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# AN EFFICIENT ACCESS TO HOMOALLYL AND HOMOCINNAMYL SKELETONS USING 1-TRIBUTYLSTANNYL-4,4-DIETHOXY-BUT-1-ENE

Jean-Luc PARRAIN[a], Alain DUCHENE[b] and Jean-Paul QUINTARD[a]

*a) Laboratoire de Synthèse Organique associé au CNRS, Faculté des Sciences et des Techniques de NANTES, 2 rue de la Houssinière 44072 NANTES - Cedex 03 . (France).*

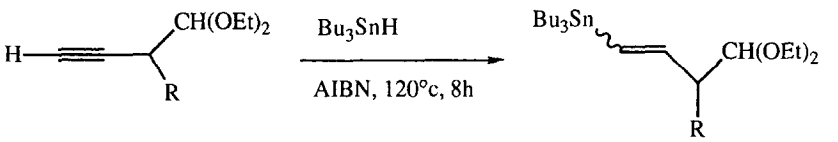
*b) Laboratoire de Synthèse Organique, Faculté des Sciences de TOURS, Parc de Grandmont, 37200 TOURS . (France).*

**Summary :** The easily prepared and stored 1-tributylstannyl-4,4-diethoxy-but-1-ene reacts like a usual vinyltin (unaffected by the presence of the acetal function) allowing easy transfer of the functionally substituted butenyl unit onto miscellaneous substrates via palladium promoted cross-coupling reactions or after transmetallation with butyllithium or high order cyanocuprates.

Vinyltin reagents have been proved to be efficient tools for the transfer of a vinyl unit with a high tolerance for numerous functionalities both on the substrate and on the reagent [1,2]. As the carbonyl group and its protected forms can be considered as key functions for multistep syntheses, it is of interest to offer to the practitionist new organotin reagents useful for the transfer of an hydrocarbon chain bearing a protected carbonyl group on miscellaneous substrates.

Until now, the more significant efforts in these series have been related to species able to transfer an "umpolung" unit of $d^1$ or $d^3$ type in order to achieve key steps in organic syntheses. α-Stannylethers [3-7], α-stannylacetals [8,9], and acyltins [10,11] have been used as $d^1$ species while the $d^3$ type synthons are often α-alkoxyallytins [12-14]. However, in this series, the use of functionally substituted vinyltins has brought some improvements because of their higher stability and we have recently proposed γ-silylated-γ-methoxypropenyltributyltin as a homoenolate equivalent [15] and 1-tributylstannyl-3,3-diethoxy-prop-1-ene as a storable β-formylvinylanion equivalent [16]. In the present paper, we wish to demonstrate that the usefulness of functionally substituted vinyltin reagents is not limited to the "umpolung" reagents area and we have focussed our interest on vinyltins reagents bearing a homoallylic acetal function in order to obtain the corresponding homoallylic acetals or aldehydes.

The organotin precursors required for such a purpose must be easily obtained and, indeed, the hydrostannation of the suitable alkynes (easily prepared via reaction of allenyl-aluminium bromides with orthoformates [17]) constitutes an efficient preparation :




**1a** (R=H)

**1b** (R=Me)

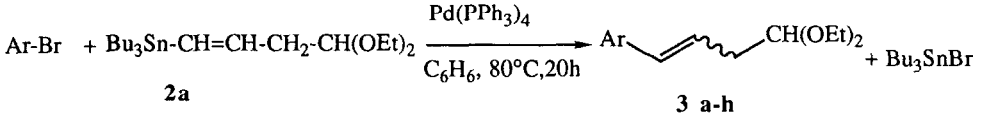
**2a** ( R=H, 90% yield, E/Z=85/15)

**2b** ( R=Me, 82% yield, E/Z = 88/12 )

## Results

Cross-coupling reactions :

