Figure 2**

Our synthesis (**Scheme 1**) began with the 1,2;3,4-di-*O*-isopropylidene-D-psicofuranose **3**, which is easily prepared from D-fructose by previously reported procedures.[7] Treatment of **3** with trimethylsilyl cyanide (TMSCN)[8] in the presence of trimethylsilyl triflate (TMSOTf) at -20 °C provided a mixture of **4** and **5** in a ratio of 4:1 in 81% combined yield, along with **6** in 16% yield. In this reaction, the 2-furaldehyde **6** was produced through acidic degradation of **3** before addition of cyanide ion. Using $SnCl_4$ instead of TMSOTf depressed the formation of the undesired **6** with a similar stereoselectivity (ratio 4.5:1) in a lower yield (66%). Separation of **4** and **5** was achieved by careful chromatography on silica gel.



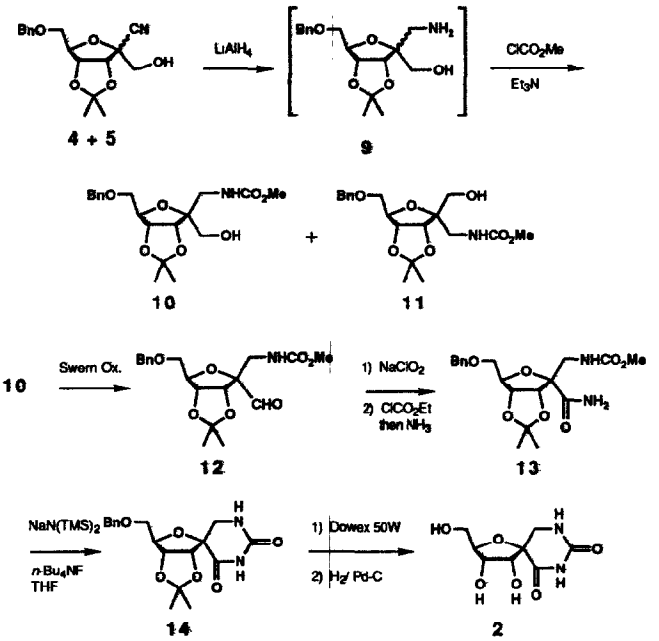

**Scheme 1**

The stereochemistry at the anomeric position in **4** was confirmed by chemical transformation into oxetane **8** (**Scheme 2**). Mesylation of **4** followed by removal of the isopropylidene moiety afforded diol **7**, which was treated with bis(trimethylsilyl)amide ($NaN(TMS)_2$), to give oxetane **8**. This chemical transformation clearly demonstrated the *cis* configuration of the C2-hydroxylmethyl and C3-hydroxy group in **4**, confirming that cyano nucleophile was introduced at the β-position.




**Scheme 2**

We next turned our attention to constructing the dihydrouracil derivative **2** (**Scheme 3**). Reduction of the mixture of **4** and **5** with lithium aluminum hydride gave aminoalcohol **9**, which was *N*-carbonylated with methyl chloroformate in the presence of triethylamine, to provide carbamates **10** and **11** in 63% and 15% yields, respectively. These stereoisomers were more readily separated than **4** and **5** by silica gel chromatography. The major isomer **10** was identical with the carbamate prepared from a pure **4**, by spectroscopic and chromatographic comparison. The conversion of a hydroxymethyl group in **10** into an amide group was performed as follows: Swern oxidation of **10** afforded the aldehyde **12**, which was oxidized with sodium chlorite in the presence of sodium dihydrogen phosphate to yield the corresponding carboxylic acid. The amide **13** was obtained by sequential treatment with ethyl chloroformate to yield the mixed anhydride and then gaseous ammonia in 91% overall yield from **12**. The final cyclization step requires intramolecular attack by the amide group at the carbonyl site of the carbamate **13**.




**Scheme 3**

Our initial attempt with $NaN(TMS)_2$ alone was not successful; however, the cyclization was successfully accomplished by using a combination of $NaN(TMS)_2$ and tetrabutylammonium fluoride in THF, to give spirodihydrouracil **14** in 86% yield. Acid hydrolysis of the isopropylidene group in **14**, followed by hydrogenolysis of the benzyl group, furnished the final compound **2** in quantitative yield from **14**.

