An Easy Access to β-Acyl- and β-Aryl-propionaldehydes through a New Silylated Organotin Homoenolate Equivalent

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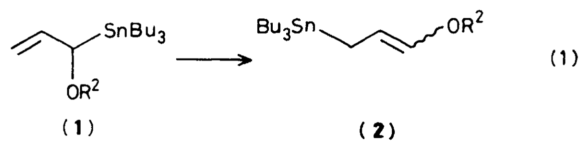
Palladium-catalysed cross-coupling of a new umpolung reagent, (α-methoxy-γ-tributylstannyl)allyltrimethylsilane, with acyl or aryl halides, involves exclusively the vinyl–tin bond and subsequent desilylation with tetrabutylammonium fluoride gives enol ethers, precursors of β-acyl- or β-aryl-propionaldehydes.

Homologation by a three-carbon reagent is a process of considerable synthetic interest[1,2] and several lithiated species have been proposed as homoenolate equivalents (d^3 propionaldehyde synthons).[3] However, such highly reactive species do not tolerate various functional groups.

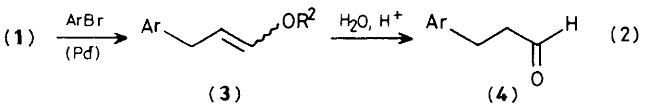
We had previously employed for this purpose α-alkoxyallyltins[4—7] but difficulties appeared with the simplest reagent, α-ethoxyallyltributyltin (**1**) which tends to isomerize readily into γ-ethoxyallyltributyltin (**2**) (reaction 1). Thus, while the palladium-catalysed couplings occurred nicely with aryl bromides,[4,8] isomerization of the allyltin was only observed with acyl halides (reactions 2 and 3). Also, the preparation of reagent (**1**) necessitates several steps including the use of a vinylmetallic compound to introduce the double bond.[8] An alternative might be the reaction of α-siloxyallylsilanes with acyl halides in the presence of $TiCl_4$[9] but this approach does not tolerate various functional groups on the substrate.

We describe herein a fast and efficient method to introduce the simplest homoenolate anion $^-CH_2CH_2CHO$ on acyl chlorides and aryl bromides *via* the easily accessible vinyltin (**7**) (Scheme 1).[10]

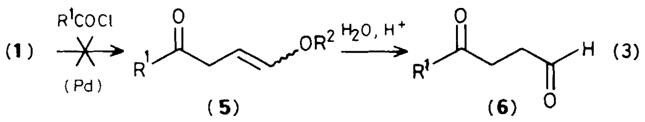
In the first series of experiments, (**7**) was treated with benzoyl chloride and bromobenzene in the presence of $PhCH_2PdCl(Ph_3P)_2$[11,12] and the corresponding allyl ethers (**8**; R^1 = Ph) and (**9**; Ar = Ph) were obtained in good yields (70—85%). It was possible to convert (**8**; R^1 = Ph) into a mixture of enol ether (**5**; R^1 = Ph, R^2 = Me) and acetal (**10**; R^1 = Ph, R^2 = Et) in ethanol, in the presence of Wilkinson's catalyst (20 h, 110 °C, sealed tube). Acid hydrolysis of the mixture (**5** + **10**) gave the expected β-benzoylpropionaldehyde in 59% overall yield from (**8**). However, we did not succeed in isomerizing (**9**; Ar = Ph) into (**3**; Ar = Ph, R^2 = Me) under the usual conditions.[13] For this reason we looked for a more efficient way and anticipated that the silylation of (**7**) would give the allylsilane (**11**). Compound (**11**) could undergo cross-coupling at the vinyl–tin bond yielding (**12**) and (**13**) before splitting of the silicon–carbon bond which would normally occur with allylic shift yielding (**5**) and (**3**), respectively.[14]



(1)

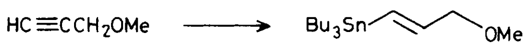


(2)



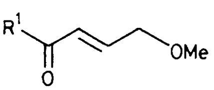
(3)

