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TARTRALDEHYDES I. SYNTHESIS OF N-ACETYL-D- AND L-DAUNOSAMINE AND THEIR XYLO ISOMERS[1]

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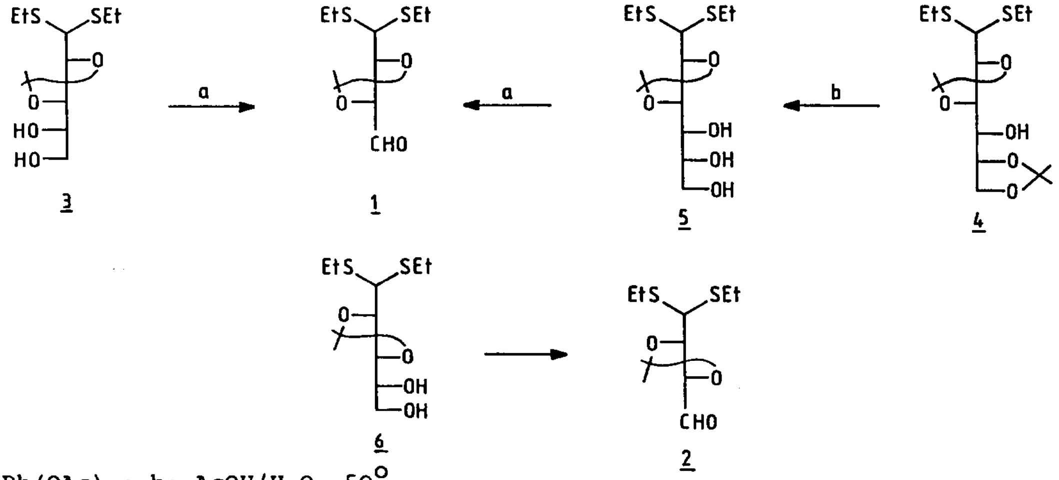
Abstract: The title compounds were prepared from tartraldehyde dithioacetals 1 and 2 using Wittig chain elongation, amino functionalization of the double bond and removal of the protective groups.

Tartraldehydes (2,3-dihydroxybutane-1,4-dials) and their derivatives have long been known[2-7]. Since they are potential C_4 dichiral synthetic units we have elaborated a simple method for the preparation of new tartraldehyde mercaptals 1 and 2[8]. The (2R,3R) isomer 1 was obtained from the easily available L-arabinose derivative[9] 3 by lead(IV)acetate oxidation. Alternatively, 1 can be prepared similarly from the 2,3-O-isopropylidene-D-glucose mercaptal 5 accessible from 4 by partial hydrolysis[10]. Glycol-cleaving reaction of 6 led to the formation of 2 (2S,3S) tartraldehyde dithioacetal.

