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Reactivity of Functionalized Allyltrihalostannanes : An Easy Entry to α-Methylene-γ-lactones

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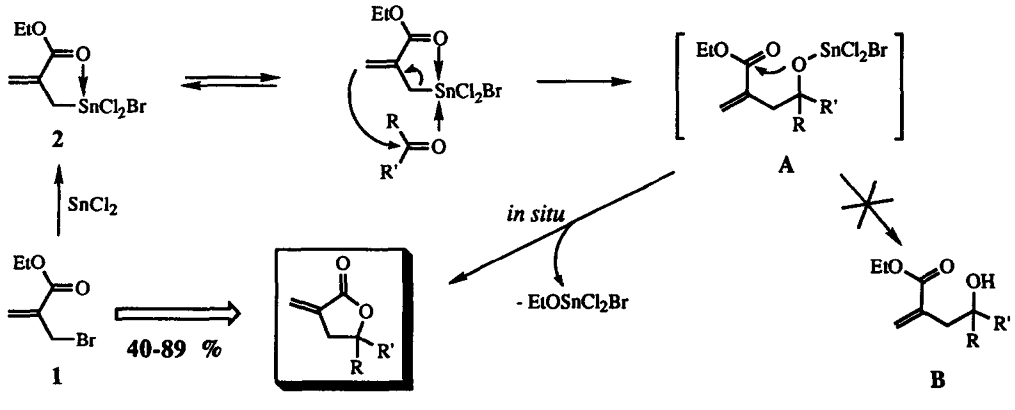
***Abstract** : Stable ester monoallyltin halides 2 are prepared in excellent yields and react easily with aldehydes and ketones under very mild conditions, to provide a usefull access to various α-methylene-γ-lactones.*

We have previously described a mild and practical process for producing monoallyltrihalostannanes starting from functionalized allylbromides and stannous halides[1]. These organometallic derivatives, which appeared to be particularly stable, from the fact they are not very sensitive to moisture, can be stored for a long period. Moreover they can be easily manipulated in air and could be of great interest in the field of synthetic chemistry. We now wish to report their reactivity as allylic carbanion equivalents in addition reactions with various carbonyl compounds. Barbier-type allylation of aldehydes using allylic halides and tin (II) halides is a well known reaction[2], and allyl transfer to various electrophiles using allylic tributyltin reagents is also well documented[3]. Most of these methods seem to be limited, however, either by the instability of the allylic tin species used or by the reactions conditions and the nature of the organotin residues. In contrast, functionalized allyltrihalostannanes 2 reacted efficiently with aldehydes and ketones under very mild conditions.



This reaction did not produce homoallylic alcohols **B**, but led directly to α-methylene-γ-lactones after cyclisation of the transient trihaloalkoxystannanes **A**. The reaction probably proceeds primarily by an equilibrium between intramolecularly complexed form **2** and an intermediate in which the tin atom is intermolecularly complexed to the carbonyl compound. Simultaneous enhancement of the nucleophilicity of the allylic moiety and activation of the carbonyl derivative allow the nucleophilic addition to proceed with allylic transposition, implying a cyclic six-centered transition state[4]. The trihaloalkoxystannane formed, **A**, is reactive enough to promote the lactonization step with elimination of ethoxytrihalostannane.

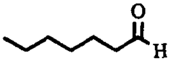
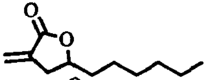
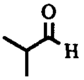
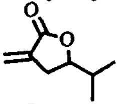
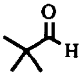
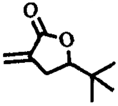
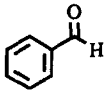
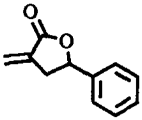
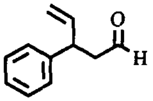
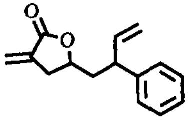
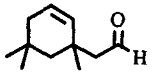
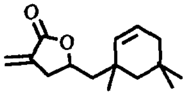
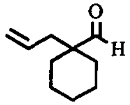
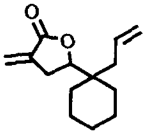
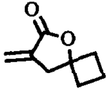
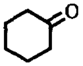
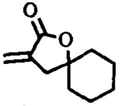
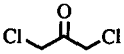
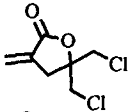
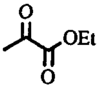
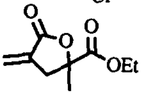
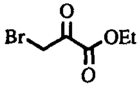
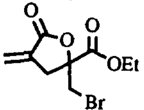
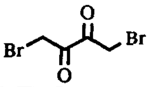
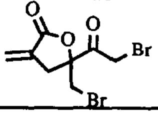
α-Bromomethylacrylates **1** are widely employed synthons for the preparation of α-methylene-γ-lactones[5]. Zinc is the most commonly used metal in these reactions, and only few examples are reported with tin halides[6]. In none of these case had an organotin intermediate been characterized or isolated, and the lactonization needed a supplementary step or an acidic medium. In contrast, the non aqueous neutral conditions used here allowed cyclisation under very mild conditions. It is noteworthy that a simple aqueous wash of the organic layer allows separation of all the product from non-toxic inorganic tin residues.