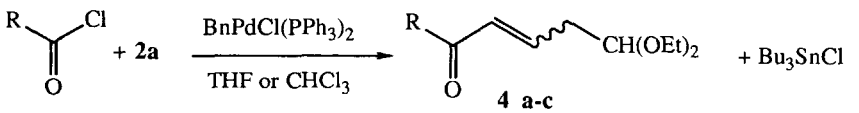
The exploration of the behaviour of **2a** has been examined in the case of cross-coupling with organic halides under palladium complexes catalysis (cf. table). With aryl or heteroaryl bromides, good yields were obtained under $Pd(PPh_3)_4$ catalysis in agreement with the results observed for other vinyltins [1,18-20]:




**2a** **3 a-h**

It is worth noting the good yields obtained with bromopyridines under mild experimental conditions (**3f**, **3h**). Furthermore, it must be stressed that cinnamyl metal reagents usually give rearranged structures or mixtures of regioisomers instead of the pure homocinnamyl derivatives when they are allowed to react with orthoformates [21].

When the cross coupling was attempted with acyl chlorides using benzyl-chloro-bis(triphenylphosphine) palladium (II) as catalyst and chloroform or tetrahydrofuran as solvent (as in previous reports for other vinyltins[1]), high yields in the expected products were obtained without the interference of a side reaction between the acyl chloride and the acetal function.(These results must be compared with the difficulties encountered when the organotin reagent contains an allylic acetal group [16]).



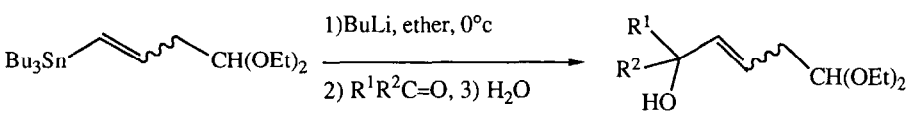

**4 a-c**

Due to the high yields obtained in these cross-coupling reactions and to the tendancy of vinyltins to react with retention of configuration [1,2], the stereochemistries of the compounds **3a-h** and **4a-c** roughly reflect the stereochemistry of **2a** (E/Z ~ 85/15). However, in the case of the cross-coupling of **2a** with p-toluenesulfonylchloride in the presence of $Pd(PPh_3)_4$, only the *trans* sulfone **5** is obtained in agreement with a recent report [22].

These few results demonstrate the efficiency with which **2a** obtains the homocinnamyl skeleton in a clean fashion and more generally transfers the $d^4$ buten-3-al diethylacetal synthon onto miscellaneous substrates. One can reasonably expect a similar reactivity for **2b** which might be a valuable tool for the synthesis of terpenic derivatives.

Transmetallation reactions

Since SEYFERTH's initial reports, the usefulness of vinyltins as precursors of vinyllithiums [2,23] has been well known. With compound **2a** , the transmetallation with n-butyllithium occurs readily in ether, allowing the new vinyllithium to be subsequently trapped by electrophiles, for instance :

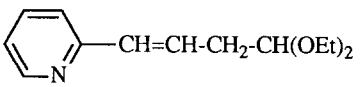
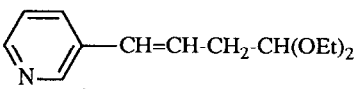
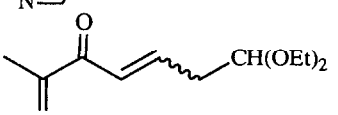
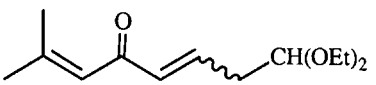
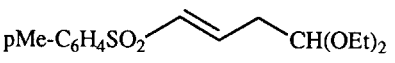



**2a** **6 a-c** (E/Z = 85/15 )

**6a** : $R^1$ = H, $R^2$ = Ph (75%) ; **6b** : $R^1$ = Me,$R^2$ = Ph (68%) ; **6c** : $R^1$=$R^2$ = Et (72%)

However, it is worth noting that vinyllithium reagents are strong bases and, as such, highly reactive with numerous functional groups. The transmetallation with softer reagents, such as high order cyanocuprates according to LIPSHUTZ procedure [24] affords vinylcyanocuprates under mild experimental conditions.