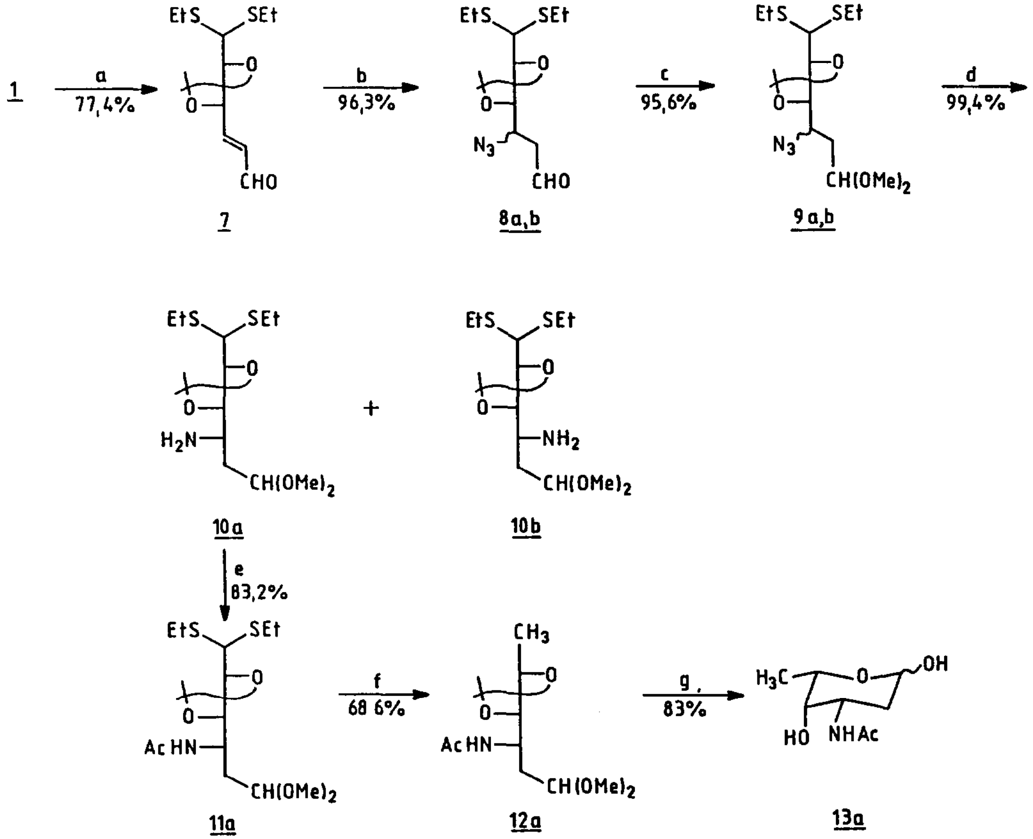


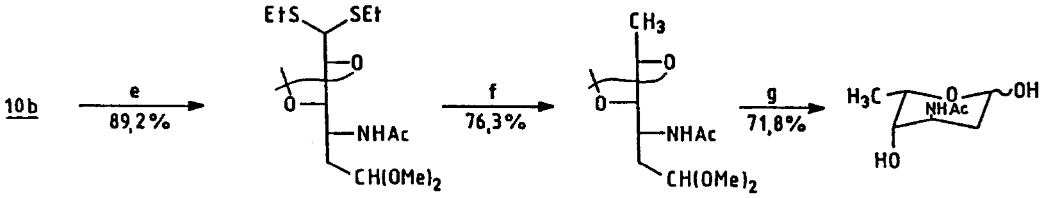
a: $Pb(OAc)_4$; b: $AcOH/H_2O$, 50°

The unstable 1 and 2 must be utilized immediately for the next step.

To demonstrate the versatility of C_4 dichiral intermediates 1 and 2 were used as starting materials for the synthesis of 3-amino-2,3,6-trideoxyhexoses important constituents of several antibiotics[11].

In a Wittig reaction of 1 with formylmethylenetriphenylphosphorane[12] the E isomer 7 was obtained exclusively[16]. That was allowed to react with sodium azide in acetic acid[13] to afford a diastereomeric mixture 8a,b containing the two isomers in a 2:3 ratio. Formyl groups in 8a,b were protected in the form of dimethyl acetal (9a,b). Without separation of the mixture the azido groups were reduced with lithium tetrahydridoaluminate to give, after column chromatography, impure 10a and 10b. The latter two on acetylation afforded pure 11a and 11b, respectively[16]. 11a and 11b were desulfurized reductively with Raney nickel to give 12a and 12b. Hydrolytic removal of the acetal type protective groups resulted N-acetyl-L-daunosamine (13a) and its L-xylo isomer (13b), respectively.

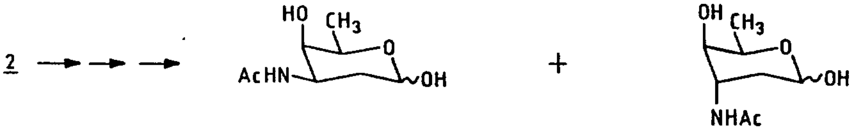




11b 12b 13b

a: $(C_6H_5)_3PCHCHO$, PhH, reflux; b: NaN_3,AcOH, RT; c: dimethoxypropane,MeOH, TsOH, RT; d: $LiAlH_4$, Et_2O, reflux; e: Ac_2O, pyridine, RT; f: Raney Ni, EtOH, reflux; g: AcOH/H_2O, 100°.

In the same sequence of reactions 2 afforded the D-lyxo (14a) and D-xylo (14b) isomers[16].