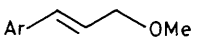
Indeed, the silylation of (**7**) gave (**11**) regiospecifically with a non-optimized yield of 56% in a process where the strong base Bu^{s}Li was used to prevent transmetallation which would have happened with BuLi (Scheme 2).[15] The reactions with acyl and aryl halides occurred as expected without cleavage of the allyl–silicon bond.[11,12] The unstable ketones (**12**) were not isolated and the reaction mixtures were immediately treated with Bu_4NF in tetrahydrofuran (THF) (attempted desilylation with CF_3CO_2H led only to heavy residues). The enol ether (**5**; R^2 = Me), easily hydrolysed to β-acylaldehydes (**6**), were obtained with non-optimized yields near 55% (Table 1). The silylated allyl ethers (**13**) were regiospecifically obtained and isolated (for comparison, direct lithiation of cinnamyl methyl ether, followed by silylation, yielded a mixture of α- and γ-silylated ethers). Desilylations were again performed with Bu_4NF, in THF (Table 1). It was found that the enol ethers (**3**; R^2 = Me) were accompanied by minor amounts of the isomeric allyl ethers (**9**) unless a strong electron-withdrawing group was present in the aromatic ring. Bu_4NF is known to



(**7**) (75%)

Scheme 1. *Reagents and conditions:* Bu_3SnH, azoisobutyronitrile (AIBN), 110 °C.


(**8**)


(**9**)

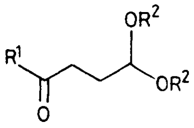
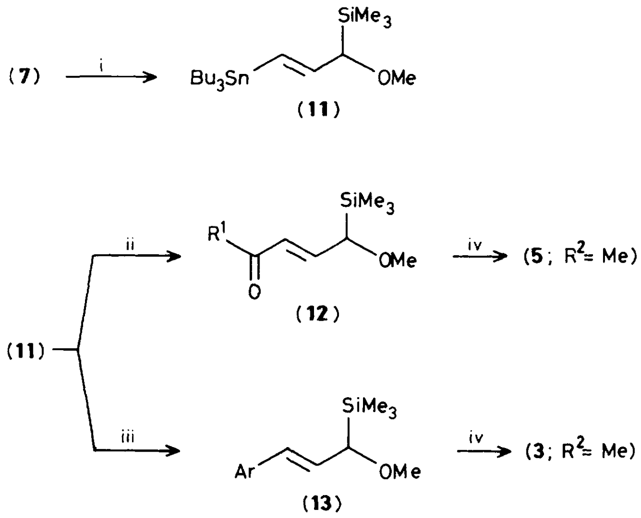

(**10**)

Table 1. Synthesis of enol ethers (**5**) and (**3**).

R^1	% Yield of (5)[a]	Ar	% Yield of (3)[b]
Ph	56	Ph	64[c]
4-$MeOC_6H_4$	53	4-$MeOC_6H_4$	56[d]
n-C_6H_{13}	51	4-ClC_6H_4	60[d]
		4-MeC_6H_4	87[c]
		4-$MeOCOC_6H_4$	82[e]
		4-NCC_6H_4	77[e]

[a] From (**11**). [b] From (**13**). [c] Plus 8% (**9**) byproduct. [d] Plus 11% (**9**). [e] No byproducts.



Scheme 2. *Reagents and conditions*: i, Bu^sLi, THF, −78 °C, then Me_3SiCl; ii, R^1COCl, $PdCl_2(PPh_3)_2$, THF, 65 °C; iii, ArBr, $Pd(PPh_3)_4$, C_6H_6, 110 °C; iv, Bu_4NF, THF, 0 °C.

generate allylic anions or their equivalents from allylsilanes[16] and the rapid protonation which follows is caused by the water contained in the commercially available reagent.

This new approach to enol ethers (**3**) and (**5**) allows an efficient access to β-aryl- and β-acylpropionaldehydes with a high tolerance for other functionalities. Thus (α-methoxy-γ-tributylstannyl)allyltrimethylsilane (**11**) appears as a reagent of choice because of easy accessibility, stability, and selectivity in the palladium-catalysed cross-couplings which occur at the vinyl–tin bond even in the presence of the highly activated silicon–carbon bond.

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