Communications to the Editor

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SYNTHESES OF PSEUDO-α-D-ARABINOFURANOSE, PSEUDO-β-D-ARABINOFURANOSE, AND PSEUDO-β-L-XYLOFURANOSE, THREE OPTICALLY ACTIVE PSEUDO-PENTOFURANOSES, FROM D-GLUCOSE

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Using lead tetraacetate oxidaton and cyclitol formation with KF in the presence of 18-crown-6 as key reactions, three optically active pseudo-pentofuranoses: pseudo-α-D-arabinofuranose, pseudo-β-D-arabinofuranose, and pseudo-β-L-xylofuranose, have been synthesized from D-glucose, via nitrofuranose derivatives which were common reaction intermediates in previous pseudo-hexopyranose synthesis.

KEYWORDS —— pseudo-pentofuranose optically active; pseudo-α-D-arabinofuranose; pseudo-β-D-arabinofuranose; pseudo-β-L-xylofuranose; pseudo-sugar synthesis; D-glucose; chemical transformation

By use of stereoselective deacetoxylation reaction effected by $NaBH_4$ and cyclitol formation from nitrofuranose with KF in the presence of 18-crown-6 as key reactions, we have recently developed a versatile method for converting carbohydrate to pseudo-hexopyranose. Using this method, pseudo-α-D-glucopyranose and pseudo-β-L-idopyranose have been synthesized from D-glucose via nitrofuranose derivatives.[1)]

As an extension of our studies on chemical transformation of carbohydrate leading to pseudo-sugar, we have found a new method for synthesizing pseudo-pentofuranose from nitrofuranose derivatives, which were common reaction intermediates in previous pseudo-hexopyranose synthesis.[1)] In this paper, we report syntheses of three optically active pseudo-pentofuranoses: pseudo-α-D-arabinofuranose (7), pseudo-β-D-arabinofuranose (8),[2)] and pseudo-β-L-xylofuranose (14) from nitrofuranose derivatives (1, 9), which were prepared from D-glucose.[3)]

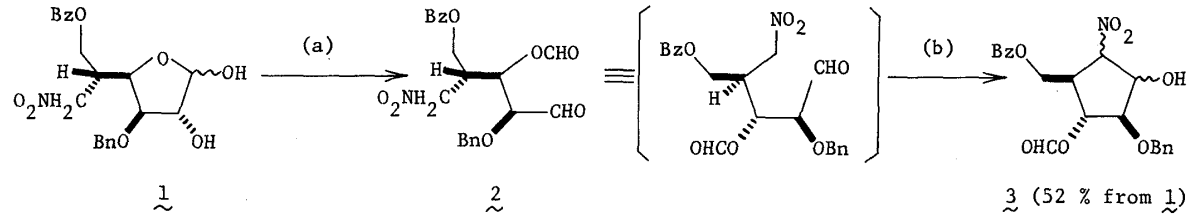
Oxidation of the nitrofuranose derivative (1)[1)] with $Pb(OAc)_4$ in benzene (25°C, 40 min) provided an unstable aldehyde (2). Treatment of 2 with KF in DMF in the presence of 18-crown-6 (2°C, 2 h) yielded a mixture of cyclization products (3, 52 % from 1), a white powder, IR ($CHCl_3$): 3403, 1716, 1544, 1361 cm^{-1}, EI-MS (m/z): 415 (M^+). Removal of the formyl group in 3 with dil. NH_4OH in EtOH (25°C, 3 min) and subsequent treatment of the product with ethyl vinyl ether and d-camphorsulfonic acid (CSA) in CH_2Cl_2 (2°C, 3 h) and elimination of the nitro group with n-Bu_3SnH in benzene in the presence of α,α'-azobis-iso-butyronitrile (AIBN) (80°C, 10 h), furnished 4 (48 %) (a mixture of 1α and 1β-epimers), colorless oil, IR ($CHCl_3$): 2905, 1715, 1280, 1095 cm^{-1}, EI-MS (m/z): 486 (M^+). Removal of the

