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 (d³ 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 TiCl₄[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 ⁻CH₂CH₂CHO 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 PhCH₂PdCl(Ph₃P)₂[11,12] and the corresponding allyl ethers (8; R¹ = Ph) and (9; Ar = Ph) were obtained in good yields (70—85%). It was possible to convert (8; R¹ = Ph) into a mixture of enol ether (5; R¹ = Ph, R² = Me) and acetal (10; R¹ = Ph, R² = 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, R² = 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]

Indeed, the silylation of (7) gave (11) regiospecifically with a non-optimized yield of 56% in a process where the strong base BuˢLi 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 Bu₄NF in tetrahydrofuran (THF) (attempted desilylation with CF₃CO₂H led only to heavy residues). The enol ether (5; R² = 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 Bu₄NF, in THF (Table 1). It was found that the enol ethers (3; R² = Me) were accompanied by minor amounts of the isomeric allyl ethers (9) unless a strong electron-withdrawing group was present in the aromatic ring. Bu₄NF is known to

$$ HC{\equiv}CCH_2OMe \longrightarrow Bu_3Sn{\diagup}{\diagdown}{\diagup}OMe $$

(7) (75%)
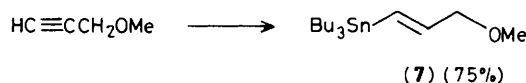
Scheme 1. Reagents and conditions: Bu₃SnH, azoisobutyronitrile (AIBN), 110 °C.
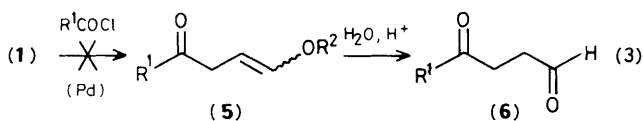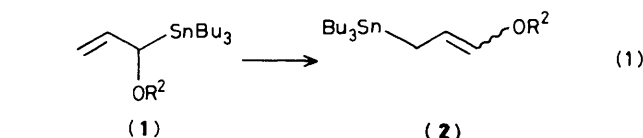
(8) (9) (10)
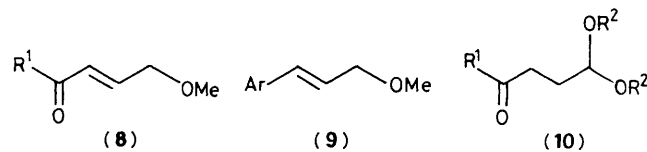
Table 1. Synthesis of enol ethers (5) and (3).

R¹	% Yield of (5)a	Ar	% Yield of (3)b
Ph	56	Ph	64c
4-MeOC₆H₄	53	4-MeOC₆H₄	56d
n-C₆H₁₃	51	4-ClC₆H₄	60d
		4-MeC₆H₄	87e
		4-MeOCOC₆H₄	82e
		4-NCC₆H₄	77e

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

(1)

(1) $\xrightarrow[\text{(Pd)}]{\text{ArBr}}$ Ar$\diagdown\diagup$OR² $\xrightarrow{\text{H}_2\text{O, H}^+}$ Ar$\diagdown\diagup$H (2)
(3) (4)

(1) $\xrightarrow[\text{(Pd)}]{\text{R}^1\text{COCl}}$ R¹—C(O)—$\diagdown\diagup$OR² $\xrightarrow{\text{H}_2\text{O, H}^+}$ R¹—C(O)—$\diagdown\diagup$H (3)
(5) (6)
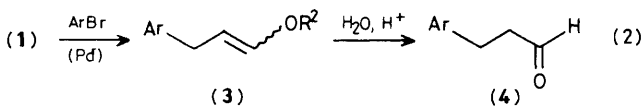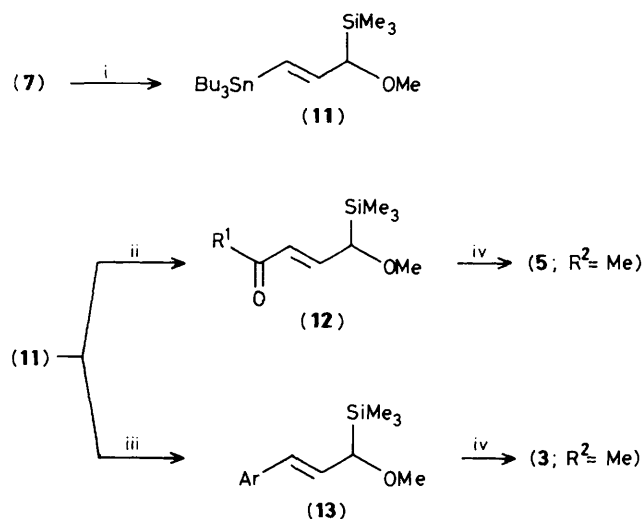
Scheme 2. *Reagents and conditions*: i, Bu^{s}Li, THF, −78 °C, then Me₃SiCl; ii, R¹COCl, PdCl₂(PPh₃)₂, THF, 65 °C; iii, ArBr, Pd(PPh₃)₄, C₆H₆, 110 °C; iv, Bu₄NF, THF, 0 °C.

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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