CHEMISTRY LETTERS, pp. 145-148, 1982.

A STEREOSELECTIVE SYNTHESIS OF 2-AMINO-2-DEOXY-D-ARABINOSE AND -D-RIBOSE

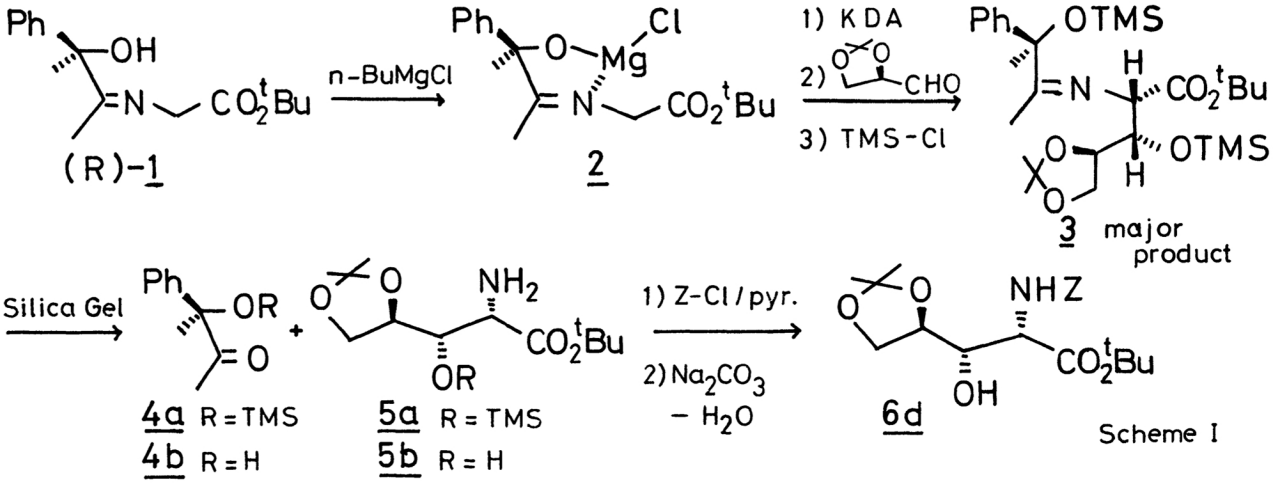
Teruaki MUKAIYAMA, Tetsuo MIWA, and Takashi NAKATSUKA

Department of Chemistry, Faculty of Science,
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

Two amino pentoses, 2-acetamido-2-deoxy-D-arabinose and -D-ribose, are conveniently synthesized from 2-amino-2-deoxy-D-pentonic acid derivatives, obtained by the stereoselective reaction of the chiral imine 1 with 2,3-O-isopropylidene-D-glyceraldehyde.

Recently the biological activities of compounds containing amino sugar moiety have been widely mentioned. Few stereoselective C-C bond formation leading to 2-amino-2-deoxypentoses have been known except for the reaction of N-pyruvylidene-glycinatoaquocopper (II) with 2,3-O-isopropylidene-D-glyceraldehyde under thermodynamic control to give 2-amino-2-deoxy-D-xylo-pentonic acid.[1] So that an efficient method for the convenient synthesis of amino sugars is still strongly desired.

In the previous paper,[2] we reported the enantioselective synthesis of β-hydroxy-α-amino acids from aldehydes and the chiral imine 1 under kinetic control condition. Now, we wish to describe a new stereoselective synthesis of 2-amino-2-deoxy-D-ribo- and -D-arabino-pentonic acids starting from the chiral imine 1 and 2,3-O-isopropylidene-D-glyceraldehyde,[3] that is, 2-amino-2-deoxy-D-ribonic acid was synthesized from the S-imine 1, and 2-amino-2-deoxy-D-arabinonic acid from the R-imine 1. We also report an efficient conversion of these intermediates to 2-acetamido-2-deoxy-D-ribose and -D-arabinose. The synthesis of these 2-amino-2-deoxy-D-pentonic acids was carried out as follows (Scheme I).



