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Syntheses of 5,6-Aziridino Sugars

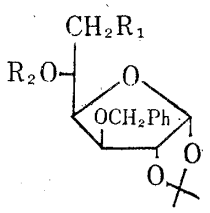
Carbohydrate epimines are not only of chemical interest because of their potency as synthetic intermediates, but also of pharmaceutical interest in cancer chemotherapy as alkylating agents. The synthesis of 2,3-epimino[1,2] or 3,4-epimino[3] carbohydrate derivatives has already been reported, while any successful approach to prepare 4,5- of 5,6-epimino derivatives is not yet found in preceding papers. We now wish to report the first synthesis of 5,6-epimino-D-*xylo*- and L-*arabino*-hexofuranoses.

Treatment of 3-O-benzyl-1,2-O-isopropylidene-6-O-tosyl-α-D-glucofuranose (I)[4] with sodium azide in dimethyl sulfoxide, followed tosylation in pyridine, or treatment of 5,6-di-O-tosylate (II)[4] with one equivalent of sodium azide in dimethyl sulfoxide[5] afforded 6-azido-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-5-O-tosyl-α-D-glucofuranose (III), mp 81.5—83°, $[\alpha]_D^{20}$ −41.2°(*c*=7.8, $CHCl_3$)(*Anal.* Calcd. for $C_{23}H_{27}O_7N_3S$: C, 56.57; H, 5.56; N, 8.59; S, 6.55. Found: C, 56.54; H, 5.72; N, 8.56; S, 6.27). Lithium aluminum hydride reduction of III in ether gave 3-O-benzyl-5,6-dideoxy-5,6-epimino-1,2-O-isopropylidene-β-L-idofuranose (IV) as needles of mp 91.5—94°, $[\alpha]_D^{21}$ −62.1°(*c*=1.8, $CHCl_3$) (*Anal.* Calcd. for $C_{16}H_{21}O_4N$: C, 65.95; H, 7.25; N, 4.81. Found: C, 65.72; H, 7.24; N, 4.90.). IV formed an acetate (V) of mp 106—107°, $[\alpha]_D^{20}$ −109.0°(*c*=5.0, $CHCl_3$)(*Anal.* Calcd. for $C_{18}H_{23}O_5N$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.83; H, 7.07; N, 4.15.). The existence of an aziridine ring in V was shown by its infrared absorption at 1700 cm^{-1}.[6]

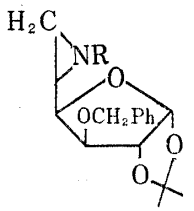
On the other hand, 5,6-anhydro-3-O-benzyl-1,2-O-isopropylidene-β-L-idofuranose (VI)[4] was treated with sodium azide in the presence of ammonium chloride in methylcellosolve[1,7] to yield an isomeric 6-azido derivative (VII) as a syrup, $[\alpha]_D^{20}$ −68.8°(*c*=4.3, $CHCl_3$) (*Anal.* Calcd. for $C_{16}H_{21}O_5N_3$: C, 57.32; H, 6.31; N, 12.53. Found: C, 57.42; H, 6.44; N, 12.54.). Lithium aluminum hydride reduction of a syrupy tosylate of VII in ether afforded an epimeric 5,6-eipmine (VIII), 3-O-benzyl-5,6-dideoxy-5,6-epimino-1,2-O-isopropylidene-α-D-glucofuranose, as a syrup which was characterized as its acetate (IX) of mp 97—99°, $[\alpha]_D^{21.5}$ −10.5°(*c*=3.9, $CHCl_3$)(*Anal.* Calcd. for $C_{18}H_{23}O_5N$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.68; H, 6.97; N, 4.27.).

Differently from the case of II, treatment of a syrupy ditosylate (X) of $[\alpha]_D^{21}$ −31.5° (*c*=3.6, $CHCl_3$), obtained from methyl 2,3-di-O-benzyl-β-D-galactofuranoside[8] (*Anal.* Calcd. for $C_{35}H_{38}O_{10}S_2$: C, 61.57; H, 5.61; S, 9.39. Found: C, 61.44; H, 5.78; S, 9.19.) with one equivalent of sodium azide in dimethyl sulfoxide afforded a mixture of a syrupy 6-azido-5-tosylate (XI) of $[\alpha]_D^{20}$ −42.8°(*c*=8.5, $CHCl_3$)(*Anal.* Calcd. for $C_{28}H_{31}O_7N_3S$: C, 60.74; H, 5.64; N, 7.59; S, 5.79. Found: C, 60.81; H, 5.74; N, 7.61; S, 5.93.) and a syrupy 5,6-diazide