The negative results of bioassay with the dihydrouracil **2** are very striking. When tested at 1000ppm, post plant emergency through a foliar application in a pot assay,[5c, 9] the spirodihydrouracil **2** exhibited no

herbicidal activity against ten representative weed species, while (+)-hydantocidin controlled all species under the same condition. This result might indicate possibly that the direction of hydrogen bonding plays a crucial role for herbicidal activity.

In summary, we have established an efficient route for synthesis of a spirodihydrouracil derivative by employing *C*-glycosidation of the protected psicose **4** with TMSCN, selective methoxycarbonylation of aminoalcohol **9**, and cyclization to dihydrouracil with the combination of $NaN(TMS)_2$ and n-$Bu_4NF$. The loss of herbicidal activity of the dihydrouracil derivative **2** might indicate the importance of the direction of hydrogen bonding. Further research on structure-herbicidal-activity relationships of (+)-hydantocidin is now in progress.

**Acknowledgment**

We wish to thank Mr. T. Honma and Mr. M. Shindou, Agroscience Research Laboratories, Sankyo Co. Ltd., for testing of the herbicidal activity of spirodihydrouracil derivative **2**.

**Experimental**

All melting points were determined on a Yanaco micro melting point apparatus and were uncorrected. $^1$H-NMR spectra (270MHz) were recorded on a JEOL GX-270 spectrometer. IR spectra were recorded on a Jasco A-102 spectrometer. Mass spectra were recorded on a JEOL JMS-D300 spectrometer. Optical rotations were measured on a Jasco DIP-360 polarimeter. Merck Kieselgel 60 was used for $SiO_2$ column chromatography. Merck TLC plate Art.5744 was used for preparative TLC.

***C*-Glycosidation of 4 with TMSCN**

**Using trimethylsilyl triflate as a Lewis acid:** To a -20 °C solution of **3** (3.99g, 11.4mmol) in $CH_2Cl_2$ (50.0ml) were added trimethylsilyl cyanide (4.6ml, 34mmol) and trimethylsilyl triflate (3.3ml, 17mmol). The resulting solution was stirred for 2 h at -20 °C, and then it was poured into saturated aqueous $NH_4Cl$. The aqueous layer was extracted with ether, and the combined organic layers were dried over $Na_2SO_4$. Filtration and concentration provided a colorless oil, which was chromatographed on silica gel (EtOAc-hexane 1:3 to 1:1) to give a mixture of **6-*O*-Benzyl-3,4-*O*-isopropylidene-β-D-psicofuranosyl cyanide 4** and **6-*O*-Benzyl-3,4-*O*-isopropylidene-α-D-psicofuranosyl cyanide 5** (2.9g, 81% combined yield) as a colorless syrup, along with **5-benzyloxymethyl-2-formylfuran 6** (0.40g, 16%). The ratio of **4** and **5** was found to be 4:1 by $^1$H-NMR analysis.

For **4**: $[\alpha]_D^{25}$ -29.7 (c 1.72, $CHCl_3$); IR ($CHCl_3$) 3600, 3000, 2950, 1710, 1600, 1450, 1390 $cm^{-1}$. NMR ($CDCl_3$) δ 7.42-7.27 (5H, m,), 5.10 (1H, d, *J* = 6.0Hz), 4.91 (1H, dd, *J* = 6.0, 1.2Hz), 4.70 (1H, d, *J* = 12.1Hz), 4.50 (1H, d, *J* = 12.1Hz), 4.43 (1H, br t, *J* = 4.0Hz), 3.89 (2H, br d, *J* = 7.0Hz), 3.63 (2H, d, ABq, *J* = 4.0, 10.5Hz), 2.40 (1H, br t, *J* = 7.0Hz), 1.53 (3H, s ), 1.35 (3H, s); MS *m/z* 319 ($M^+$), 304, 289, 277, 187, 127, 91 ; HRMS : 319.1410 Calcd for $C_{17}H_{21}NO_5$: 319.1420