14a 14b

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References and Notes

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16. Selected physical parameters of new compounds:

7: $[\alpha]_D^{21}$ -38.8 (c 0.60, $CHCl_3$), Anal. Calcd for $C_{13}H_{22}O_3S_2$: C, 53.76; H, 7.64; Found: C, 53.49; H, 7.48; 8a,b: Anal. Calcd for $C_{13}H_{23}N_3O_3S_2$: N, 12.72; Found: 12.55; 9a,b: Anal. Calcd for $C_{15}H_{29}N_3O_4S_2$: N, 11.07; S, 16.89; Found: N, 10.83; S, 16.67. 10a: Anal. Calcd for $C_{15}H_{31}NO_4S_2$: N, 3.96; Found: N, 3.75. 10b: Anal. Calcd for $C_{15}H_{31}NO_4S_2$: N, 3.96; Found: N, 3.71. 11a: $[\alpha]_D^{21}$ -51.2 (c 0.65, $CHCl_3$); Anal. Calcd for $C_{17}H_{33}NO_5S_2$: S, 16.21; Found: S, 16.37. 11b: $[\alpha]_D^{21}$ -38.0 (c 0.58, $CHCl_3$) Anal. Calcd for $C_{17}H_{33}NO_5S_2$: S, 16.21; Found: S, 16.40. 12a: $[\alpha]_D^{21}$ -33.2 (c 0.81, $CHCl_3$); Anal. Calcd for $C_{13}H_{25}NO_5$: N, 5.09; Found: N, 5.16. 12b: $[\alpha]_D^{21}$ 21.0 (c 0.74, $CHCl_3$); Anal. Calcd for $C_{13}H_{25}NO_5$: N, 5.09; Found: N, 5.06. 13a: $[\alpha]_D^{21}$ -121.4 $\longrightarrow$ -93.1 (equilibrium, c 0.38, H_2O); m.p. 155-156°; lit.[14]: $[\alpha]_D^{21}$ -100 (equilibrium, H_2O); m.p. 162°; ^{1}H-NMR: δ (D_2O, equilibrium), α-pyranoside: 5.32 (dd, $J_{1,2eq}$= 0.5 Hz, $J_{1,2ax}$= 3 Hz, H-1); 4.22 (m, H-5); 4.20 (m, $J_{3,4}$= 3 Hz, $J_{2ax,3}$= 13 Hz, $J_{2eq,3}$= 5 Hz H-3); 3.66 (dd, $J_{4,5}$= 0.7 Hz); 1.95 (m, H-2); 1.75 (m, H-2'); 1.19 (d, $J_{5,6}$= 6 Hz, 6-CH_3). β-pyranoside: 4.88 (dd, $J_{1,2eq}$= 2.3 Hz, $J_{1,2ax}$= 9.5 Hz, H-1); 4.0 (ddd, $J_{3,4}$= 3 Hz, $J_{2ax,3}$= 12.7 Hz, $J_{2eq,3}$= 4.5 Hz, H-3) 3.75 (m, $J_{4,5}$= 1 Hz, H-5); 3.58 (dd, H-4); 1.85 (m, H-2); 1.60 (m, H-2'); 1.22 (d, $J_{5,6}$= 6.2 Hz, 6-CH_3). Anal. Calcd for $C_8H_{15}NO_4$: N, 7.40; Found: N, 7.36. 13b: $[\alpha]_D^{21}$ -37.3 $\longrightarrow$ -12.4 (equilibrium, c 0.86, MeOH); m.p. 120-122°; lit.[15]: $[\alpha]_D^{29}$ -11.5 (equilibrium, c 0.7, MeOH); m.p. 119-121°; ^{1}H-NMR: δ (D_2O, equilibrium), α-pyranoside: 5.30 (dd, $J_{1,2eq}$= 3 Hz, $J_{1,2ax}$= 3 Hz, H-1); 4.35 (m, $J_{4,5}$= 2.3 Hz, H-5); 4.0 (m, $J_{3,4}$= 4.5 Hz H-3); 3.54 (dd, H-4); 2.20 (m, H-2); 1.62 (m, H-2'); 1.19 (d, $J_{5,6}$= 6 Hz, 6-CH_3). β-pyranoside: 5.04 (dd, $J_{1,2eq}$= 3.3 Hz, $J_{1,2ax}$= 9.5 Hz, H-1); 4.05 (m, H-3); 3.94 (m, $J_{4,5}$= 1.2 Hz, H-5); 3.43 (dd, $J_{3,4}$= 3 Hz, H-4); 2.15 (m, H-2); 1.83 (m, H-2'); 1.22 (d, $J_{5,6}$= 6 Hz, 6-CH_3). Anal. Calcd for $C_8H_{15}NO_4$: N, 7.40; Found: N, 7.32. ^{1}H-NMR spectra of 14a and 14b were superimposable with those of 13a and 13b, respectively.

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