The Stannyl–Cupration of Acetylenes and the Reaction of the Intermediate Cuprates with Electrophiles as a Synthesis of Substituted Vinylstannanes

Asunción Barbero,[a] Purificación Cuadrado,[a] Ian Fleming,[b] Ana M. González[a] and Francisco J. Pulido*[a]

[a] Departamento de Química Orgánica, Universidad de Valladolid, 47011-Valladolid, Spain
[b] University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK

Stannyl–cupration of acetylenes followed by electrophilic attack with a variety of electrophiles gives vinylstannanes.

The stannyl–cupration of acetylenes was discovered ten years ago, when Piers and his co-workers found that a trimethyl-stannyl–copper[1] or cuprate[2] reagent added to acetylenic esters. Since then he, and others,[3–6] have found that stannyl-copper reagents and stannyl–cuprates also add to simple alkyl-substituted acetylenes.[3] However, a major limitation of these otherwise powerful reactions has been the difficulty in persuading the vinyl-copper or vinyl-cuprate intermediate to react with anything more interesting than a proton. The problem appears to be that the stannyl–cupration step, although well to the right at equilibrium, is easily reversible,[4] and the stannyl-copper reagent itself is more reactive towards most electrophiles than the vinyl-copper intermediate is. Stannyl-copper and cuprate reagents are not very basic, with the result that a proton, usually delivered from methanol included in the reaction mixture, is relatively selective for the vinyl-copper intermediate, making the formation of the addition product high yielding. The only successes in achieving more substantial reactions have been (i) with an acetylenic ester carrying an internal alkyl halide electrophile;[1,2] (ii) with methylation, allylation and propynylation, in the presence of hexamethylphosphoramide (HMPA), of an acetylenic ester carrying a β-siloxymethyl substituent treated with a mixed higher-order cyanothiophenyl-trimethylstannyl cuprate reagent,[2] and (iii) with methylation, allylation and ethynylation, again in the presence of HMPA, of acetylene itself treated with a triphenylstannyl-copper or cuprate reagent.[5] It is not clear how general these reactions are. The usual solution to
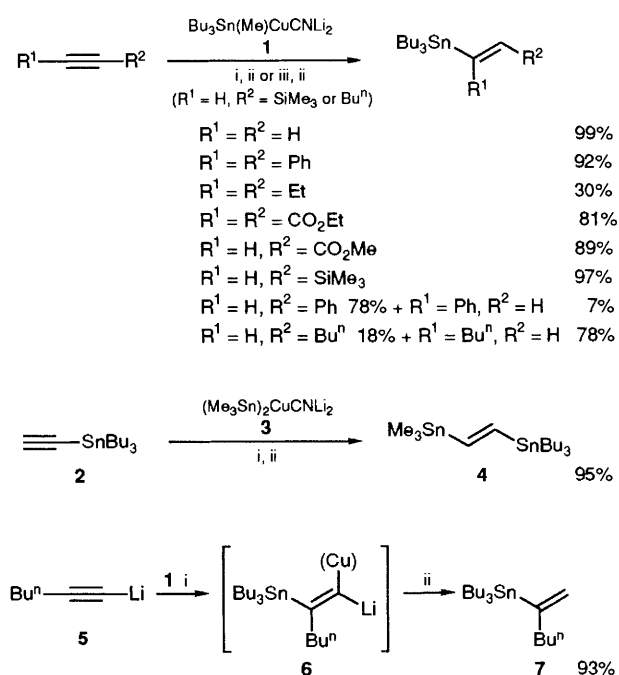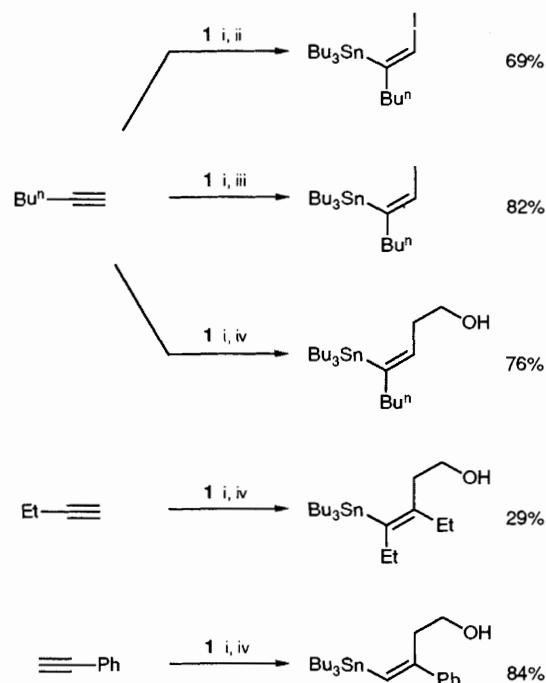