For **5**: $[\alpha]_D^{25}$ -13.1 (c 1.22, MeOH); IR ($CHCl_3$) 3440, 1082$cm^{-1}$; NMR ($CDCl_3$) δ 7.41-7.28 (5H, m), 4..87 (1H, d, *J* = 6.4Hz), 4.83 (1H, dd, *J* = 6.4, 2.8Hz), 4.56 (2H, ABq, *J* = 12.1Hz), 4.42 (1H, q, *J* = 2.8Hz), 3.94 (1H, dd, *J* = 11.8, 3.6Hz), 3.80 (1H, dd, *J* = 11.8, 10.2Hz), 3.75 (1H, dd, *J* = 10.7, 2.8Hz), 3.63 (1H, dd, *J* = 10.7, 2.8Hz), 3.08 (1H, dd, *J* = 11.8, 10.2Hz), 1.67 (3H, s), 1.37 (3H, s); MS *m/z* 319 ($M^+$), 304, 140, 107,

91 ; HRMS : 319.1408 Calcd for $C_{17}H_{21}NO_5$: 319.1420

For **6**: NMR ($CDCl_3$) δ 9.62 (1H, s), 7.37-7.28 (5H, m), 7.21 (1H, d, *J* = 3.4Hz), 6.54 (1H, d, *J* = 3.4Hz), 4.61 (2H, s), 4.58 (2H, s); MS *m/z* 216 ($M^+$), 110, 91, 81.

**Using $SnCl_4$ as a Lewis acid**: To a -20°C solution of **3** (0.61g, 1.7mmol) in $CH_2Cl_2$ (9ml) were added trimethylsilyl cyanide (0.7ml, 2.8mmol) and $SnCl_4$ (1.0M in $CH_2Cl_2$, 2.6mmol). After being stirred at -20 °C for 1h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. The product mixture was extracted with ether, and the combined organic layers were dried over $Na_2SO_4$. Filtration and concentration provided a colorless oil, which was chromatographed on silica gel, to give a mixture of **4** and **5** (0.37g, 66% combined yield) as a colorless syrup. The ratio of **4** and **5** was found to be 4.5:1 by $^1$H-NMR analysis.

**6-*O*-Benzyl-1-*O*-methanesulfonyl-D-psicofuranosyl cyanide 7:** To a solution of **4** (0.99g, 3.1mmol) and $Et_3N$ (0.65ml, 4.6mmol) in $CH_2Cl_2$ (12ml) at 0 °C was added MsCl (0.29ml, 3.7mmol), and the mixture was stirred for 30 min. The reaction mixture was poured into water, and the water layer was extracted with ether. The combined extracts were washed with brine. After drying ($Na_2SO_4$) and evaporation of the solvent, the residue was chromatographed on silica gel (EtOAc-hexane 1:3), to give **6-*O*-Benzyl-3,4-*O*-isopropylidene-1-*O*-methanesulfonyl-D-psicofuranosyl cyanide** (1.0g, 81%) as a colorless solid; m.p. 100-101°C ; $[\alpha]_D^{25}$ -37.8 (c= 1.23 MeOH); IR ($CHCl_3$) 3600, 3580, 3030, 2940, 1720, 1450, 1370 $cm^{-1}$; NMR ($CDCl_3$) δ 7.40-7.31 (5H, m), 5.11 (1H, d, *J* = 6.0Hz), 4.93 (1H, d, *J* = 6.0Hz), 4.70 (1H, d, *J* = 11.8Hz), 4.50-4.46 (1H, m), 4.44 (1H, d, *J* = 11.0Hz), 4.38 (1H, d, *J* = 11.0Hz), 3.63 (2H, ABq d, *J* = 10.4, 3.6 Hz), 3.14 (3H, s), 1.52 (3H, s), 1.34 (3H, s) ; MS *m/z* 397($M^+$), 382, 286, 265, 180, 91; Anal. found: C, 54.47; H, 5.65; N, 3.65; S, 8.30. Calcd. for $C_{18}H_{23}NO_7S$: C, 54.40; H,5.83; N, 3.52; S, 8.07 %