**Table : Cross-coupling of 2a with Organic halides**

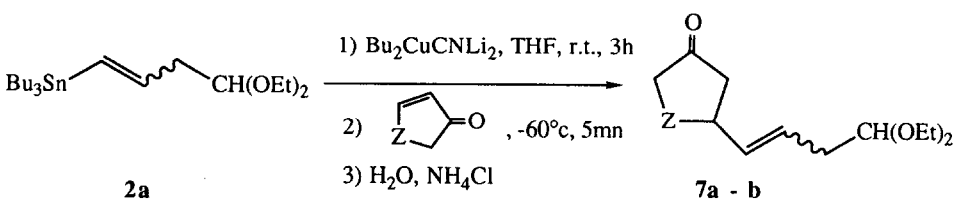
| Organic halides | Experimental conditions (a) | Products (b) | N° | Yields (c) |
|---|---|---|---|---|
| PhBr | A | Ph-CH=CH-$CH_2CH(OEt)_2$ | **3a** | 75 (85) |
| pF-$C_6H_4$Br | A | pF-$C_6H_4$-CH=CH-$CH_2CH(OEt)_2$ | **3b** | 60 (69) |
| pMeO-$C_6H_4$Br | A | pMeO-$C_6H_4$-CH=CH-$CH_2CH(OEt)_2$ | **3c** | 55 (61) |
| pAc-$C_6H_4$Br | A | pAc-$C_6H_4$-CH=CH-$CH_2CH(OEt)_2$ | **3d** | 78 |
| pHCO-$C_6H_4$Br | A | pH-CO-$C_6H_4$-CH=CH-$CH_2CH(OEt)_2$ | **3e** | 85 |
| 2-bromopyridine | A |  | **3f** | 88 (98) |
| 3-iodopyridine | A |  | **3h** | 65 |
| $CH_2$=CMe-COCl | B |  | **4a** | 80 |
| $Me_2C$=CH-COCl | B |  | **4b** | 85 |
| Ph-COCl | B' |  | **4c** | 81 |
| pMe-$C_6H_4SO_2Cl$ | C |  | **5** | 85 |

(a) The reactions were conducted under nitrogen using 1.1 eq of **2a** (E/Z=85/15,4.77g) for 1 eq of halide. A = sealed tube, benzene 80°C, 2% $Pd(PPh_3)_4$, 20h ; B = 2% $BnPdCl(PPh_3)_2$, $CHCl_3$, 65°C, 17h ; B' = same conditions but with THF as solvent ; C = 2% $Pd(PPh_3)_4$, THF, 55°C, 30mn.

(b) mixture of isomers E/Z ~ 85/15 excepted for **5** (100% E): physicochemical data (i.r, m.s., $^1H$ and $^{13}C$ n.m.r.) are consistent with the above mentionned structures.

(c) isolated yields ; values in brackets are conversion rates (n.m.r. evaluation).

These new reagents are very efficient tools for achieving 1,4-addition on α-β enones, for instance :




**2a** **7a - b**

( **7a** , Z = $CH_2$, 82 % ; **7b** , Z = $CH_2$-$CH_2$ , 75 % )

In this last example, the nature of the entering vinyl unit (homoallylic acetal function) can formally provide a common precursor for prostaglandin analogues bearing a homoallylic hydroxy group on the β-chain (compounds of this type have been already proposed as ulcer inhibitors, hypotensives or vasodilatators [25,26]).

In conclusion, 1-tributylstannyl-4,4-diethoxy-but-1-ene **2a** and its analogue **2b** are readily prepared, easily stored organotin precursors, useful for the transfer of a homoallylic acetal (or its derivatives) onto miscellaneous substrates under mild experimental conditions. We are currently developping our research to evaluate the potential of this type of reagents for the synthesis of unusual terpenes and prostaglandin analogues.

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