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A USEFUL PREPARATION OF 4-SUBSTITUTED 5-HYDROXY-3-OXOCYCLOPENTENE

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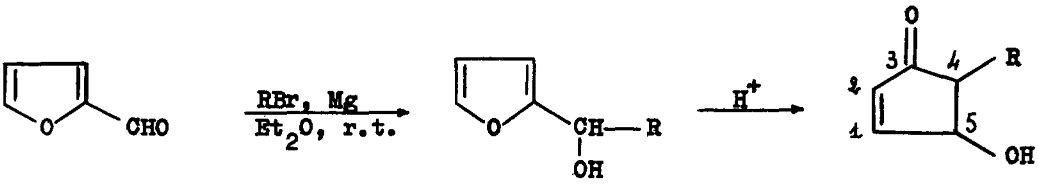
The 3-oxocyclopentene molecule and its 5-hydroxy derivative are present in several biologically active natural products as major structural features: this has given rise to considerable interest and efforts to develop efficient syntheses of these molecules (1). In this letter we wish to describe a useful two-step synthesis of 4-substituted 5-hydroxy-3-oxocyclopentene by molecular rearrangement of 2-furyl carbinols.

In fact, 2-furyl carbinols 1, easily obtained through the usual procedure of a Grignard reaction (2), were submitted to acid-catalyzed hydrolysis in acetone-water mixture; under these conditions, the compounds 1a, 1b, and 1c undergo a molecular rearrangement, yielding directly 2a, 2b, and 2c (Table 1).

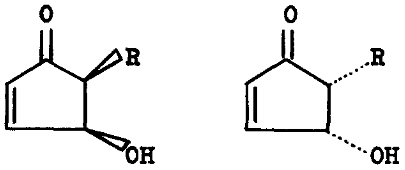


1 2

a: R = C_6H_5-
b: R = $CH_3(CH_2)_4CH_2$-
c: R = CH_3-

The rearrangement proceeds stereospecifically: the ^{1}H-NMR data show the formation of one only enantiomeric pair. In fact, both the compounds 2b and 2c afford monoacetoxy derivatives, which show only clear singlets for the acetoxy groups (C_6D_6, respectively at 1.71 δ and 1.68 δ). Between the two possible pairs, (I) and (II), only (I) is formed, as indicated by the spectroscopic data:

(I)



(II)

a) In the ^{1}H-NMR spectrum of 2a, the C_4 proton shows as a neat doublet ($J = 2.5$ Hz), in agreement with a trans coupling of C_4 and C_5 protons; it is well known that in cyclopentene derivatives $J_{cis} > J_{trans}$ ($J_{cis} = 6$–8 Hz, $J_{trans} = 2$–3 Hz) (3).

b) In the ^{1}H-NMR spectrum of 2c, the secondary methyl shows as a clear doublet at 1.26 δ ($J = 7$ Hz); by double irradiation at 1.26 δ , the signal of the C_4 proton at 2.27 δ turns into a doublet ($J = 2$ Hz), again in agreement with a trans disposition of the C_4 and C_5 protons.

