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A STEREOSELECTIVE SYNTHESIS OF METHYL D-GLUCOSAMINATE VIA TIN(II) ENEDIOLATE FORMED FROM FURYLGLYOXAL

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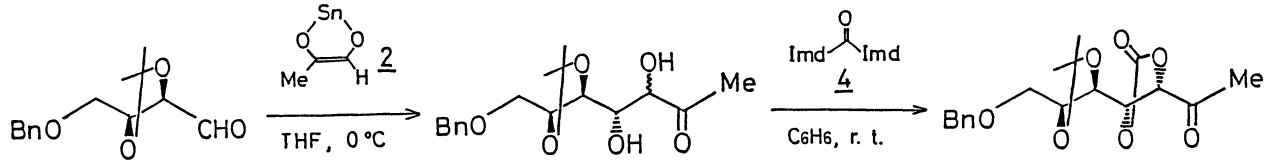
The tin(II) enediolate, formed in situ from furylglyoxal, reacts with polyoxyaldehydes such as 2,3-O-isopropylidene-D-glyceraldehyde and 4-O-benzyl-2,3-O-isopropylidene-L-threose to give the cross aldol adducts in good yields. This reaction is successfully applied to the synthesis of methyl D-glucosaminate.

In the previous paper,[1] we reported that the tin(II) enediolate (2), formed in situ from methylglyoxal, reacted with the polyoxyaldehyde (1) to give the cross aldol adduct (3), and this adduct, a mixture of two diastereomers, was converted into the cyclic carbonate (5) predominantly on treatment with N,N'-carbonyldiimidazole (4) (Scheme 1).

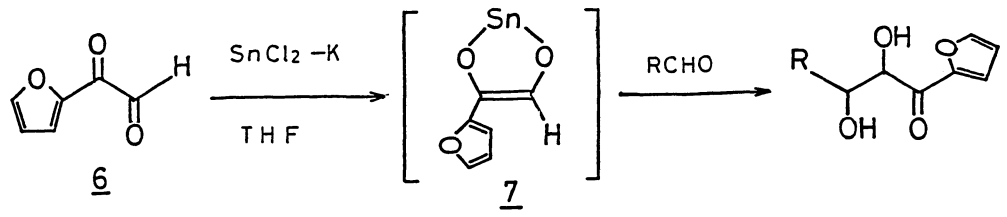


1 → 3 (88 %) → 5 (72 %)

Scheme 1.

Bn-= $PhCH_2$-

During our studies on the exploration of new methods for the synthesis of various sugars by the use of 5, it was found that the tin(II) enediolate (7) derived from furylglyoxal (6)[2] has advantages over 2, because it can be prepared from the stable α-ketoaldehyde and be efficiently utilized as a three-carbon synthetic unit containing three functional groups in the subsequent carbon chain extension on treatment with polyoxyaldehydes (Scheme 2).



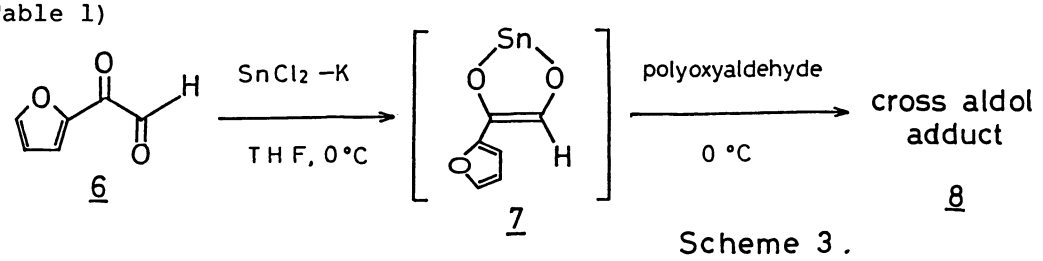
6 → 7

Scheme 2. X = OH, NH_2, etc.

In this communication, we wish to describe the cross aldol reaction of the

tin(II) enediolate (7) and the application of this reaction to the synthesis of methyl D-glucosaminate.