To a solution of the above mesylate (0.70g, 1.8mmol) in a mixture of MeOH and water (2:1, 20ml), was added Dowex$^R$ 50W (3.0g) at 80 °C, and then the mixture was stirred overnight. After filtration through a pad of Celite$^R$, the filtrate was concentrated. Silica gel chromatography (EtOAc-hexane 5:1) of the residue gave **7** (0.58g, 92%) as a colorless oil;

For **7**: $[\alpha]_D^{25}$ -1.6 (c= 1.23, MeOH); IR ($CHCl_3$) 3580, 3530, 3300, 3020, 2940, 2860, 1720, 1600, 1450, 1360 $cm^{-1}$; NMR ($CDCl_3$) δ 7.39-7.28 (5H, m), 4.66-4.62 (1H, m), 4.64 (1H, d, *J* = 12.2Hz), 4.59(1H, d, *J* = 11.4Hz), 4.55 (1H, d, *J* = 12.2Hz), 4.50-4.42 (1H, m), 4.43(1H, d, *J* = 11.4Hz), 4.20-4.15 (1H, m), 3.67 (2H, d, *J* = 4.0Hz), 3.52(1H, d, *J* = 4.8Hz), 3.14(3H, s), 2.78(1H, d, *J* = 6.4Hz) ; MS *m/z* 357($M^+$), 261, 155, 107, 91 ; Anal. found: C, 50.56; H, 5.17; N, 3.99; S, 9.15. Calcd. for $C_{15}H_{19}NO_7S$: C, 50.41; H, 5.36; N, 3.92; S, 8.97%

**1,3-Anhydro-6-*O*-benzyl-D-psicofuranosyl cyanide 8:** $NaN(TMS)_2$ (1.0M in THF, 2.0mmol) was added to a solution of **7** (0.37g, 1.0mmol) in THF (15ml) at 0 °C, and the mixture was stirred at room temperature for 30min. The reaction mixture was poured into sat. $NH_4Cl$ and extracted with ether (x3). The combined extracts were washed with brine, dried ($Na_2SO_4$), and concentrated. The resulting residue was chromatographed on silica gel (EtOAc-hexane 1:2) to give **8** (80mg, 30%) as a colorless oil;

For **8**: $[\alpha]_D^{25}$ +74.5 (c= 1.10 MeOH); IR ($CHCl_3$) 3580, 3555, 3020, 2880, 2360, 1450, 1390 $cm^{-1}$; NMR ($CDCl_3$) δ 7.39-7.28 (5H, m), 5.33 (1H, d, *J* = 5.0Hz), 5.07 (1H, d, *J* = 8.0Hz), 4.34-4.29 (1H, m), 4.14 (1H, ddd, *J* = 8.8, 6.5, 5.0Hz), 3.81 (1H, dd, *J* = 10.9, 2.8Hz), 3.71 (1H, dd, *J* = 10.9, 4.4Hz), 2.52 (1H, d, *J* =

8.8Hz) ; MS *m/z* 261 ($M^+$), 140, 107, 91; Anal. found: C, 64.08; H, 5.59; N, 5.48. Calcd. for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36%

**6-*O*-Benzyl-3,4-*O*-isopropylidene-β-D-psicofuranosyl (methoxycarbonylamino methane) 10 and its isomer 11:** To a mixture of **4** and **5** (506.7mg, 1.59mmol) in ether (17ml), was added $LiAlH_4$ (120mg, 3.15mmol) at 0 °C. The solution was stirred at 0 °C for 30 min, and then at room temperature for 2h. The mixture was quenched with aqueous [1.0M] $K_2CO_3$ (0.8ml), and then the grey precipitate was removed by filtration through a pad of Celite®. The organic layer was washed with brine and dried over $Na_2SO_4$. Evaporation of the solvent under reduced pressure gave a colorless syrup (2.10g).

The resulting syrup (2.10g) was dissolved in dry $CH_2Cl_2$ (100ml), and $Et_3N$ (3.6ml, 26mmol) and methyl chloroformate (0.76ml, 9.7mmol) were added. The solution was stirred at 0 °C for 20 min. The reaction mixture was poured into water, and the water layer was extracted with ether (x3). The combined extracts was washed with water and brine. After drying ($Na_2SO_4$) and evaporation of the solvent, the residue was subjected to chromatography on silica gel (EtOAc-hexane 1:1) to afford carbamates **10** (0.38g, 63%) and **11** (91mg, 15%) as colorless syrups.