ethoxyethyl group in 4 with 10 % aq. AcOH in acetone (40°C, 5 h) and subsequent acetylation with Ac_2O and pyridine provided 5 (65 %), colorless oil, $[\alpha]_D^{20}$ +15° ($CHCl_3$), $C_{24}H_{26}O_7$,[4] IR ($CHCl_3$): 1721, 1270, 1220, 1100 cm^{-1}, EI-MS (m/z): 426 (M^+) and 6 (25 %), colorless oil, $[\alpha]_D^{20}$ +38° ($CHCl_3$), $C_{24}H_{26}O_7$, IR ($CHCl_3$): 1723, 1270, 1220, 1100 cm^{-1}, EI-MS (m/z): 426 (M^+). The detailed ^1H NMR decoupling experiments (500 MHz, $CDCl_3$) of 5 and 6 resulted in the following assignment (J in Hz): 5, δ 2.04 (ddd, J=3, 3, 14, 5β-H), 2.11 (ddd, J=6, 10, 14, 5α-H), 2.66 (m, 4α-H), 3.92 (dd, J=3, 4, 2α-H), 4.38 (d, J=6, 6-H_2), 5.13 (ddd, J=3, 3, 6, 1β-H), 5.19 (dd, J=4, 7, 3β-H); 6, δ 1.69 (ddd, J=7, 11, 13, 5α-H), 2.52 (ddd, J=8, 8, 13, 5β-H), 2.80 (m, 4α-H), 3.94 (dd, J=3, 3, 2α-H), 4.68 (d, J=10, 6-H_2), 5.11 (ddd, J=3, 7, 8, 1α-H), 5.24 (dd, J=3, 5, 3β-H). The NOE's were observed between the following pairs of protons[5]: 5, 1β-H & 5β-H (12 %), 2α-H & 4α-H (3 %), 4α-H & 2α-H (3 %), 4α-H & 5α-H (9 %); 6, 1α-H & 2α-H (6 %), 1α-H & 4α-H (1 %), 1α-H & 5α-H (2 %), 2α-H & 1α-H (3 %), 3β-H & 5β-H (2 %), 4α-H & 1α-H (3 %). Based on these spectral findings, the stereostructures of 5 and 6 were clarified.

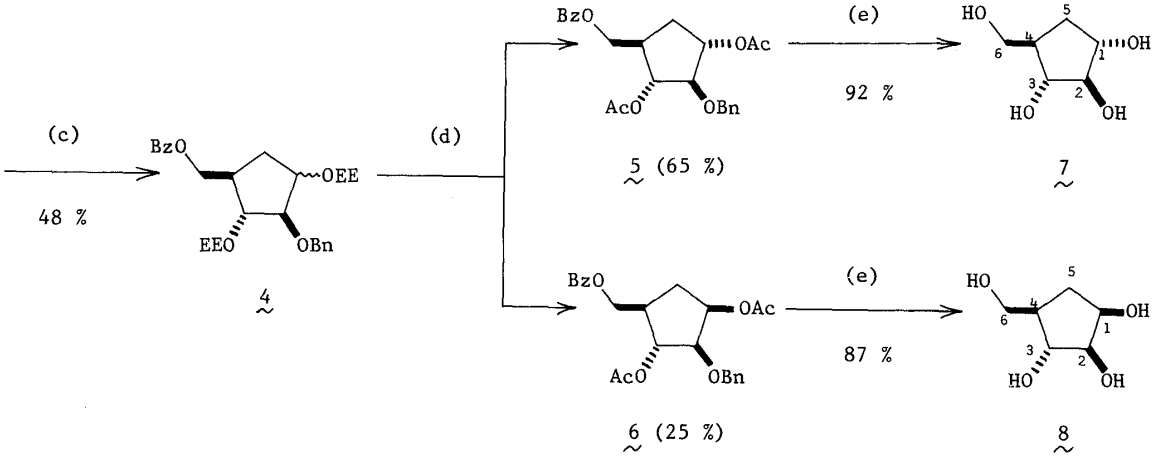
Deacetylation of 5 with 1 % NaOH-MeOH (25°C, 3 h) followed by Birch reduction (Na, liq.NH_3, -78°C, 30 min), furnished the new optically active pseudo-sugar pseudo-α-D-arabinofuranose (7, 92 %), colorless oil, $[\alpha]_D^{20}$ +40° (MeOH), $C_6H_{12}O_4$, ^1H NMR (500 MHz, d_5-pyridine-D_2O, J in Hz): δ 2.33 (ddd, J=4, 6, 13), 2.38 (ddd, J=7, 7, 13) (5-H_2), 2.76 (m, 4α-H), 4.04 (dd, J=6, 10), 4.12 (dd, J=5, 10) (6-H_2), 4.44 (dd, J=8, 8, 3β-H), 4.59 (dd, J=3, 8, 2α-H), 4.60 (ddd, J=3, 4, 7, 1β-H). ^{13}C NMR (125 MHz, d_5-pyridine): δc 33.9 (5-C), 45.8 (4-C), 64.8 (6-C), 76.0, 79.5 (1, 3-C), 86.2 (2-C). Removal of the protecting groups in 6 as described above for 5 furnished pseudo-β-D-arabinofuranose (8, 87 %).[6]

