ACCESS TO A CHIRALLY SUBSTITUTED FURAN. SYNTHESIS OF 5-(D-GLYCERO-1,2-DIHYDROXYETHYL)-2-FURALDEHYDE FROM A NATURAL HEPTULOSE[1]

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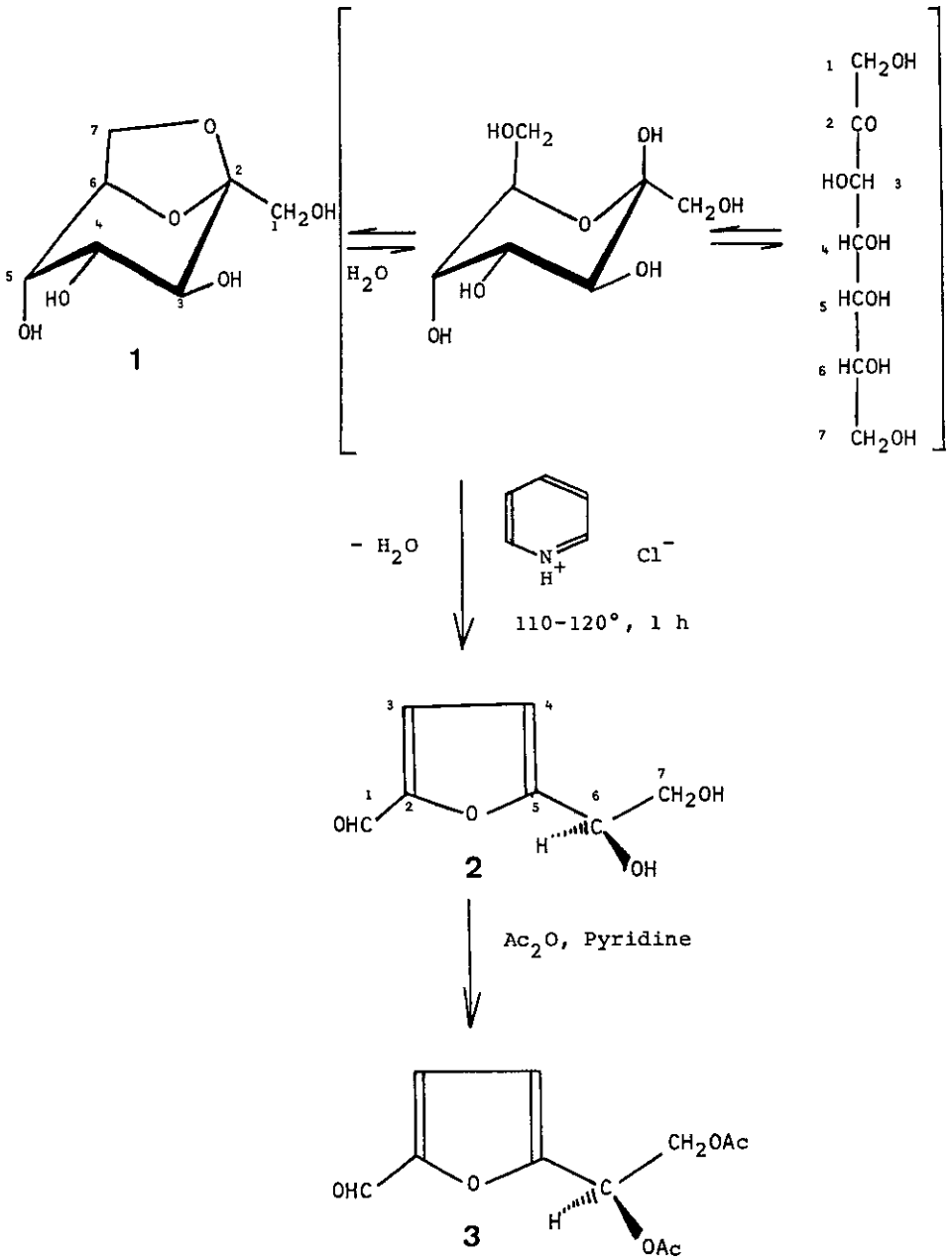
Abstract - A simple preparative one-step access to a chiral furan [5-(1',2'(R)-dihydroxyethyl)-2-furaldehyde] from a natural sugar (sedoheptulosan) is described.