For **10**: $[\alpha]_D^{25}$ +24.0 (c 1.10, MeOH); IR ($CHCl_3$) 3460, 1710, 1075 $cm^{-1}$. NMR ($CDCl_3$) δ 7.40-7.27 (5H, m), 5.64 (1H, brd), 4.79 (1H, dd, *J* = 6.6Hz, 4.4Hz), 4.61 (1H, d, *J* = 6.6Hz), 4.58 (2H, ABq, *J* = 11.9Hz), 4.16-4.08 (1H, m), 3.79 (2H, dd, *J* = 17.0, 11.9Hz), 3.68-3.51 (2H, m), 3.64 (3H, s), 3.34 (1H, dd, *J* = 14.1, 4.4Hz), 2.63 (1H, brd.), 1.54 (3H, s,), 1.33 (3H, s) ; MS *m/z* 382 ($M^+$+1), 366, 350, 334, 293, 143, 213, 185, 173, 148, 141, 127, 97, 92; HRMS : 381.1770 Calcd for $C_{19}H_{27}NO_7$: 381.1787

For **11**: $[\alpha]_D^{25}$ +24.1 (c=0.97 MeOH); IR ($CHCl_3$) 3460, 1715, 1075 $cm^{-1}$; NMR ($CDCl_3$) δ 7.39-7.27(5H, m), 5.14(1H, brd.), 4.82(1H, t, *J* = 6.4Hz), 4.71(1H, d, *J* = 6.4Hz), 4.56(2H, ABq, *J* = 12.1Hz), 4.11-4.16(1H, m), 3.68(1H, s), 3.68-3.45(7H, m), 1.54(3H, s), 1.34(3H, s) ; MS m/z 382($M^+$+1), 366, 350, 334, 293, 243, 213, 185, 173, 92; HRMS. found: 381.1775. Calcd. for $C_{19}H_{27}NO_7$: 381.1787

**6-*O*-Benzyl-3,4-*O*-isopropylidene-β-D-*ribo*-hexos-2-ulo-2,5-furanosyl (methoxycarbonylamino methane) 12:** To a cooled solution of oxalyl chloride (0.15ml, 1.71mmol) in $CH_2Cl_2$ (10ml) was added a solution of DMSO (0.24ml, 3.41mmol) in $CH_2Cl_2$ (0.2ml) at -60 °C, and stirred for 20 min. A solution of **12** (0.50g, 1.31mmol) in $CH_2Cl_2$ (2ml) was added dropwise to the reaction mixture, and stirred for 30min at -60 °C. $Et_3N$ (0.95ml, 6.83mmol) was added to the mixture and followed by stirring for 20min, then further stirring at 0 °C for 90min. The resulting mixture was poured into saturated $NH_4Cl$ solution and acidified with 1N-HCl. The water layer was extracted with ether and the combined organic phases were washed with brine, dried($Na_2SO_4$), and concentrated in vacuo. The residue was chromatographed on silica gel (EtOAc-hexane 1:3), to give **12** (0.43g, 86%) as a colorless syrup. $[\alpha]_D^{25}$ +42.3 (c= 1.09 MeOH); IR ($CHCl_3$) 3450, 1685, 1078 $cm^{-1}$; NMR ($CDCl_3$) δ 9.57(1H, s), 7.28-7.41(5H, m), 5.62(1H, brd.), 4.85(1H, dd, *J* = 6.0, 3.0Hz), 4.77(1H, d, *J* = 6.0Hz), 4.61(2H, ABq, *J* = 12.1Hz), 4.45(1H, q, *J* = 3.0Hz), 3.75-3.57(3H, m), 3.63(3H, s), 3.45(1H, dd, *J* = 14.1, 5.0Hz), 1.46(3H, s), 1.29(3H, s) ; MS *m/z* 380 ($M^+$+1), 364, 350, 306, 292, 279, 263, 244, 218, 183, 158, 143, 127, 113, 105, 97; HRMS. found: 379.1620. Calcd. for $C_{19}H_{25}NO_7$: 379.1631