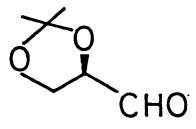
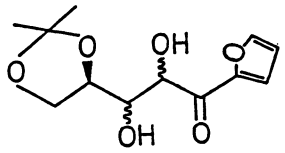
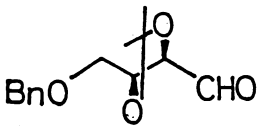
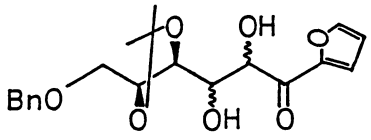
In the first place, the cross aldol reactions of the tin(II) enediolate (7) with polyoxyaldehydes were examined, and as shown in Scheme 3, the cross aldol adducts (8) were obtained in high yields when two times molar excess of furylglyoxal was added in 3 h to the mixture of an aldehyde and metallic tin at 0 °C. (See Table 1)



6 7 8

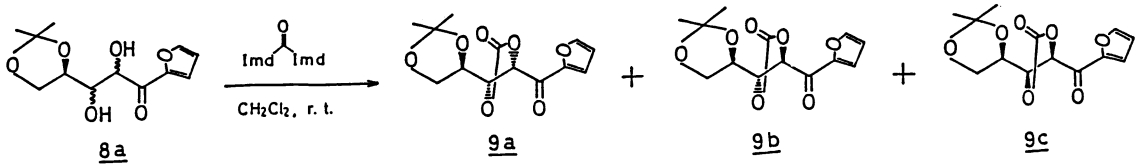
Scheme 3.

Table 1. Cross aldol reactions of furylglyoxal.

polyoxyaldehyde	adduct (8)	yield/%[a]
	 8a	88
	 8b	91

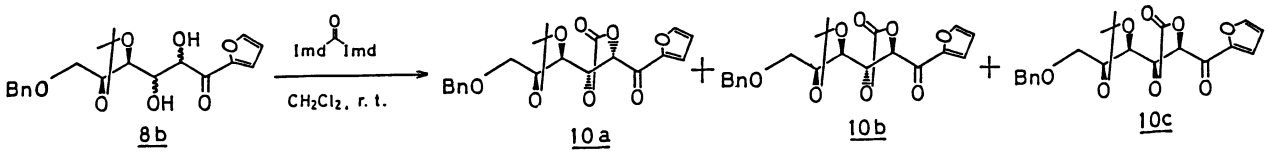
a) The yield as a mixture of the diastereomers.

Then these adducts, similarly to the case of methylglyoxal,[1] were converted into the cyclic carbonates (9a, 10a)[3] predominantly as shown in Scheme 4.[4]



8a 9a 9b 9c

68 % (9a:9b:9c = 4.8 : 1 : 1.2)[a]



8b 10a 10b 10c

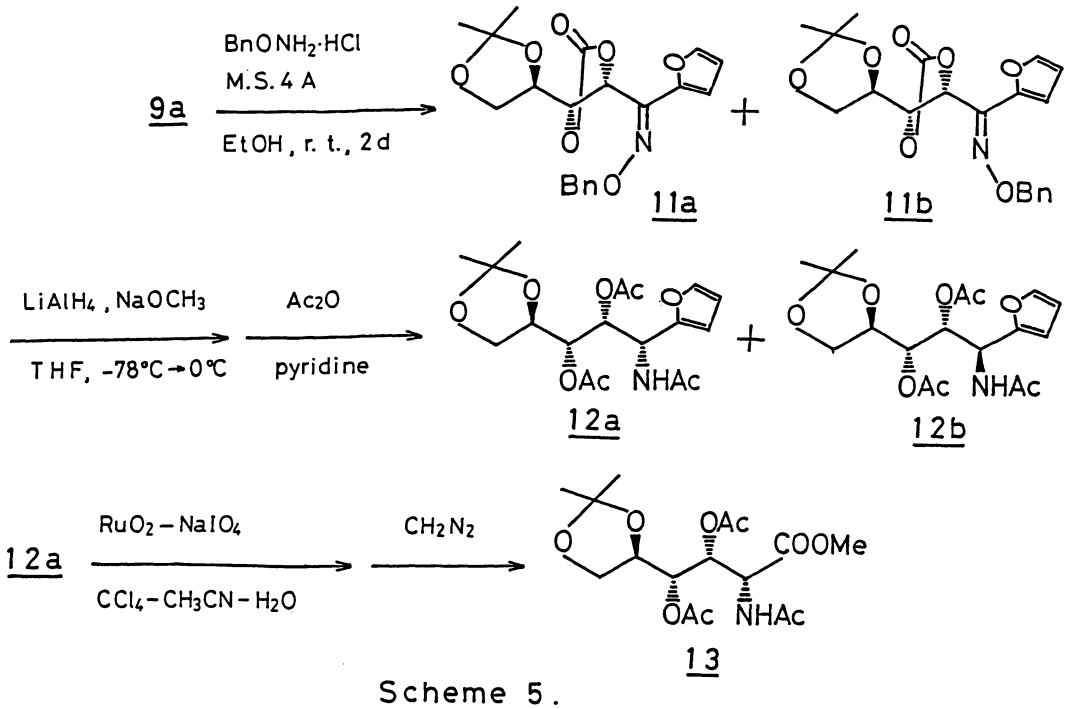
72 % (10a:10b:10c = 32 : 5 : 1)[a]