Scheme I

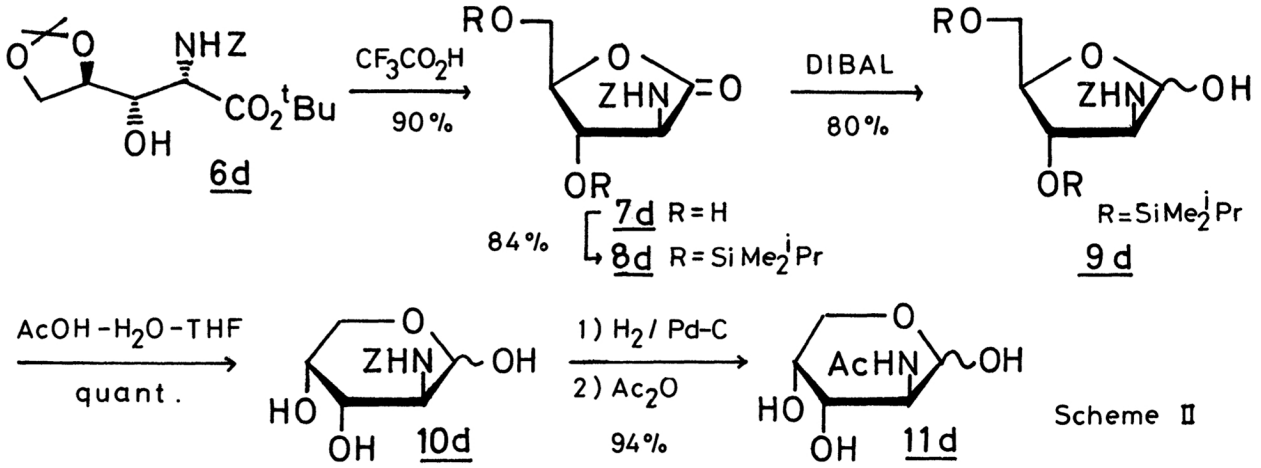
The optically pure imine 1[2] was converted to the alkoxide 2 with a rigid five membered chelate structure. Then the alkoxide 2 was treated successively with a pottasium diisopropylamide[4] (KDA), 2,3-O-isopropylidene-D-glyceraldehyde, and trimethylchlorosilane to give the silylated adduct 3 as a diastereomeric mixture. After the imine part of the adduct 3 was hydrolyzed, the resulting amino group was benzyloxycarbonylated, and the silyl group was removed to afford the diastereomeric mixture of 2-amino-2-deoxy-D-pentonic acid derivatives 6 in 58% yield based on the chiral imine 1. The diastereomeric ratio determined by HPLC (Lichrosorb Si 60, ethyl acetate : chloroform, 8 : 92), is shown in Table.

Table The diastereomeric ratios of 6

configuration of the starting imine 1	diastereomeric ratio (in order of their appearing) 6a[a] : 6b[a] : 6c : 6d
R	6 : 9 : 12 : 73
S	16 : 2 : 62 : 20

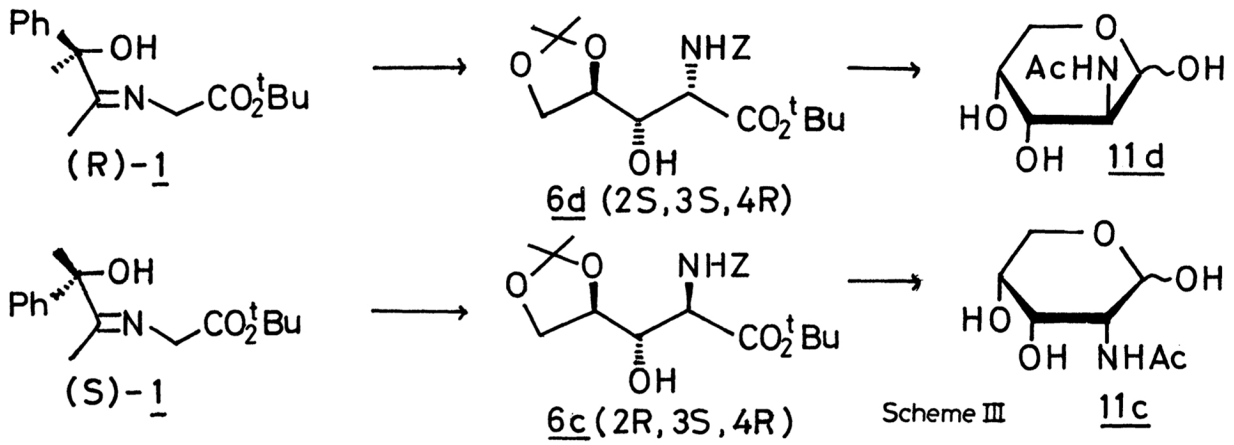
a) The configurations of 6a and 6b are not determined.

