

1-Tributylstannyl-3,3-diethoxyprop-1-ene as a d³ Acrolein Equivalent

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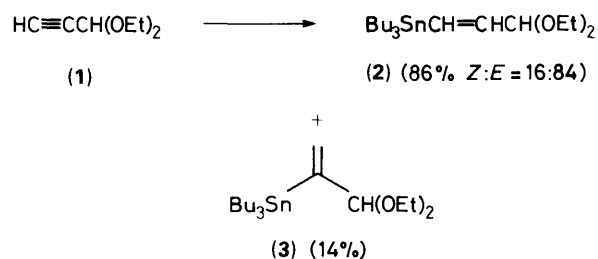
1-Tributylstannyl-3,3-diethoxyprop-1-ene has proved to be a readily available β-formylvinyl anion equivalent which under mild experimental conditions gives ready access to cinnamic skeletons and 4-oxo- or 6-oxo-α,β-enals.

Organotin compounds with an umpolung character¹ are useful reagents for the introduction of carbonyl-containing side chains. For instance, α-alkoxyalkyltins,² α-stannylacetals,³ or acyltins⁴ can be used in this way and act as typical d¹ umpolung reagents while α-alkoxyallyltins derivatives react either as d¹ or d³ umpolung reagents depending on the experimental conditions.^{2,5,6}

In the vinyltin series, appropriate precursors have been used as d³ propionaldehyde equivalents⁷ but until now, there have been no reports of the use of vinyltins as a d³ acrolein equivalent (–CH=CH–CHO) despite of the synthetic importance of β-acylvinyl anions and β-formylvinyl anions.^{8–13}

Herein, we report a readily accessible organotin reagent which is competitive with others previously described, in terms of yields and mildness of experimental conditions. Hydrostannation of the readily available 3,3-diethoxypropyne¹⁴ in the presence of azoisobutyronitrile (AIBN) using a slight excess of tributyltin hydride affords, after distillation, a mixture of the expected adducts (b.p._{0.8} 110–118 °C, 92% yield) on a 50–100 g scale † (see Scheme 1).

The obtention of a mixture of stereoisomers, *Z,E*-(2), and regioisomers, (2) + (3), which could have been a major problem for further syntheses appeared, in fact, to be only a minor one for two reasons. (i) Compound (3) is generally unreactive under the experimental conditions where (2) is reactive. (ii) After reaction, deprotection of the acetal function induces isomerization of *cis* enal into *trans* enal at least in the case of cinnamic skeletons.



Scheme 1. Reagents and conditions: Bu₃SnH (1.2 equiv.), AIBN, 120 °C, 4 h, 92%.

In consequence, the use of a slight excess of (2) + (3) (*ca.* 1.15 equiv.) allows good yields of the expected products. In the reaction schemes where a mixture of (2) + (3) is used, (3) will be ignored. Initially, we took advantage of the mildness of the experimental conditions to cross-couple vinyltins with aryl and heteroaryl bromides in the presence of a palladium complex catalyst^{2,16} to obtain the corresponding α,β-enals (6) (*cf.* the Table).

Tributyltin bromide was converted into insoluble tributyltin fluoride upon treatment with potassium fluoride–acetone and the crude mixtures of (5a–h) were submitted to liquid chromatography (silica gel 230–400 mesh using hexane–ether as eluant) which converts the allylic acetals (5) into the *trans*-α,β-enals (6) ‡ (See Scheme 2). It is noteworthy that clean

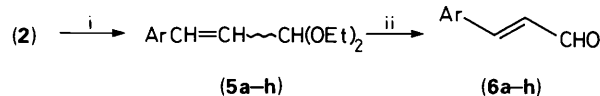
† An attempt to add Bu₃SnMgCl to the triple bond of (1) in the presence of CuBr (5%) according to Takeda¹⁵ affords the allenic derivative Bu₃SnCH=C=CHOEt (4) in poor yield (*ca.* 20%). To our knowledge it is the first unsubstituted γ-alkoxyallenyltin.