**[6-*O*-Benzyl-3,4-*O*-isopropylidene-β-D-*ribo*-hex-2-ulofuranosyl (methoxycarbonylaminomethane)]onic**

**acid amide 13:** A solution of $NaClO_2$ (0.22g, 2.4mmol) and $NaH_2PO_4$ (0.28g, 1.8mmol) in $H_2O$ (4ml) was added to a solution of **12** (0.30g, 0.8mmol) and 2-methyl-2-butene (0.26ml, 2.41mmol) in t-BuOH (5ml) at room temperature, and followed by stirring for 1.5 h. Saturated $NaHSO_3$ solution (5ml) was added, and the resulting mixture was stirred for 10 min. The mixture was acidified with 1N-HCl and extracted with $CH_2Cl_2$ (x2). The combined extracts were washed with brine, and dried ($Na_2SO_4$). Evaporation of the solvent afforded **[6-*O*-Benzyl-3,4-*O*-isopropylidene-β-D-*ribo*-hex-2-ulofuranosyl (methoxycarbonylamino methane)]onic acid** (0.35g), which was directly subjected to the next reaction.

To a cooled (0 °C) solution of the above carboxylic acid (0.35g) in THF (14ml) were added $Et_3N$ (0.37ml, 2.7mmol) and ethyl chloroformate (0.10ml, 1.1mmol), and the reaction mixture was maintained at 0 °C for 15 min. $NH_3$ gas was bubbled through the reaction mixture for 5min, followed by stirring at room temperature for 30 min. The resulting mixture was acidified with 1N-HCl and extracted with EtOAc (x3). The combined organic layers were washed with brine and dried over $Na_2SO_4$. After evaporation of the solvent, the residue was chromatographed on silica gel (EtOAc-hexane 5:1 to EtOAc only), to give **13** (0.29g, 91% from **12**) as a colorless syrup. $[\alpha]_D^{25}$ -7.2 (c= 1.18 MeOH); IR ($CHCl_3$) 3420, 3550, 1720, 1075 $cm^{-1}$; NMR ($CDCl_3$) δ 7.40-7.28(5H, m), 6.72(1H, brd.), 5.68-5.55(2H, brd.), 4.81(1H, dd, *J* = 5.8, 3.6Hz), 4.70(1H, d, *J* = 5.8Hz), 4.60(2H, ABq, *J* = 11.8Hz), 4.43(1H, q, *J* = 3.6Hz), 3.71-3.53(4H, m), 3.64(3H, s), 1.49(3H, s), 1.31(3H, s); MS *m/z* 394($M^+$), 363, 347, 307, 289, 249, 198, 173, 154, 141, 128, 111, 97, 92 ; Anal. found: C, 57.67; H, 6.69; N, 7.05. Calcd. for $C_{19}H_{26}N_2O_7$: C, 57.86; H, 6.64; N, 7.10%

**(2R,3R,4R,5S)-2-benzyloxymethyl-3,4-(dimethylmethylenedioxy)-1-oxa-7,9-diazaspiro[4.5]decane-6,8-dione 14:** To a solution of **13** (1.67g, 4.24mmol) in anhydrous THF (160ml), were added 1M solution of $NaN(TMS)_2$ in THF (8.4ml, 8.4mmol) and 1M solution of n-$Bu_4NF$ in THF (8.4ml, 8.4mmol), and the mixture was heated at 70°C for 30 min. The reaction mixture was poured into $H_2O$, acidified with 1N HCl, and extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried ($Na_2SO_4$), and evaporated. The residue was purified by chromatography on silica gel (EtOAc-hexane 2:1 to EtOAc only), to give **14** (1.32g, 86%) as a colorless solid. m.p. 236-237°C ; $[\alpha]_D^{25}$ +40.1 (c= 0.70 MeOH); IR ($CHCl_3$) 3400, 1720, 1075 $cm^{-1}$; NMR ($CDCl_3$) δ 7.58(1H, brd.), 7.40-7.27(5H, m), 5.80(1H, brd.), 4.86(1H, dd, *J* = 6.4, 2.4Hz), 4.75(2H, d, *J* = 6.4Hz), 4.75-4.72(1H, m), 4.55(2H, ABq, *J* = 12.1Hz), 3.64(1H, dd, *J* = 10.7, 2.6Hz), 3.58(1H, dd, *J* = 10.7, 2.8Hz), 3.41(1H, dd, *J* = 12.5, 4.8Hz), 3.35(1H, d, *J* = 12.5Hz), 1.45(3H, s), 1.30(3H, s); MS *m/z* 362 ($M^+$), 347, 278, 233, 217, 186, 167, 149, 91; HRMS. found: 362.1462. Calcd. for $C_{18}H_{22}N_2O_6$: 362.1478