The conversion of hexoses to 5-hydroxymethyl-2-furaldehyde (HMF) is an old reaction, the importance of which has been limited essentially to its implication in the food technology (non-enzymatic browning) and in the analytical determination of hexoses[2]. However, an industrial interest is rising due to the possibility of preparing it from renewable resources. We recently described a new and easy process for dehydrating some mono-, oligo- and poly-saccharides to HMF or to 5-halogenomethyl-2-furaldehydes[3]. We present here an extension of the method to the synthesis of a chiral furan, namely 5-(1',2'(R)-dihydroxyethyl)-2-furaldehyde(DHEF, 2). The use of carbohydrates as chiral synthons is now a well-established route to the synthesis of optically active non-carbohydrate compounds[4]. This strategy requires in general many steps, and to our knowledge, there is practically no example of a simple and readily one-step preparative access to an optically active non-carbohydrate molecule from sugars. Applying our method[3] of direct heating of a crystalline sugar with anhydrous pyridinium hydrochloride without any solvent, we were able to obtain directly in a reasonable yield (20-25%)[5] a practically pure sample of DHEF (2) starting from 2,7-anhydro-β-D-altro-heptulopyranose (1) (or sedoheptulosan, a natural heptulose present to some extent in green plants and an important intermediate in photosynthesis). This furan had been previously claimed to be isolated in traces by thick-paper chromatography from the action of sulfuric acid upon sedoheptulosan and identified only on the basis of U.V. spectrum similar to that of HMF[6].


1
H_2O
CH_2OH
CO
HOCH
HCOH
HCOH
HCOH
CH_2OH
- H_2O
Cl^-
110-120°, 1 h
2
OHC
CH_2OH
Ac_2O, Pyridine
3
CH_2OAc
OAc

We characterized the furan 2 by analytical and spectral data (see Experimental Section for analysis and ^{1}H, ^{13}C, and mass spectra) and by its conversion to the diacetate 3 (analysis and ^{1}H, ^{13}C and mass spectra). It appears to be the aldehydo-substituted homolog of the furan [namely 2-(D-glycero-1,2-dihydroxyethyl) furan] obtained by acid hydrolysis of an unsaturated sugar (methyl 4,6-O-benzylidène-α-D-erythro-hex-2-enopyranoside) by Horton et al[7].

Compounds 2 and 3 are useful polyfunctional starting chiral synthons for valuable structural modifications in the furan series.

EXPERIMENTAL

Evaporations were performed under diminished pressure. Optical rotations were measured on a Perkin-Elmer 141 polarimeter in 1-dm tubes. Column chromatography was performed with Kieselgel 60 Merck and t.l.c. with pre-coated plates (Merck 5724), with detection by charring with sulfuric acid. ^{1}H-NMR spectra were performed on Varian T60 spectrometer (s : singlet, d : doublet, t : triplet, m : multiplet ; δ are given in ppm and coupling in Hz). ^{13}C-NMR spectra were recorded with a Jeol FX 60 instrument, and electron-impact mass spectra with a AEI-Kratos MS 30.

Reaction of sedoheptulosan with anhydrous pyridinium chloride. Synthesis of 5-(D-glycero-1,2-dihydroxyethyl)-2-furaldehyde (2). Commercial sedoheptulosan monohydrate (2,7-anhydro-β-altro-heptulopyranose hydrate, 2 g, 0.0095 mol) and anhydrous pyridinium chloride (2 g prepared by bubbling anhydrous hydrogen chloride in anhydrous ethyl ether, filtration of the precipitate and washing with anhydrous ethyl ether), both in solid phase, were mixed at room temperature. The reagents were then heated (oil-bath at 120°) during 90 minutes, the reaction being monitored by t.l.c. (ethyl acetate). After cooling at room temperature, 30 or 40 ml of water were added. Aqueous phase was extracted with ethyl acetate (continuous extraction during 36 to 48 h). The organic layer was dried on sodium sulfate. Evaporation of the solvent gave 0.6 g of crude product which was further purified on a silica gel column (ethyl acetate) to give pure dihydroxyethylfuraldehyde (2) : yield 0.3-0.35 g (20-25 %) ; m.p. 44-45° ; $[\alpha]_D^+$ 60° (c 0.1, acetone). ^{1}H-NMR ($CDCl_3$) : d 6.57 (H-3), d 7.25 (H-4), t 4.90 (H-6), d 3.90 (CH_2-7) ; s 4.03 (OH), s 9.50 (CHO) ; $J_{3,4}$ 3.8, $J_{6,7}$ 5.5. ^{13}C-NMR ($CDCl_3$) : 177.6 (CHO) ; 161.0 and 152.0 (C-2 and C-5) ; 123.1 and 109.8 (C-3 and C-4) ; 68.6 and 64.8 (C-1' and C-2'). Mass spectrum : m/e 156 (M^{+}, 2 %) ; 127 (M^{+}-.CHO, 11 %) ; 125 (M^{+}-$\dot{C}H_2OH$, 100 %). Anal. calc. for $C_7H_8O_4$: C 53.85, H 5.13, O 41.03 ; tr. : C 53.73, H 5.35, O 41.05.