‡ An authentic sample of (3) obtained from 2-bromo-3,3-diethoxypropene on treatment with butyl-lithium and subsequent trapping with tributyltin chloride remains unchanged after 3 days under similar experimental conditions even at a higher temperature (120 °C).

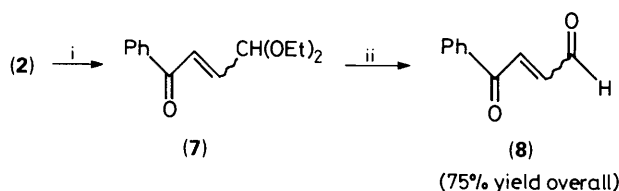
Table. Synthesis of α,β -enals (**6**) via allylic acetals (**5**).

Entry	Ar	(6) (%)
a	Ph	90
b	4-FC ₆ H ₄	70
c	2,4-(MeO) ₂ C ₆ H ₃	75
d	4-AcC ₆ H ₄	62
e	4-HCOC ₆ H ₄	65
f	2-Pyridyl	88 ^a
g	2-(4-Ethoxycarbonyl)furyl	55
h	5-(1-Phenyl-1,2,4-triazolyl)	45

^a After a hexane-acetonitrile partition, (**5f**) was obtained as a mixture of isomers (*Z*:*E* = 15:85).



Scheme 2. Reagents and conditions: i, ArBr, Pd(PPh₃)₄, C₆H₆, 100 °C, ca. 18 h, sealed tube; ii, SiO₂.



Scheme 3. Reagents and conditions: i, PhCOCl, Et₃N (1 equiv.), PdCl₂(PPh₃)₂, C₆H₆, 80 °C, 15 h; ii, CF₃CO₂H, CHCl₃.

conversions were observed even in the presence of functional groups such as ketones, aldehydes, or esters.

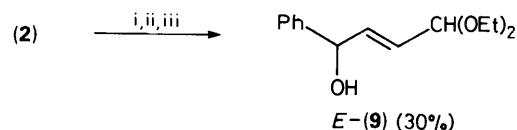
The extension of this reaction to the synthesis of 1,4-ketoaldehydes has also been attempted using palladium complexes for cross-coupling of (**2**) with acyl chlorides.¹⁷ While (3,3-diethoxyalkynyl)triorganotin react at the tin-carbon bond with acyl halides,¹⁸ the vinyltin (**2**) reacts usually at the acetal function. However, in the case of benzoyl chloride, using benzene as solvent and bis(triphenylphosphine)palladium dichloride as catalyst, this cross-coupling occurs when the experiment is conducted in the presence of triethylamine* (See Scheme 3).

A further interesting aspect is the use of (**2**) as a precursor for the corresponding vinyl-lithium or vinylcuprate reagents. In the first case, transmetalation of (**2**) by butyl-lithium in THF-ether-pentane at -120 °C during 5 min followed by quenching with benzaldehyde affords (**9**) in moderate yield (ca. 30%) and with a *trans* configuration (NMR data are consistent with those reported by Meyers for this compound).¹¹ (See Scheme 4).

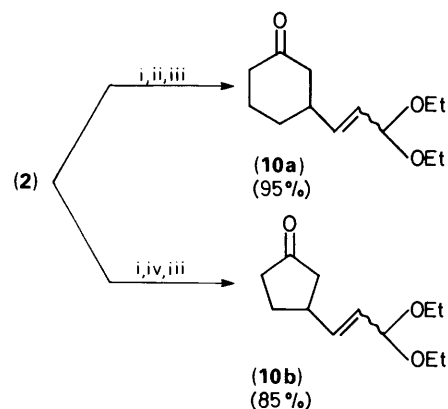
More interestingly, transmetalation of (**2**) with Bu₂CuCNLi₂ using the experimental procedure¹⁹ described by Lipshutz gives access to vinylcuprate reagents at room temperature and opens an efficient route for the introduction a β -formylvinylanion equivalent to the α,β -enones [here again (**3**) appears nearly unreactive in the suitable experimental conditions and the configuration of (**2**) is maintained in (**10a**) and (**10b**)] (See Scheme 5).