On the other hand, $Pb(OAc)_4$ oxidation of the nitrofuranose derivative (9)[1] furnished an aldehyde (10) which, on treatment with KF in DMF in the presence of 18-crown-6 (2°C, 2 h), was converted to a mixture of cyclization products 11 (52 % from 9), IR ($CHCl_3$): 3403, 1716, 1544, 1361 cm^{-1}, EI-MS (m/z): 415 (M^+). Deformylation of 11 and subsequent ethyl vinyl ether treatment and elimination of the nitro group as described above for 3 yielded 12 (45 %), colorless oil, $[\alpha]_D^{20}$ +70° ($CHCl_3$), $C_{28}H_{38}O_7$, IR ($CHCl_3$): 2890, 1710, 1277, 1100 cm^{-1}, EI-MS (m/z): 486 (M^+). Elimination of the ethoxyethyl group in 12 and subsequent acetylation provided 13 (90 %), colorless oil, $[\alpha]_D^{20}$ +13° ($CHCl_3$), $C_{24}H_{26}O_7$, IR ($CHCl_3$): 1724, 1275, 1220, 1100 cm^{-1}, EI-MS (m/z): 426 (M^+). The ^1H NMR decoupling experiments (500 MHz, $CDCl_3$) of 13 resulted in the following assignment (J in Hz): δ 1.84 (ddd, J=6, 6, 13, 5β-H), 2.32 (ddd, J=6, 10, 13, 5α-H), 2.37 (m, 4β-H), 3.91 (dd, J=5, 5, 2α-H), 4.39 (dd, J=7, 11), 4.44 (dd, J=6, 11) (6-H_2), 5.22 (ddd, J=5, 6, 6, 1β-H), 5.25 (dd, J=5, 6, 3β-H). The detailed comparisons of the ^1H NMR data for 13 with those for 5 and 6 led us to assign the structure 13, the stereostructure of which was corroborated by examination of the NOE's.[7]

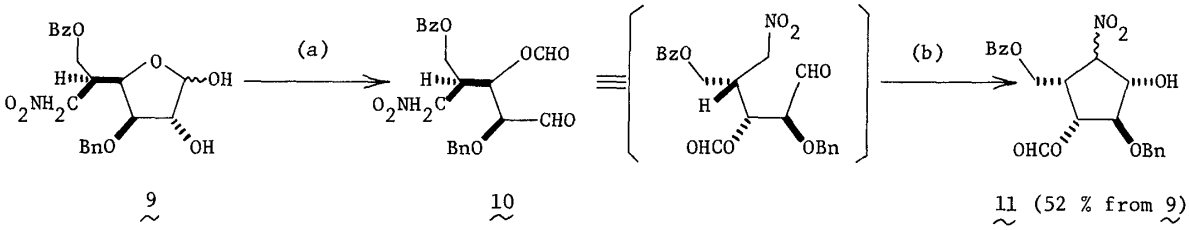
Deprotection of 13 as described above for 5 and 6 furnished the new optically active pseudo-sugar pseudo-β-L-xylofuranose (14, 90 %), colorless oil, $[\alpha]_D^{20}$ +5° (MeOH), $C_6H_{12}O_4$, ^1H NMR (500 MHz, d_5-pyridine-D_2O, J in Hz): δ 2.07 (ddd, J=6, 6, 13), 2.47 (ddd, J=6, 6, 13) (5-H_2), 2.50 (m, 4β-H), 4.10 (dd, J=5, 10), 4.20 (dd, J=6, 10) (6-H_2), 4.39 (dd, J=6, 6, 2α-H), 4.54 (ddd, J=6, 6, 6, 1β-H), 4.62 (dd, J=6, 6, 3β-H). ^{13}C NMR (125 MHz, d_5-pyridine): δc 33.7 (5-C), 45.9 (4-C), 65.1 (6-C), 71.4, 79.2 (1, 3-C), 80.4 (2-C).