Scheme 4.

a) The diastereomer ratio was determined by ^{1}H-NMR.

These cyclic carbonates (9a, 10a) are expected to be useful intermediates for the synthesis of sugars, and, to show the utilities of these carbonates, we next

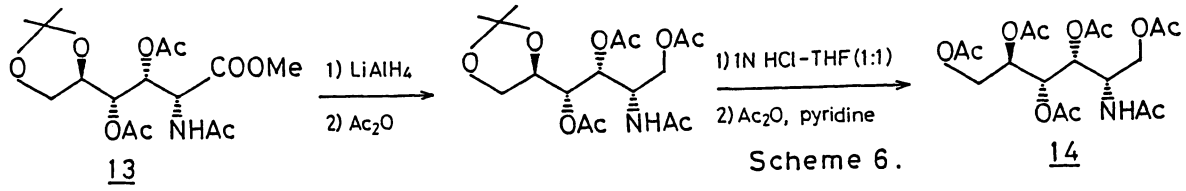
tried to synthesize methyl D-glucosaminate (13)[5] from 9a as shown in Scheme 5.



Scheme 5.

The cyclic carbonate (9a) was converted into the O-benzyl oximes (11, 86%, 11a : 11b = 2 : 1)[6] on treatment with O-benzylhydroxylamine hydrochloride and molecular sieves 4A. Then, these O-benzyl oximes (11) were reduced by lithium aluminum hydride in the presence of sodium methoxide,[7] and further treatment with acetic anhydride and pyridine gave the amide (12a, 75%)[8] stereoselectively along with a small amount of the isomer (12b, 8%).[8] Finally, the amide (12a) was oxidized by ruthenium tetraoxide[9], and a following esterification with diazomethane yielded methyl D-glucosaminate (13, 78%).

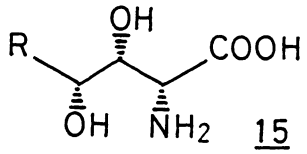
In order to confirm the configuration of the product, conversion to 2-acetamido-2-deoxy-D-glucitol pentaacetate (14)[10] was tried as shown in Scheme 6.



Scheme 6.

The ^{1}H-NMR, ^{13}C-NMR, IR spectra, and the optical rotation of 14 agreed well with those of the authentic sample prepared by the reduction and acetylation of D-glucosamine hydrochloride.[11]

Thus, the tin(II) enediolate (7) was efficiently utilized in the synthesis of methyl D-glucosaminate (13), and it is noteworthy that this method can generally be applied to the synthesis of β,γ-dihydroxy-α-amino acid derivatives (15).



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Now, further utilization of this novel tin(II) enediolate (7) to various synthetic purposes is in progress.

References

1) T. Mukaiyama, R. Tsuzuki, and J. Kato, Chem. Lett., 1983, 1825.

2) F. Kipnis and J. Ornfert, J. Am. Chem. Soc., 70, 3948 (1948).

3) 9a: NMR ($CDCl_3$) δ 1.26 (3H, s), 1.32 (3H, s) 3.7-4.1 (2H, m), 4.1-4.5 (1H, m), 4.6 (1H, dd, J_1=4 Hz, J_2=6 Hz) 5.3 (1H, d, J=4 Hz), 6.5 (1H, dd, J_1=2 Hz, J_2=4 Hz), 7.4 (1H, d, J=4 Hz), 7.6 (1H, d, J=2 Hz). IR (KBr) 1800, 1660 cm^{-1}. 10a: NMR ($CDCl_3$) δ 1.5 (6H, s), 3.6-3.7 (2H, m), 3.8-4.5 (2H, m), 4.5 (2H, s), 5.0 (1H, dd, J_1=J_2=5 Hz), 5.3 (1H, d, J=5 Hz), 6.6-6.7 (1H, m), 7.3 (5H, s), 7.5 (1H, d, J=3 Hz), 7.7 (1H, s). IR (NaCl) 1810, 1680 cm^{-1}.

