

OXIDATION OF FURANS - I. SYNTHESIS OF 6-HYDROXY-2H-PYRAN-3(6H)-ONES

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For several years, we have been studying the transformation of furans under various oxidative conditions. As already reported, treatment of 3-substituted furan derivatives with peracids or N-bromosuccinimide led to the formation of isomeric butenolides and application of these reactions in the cardenolide field yielded interesting analogues of digitoxigenin¹.

Recent reports on the conversion of furans to pyran derivatives^{2,3} prompt us to present some of our work on the oxidation of furanmethanols⁴.

17 α -[2-Furyl]-3-methoxy-1,3,5(10)-estratrien-17-ol I, mp 117-119°, $[\alpha]_D = +54.6^\circ$, readily prepared from estrone methyl ether upon reaction with 2-furyllithium⁵, was treated with peracetic acid or *m*-chloroperbenzoic acid affording in approximately 65% yield 17 β ,24-epoxy-24 α -hydroxy-19,21-dinorchola-1,3,5(10),22-tetraen-20-one II, mp 191.5-192.5°, $[\alpha]_D = +95^\circ$, characterized by the presence of a 6-hydroxy-2H-pyran-3(6H)-one system (at position 17), attached in a spiral manner. A mixture of isomers in position 24 was obtained. The structure of II was ascertained by spectral analysis. The infrared spectrum indicated the presence of an alcohol group at 3580 and 3410 cm^{-1} and a conjugated ketone at 1680 cm^{-1} . The NMR spectrum confirmed the presence of two isomers:

Major isomer: 18CH₃:1.03; H₂₂:6.00 (doublet, J=10 cps); H₂₃:in the aromatic region - the proton is centered at 6.90 (J=10 cps) and H₂₄:5.76 (multiplet).

Minor isomer: 18CH₃:1.00; H₂₂:5.96 (doublet; J=10 cps); H₂₃:in the aromatic region and H₂₄:5.53 (multiplet).

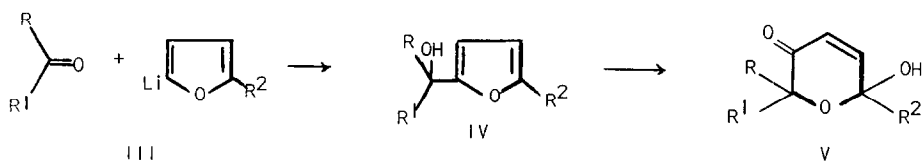
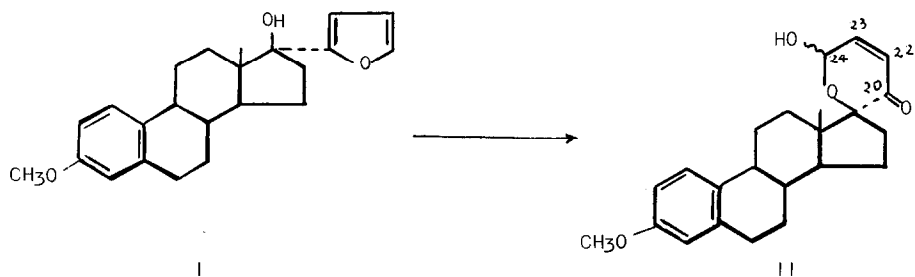
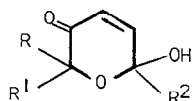


Table I



Starting Material	R	R ¹	R ²	mp	Yields
	H	H	H	58-59° ⁷	48%
		H	H	124-126°	75%
		CH ₃	H	166-167°	80%
		H	H	159-160°	62%
		CH ₃	CH ₃	85-87°	40%

The two isomers could only be separated as the corresponding acetates: major isomer, mp 169-171°; $[\alpha]_D +126.7^\circ$: minor isomer, mp 151-152°; $[\alpha]_D = +73.8^\circ$.

In this manner a series of 17 α -[2-furyl]-17-hydroxy steroids of the estrane and androstane series led to the corresponding 17 β ,24-epoxy-24-hydroxy-19,21-dinorchol-22-en-20-ones and 17 β ,24-epoxy-24-hydroxy-21-norchol-22-en-20-ones, as well as their 24 esters and ethers.

It was readily apparent that the above oxidation reaction was general and could also be applied to non-steroidal 2-furanmethanols of type IV, thus affording the 6-hydroxy-2H-pyran-3(6H)-ones⁶. A large number of pyranones were prepared and the few examples given in Table I serve only to illustrate the potential of the reaction. The starting furanmethanols were in most cases obtained from the appropriate carbonyl-containing compounds III by reaction with 2-furyllithium or a 5-substituted 2-furyllithium, i.e. 5-methyl 2-furyllithium.

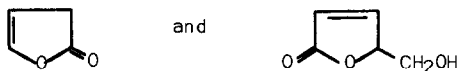
Conventional derivatives of the ketolactols such as esters, ethers and carbamates were also prepared. A full account of this work will be reported elsewhere.

It should finally be mentioned that the 6-hydroxy-2H-pyran-3(6H)-ones constitute a group of substances very useful as starting materials for the preparation of new classes of compounds otherwise not readily available by synthesis⁸.

References

1. J.M.-Ferland, Y. Lefebvre, R. Deghenghi, and K. Wiesner, Tetrahedron Letters, No. 30, 3617 (1966).
2. G.W. Cavill, D.G. Laing, and P.J. Williams, Aust. J. Chem., 22, 2145 (1969).
3. O. Achmatowicz, Jr., P. Bukowski, B. Szechner, Z. Zwierzchowska, and A. Zamojski, Tetrahedron, 27, 1973 (1971).
4. All new compounds had consistent microanalytical and spectroscopical data. Rotations were measured in chloroform. Infrared spectra were recorded in chloroform solutions on a Perkin-Elmer spectrophotometer Model 225. The NMR spectra were taken in DMSO- d_6 solutions at 60 mC with TMS as internal reference, and were recorded as δ values, in ppm.
5. V.R. Ramanathan, and R. Levine, J. Org. Chem., 27, 1216 (1962).
6. Several patent applications have been filed on the subject in the United States. The original case, filed on July 29, 1968, was granted on December 15, 1970 as U.S. Pat. No. 3,547,912. The full scope of the process is described in the specification.

7. The oxidation of furfural by peracetic acid was previously reported by J. Bösenken and co-workers: Rec. Trav. Chim., 50, 1023 (1931), Chem. Abst., 26, 983 (1932). They isolated two products to which they assigned the following structures:



In our hands, oxidation of furfural with m-chloroperbenzoic acid only yielded 6-hydroxy-2H-pyran-3(6H)-one V ($R = R^1 = R^2 = H$).

8. R. Laliberté: to be published.