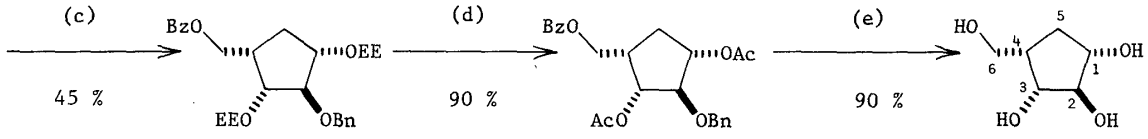
1 2 3 (52 % from 1)



4 5 (65 %) 6 (25 %) 7 8



9 10 11 (52 % from 9)



12 13 14

Bz : C_6H_5CO , EE : ethoxyethyl

Bn : $C_6H_5CH_2$, AIBN : α,α'-azobis-iso-butyronitrile

(a) $Pb(OAc)_4$ / benzene (25°C, 40 min) (b) KF / 18-crown-6 / DMF (2°C, 2 h) (c) 28 % aq. NH_4OH / EtOH (25°C, 3 min); ethyl vinyl ether / d-camphorsulfonic acid / CH_2Cl_2 (2°C, 3 h); n-Bu_3SnH / AIBN / benzene (80°C, 10 h) (d) 10 % aq. AcOH / acetone (40°C, 5 h); Ac_2O / pyridine (25°C, 2h) (e) 1 % NaOH-MeOH (25°C, 3 h); Na / liq.NH_3 (-78°C, 30 min)

Following our previous paper on the synthesis of optically active pseudo-hexopyranose,[1] we have now shown that optically active pseudo-pentofuranose may be conveniently synthesized from carbohydrate via nitrofuranose which is a common intermediate in our previous pseudo-hexopyranose synthesis.

We are currently extending this conversion method to the synthesis of other pseudo-sugars.

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REFERENCES AND NOTES

1) M. Yoshikawa, B. C. Cha, T. Nakae, and I. Kitagawa, Chem. Pharm. Bull. (1988), submitted.

2) K. Tadano, H. Kimura, M. Hoshino, S. Ogawa, and T. Suami, Bull. Chem. Soc. Jpn., 60, 3673 (1987).

3) M. Yoshikawa, B. C. Cha, T. Nakae, Y. Yokokawa, Y. Okaichi, and I. Kitagawa, presented at the 37th Annual Meeting of the Kinki Branch of the Pharmaceutical Society of Japan, Abstract p. 40 (Nov. 1987, Kobe).

4) The molecular composition of the compound given with the chemical formula was determined either by elemental analysis or by high resolution mass spectrometry.

5) The magnitude of NOE (%) given in the parenthesis was obtained when the underlined proton was irradiated.

6) 8, colorless oil, $[\alpha]_D^{20}$ +6° (MeOH), ^{1}H NMR (500 MHz, d_5-pyridine-D_2O, J in Hz): δ 2.15 (ddd, J=8, 8, 13), 2.46 (ddd, J=8, 8, 13) (5-H_2), 2.73 (m, 4α-H), 4.14 (dd, J=6, 11), 4.31 (dd, J=7, 11) (6-H_2), 4.55 (ddd, J=5, 8, 8, 1α-H), 4.65 (dd, J=5, 5, 2α-H), 4.69 (dd, J=5, 7, 3β-H).
^{13}C NMR (125 MHz, d_5-pyridine): δc 34.9 (5-C), 42.1 (4-C), 62.8 (6-C), 77.2, 78.7 (1, 3-C), 85.6 (2-C).

7) The NOE's of 13: 4β-H & 1β-H (7 %), 4β-H & 3β-H (4 %), 4β-H & 5β-H (15 %).[5]

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