Preparation of 5-(D-glycero-1,2-diacetoxyethyl)-2-furaldehyde (3). A stirred solution of the diol 2 in pyridine was treated at 0°C by twice the stoichiometric amount of acetic anhydride in solution in pyridine. After 24 h the solution was pourred onto ice-water with sodium carbonate.

The mixture was extracted with dichloromethane. The extract was washed with a saturated aqueous solution of sodium bicarbonate and dried (sodium sulfate). The solvent was evaporated with addition of toluene during evaporation to give compound 3 practically pure in t.l.c. : syrup ; $[\alpha]_D$ + 124° (c 0.1, chloroform). ^{1}H-NMR ($CDCl_3$) : d 6.60 (H-3), d 7.25 (H-4), t 6.13 (H-6), m 4.50 (CH_2-7), s 9.66 (CHO), 2s 2.10 (OAc) ; $J_{3,4}$ 3.8, $J_{6,7}$ 5.6. ^{13}C-NMR ($CDCl_3$) : 177.8 (CHO) ; 170.3 and 169.7 (CO) ; 155.3 and 152.7 (C-2 and C-5) ; 121.6 and 111.8 (C-3 and C-4) ; 66,4 and 62.9 (C-1' and C-2') ; 20.6 (CH_3). Mass spectrum : m/e 181 (M^+-.OAc, 11 %) ; 180 (M^+-AcOH, 35 %) ; 167 (M^+-.CH_2OAc, 3 %) ; 139 (M^+-.OAc-CH_2CO, 34 %) ; 138 (M^+-AcOH-CH_2CO, 100 %). Anal. calc. for $C_{11}H_{12}O_6$: C 55.00, H 5.00, O 40.00 ; tr. : C 54.65, H 4.95, O 39,62.

REFERENCES

1. Taken from the Docteur-Ingénieur thesis to be presented by C. Fayet. Supported, in part, by ATP CNRS "Chimie Fine : Valorisation de la Matière Première Végétale".
2. (a) F.H. Newth, Adv. Carbohydr. Chem. 1951, 6, 83-106 ; (b) M.S. Feather et J.F. Harris, Adv. Carbohydr. Chem. Biochem. 1973, 28, 161-224 ; (c) W. Pigman et E.F.L.J. Anet, in The Carbohydrates, W. Pigman et D. Horton Ed., Acad. Press, N.Y. 1972, vol. IA, 165-194.
3. C. Fayet and J. Gelas, Carbohydr. Res. 1983, in press.
4. (a) T.D. Inch, Adv. Carbohydr. Chem. Biochem. 1972, 27, 191-225 ; (b) S. Hanessian, Acc. Chem. Res. 1979, 12, 159-165 ; (c) B. Fraser-Reid and R.C. Anderson, Fortsch. Chem. Org. Nat. 1980, 39, 1-61.
5. This yield is not optimized and would be easily improved, for instance starting from the free heptulose instead of its 2,7-anhydride.
6. L.P. Zill and N.E. Tolbert, J. Am. Chem. Soc. 1954, 76, 2929-2933.
7. (a) E. Albano, D. Horton, and T. Tsuchiya, Carbohydr. Res. 1966, 2, 349-362 ; (b) D. Horton and T. Tsuchiya, Carbohydr. Res. 1966, 3, 257-259.

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