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# A Novel Tetrahydrofuran Derivative Via a Tertiary Ketol-Type Rearrangement

Siegfried E. Drewes*, Neville D. Emslie, John S. Field,
Abdullah A. Khan and Niyum S. Ramesar

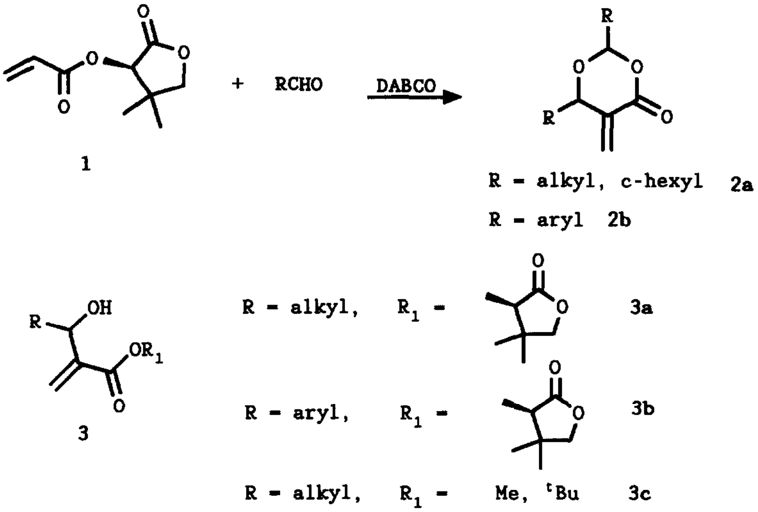
Department of Chemistry, University of Natal,
Pietermaritzburg, 3201, South Africa

**Abstract:** Hexahydro-3a,7a-dihydroxy-3,7,7-trimethyl-2-phenyl-4H-furo[3,2-c]pyran-4-one **6** has been obtained from the reaction between tetrahydro-4,4-dimethyl-2-oxo-3-furanyl propanoate **4**, benzaldehyde and base. The product is the result of a modified benzilic acid rearrangement.

The Baylis-Hillman reaction,[1] which involves the coupling of acrylic systems with electrophiles (usually aldehydes) in the presence of a catalyst (usually DABCO) continues to generate interest.[1,2] Current endeavours in this area are focused on the stereochemical control of the new chiral centre.[3]

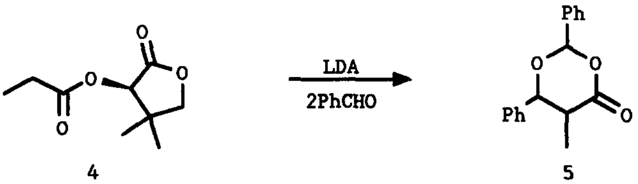
In our endeavours to extend this reaction to chiral acrylic systems we have discovered a novel cyclisation reaction[3c] which leads to multi-functional compounds. When the chiral acrylate **1** was treated with aliphatic aldehydes, the 2,6-disubstituted-5-methylene-1,3-dioxan-4-one **2a** was obtained instead of the desired Baylis-Hillman product **3a**. Formation of **2a** results from sequential condensation of 2 equivalents of aldehyde followed by an intramolecular transesterification (**Scheme 1**).

While the above cyclisation has been established as a general method for the synthesis of **2a** using aliphatic aldehydes, aromatic aldehydes only yield the conventional products **3b**.[4] It was speculated that under different reaction conditions the corresponding dioxanones **2b** may be produced, by using, for example, the masked acrylate procedure described earlier by us.[5]



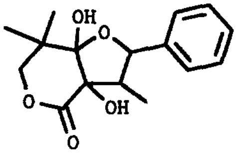
Scheme 1

Initial studies were focused on using a simple model compound such as the chiral ester **4**. This would obviate the need for masking and removal of the amino group. Reaction with benzaldehyde in the first instance was expected to produce the dioxanone **5** (**Scheme 2**) but spectral information on the major product indicated otherwise.