These diastereomers were easily separated by the flash column chromatography to give two pure main diastereomers 6c[5),6)] and 6d.[5)] Next, in order to confirm the configurations of 2-amino-2-deoxy-D-pentonic acid derivatives 6c and 6d, they were converted to the known 2-acetamido-2-deoxy-D-pentoses, according to the reaction shown in Scheme II.



Scheme II

The 2-amino-2-deoxy-D-arabinonic acid derivative 6d was treated with trifluoroacetic acid to give a γ-lactone 7d,[5)] which in turn is converted to a disilylated lactone 8d[5)] by dimethylisopropylchlorosilane. The lactone 8d was reduced to a lactol 9d[5)] by diisobutylaluminiumhydride (DIBAL), then the silyl groups were removed under acidic condition to give a N-benzyloxycarbonylated amino sugar 10d.[5)] This amino sugar 10d was converted to 2-acetamido-2-deoxy-D-arabinose which was identified by melting point and specific rotation.[7)] In the same way, 2-acetamido-2-deoxy-D-ribose was obtained from 6c.[7)] These results are summarized in Scheme III.



Scheme III

These results indicate that the chirality of C-2 position of 2-amino-2-deoxy-D-pentonic acid was induced by the chirality of imine 1 and that of C-3 position was induced by the chirality of D-glyceraldehyde.[8)]

A typical procedure for the preparation of 2-acetamido-2-deoxy-D-arabinose (11d) is as follows. To a THF solution of the chiral imine 1 (3.0 mmol) was added n-butylmagnesium chloride (3.0 mmol; in THF solution) at -78°C and then the reaction mixture was warmed to room temperature. To an ethereal suspension of KDA (3.3 mmol) was added dropwise the solution of the previously prepared magnesium alkoxide at -123°C (liquid N_2-ether), and the reaction mixture was stirred for 10 min at this temperature and for 15 min at -78°C. To the resulting solution was added 2,3-O-isopropylidene-D-glyceraldehyde (3.6 mmol) in ether (5 ml) at -123°C and after 5 min was added excess trimethylchlorosilane in THF (10 ml), and the reaction mixture was gradually warmed to room temperature. After the solvents and the excess amount of trimethylchlorosilane were evaporated under reduced pressure, a phosphate buffer solution (pH 7) was added to the residue at 0°C, and the adduct was extracted with ethyl acetate. After the removal of the solvent, the residue was charged on a silica gel column and eluted with dichloromethane. First the ketones 4a and 4b were eluted and next the amino esters 5a and 5b were eluted (dichloromethane : methanol, 9 : 1). The amino esters 5a and 5b were treated with benzyloxycarbonyl chloride (3.9 mmole) and pyridine (4.5 mmole) in THF at 0°C for an hour. The resulting pyridine hydrochloride was filtered off, and then ether was added to the filtrate, which was washed with sat. $CuSO_4$ solution and brine successively and dried over $MgSO_4$. After the removal of the solvents, the residue was treated with Na_2CO_3 (3.0 mmole) in methanol-water (1 : 1) at room temperature for an hour. The organic compounds were extracted with ether and the ethereal layer was washed with brine and dried over $MgSO_4$. Four diastereomers 6a-d were separated each other by the flash column chromatography (Silica gel. ethyl acetate: petroleum ether, 1 : 5, total yield 58% based on 1). Then the pure 6d (2.3 mmole) was treated with trifluoroacetic acid (10 ml) containing a small amount of water (0.5 ml) for 7 hours at 0°C, and the solvents were evaporated. In order to complete the lactonization to the residue was added the mixture of toluene and ethanol (5 : 1, 5 ml) and azeotropically evaporated three times, to afford the γ-lactone 7d (2.0 mmole) in 90% yield. After the protection of hydroxyl groups [dimethyliso-

