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Improved Synthesis of α-Methylene-γ-lactones *via* organotin reagents

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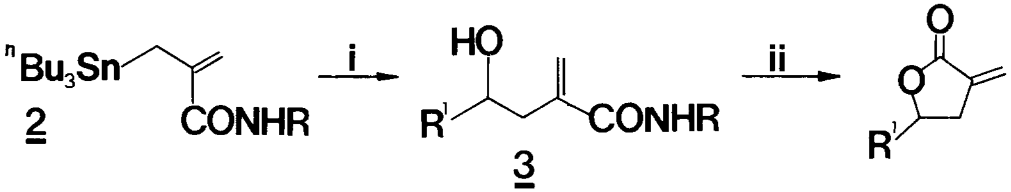
Summary: The products of the reaction between aldehydes and the organotin reagent (1) have been converted to the corresponding α-methylene-γ-lactones in excellent yield under extremely mild conditions.

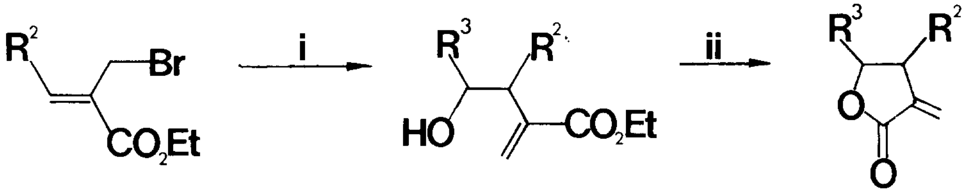
As the α-methylene-γ-lactone functionality has been estimated to occur in almost 10% of all structurally elucidated natural products,[1] great interest has recently been generated in the development of new synthetic routes to these ubiquitous compounds.[2]

The reaction of the known acrylamide reagents (2) with aldehydes and the subsequent transformation of the intermediate γ-hydroxyacrylamides (3) to the corresponding lactones is documented[3] (Scheme 1). The conversion of the amides to the desired lactones, however, requires rather drastic conditions *viz.* reflux in 10% HCl. To increase the generality of this potentially useful method, a milder alternative would be desirable.



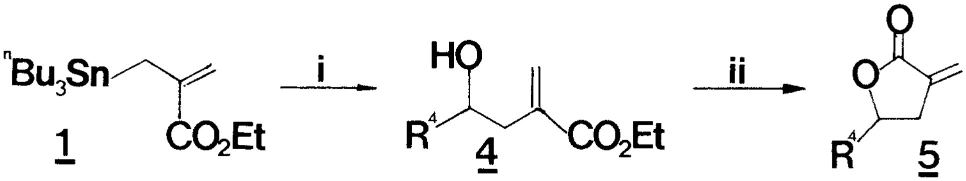
Scheme 1 (i) R^1CHO, CH_2Cl_2, $BF_3.Et_2O$ (4 eq.), -78°→RT
(ii) 10% HCl, reflux, 3hr.

A similar synthetic route to these lactones has been reported (Scheme 2) in which the one-pot reaction of (α-bromomethyl)acrylates with aldehydes in the presence of elemental tin furnishes α-methylene lactones in moderate yields.[4]



Scheme 2 (i) R^3CHO, Sn(powder), H_2O, AcOH (cat.), Et_2O, reflux.
(ii) p-TSA, benzene, RT.

During the course of our own studies concerning reactions of functionalized allyl stannanes, we developed the 2-ethoxycarbonylallylstannane (1) and firstly demonstrated its suitability to provide efficient transfer of the methacrylyl moiety via radical reaction pathways.[5] Secondly, we considered that (1) should prove a substantial improvement upon (2) as a precursor to α-methylene-γ-lactones by virtue of the fact that the hydrolytically resistant amide group is replaced by an ester moiety. We now report the preparation of α-methylene-γ-lactones via (1) according to Scheme 3. Thus, reaction of 1 equivalent of (1) with aldehydes in the presence of $BF_3.Et_2O$ furnished the γ-hydroxyacrylates (4) in high yield after chromatography. These compounds were then converted to the corresponding lactones (5) in excellent yield through reaction with 1 equivalent of trifluoroacetic acid in CH_2Cl_2 at ambient temperature (Table 1).



Scheme 3 (i) R^4CHO, CH_2Cl_2, $BF_3.Et_2O$ (4 eq.), -78°→ RT
(ii) CF_3CO_2H (1 eq.), CH_2Cl_2, RT overnight.

R^4	Yield 4 (%)	Yield 5 (%)
Ph	85	90
Et	87	92
ⁿPr	86	98
ⁱBu	94	92

Table 1

In summary, the novel allylstannane (1) has been shown to function as an efficient precursor to α-methylene-γ-lactones; the mildness of the overall process makes this an attractive synthetic method.

References

1. H.M.R. Hoffmann and J. Rabe, Angew.Chem., Int.Ed.Engl., 1985, 24, 94.
2. For reviews see: (a) J.C. Sarma and R.P. Sharma, Heterocycles, 1986, 24, 441. (b) P.A. Grieco, Synthesis, 1975, 67. (c) R.B. Gammill, C.A. Wilson and T.A. Bryson, Synth.Commun., 1975, 5, 245, and references therein.
3. K. Tanaka, H. Yoda, Y. Isobe and A. Kaji, J.Org.Chem., 1986, 51, 1856.
4. J. Nokami, T. Tamaoka, H. Ogawa and S. Wakabayashi, Chem.Lett., 1986, 541.
5. J.E. Baldwin, R.M. Adlington, D.J. Birch, J.A. Crawford and J.B. Sweeney, J.Chem.Soc., Chem.Commun., 1986, in press.

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