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ON THE ACETOXYLATION OF 2,3-DIHYDRO-4-PYRONES: A CONCISE, FULLY SYNTHETIC ROUTE TO THE GLUCAL STEREOCHEMICAL SERIES

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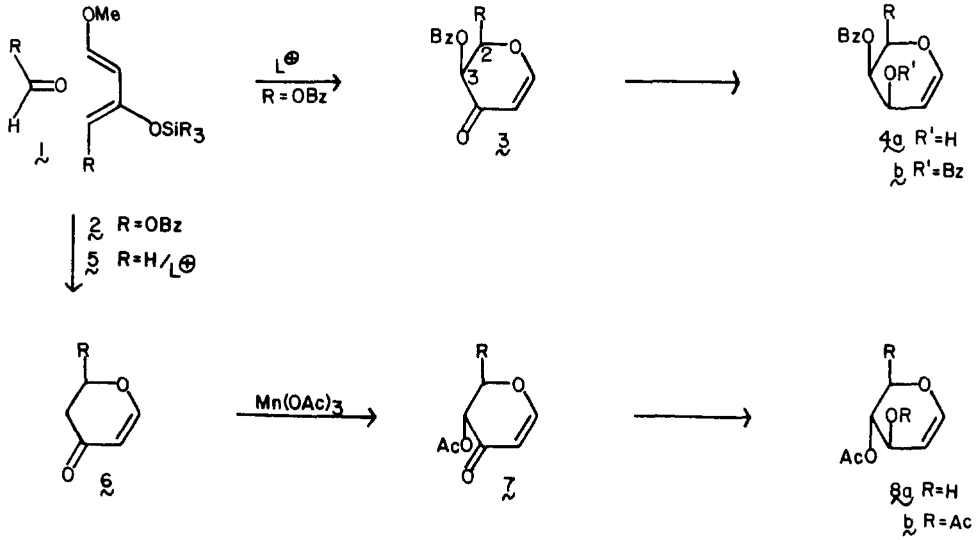
Summary: The acetoxylation of the title compounds at C_3 with $Mn(OAc)_3$ is described.

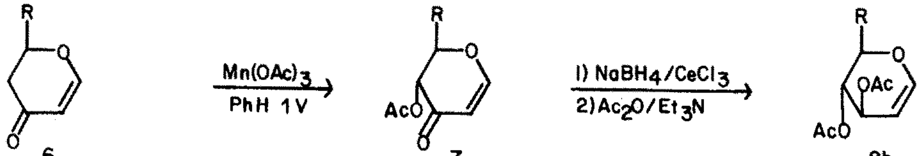
Cyclocondensation of diene type **2** with aldehydes in the presence of various catalysts affords dihydropyrones of the type **3** with a cis relationship between the 2- and 3-substituents.[1] Subsequent reduction of such systems with sodium borohydride-$CeCl_3$[1,2] provides a concise route to "galactal"[3] structures (cf **4**). This methodology allows for rapid access to compounds with a broad range of R functions at C_2 of the pyrone (i.e. C_5 of the "pyranose").

For many applications it would be helpful to have a correspondingly simple access to "glucals"[3] (cf **8**). Below we describe a solution to this problem in which the key step is the acetoxylation of pyrones **6** at C_3. Compounds such as **6** are available by cyclocondensation of aldehydes **1** with the commercially available diene **5**.[4] Following a lead provided in a recent disclosure by Watt,[5] we found that this acetoxylation could be achieved with manganese triacetate.[6]



With all substrates except **6** (R=Me),[7] the oxidation is a stereoselective process yielding almost exclusively the trans-products **7**. Also, the conditions are mild enough to allow for the survival of potentially sensitive functionality. Moreover, the Luche reductions[2] of **7** give, with high selectivity

(>10:1), the equatorial alcohols which, upon acetylation, yield diacetates **8b**. This methodology allows for access to "glucals" of a type which are not readily available via glucose itself.



6	7	8b
R=Ph	64%	89%
R=2-furyl	53%	78%
$R=CH_2\text{-}CH{=}^{t}CHMe$	51%	83%
R=Me[7]	44%	78%

A typical experimental procedure is given below. To 50 mg (0.287 mmol) of pyrone **6** (R=Ph) in 5 mL of dry benzene was added 350 mg (1.5 mmol) of $Mn(OAc)_3$, which was previously dried over P_2O_5 under high vacuum. The reaction mixture was heated under reflux for 12 hours and an additional 350 mg of $Mn(OAc)_3$ was added. After reflux was continued for another 12 hours, no starting material was observed by TLC analysis. Dilution with ethyl acetate followed by standard workup[5] and flash chromatography gave 40 mg of pyrone **7** (R=Ph) in 64% yield.

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1. S.J. Danishefsky, C.J. Maring. J. Am. Chem. Soc. 107, 1269 (1985).
2. J.L. Luche, A.L. Gemal. J. Am. Chem. Soc. 101, 5848 (1979).
3. The term "galactal" refers to a cis-cis relationship between the C_3, C_4 and C_5 substituents (carbohydrate numbering). This corresponds to the C_2, C_3 and C_4 substituents based on the strictly conventional dihydropyran view (cf compound **4**). Similar considerations apply to our use of the descriptor "glucal".
4. S.J. Danishefsky, J.F. Kerwin, Jr. J. Am. Chem. Soc. 104, 358 (1982). Also see: M. Bednarski, S.J. Danishefsky. J. Am. Chem. Soc. 105, 3716 (1983).
5. N.K. Dunlap, M.R. Sabol, D.S. Watt. Tetrahedron Lett. 5839 (1984).
6. For some previous uses of manganese triacetate in quite different contexts see: (a) E.I. Heiba, R.M. Dessau, P.G. Rodewald. J. Am. Chem. Soc. 96, 7977 (1974). (b) E.J. Corey, M. Kang. J. Am. Chem. Soc. 106, 5384 (1984). (c) W.E. Fristad, J.R. Peterson. J. Org. Chem. 50, 10 (1985). In our hands, attempts at acetoxylation with lead tetraacetate were not successful.
7. A 3:1 mixture of C_2-C_3 trans to cis was observed in this example. The mixture was, however, separable by chromatography.

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