Tetrahedron Letters,Vol.28,No.40,pp 4757-4758,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

L-(S)-ERYTHRULOSE
A NOVEL PRECURSOR TO L-2,3-O-ISOPROPYLIDENE-C_3 CHIRONS

H. De Wilde, P. De Clercq[1] and M. Vandewalle*
State University of Ghent, Department of Organic Chemistry,
Laboratory for Organic Synthesis,
Krijgslaan, 281 (S.4), B-9000 GENT (Belgium)
and

H. Röper
CPC Europe Industrial Products, Research and Development Centre,
Havenstraat, 84, B-1800 VILVOORDE (Belgium)

Abstract : Starting from L-(S)-erythrulose, now available in larger quantities, the preparation of L-(S)-glyceraldehyde, L-(R)-glycerol and L-(S)-methyl glycerate acetonides, via the protected L-(S)-3,4-O-isopropylideneerythrulose, is described.

One of the inherent limitations of the now established chiron approach to the synthesis of natural products remains the limited number of chiral starting materials, which are, at the same time, readily available and easily adaptable[2]. Among the sugar-derived C_4 aldoses and ketoses, L-(S)-erythrulose (1) has now become available in larger quantities[3]. Due to the presence of the 2-carbonyl group and to its stereogenic centre (enantiomeric with the natural D-sugars), L-(S)-erythrulose (1) constitutes a novel and promising C_4 chiral building block.

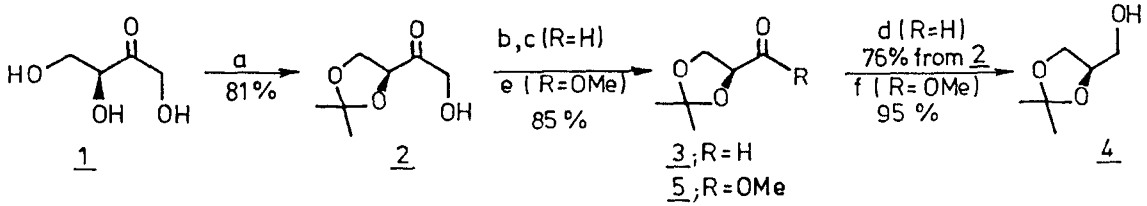
Herein, we wish to describe the conversion of 1 to the corresponding acetonide 2, and transformations to the acetonides of L-(S)-glyceraldehyde (3), L-(R)-glycerol (4) and L-(S)-methylglycerate (5).

D-(R)-glyceraldehyde acetonide and D-(S)-glycerol acetonide are available from inexpensive D-mannitol and have been widely used as versatile substrates in asymmetric synthesis[4]. The enantiomers 3 and 4, however, have found comparatively few applications mainly because of the relative unavailability of L-mannitol[5]. Alternative syntheses to 3 and 4 include : (1) oxidative α-diol cleavage of derivatives of D-sorbitol[6], ascorbic acid[7,8], L-galactono-1,4-lactone[9], L-arabinose[10], and (2R,3R)-dimethyl tartrate[11]; (2) conversion of L-serine to 4 via 5[12]; and (3) a 6-step process from allyl alcohol[13].

L-(S)-Erythrulose (1) is available as an aqueous solution (70.3 %; pH 4-5)[3]. Anhydrous 1 is obtained via azeotropic concentration with methanol-toluene. No racemisation is observed during this process; 1 has $|\alpha|_D^{20} = +13°$ (c = 2.44, H_2O); lit.[14] $|\alpha|_D^{20} = +13.3°$ (c = 2.25, H_2O). The acetonide 2 was obtained upon $ZnCl_2$ mediated reaction at r.t. of 1 and acetone in the presence of anhydrous Na_2SO_4; distillation (b.p. 55-60°C/0.1 mm Hg) gave 2; $|\alpha|_D^{20} = -56°$ (c = 1.87, THF). Heating of a sample of 2 in dil. H_2SO_4 led back to 1; $|\alpha|_D$ measurement showed that no racemisation had occurred.

