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A SHORT SYNTHESIS OF (S)-5-HYDROXYMETHYL-(5H)-FURAN-2-ONE AND DERIVATIVES FROM D-RIBONOLACTONE

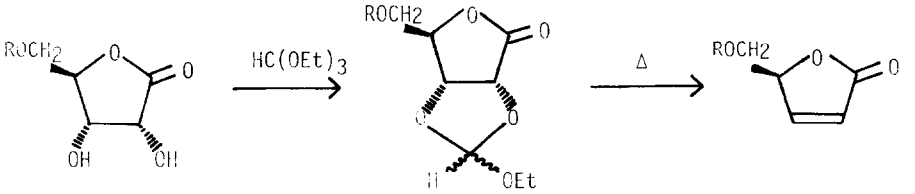
P. Camps, J. Font* and O. Ponsatí
Departament de Química Orgànica, Facultat de Ciències, Universitat Autònoma de Barcelona, Bellaterra, Barcelona, Spain.

Abstract.- *We describe a short synthesis of (S)-5-hydroxymethyl-(5H)-furan-2-one and some 5-O-derivatives, which are being used as key starting products for the synthesis of several antileukaemic lignan lactones, from D-ribonolactone.*

Recently, Koga has published two articles describing the use of (S)-5-benzyloxymethyl-(5H)-furan-2-one[1], 8, and (S)-5-trityloxymethyl-(5H)-furan-2-one[2], 10, as starting chiral compounds for the synthesis of the antileukaemic lignan lactones (+)-trans-burseran, (-)-isostegane and (+)-steganacin. Compounds 8 and 10 were synthesized by Koga[1,2] in three steps from (S)-4,5-dihydro-5-hydroxymethyl-(3H)-furan-2-one, which in turn had been prepared in three steps from L-glutamic acid[3]. The total yield of 8 from L-glutamic acid is 19,5% while that of 10 cannot be determined because the yield of the tritylation step is not specified, but it should be < 39%.

We describe in this communication a facile preparation of butenolides[4] 7-10 in good yield from readily available D-ribonolactone, 1. D-Ribonolactone has the required configuration at C-4 for its conversion into 7-10. Only two transformations are needed: a) conversion of the vic-diol function into a C=C double bond and b) etherification of the hydroxyl group at C-5.

Refluxing 1 with one equiv. of triethyl orthoformate in anh. THF (2ml/mmol) for 12 hours gave, after evaporation of the solvent and the ethanol formed, a mixture of stereoisomers of cyclic orthoformates[5], 4, in quantitative yield. Pyrolysis[6] of 4, in a 0,5 g scale, by heating at 220°C/40 torr in a rotatory microdistillator, followed by chromatography and distillation, gave (S)-5-hydroxymethyl-(5H)-furan-2-one, 7($\{\alpha\}_D^{20}$=-143°, c=1,14 in H_2O), in 68% yield[7], identical with that obtained by enzymatic hydrolysis of the glycoside ranunculin[8].



1, R=H
2, R=$PhCH_2$
3, R=Me

4, R=H
5, R=$PhCH_2$
6, R=Me

7, R=H
8, R=$PhCH_2$
9, R=Me
10, R=Tr

Reaction of 7 with benzyl bromide/Ag_2O in anh. DMF[3] gave 8 ($[\alpha]_D^{20}$=-10,6°, c=2,1 in EtOH) in 73% yield. Similarly, reaction of 7 with trityl chloride in pyridine gave 10 (m.p.=152-154°C, $[\alpha]_D^{20}$=-95,1°, c=3,42 in $HCCl_3$) in 65% yield.

Alternatively compound 8 was also prepared form 5-O-benzyl-D-ribonolactone[9], 2, in 66% overall yield by orthoesterification with triethyl orthoformate, which gave quantitatively the mixture of cyclic orthoformates, followed by heating in diglyet in a sealed Pyrex tube at 200°C for 7 hours in the presence of a small quantity of glacial AcOH as catalyst. In a similar way (S)-5-methoxymethyl-(5H)-furan-2-one, 9, was prepared from 5-O-methyl-D-ribonolactone[10], 3, in 66,5% overall yield. In this case, the cyclic orthoformate pyrolysis was carried out by heating the compound at 176°C for 14 hours with neither solvent nor catalyst.

It is noteworthy that Corey-Winter[11] and Hanessian[12] methods for stereospecific conversion of 1,2-diols into olefines did not give satisfactory results when applied to 3.

The use of (S)-hydroxymethyl-(5H)-furan-2-one as a chiral synthon for the synthesis of natural products is under study.

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References and notes

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2. K. Tomioka, T. Ishiguro and K. Koga, Tetrahedron Letters, 2973 (1980).
3. M. Taniguchi, K. Koga and S. Yamada, Tetrahedron, 3547 (1974).
4. In the preceding communication the synthesis of racemic 7 and some derivatives is described.
5. No orthoesterification of the hydroxyl at C-5 was detected. When an excess of triethyl orthoformate is used, orthoesterification of the hydroxyl at C-5 takes also place and 5-methylene-furan-2-one (protoanemonin) is the major product formed during the pyrolysis of the mixture of orthoesters at 220°C/18 torr, which agrees with the easy conversion of 7 and derivatives into protoanemonin.
6. The method of Crank and Eastwood (G. Crank and F. W. Eastwood, Aust. J. Chem., 17, 1385 (1964)) was followed. The temperature and the pressure of the pyrolysis were chosen in order to get a clean and fast reaction in which the formation of protoanemonin, which is a by-product of this reaction, was minimized, and distillation of orthoformate 4, was avoided.
7. Working on a 2 g scale the yield was about 52%.
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9. Compound 2 was prepared in three steps from 1 in 73% overall yield. Satisfactory elemental analyses and spectroscopic data were obtained for the new compounds 2 and 9 described in this communication.
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