Scheme 2

X-ray crystallography (**Figure 1**)[6] permitted the assignment of structure **6** to the unknown product. It bears some resemblance to **7** which was isolated by Loder and Nearn[7] from the bark of an unnamed *Polyalthia sp.*.



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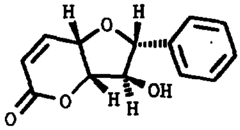

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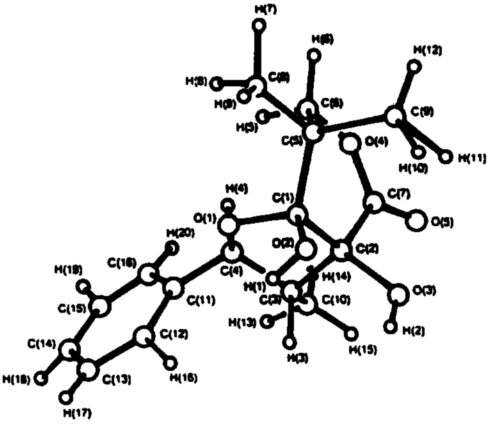
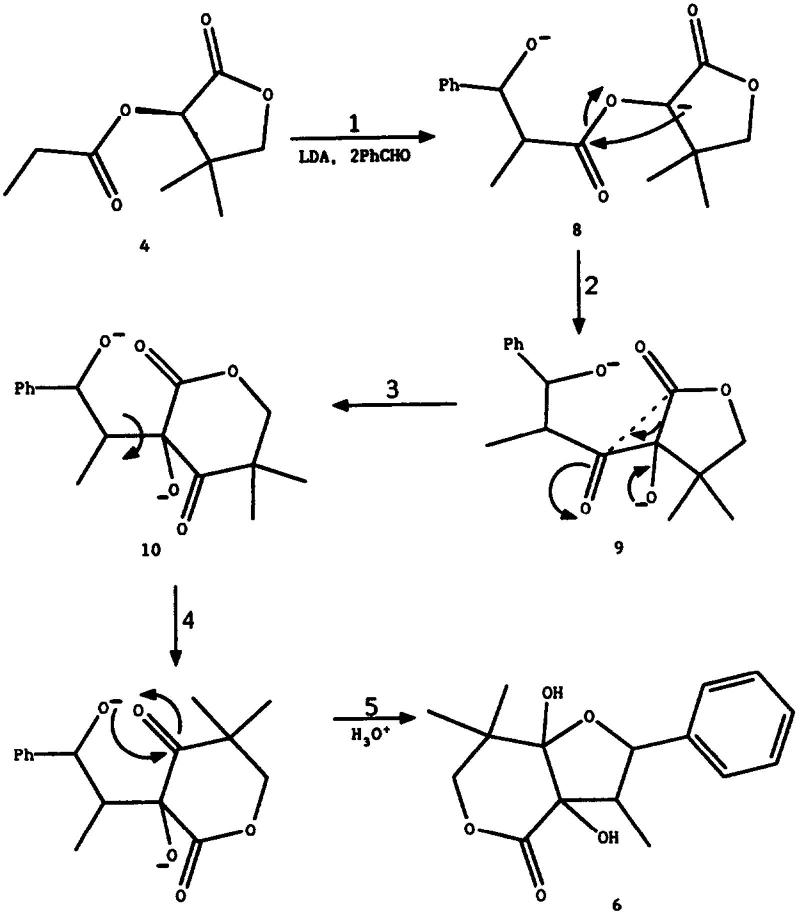


Figure 1



Scheme 3

To explain the formation of **6** it is proposed (**Scheme 3**) that LDA produces the dianion which, after condensation with benzaldehyde affords the intermediate **8** which rearranges to **9** as shown. This is followed by a novel example of a tertiary ketol rearrangement as described by Selman and Eastham[8] to produce **10**. The final step is simply the cyclisation of the alkoxy anion onto the ketone carbonyl which on work up, affords the diol **6**.

The absence of any optical activity in **6** shows that the dianion does form and the fact that similar rearrangements were reported in the steroid field,[9] gives us some confidence in this proposal.

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