Scheme 1 Reagents and conditions: i, −78 to 0 °C; ii, NH₄Cl; iii, −78 °C
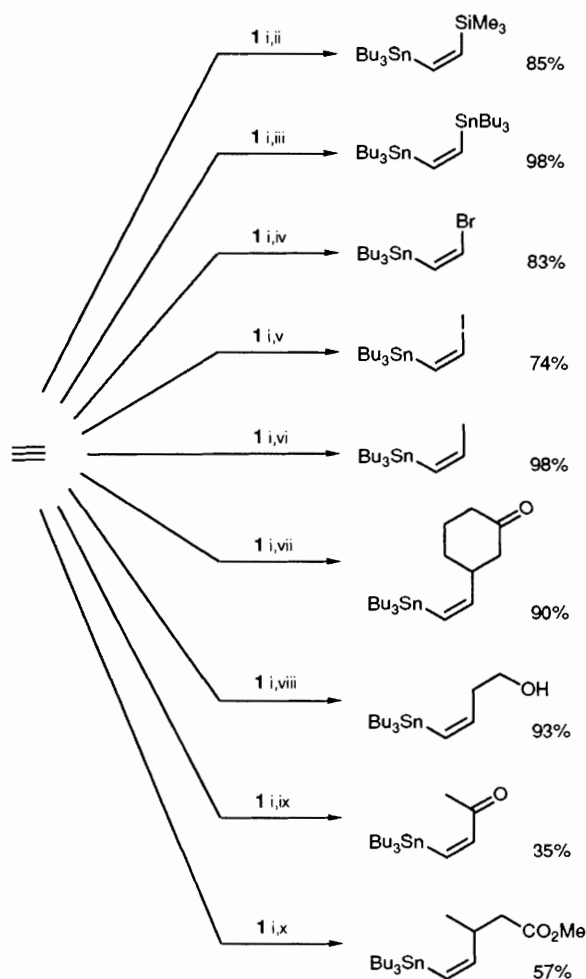
Scheme 2 *Reagents and conditions*: i, THF, −78 °C; ii, Me₃SiCl, −78 to 0 °C; iii, Bu₃SnCl, −78 to 0 °C; iv, Br₂ −78 to 0 °C; v, I₂, −78 to 0 °C; vi, MeI, −78 to 0°; vii, cyclohexenone, −78 to 0 °C; viii, ethylene oxide, −78 to 0 °C; ix, AcCl, −78 to 0 °C; x, MeCH=CH-CO₂Me, −78 to 0 °C

Scheme 3 *Reagents and conditions*: i, −78 °C; ii, I₂, −78 to 0 °C; iii, MeI, −78 to 0 °C; iv, ethylene oxide, −78 to 0 °C

the problem has been to use copper or palladium to *catalyse* the addition of the tin and another main-group metal, such as boron, aluminium, magnesium or zinc, across the triple bond.[7] The other main-group metal can then be replaced in a second step by a variety of electrophiles. Another solution is the addition of *two* trimethyltin groups across the triple bond, with selective replacement of one or both of them by tin–lithium exchange followed by treatment with carbon electrophiles.[8] A third solution is simply to use a large excess of the stannyl–cupration product to make the yield based on the electrophile high.[9]

We have been using the mixed higher-order cyano-methyl-tributylstannyl cuprate 1[6,10] on some simple acetylenes, working up with a proton source in the usual way, to make unexceptionally a number of potentially useful small synthons (Scheme 1). The only complications were that the stannyl-acetylene 2 did not react with the mixed cuprate 1, but did with the bis(trimethyl)stannyl cuprate 3, and the reaction with hex-1-yne was not very regioselective, as expected by analogy with Piers' work. We find that high regioselectivity in the same sense, giving the 2-stannylated hex-1-ene 7, can be achieved, without necessarily committing oneself to a proton electrophile, by carrying out the addition of the stannyl–cuprate 1 to the corresponding lithium acetylide 5, with reaction presumably taking place by way of the three times over differentially metallated alkene 6.