propylchlorosilane (6.12 mmole), triethylamine (8.2 mmole), 4-(dimethylamino)-pyridine (0.60 mmole) /DMF, 0°C, one hour / 84% yield], the lactone 8d (1.7 mmole) was reduced by DIBAL (2.9 mmole) in toluene at -78°C to give the lactol 9d (1.4 mmole) in 80% yield. The lactol 9d (1.4 mmole) was quantitatively deprotected in acetic acid-THF-water (3 : 2 : 2) in two hours at room temperature to give 10d (1.4 mmole). Then the benzyloxycarbonyl group of 10d (1.4 mmole) was converted to acetyl group by known methods to give 2-acetamido-2-deoxy-D-arabinose (11d) (mp 160-163°C (decompose); $[\alpha]_D^{24}$ -98° (equilibrium, c 1.0, H_2O)/ lit.[7] $[\alpha]_D^{24}$ -97° (equilibrium, c 0.94, H_2O)). In the same way, 2-acetamido-2-deoxy-D-ribose (11c) was obtained (mp 140-143°C (decompose); $[\alpha]_D^{23}$ -39° (equilibrium, c 1.1, H_2O)/ lit.[7] $[\alpha]_D^{23}$ -39° (equilibrium, c 1.1, H_2O)) from 6c.

It is noted that according to the present method, 2-amino-2-deoxy-D-ribose and 2-amino-2-deoxy-D-arabinose are conveniently prepared stereoselectively from S- and R-1, respectively.

References

1) S. Ohdan, T. Okamoto, S. Maeda, T. Ichikawa, Y. Araki, and Y. Ishido, Bull. Chem. Soc. Jpn., 46, 981 (1973).
2) T. Nakatsuka, T. Miwa, and T. Mukaiyama, Chem. Lett., 1981, 279.
3) E. Baer and H. O. Fischer, J. Biol. Chem., 128, 463 (1939).
4) B. Renger, H. Hugel, W. Wykypiel, and D. Seebach, Chem. Ber., 111, 2630 (1978).
5) Satisfactroy elemental analyses, IR data, and NMR data were obtained for these new compounds.
6) The absolute configuration of 6c was determined as (2R, 3S, 4R) by X-ray analysis. We are grateful to Sumitomo Chemical Co., Ltd. for X-ray analysis.
7) R. Kuhn and G. Baschang, Justus Liebigs Ann. Chem., 682, 193 (1959).
8) The stereochemistry of C-3 position is explained according to the Felkin's model. M. Chérest, H. Felkin, and N. Prudent, Tetrahedron Lett., 1968, 2199.
9) Melting points and specific rotations of the intermediates for the synthesis of 2-acetamido-2-deoxy-D-ribose and arabinose, indicated by c, and d, respectively, are as follows: 6c: mp 83-84°C (hexane); $[\alpha]_D^{20}$-46° (c 0.99, $CHCl_3$). 6d: oil; $[\alpha]_D^{20}$-6.6° (c 1.23, $CHCl_3$). 7c: oil; $[\alpha]_D^{23}$+16° (c 0.90, EtOH). 7d: mp 134°C ($CHCl_3$-MeOH); $[\alpha]_D^{22}$ 0° (c 0.77, EtOH). 8c: oil; $[\alpha]_D^{24}$-1.5° (c 0.97, $CHCl_3$). 8d: oil; $[\alpha]_D^{24}$+16.4° (c 0.96, $CHCl_3$). 9c: oil; $[\alpha]_D^{25}$+5.8° (c 0.98, $CHCl_3$). 9d; oil; $[\alpha]_D^{25}$+3.9° (c 1.0, $CHCl_3$). 10c: mp 146-148°C (MeOH); $[\alpha]_D^{20}$-10.7° (c 1.07, MeOH). 10d: mp 171-172°C (MeOH); $[\alpha]_D^{20}$-63.3° (c 1.74, MeOH).

(Received October 31, 1981)