The above examples demonstrate clearly the versatility of 1-

* Once more, the reactivity of (**3**) appears to be poor compared to (**2**): a sample of pure (**3**) affords the cross-coupled product in 50% yield after 3 days at 120 °C when it is treated with benzoyl chloride under similar experimental conditions.



Scheme 4. Reagents and conditions: i, BuLi, THF-ether-pentane, -120 °C; ii, PhCHO, -120 °C; iii, H₂O-NH₄Cl.



Scheme 5. Reagents and conditions: i, Bu₂CuCNLi₂, THF, 25 °C, 2 h; ii, cyclohex-2-enone, -65 °C, 3 min; iii, H₂O/NH₄Cl; iv, cyclopent-2-enone, -50 °C, 10 min.

tributylstannyl-3,3-diethoxyprop-1-ene as a storable β -formylvinyl anion equivalent and work is in progress to illustrate more extensively the potentialities of this new reagent.

Acknowledgements

The authors are grateful to Schering and Rhône-Poulenc for their gift of the organometallic starting materials.

Experimental

Preparation of Compounds (2) and (3).—3,3-Diethoxypropyne (32 g, 0.25 mol) was heated with tributyltin hydride (87.6 g, 0.3 mol) at 120 °C in the presence of a catalytic amount of azoisobutyronitrile (AIBN, 0.3 g) over 4 h. After distillation the adducts (96.6 g) were isolated (b.p._{0.5} 110–118 °C): *E*-(**2**) (72%), *Z*-(**2**) (14%) and (**3**) (14%); δ_{H} (CDCl₃/Me₄Si; vinylic and allylic protons) *E*-(**2**) 6.35 (1 H, ³J_{1H} 19.5 Hz, ⁴J_{1H} 0.95 Hz, ²J_{SnH} 69/72 Hz), 5.97 (1 H, ³J_{1H} 19.5 Hz, ³J_{1H} 4.8 Hz, ³J_{SnH} 61/64 Hz), 4.808 (1 H, ³J_{1H} 4.8 Hz, ⁴J_{1H} 0.95 Hz); *Z*-(**2**) 6.51 (1 H, ³J_{1H} 13.3 Hz, ³J_{1H} 4.9 Hz, ³J_{SnH} 130/136 Hz), 6.20 (1 H, ³J_{1H} 13.3 Hz, ⁴J_{1H} 1.2 Hz, ²J_{SnH} 58.5/61 Hz), 4.814 (1 H, ³J_{1H} 4.9 Hz, ⁴J_{1H} 1.2 Hz); (**3**) 5.90 (1 H, ²J_{1H} 2.46 Hz, ⁴J_{1H} 1 Hz, ³J_{SnH} 128/132 Hz), 5.39 (1 H, ²J_{1H} 2.46 Hz, ⁴J_{1H} 1 Hz, ³J_{SnH} 60.5/63.5 Hz) 4.76 (1 H, ⁴J_{2H} 1 Hz, ³J_{SnH} 38 Hz).

¹¹⁹Sn NMR data (C₆D₆/Me₄Sn) *E*-(**2**) = -46.4 ppm, *Z*-(**2**) = -60.6 ppm, (**3**) = -46.1 ppm.

Cross-coupling Reactions—All these reactions were conducted under an inert atmosphere (N₂) from 10 mmol of organotin reagent using conventional experimental conditions for palladium-promoted cross-coupling reactions of vinyltins with organic halides.¹⁶

Transmetalation Reactions with BuLi or Bu₂CuCNLi₂.—These reactions were achieved under an inert atmosphere (dry

nitrogen) in a Schlenk reactor from 10 mmol of organotin reagent in 70 ml of the appropriate solvent. Quenching of the vinyl anion was subsequently achieved by addition of the electrophile (10 mmol in 10 ml of solvent) using the above mentioned experimental conditions (*c.f.* details on the reaction schemes).

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Paper 9/04015C

Received 22nd May 1989

Accepted 4th August 1989