**(2R,3R,4R,5S)-3,4-Dihydroxy-2-hydroxymethy-1-oxa-7,9-diazaspiro[4.5]decane-6,8-dione 2:** A mixture of **14** (0.70g, 1.94mmol) and Dowex$^R$ 50W (2.1g) in MeOH (50ml) and $H_2O$ (25ml) was maintained at 70°C for 5 h. After filtration with a pad of Celite$^R$, the filtrate was concentrated in vacuo, to give a crude sample of **(2R,3R,4R,5S)-2-Benzyloxymethyl-3,4-dihydroxy-1-oxa-7,9-diazaspiro[4.5]decane-6,8-dione** (0.62g) as a colorless solid. An analytical sample was obtained by recrystallization from i-$Pr_2O$. m.p. 174-175°C ; $[\alpha]_D^{25}$ +51.2 (c=0.82 MeOH ); IR (Nujol) 3520, 3410, 1720, 1750, 1110$cm^{-1}$; NMR ($CD_3OD$) δ 7.23-7.34(5H, m), 4.57(2H, s), 4.27(1H, ddd, *J* = 7.2, 4.2, 2.4Hz), 4.24(1H, d, *J* = 5.8Hz), 4.09(1H, dd, *J* = 7.2, 5.8Hz), 3.74(1H, dd, *J* = 11.0, 2.4Hz), 3.60(1H, dd, *J* = 11.0, 4.2Hz), 3.38(1H, d, *J* = 12.9Hz), 3.16(1H, d, *J* =

12.9Hz); MS *m/z* 322($M^+$), 304, 279, 256, 216, 180, 167, 143, 129, 107, 97, 91; HRMS. found: 322.1158. Calcd. for $C_{15}H_{18}N_2O_6$ : 322.1165

A mixture of the above diol (0.62g) and Pd-C (10%) in MeOH (300ml) was heated at 55°C under hydrogen atmosphere (3Kg/cm$^2$) for 5.5 h. After filtration with a pad of Celite$^R$, the filtrate was concentrated in vacuo, and the residue was chromatographed on Diaion CHP20P (water), to give **2** ( 0.45g, quantitative yield from **14**) as a colorless solid. m.p. 205-206°C ; $[\alpha]_D^{25}$ +63.8 (c=0.98 MeOH ); IR (KBr) 3470, 1690, 1090cm$^{-1}$; NMR ($CD_3OD$) δ 4.23(1H, d, *J* = 5.6Hz), 4.12(1H, ddd, *J* = 7.6, 3.4, 2.4Hz), 4.07(1H, dd, *J* = 7.6, 5.6Hz), 3.82(1H, dd, *J* = 12.3, 2.4Hz), 3.60(1H, dd, *J* = 12.3, 3.4Hz), 3.40(1H, d, *J* = 12.7Hz), 3.17(1H, d, *J* = 12.7Hz) ; MS *m/z* 232($M^+$), 214, 201, 196, 159, 143, 129, 113, 100, 83; Anal. found: C, 41.16; H, 5.27; N, 11.90. Calcd. for $C_8H_{12}N_2O_6$: C, 41.38; H, 5.21; N, 12.07%

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9. The herbicidal activity of **2** was evaluated against ten representative weeds; barnyard grass, crab grass, fall panicum, green foxtail, Johnson grass, black nightshade, cocklebur, tall morning glory, ragweed, and velvet leaf.


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