Reduction of 2 to intermediate diol (91 % yield) and subsequent α-diol cleavage, in a two-phase system, afforded crude 3. A freshly distilled sample (b.p. 70°/15 mm) has $|\alpha|_D^{20}$ =

-64° (c = 8.2, benzene). Because of its known instability and in order to establish the optical purity 3 was directly reduced to 4 after distillation (b.p. 80°C/12 mm Hg) 4 was obtained in 76 % yield from 2. (R)-Glycerol acetonide 4 has $|\alpha|_D^{21}$ = -11.1° (c = 2.3, MeOH). The optical purity was checked by ^{1}H NMR in the presence of tris-(3-heptafluoropropylhydroxymethylene-(+)-camphorato)-europium; no enantiomer could be detected. Racemic 4 showed splitting of the high-field CH_3-signal.



(a) Me_2CO, $ZnCl_2$, Na_2SO_4, 1,4-dioxane-MeOH (10:1), r.t., 15 h; (b) $NaBH_4$, MeOH, r.t., 15 min; (c) $NaIO_4$, $(nBu)_4NBr$, CH_2Cl_2-H_2O, r.t., 30 min; (d) $NaBH_4$, MeOH, 0°C, 30 min; (e) $Pb(OAc)_4$, benzene, MeOH, 50°C, 30 min; (f) $LiAlH_4$, Et_2O, r.t., 1 h.

The (S)-methyl glycerate acetonide (5) is available in two steps from (S)-erythrulose (1) upon oxidative cleavage of 2. The best result was obtained with $Pb(OAc)_4$ in a benzene-methanol (9:1) solution. After distillation (b.p. 80°-85°C/12 mm Hg) methyl ester 5 has $|\alpha|_D^{20}$ = -9.4° (c = 1.7, MeOH). The optical purity of 5 was determined after reduction to 4; $|\alpha|_D^{20}$ = -11.4° (c = 2.1 in MeOH) and ^{1}H NMR control (vide supra).

Acknowledgements
We thank the "Instituut ter Bevordering van het Wetenschappelijk Onderzoek in Nijverheid en Landbouw" (IWONL) and the Belgian National Fund for Scientific Research (NFWO-FNRS) for financial assistance to the laboratory.

References and notes

1. Senior Research Associate of the National Fund for Scientific Research.
2. Total Synthesis of Natural Products. The "Chiron" Approach, S. Hanessian, Pergamon Press, 1983.
3. (a) for information contact Dr. H. Röper; (b) presently available from Aldrich.
4. J. Jurczak, S. Pikul, T. Bauer, Tetrahedron, (1986), 42, 447.
5. E. Baer, H.O.L. Fischer, J. Am. Chem. Soc., (1939), 61, 761. For 3, $|\alpha|_D^{20}$: -67.9° (c = 8, benzene) and for 3, $|\alpha|_D^{20}$: -10.8° (c = 23, methanol), $|\alpha|_D$: -13.4° (neat).
6. B.C. Pressman, L. Anderson, H.A. Lardy, J. Am. Chem. Soc., (1950), 72, 2404.
7. M.E. Jung, T.J. Shaw, J. Am. Chem. Soc., (1980), 102, 6304, 4; $|\alpha|_D^{25}$: -10.76° (c = 16.9, methanol).
8. C. Hubschwerlen, Synthesis, (1986), 962; 4, $|\alpha|_D^{20}$: -63.5° (c = 8, benzene); 4, $|\alpha|_D^{20}$: -10.9° (c = 1, methanol)
9. S. Morgenlie, Carbohydr. Res., (1982), 107, 137.
10. K.E. MaloneyHuss, Synthet. Commun., (1985), 15, 273; 3, $|\alpha|_D$: -69.7° (c = 2.22, benzene); 4, $|\alpha|_D$: -10.7° (c = 1.55, methanol).
11. A.H. Al-Hakim, A.H. Haines, C. Morley, Synthesis, (1985), 207; 4 $|\alpha|_D$: -10.6° (c = 4, methanol).
12. C.M. Lok, J.P. Ward, D.A. Van Dorp, Chem. Phys. Lipids, (1976), 16, 115; 5, $|\alpha|_D^{22}$: -10.1° (neat); 4, $|\alpha|_D^{22}$: -13.2° (neat).
13. S.K. Kang, D.S. Shin, Bull. Korean Chem. Soc., (1986), 7, 159.
14. Carbohydrates, Ed. P.M. Collins; Chapman and Hall Chemistry Sourcebooks 1987.

(Received in UK 22 July 1987)