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A NEW APPROACH TO δ-LACTONES, RELATED TO THE PRELOG-DJERASSI LACTONE.

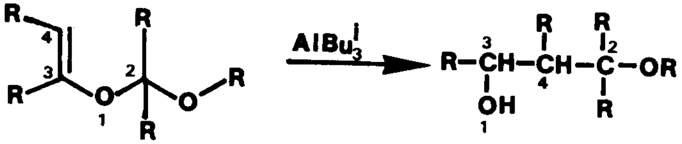
C.Malanga,[*,a] R.Menicagli,[a,b] M.Dell'Innocenti,[a] L.Lardicci[a,b]

[a]Dipartimento di Chimica e Chimica Industriale, [b]Centro delle Macromolecole Stereordinate ed Otticamente Attive, via Risorgimento 35-56100 Pisa-Italy.

Summary: The reductive rearrangement of 2-ethoxy-5-(2-alkenyl)-2H-tetrahydropyrane systems, in the presence of $AlBu^i_3$, was used as the key-step in the synthesis of Prelog-Djerassi related lactones.

Recent synthetic elaborations in the field of macrolides have prompted the development of some useful syntheses of δ-lactones[1,2], related to the Prelog-Djerassi lactone[2]. However, such approaches often involve many steps that cause the drop in final overall yields. Here we wish to report a very efficient new synthetic route to the synthesis of δ-lactones employing, as the key step, the reductive rearrangement of suitable alkyl, 1-alkenyl acetals (**1**) promoted by $AlBu^i_3$[3]; since such a reaction makes it possible to convert the C_2-O_1 bond into the C_2-C_4 bond, as shown in Scheme 1, we have concentrated our attention on the sequence of reactions reported in Scheme 2.

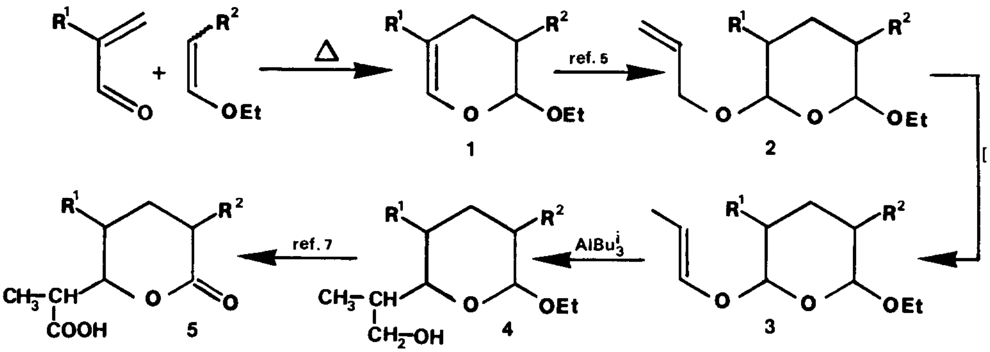
Scheme 1



In a typical experiment the required 2-ethoxy-3,4-dihydro-2H-pyrane derivative **1**, easily obtained from the Diels-Alder reaction[4] was reacted with allylic alcohol, in the reaction conditions already described,[5] to give (70-80% yields) **2** that was purified from smaller amounts of trans-acetalization products[5] by careful distillation, using a Fisher-Spalthror apparatus. Compounds **2b,c** were reacted with $RuH_2(Ph_3)_4$ (1/100, molar ratio, 150° C, 4h) to give compounds **3b,c** in quantitative yields, after elimination of the catalyst by bulb to bulb distillation. To the experimental conditions already reported,[3] the reaction of **3b,c** with

$AlBu^i_3$ gave compounds **4b,c** in 70-90% overall yields. These last products were oxidized by the Jones reagent[7] to give the corresponding lactones **5b,c** in good overall yields (70%).

Scheme 2[6]



$R^1=R^2=H$ (a); $R^1=Me$, $R^2=H$ (b); $R^1=R^2=Me$ (c)

This synthetical approach, characterized by only a few steps and high yields, gives diastereomeric mixtures that can be separated by chromatographic techniques. Owing to the general applicability of the reductive rearrangement,[3] the sequence reported (Scheme 2), might allow the preparation of a wide range of δ-lactones suitable as intermediates in macrolide syntheses.

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