More significantly, we now report that we have easily achieved the successive addition of a stannyl–cuprate and carbon and other electrophiles to unactivated acetylenes. Thus the mixed cuprate 1 reacts with acetylene itself, and the intermediate cuprate reacts well with trimethylsilyl chloride, tributyltin chloride, bromine, iodine, methyl iodide, cyclohexenone and ethylene oxide (Scheme 2) and moderately well with methyl crotonate and acetyl chloride. HMPA was not used in any of these reactions. The reaction is not, however, limited to acetylene itself—the mixed cuprate also reacts with hex-1-yne, and the intermediate vinyl-cuprate can be trapped with iodine, methyl iodide and ethylene oxide (Scheme 3). Hex-3-yne and phenylacetylene also react, and in both cases the intermediate reacts with ethylene oxide as a representative carbon electrophile. The regiochemistry shown by phenylacetylene, in the reactions in Schemes 1 and 2, is that expected by analogy with the catalysed reactions.[7] It is clear that stannyl–cupration is not limited merely to the addition of tin and a proton across a triple bond, powerful though that reaction is already.[11] We note in particular that between the reactions in Schemes 1 and 2, we now have easy methods for preparing both *E*- and *Z*-2-silylvinylstannanes, and *E*- and *Z*-vinylbisstannanes.

We are unclear why we have been able so easily to overcome the limitations experienced by others, but most probably it is connected with the fact that we have used a cuprate, where earlier work has most often been carried out using stannyl–copper reagents. It is significant that Piers used a cuprate in the only reactions in which he was able to achieve intermolecular reaction with carbon electrophiles, although in his case he needed HMPA, and still found substantial amounts of protonation.[2] What is clear is that it is not just the fact that we have usually used a mixed cuprate, for we find that the corresponding bistributylstannyl cuprate behaves very similarly in several of these reactions, and we have also found that the carbon ligand can equally well come from butyllithium as from methyllithium. We note also, that after submission of this manuscript, two papers reporting stannyl–cuprate additions to 3,3-diethoxypropyne and subsequent reaction with electrophiles have appeared.[12]

The following is a general recipe. Methyllithium (1.25 cm^3 of a 1.6 mol dm^{-3} solution in diethyl ether, Merck) was added by syringe to a solution of tributylstannyllithium [2 mmol, prepared from hexabutylditin (Aldrich) and butyllithium (Carlo-Erba) in dry tetrahydrofuran (THF) (2 cm^3), following Still[13] at −20 °C and the mixture stirred for 2 min. This mixture was added by syringe to a stirred suspension of copper(I) cyanide (179 mg, 2 mmol, dried at 100 °C overnight, Fluka >99%) in THF (2 cm^3) at −20 °C and the resulting red–black solution (green–black when prepared from tributyl-tin chloride) stirred at this temperature for 15 min. The mixture was cooled to −78 °C and the acetylene (2 mmol, from a balloon or by syringe) added, followed, after 30 min, by the neat electrophile (2 mmol usually, 4 mmol for ethylene oxide, 10 mmol for methyl iodide). After 15 to 30 min, the mixture was allowed to warm to 0 °C, and held at that temperature for 1 h before being quenched with ammonium chloride solution. In view of the recent report[14] that stannyl–cupration of acetylenes does not take place below −35 °C, we checked that our solution had not in fact warmed up to this temperature before we had added the electrophile; the temperature in the flask did not rise above −67 °C. We conclude that, in our conditions at least, the stannyl–cupration must have taken place below this temperature, since the stannyl–cuprate, if there were any still in the reaction mixture when the electrophile was added, would surely have reacted with most of the electrophiles before it reacted with the acetylene.

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