The reaction appears to be quite general with aldehydes, and shows some chemoselectivity. The reactivity differences observed for the various aldehydes is mainly due to steric hindrance. Indeed, when the carbonyl group is shielded (entries 3 and 7), the reaction must be performed in refluxing THF instead of ether. At first, the scope of this reaction with ketones seemed to be more limited, due to the lower nucleophilicity of the organotin reagent in comparison with more reactive organometallic species such as, for instance, organozincs[7]. This lack of reactivity goes together with a fairly good selectivity, according to the nature of the carbonyl compounds, as the reaction did not occur with acyclic ketones but did proceed with cyclic ketones (entries 8 and 9). More interestingly, reaction of **2** with ketones activated by electron withdrawing groups (halogen or carbonyl) led to the corresponding functionalized α-methylene-γ-lactones in good yields (entries 10 to 13). It is worth noting that the sensitivity of the reaction to the steric effects above-mentioned allowed the synthesis of lactone **15** functionalized by a keto group, simply starting from the corresponding diketone. The reaction of the second carbonyl group, though activated, is avoided.

Organotin chemistry may be an expedient entry into the chemistry of α-methylene-γ-lactones. Moreover, the mildness of the reaction conditions and the ability to obtain various functionalizations offers a powerful methodology for the synthesis of many natural products that include the α-methylene-γ-lactone subunit. Further extensions of this reaction are currently under study.

Experimental details

Preparation of the organotin reagent : In a 50 ml three-neck round-bottom flask were mixed the allylic bromide **1** (5.00 g, 25.9 mmol) and stannous chloride (4.91 g, 25.9 mmol) under an inert atmosphere. After addition of dichloromethane (10 ml), anhydrous ether (10 ml) and lithium bromide (225 mg, 2.6 mmol), the mixture was heated at reflux for two hours. After cooling and concentration under reduced pressure, the residue was dissolved in chloroform (50 ml) and filtered. Removal of the solvent gave the crude monoallylstannane **2** as a yellow oil (9.65 g, 97%) which can be stored or used for the lactonization reactions without any further purification. However, the product can be distilled (130°C / 10^{-4} mm Hg) providing with a minimum of decomposition, ethyl 2-(bromodichlorostannylmethyl)prop-2-enoate **2** as a colourless liquid. Spectral data for **2** : ^{1}H NMR (250 MHz in $CDCl_3$) δ (ppm) *J (Hz)* : 6.43 (1H, bs), 6.04 (1H, bs,${}^4J_{1H\text{-}119Sn}$

Entry	Carbonyl Compounds	Conditions	Methylenelactones	(Yields %)[8]
1		Et_2O (R.T.)		**3** (89)
2		Et_2O (R.T.)		**4** (81)
3		THF (Reflux)		**5** (68)
4		Et_2O (R.T.)		**6** (87)
5		Et_2O (R.T.)		**7** (62)
6		Et_2O (R.T.)		**8** (71)
7		THF (Reflux)		**9** (42)
8		THF (Reflux)		**10** (54)
9		THF (Reflux)		**11** (40)
10		THF (Reflux)		**12** (66)
11		THF (Reflux)		**13** (69)
12		THF (Reflux)		**14** (70)
13		THF (Reflux)		**15** (51)

<u>Table</u> : Addition of **2** onto Carbonyl Compounds

30.8), 4.43 (2H, q, *7.1*), 2.96 (2H, bs, $^{2}J_{1H\text{-}119Sn}$ *118.1*), 1.39 (3H, t, *7.1*). ^{13}C NMR (63 MHz in $CDCl_3$) δ (ppm) *J* (Hz) : 172.9 (C=O), 129.4 (=CH_2, $^{3}J_{13C\text{-}119Sn}$ *158*), 125.4 (=C<), 65.6 (O-CH_2), 31.9 (CH_2-Sn, bs), 14.0 (CH_3). ^{119}Sn NMR (75 MHz in $CDCl_3$) δ (ppm) : -144.0 (R-$SnCl_3$), -204.4 (R-$SnCl_2Br$), -264.0 (R-$SnClBr_2$), -322.2 (R-$SnBr_3$)[9]. IR (film) ν (cm^{-1}) : 1640 (C=C), 1600 (C=O), 1205 (C-O).

Typical procedure for the lactonization reaction : Benzaldehyde (555 mg, 5.23 mmol) and crude organotin **2** (2.00 g, 5.23 mmol) were mixed in anhydrous ether (20 ml). After stirring for three hours at 25°C the reaction mixture were pourred into water and extracted with ether three times. The combined organic layer was washed with brine, dried over Na_2SO_4. After concentration under reduced pressure the residual oil was purified by flash chromatography on silica gel, providing **6** as a white solid (793 mg, 87 %).

References and Notes

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4. This transition state appears to be close to Zimmerman-Traxler model invoked for many aldol reactions. Further experiments with ester monocrotyltin halides confirmed this assumption and exhibited the unicity of this mechanism. For a discusion of the transition state of allyl metal reagents, see Roush, W.R. in Trost, B. M.; Fleming, I. *Comprehensive Organic Synthesis*, Vol. II, Pergamon Press, Oxford, **1991**, 6-8 and references cited.
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7. Lambert, F.; Kirschleger, B.; Villieras, J. *J. Organomet. Chem.*, **1991**, *406*, 71-86.
8. Yields given are calculated relatively to the allyl bromide precursor **1**. All the lactones synthetized gave satisfactory mass spectra or elemental analyses. Structures were established by IR and NMR (^{1}H and ^{13}C).
9. As a result of rapid halogen exchange, **2** is in fact, a mixture of the four isomers R-$SnCl_3$, R-$SnCl_2Br$, R-$SnClBr_2$, R-$SnBr_3$ distinguished by ^{119}Sn NMR and mass spectroscopy. The proportions are close to the statistical values (30%, 44%, 22%, 4%). On the other hand, ^{1}H and ^{13}C NMR gave average values.

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