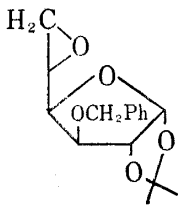
1) R.D. Guthrie and D. Murphy, *J. Chem. Soc.*, **1963**, 5288.
2) R.D. Guthrie and D. Murphy, *J. Chem. Soc.*, **1965**, 3828. D.H. Buss, L. Hough, and A.C. Richardson, *J. Chem. Soc.*, **1963**, 5295; *J. Chem. Soc.*, **1965**, 2736. C.F. Gibbs, L. Hough, and A.C. Richardson, *Carbohyd. Res.*, **1**, 290 (1965). B.R. Baker and T. Neilson, *J. Org. Chem.*, **29**, 1047, 1051, 1057 (1964). B.R. Baker and T.L. Hullar, *J. Org. Chem.*, **30**, 4045, 4038 (1965). J.E. Christensen and L. Goodman, *J. Am. Chem. Soc.*, **82**, 4738 (1960). W. Meyer zu Reckendorf, *Chem. Ber.*, **97**, 325 (1964).
3) H.H. Baer and T. Neilson, *Can. J. Chem.*, **43**, 840 (1965). A.D. Barford and A.C. Richardson, *Carbohyd. Res.*, **4**, 408 (1967).
4) A.S. Meyer and T. Reichstein, *Helv. Chim. Acta*, **29**, 152 (1946).
5) Nucleophilic substitution of 5,6-di-O-tosylate for 5,6-di-O-mesylate of hexofuranosides fell at the 6-position predominantly. *cf.* W. Meyer zu Reckendorf, *Tetrahedron*, **19**, 2033 (1963); D.H. Buss, L.D. Hall, and L. Hough, *J. Chem. Soc.*, **1965**, 1616.
6) H.L. Spell, *Analyt. Chem.*, **39**, 185 (1967).
7) S. Hanessian and T.H. Haskell, *J. Org. Chem.*, **30**, 1080 (1965).
8) H. Saeki, T. Iwashige, and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), in press.



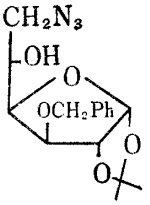
I : R_1=OTs, R_2=H
II : R_1=OTs, R_2=Ts
III : R_1=N_3, R_2=Ts



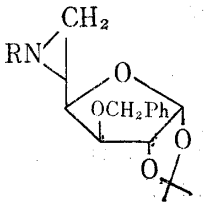
IV : R=H
V : R=$COCH_3$



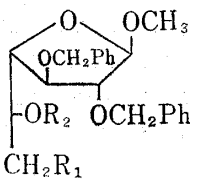
VI



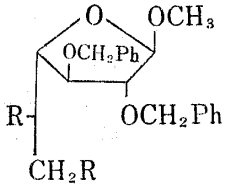
VII



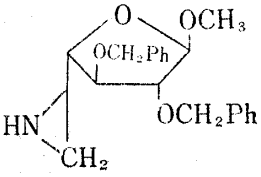
VIII : R=H
IX : R=$COCH_3$



X : R_1=OTs, R_2=Ts
XI : R_1=N_3, R_2=Ts



XII : R=N_3
XIV : R=$NHCOCH_3$



XIII

(XII) of $[\alpha]_D^{21.5}$ −61.7°(c=5.5, $CHCl_3$)(*Anal.* Calcd. for $C_{21}H_{24}O_4N_6$: C, 59.42; H, 5.70; N, 19.82. Found: C, 59.38; H, 5.67; N, 19.26.). Lithium aluminum hydride reduction of XI in ether also yielded methyl 2,3-di-O-benzyl-5,6-dideoxy-5,6-epimino-α-L-altrofuranoside (XIII) as a syrup, which was also characterized as its syrupy acetate of $[\alpha]_D^{21}$ −107.3°(c=6.1, $CHCl_3$) (*Anal.* Calcd. for $C_{23}H_{27}O_5N$: C, 69.50; H, 6.85; N, 3.59. Found: C, 69.27; H, 6.79; N, 3.46.). Treatment of the acetate of XIII with sodium azide and lithium aluminum hydride reduction of the resulting azide, followed by acetylation, gave methyl 5,6-diacetamido-2,3-di-O-benzyl-5,6-dideoxy-α-L-altrofuranoside (XIV) of mp 187—188°, $[\alpha]_D^{20}$ −55.1°(c=2.3, $CHCl_3$) (*Anal.* Calcd. for $C_{25}H_{32}O_6N_2$: C, 65.77; H, 7.07; N, 6.14. Found: C, 65.74; H, 6.98; N, 6.01.). XIV was identified with the sample obtained from the diazide (XII) by lithium aluminum hydride, followed by acetylation.

Further studies on solvolysis of these epimino carbohydrate derivatives, which were found to be unstable to acids, are now in progress.

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