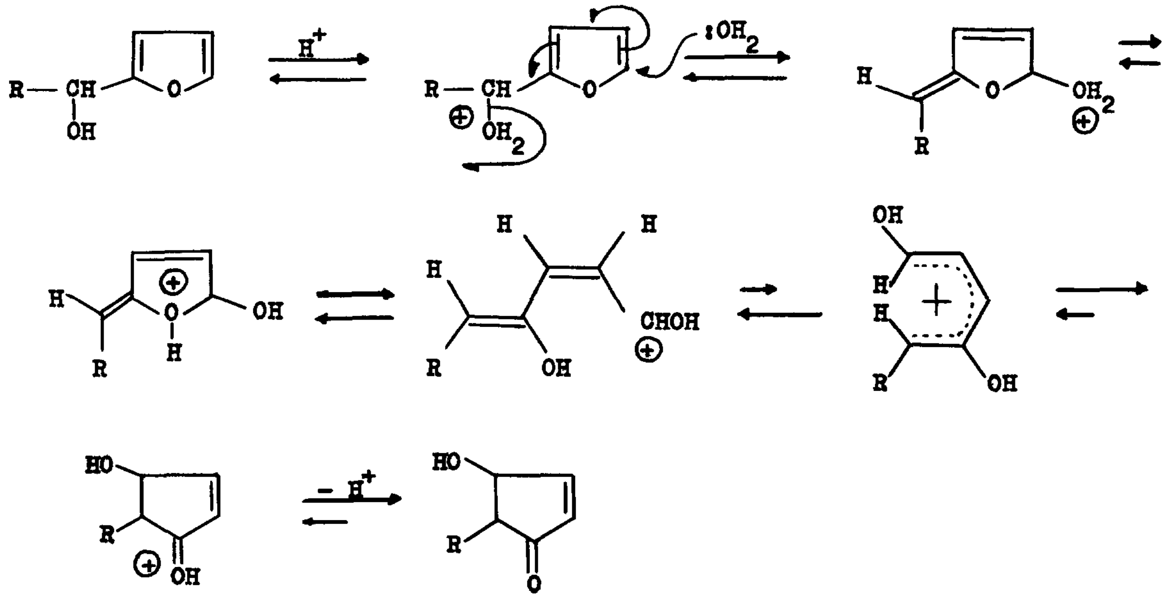
TABLE 1*

	^{1}H-NMR data**				IR data**		
compounds	C_1-H	C_2-H	C_4-H	C_5-H	C=O	C=C	Yield
2a	d of d 7.38 J_1= 3 J_2= 6	d of d 6.10 J_1= 1.5 J_2= 6	d 3.28 J = 2.5	broad s 4.70	1714	1602	65%
2b	d of d 7.45 J_1= 3 J_2= 6	d of d 6.07 J_1= 1.5 J_2= 6	m 2.12	broad s 4.57	1710	1597	70%
2c	d of d 7.51 J_1= 3 J_2= 6	d of d 6.18 J_1= 1.5 J_2= 6	d of q 2.27 J_1= 2 J_2= 7	broad s 4.58	1715	1600	30%

* The IR and ^{1}H-NMR data were completely in agreement with the ones reported for similar compounds (4).

** ^{1}H-NMR ($CDCl_3$, δ ; J values are reported in Hz); IR (1% $CHCl_3$, ν_{max}, cm^{-1}).

The reaction mechanism can be explained in terms of a thermal electrocyclic reaction of a 4π electron system, that is conrotatory (5).



Typical procedure:

3 g of 1a, (1b or 1c), are dissolved in 2:1 acetone-water mixture (40 ml); then the acid is added (6) and the solution is stirred at 50 °C for 24 h. The usual work-up (dilution with AcOEt, washing with $NaHCO_3$ and H_2O, drying over anhydrous Na_2SO_4 and evaporation of the solvent) yields a reddish oil that is chromatographed on SiO_2: elution with 2:1 benzene-diethyl ether gives respectively 2a (1.950 g), 2b (2.1 g), and 2c (0.9 g), as oils.

We are now studying the synthetic utility of this rearrangement.

Acknowledgement: we are grateful to the Italian CNR for financial support.

References and remarks

1) R. A. Ellison, *Synthesis*, 397 (1973).
2) The analytical and spectroscopic data (MS, IR, and ^{1}H-NMR) were completely in accord with the proposed structures 1a, 1b, and 1c.
3) a) K. Ogura, M. Yamashita, and G. Tsuchihashi, *Tetrahedron Lett.*, 759 (1976) and references therein; b) F. A. L. Anet and R. Anet in " Determination of Organic Structures by Physical Methods ", F. C. Nachod and J. J. Zuckermann eds., Academic Press, New York, 1971 vol. 3, p. 340; c) H. Booth in " Progress in NMR Spectroscopy ", J. W. Ensley, J. Feeney, and L. H. Sutcliffe eds., Pergamon Press, Oxford, 1969, pp. 215-16.
4) See ref. 3a).
5) R.B. Woodward and R. Hoffmann," The Conservation of Orbital Symmetry ", Verlag Chemie, GmbH, Weinheim, 1970, pp. 45, 58.
6) The best yields were given by the following acids: formic acid for 1a (0.15 ml), polyphosphoric acid (0.5 g) for 1b, and p-toluenesulfonic acid (0.3 g) for 1c.