4) Configurations of 9a-c and 10a-c were determined by NMR spectra. Important data are as follows. 9b 5.7 (1H, d, J=8 Hz). 9c 5.46 (1H, d, J=4 Hz). 10b 5.8 (1H, d, J=8 Hz). 10c 5.3 (1H, d, 4 Hz). Relative configuration of C3 and C4 in 9 and 10 is assumed to be predominantly anti. See: T. Mukaiyama, K. Suzuki, and T. Yamada, Chem. Lett., 1982, 929.

5) 13: NMR ($CDCl_3$) δ 1.32 (3H, s), 1.38 (3H, s), 2.1 (9H, s), 3.7 (3H, s), 3.8-4.3 (3H, m), 5.0 (1H, dd, J_1=5 Hz, J_2=9 Hz), 5.1 (1H, dd, J_1=J_2=6 Hz), 5.4 (1H, dd, J_1=5 Hz, J_2=6 Hz), 6.2 (1H, d, J=9 Hz). IR (NaCl) 3320, 1740, 1686, 1076 cm^{-1}.

6) 11 (as a mixture of isomers): NMR ($CDCl_3$) δ 1.26 (4H, s), 1.29 (2H, s), 3.5-4.4 (3H, m), 4.4 (0.67H, t, J=5 Hz), 4.8 (0.33H, t, J=5 Hz), 5.1 (2H, s), 5.5 (0.33 H, d, J=5 Hz), 5.6 (0.67H, d, J=5 Hz), 6.2-6.4 (1H, m), 6.7 (0.67H, d, J=3 Hz), 7.2 (5.33H, s), 7.3 (1H, d, J=2 Hz). IR (NaCl) 1810, 1660 cm^{-1}.

7) K. Narasaka, S. Yamazaki, and Y. Ukaji, Chem. Lett., 1984, 2065.

8) 12a: NMR ($CDCl_3$) δ 1.2 (6H, s), 2.0 (3H, s), 2.1 (6H, s), 3.5-4.4 (3H, m), 4.9 (1H, dd, J_1=3 Hz, J_2=7 Hz), 5.2-5.6 (2H, m), 5.9-6.5 (3H, m), 7.2 (1H, d, J=2 Hz). IR (NaCl) 3280, 1740, 1660 cm^{-1}. 12b: NMR ($CDCl_3$) δ 1.16 (3H, s), 1.21 (3H, s), 1.78 (3H, s), 1.81 (3H, s), 2.00 (3H, s), 3.6-4.2 (3H, m), 5.1-5.5 (3H, m), 5.9-6.4 (3H, m), 7.2 (1H, d, J=1 Hz). IR (KBr) 3420, 3270, 1744, 1650 cm^{-1}.

9) P. H. Carlsen, T. Katsuki, V. S. Martin, and K. B. Sharpless, J. Org. Chem., 46, 3936 (1981).

10) 14: ^{1}H-NMR ($CDCl_3$) δ 1.7-2.1 (18H, m), 3.7-4.2 (4H, m), 4.2-4.6 (1H, m), 4.7-5.3 (3H, m), 5.7 (1H, d, J=9 Hz). ^{13}C-NMR ($CDCl_3$) δ 20.5, 20.6, 23.0, 48.2, 61.6, 62.8, 69.2, 69.3, 69.6, 169.6, 169.9, 170.1, 170.2, 170.4. IR (KBr) 3360, 1734, 1668, 1652 cm^{-1}. $[\alpha]_D^{17}$ +20.7 °(c 1.03, $CHCl_3$). For the reduction of 13, see B. A. Lewis, F. Smith, and A. M. Stephen, "Methods in Carbohydrate Chemistry," ed by R. L. Whistler and M. L. Wolfrom, Academic Press, New York (1963), Vol.II, Section III, pp. 73-74.

11) W. Roth, W. Pigman, and I. Danishefsky, Tetrahedron, 20, 1675 (1964).

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