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Cobalt-catalysed synthesis of highly substituted styrene derivatives *via* arylzincation of alkynes†

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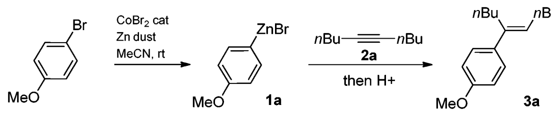
A new two-step procedure was developed by carbozincation of internal and terminal alkynes to synthesise highly functionalised vinylzinc bromides. Various tri and tetrasubstituted alkenes were prepared in moderate to good yields under mild reaction conditions in a stereo-selective manner. This methodology represents an interesting alternative to previously known methods.

Among all the routes to alkenes, few are as convenient as carbometallation reactions.[1] These reactions allow direct formation of stereodefined tri- and tetrasubstituted alkenes in a minimum number of steps which is still very difficult to achieve. Among those, carbozincation is especially useful, as organozinc reagents are readily accessible, as well as very tolerant towards functional groups. In addition, carbozincation of internal alkynes is always *syn*-selective.[1e] Although addition of organozinc to activated alkynes has been well studied,[2–5] a single and elegant report of cobalt catalysed arylzincation of unactivated alkynes exists.[6] However, the methodology proposed relies on a activated substrate (*e.g.* aryl iodide) and tight temperature control for the synthesis of the arylzinc species, as well as a change of solvent between the synthesis of the arylzinc (conducted in THF) and the carbozincation itself, which has to be conducted in acetonitrile to occur. Recently, Yoshikai *et al.*[7] showed that, under different conditions, arylzinc species could be added across triple bonds, but instead of furnishing the expected vinylzinc species, the metal was transferred back to the *ortho* position of the aromatic group. As our group has already reported, the synthesis of the arylzinc species is possible in acetonitrile, under cobalt catalysis, from the cheaper aryl bromides.[8] In addition, we have been interested in the formation of styrene derivatives through cobalt-catalysed cross-coupling reactions of aryl halides with vinylic substrates.[9] The aforementioned report[6] spurred us to investigate the possibility for the arylzinc synthesised under cobalt catalysis to react with alkynes to afford trisubstituted vinylzinc species, which could then react with various electrophiles, in a simple "bench-friendly" manner.



Scheme 1 Cobalt-catalysed arylzincation of 5-decyne.

We first investigated the possibility of a one-pot procedure allowing the carbometallation to directly take place in the same pot as the formation of the arylzinc bromide (Scheme 1). However, although the desired carbometallation product was formed at room temperature, the yield was severely limited by the formation of an untractable mixture of products incorporating several alkene moieties (Table 1, entry 1). Changing the conditions for the formation of the arylzinc bromide barely improved the yield, and the amount of unseparable byproducts remained high (Table 1, entry 2).

Filtration of the medium, by eliminating the excess metallic zinc, allowed the reaction to occur with slightly improved yield and rate (Table 1, entry 3). The use of an easily synthesised and shelf-stable preformed $CoBr_2$(bipy) complex instead of the simple $CoBr_2$ allows the rapid formation of the arylzinc bromide under the same conditions. Moreover, the amount of unidentifiable-products detected by GC analysis (Table 1, entry 4) is lower in this case. Additionally, the yield increases with simple filtration of the arylzinc compound by avoiding the rapid cyclotrimerisation of the alkyne (Table 1, entry 5). Under these last conditions, 3 equivalents of arylzinc species, instead of 2 or 4, were necessary to limit the amount of by-products (entries 6 and 7).

With these results in hand, the scope of the arylzincation was then examined with various arylzinc species and alkynes (Scheme 2) and results are reported in Table 2.

Table 1 Cobalt-catalysed arylzincation of 5-decyne: optimization of the reaction conditions

Entry	[Co]	Zn (equiv.)	Ligand	Alkyne added (equiv.)	Filtration	Yield[a]
1	13%	2.6	None	0.33	No	53%
2	10%	2	None	0.33	No	55%
3	13%	2.6	None	0.33	Yes	57%
4	10%[b]	2	Bipy	0.33	No	59%
5	10%[b]	2	Bipy	0.33	Yes	75%
6	10%[b]	2	Bipy	0.25	Yes	53%
7	10%[b]	2	Bipy	0.5	Yes	49%

[a] GC yield *vs.* decane as internal standard. [b] Preformed $CoBr_2$(bipy) was used.

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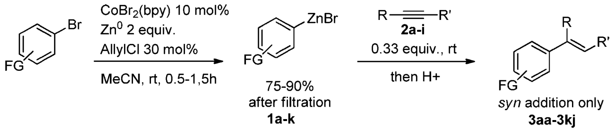


Scheme 2 Reaction scope under the optimized conditions.

Internal symmetrical alkynes reacted well under the optimized conditions, with electron-neutral, -rich, or -poor arylzinc bromides, affording the desired isolated trisubstituted alkenes in good yield after hydrolysis (Table 2, entries 1–4).

Various functional groups were well tolerated on both partners: nitrile (entries 3, 10 and 11), ester (entries 4, 8 and 15), methoxy (entries 2 and 11), fluoride (entry 9), methyl (entries 10 and 11), chloride (entries 6, 13 and 14), trifluoromethyl (entries 10 and 15), methylsulfanyl and methyl sulfone (entry 13). In contrast to previous reports,[6] sterically hindered alkynes could also react: while an isopropyl group failed to impose a significant regioselectivity (entry 6), a tertiobutyl group oriented the reaction effectively, affording a single isomer in useful yield (entry 7). On the other hand, *ortho*-substituted arylzinc bromides did not react (entry 5). When the alkyne was a phenylacetylene derivative, the reaction was generally high yielding and always chemoselective, affording a single isomer, where the zinc was introduced solely at the benzylic position. Steric hindrance on the aryl group (entry 10), electron-rich (entry 11) and -poor aromatic groups (entries 13 and 15) and heteroaromatic substituents (entry 14) were well tolerated on the alkyne. Even a challenging substrate, bearing both an electron poor aromatic group and a bulky substituent, afforded the desired product in acceptable yield in 5 h. However the temperature had to be raised to 50 °C (entry 15). Phenylacetylene could also be made to react under those conditions, to afford the corresponding *trans*-stilbene in moderate yield (entry 16).

Finally, we tried to functionalise the newly-formed vinylzinc compound with various electrophiles (Scheme 3). This organometallic species could react almost quantitatively with molecular iodine to afford the vinyl iodide in good isolated yield. It could also be made to react under Negishi-type cross-coupling conditions,[10] to afford the tetrasubstituted alkene in good yield, in a single pot, two-step procedure, from a simple alkyne.

In conclusion, we have managed to devise a new set of conditions to allow the synthesis of tri and tetrasubstituted alkenes from internal and terminal alkynes, under cobalt catalysis. The catalyst used for both the synthesis of the arylzinc species and the carbometallation reaction is an easily synthesised and shelf-stable $CoBr_2$(bipy) complex. The conditions for both steps are very simple, and do not necessitate

Table 2 Scope of arylzinc bromides and alkynes

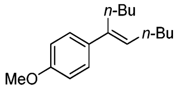
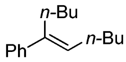
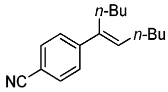
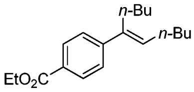
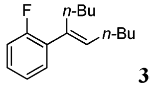
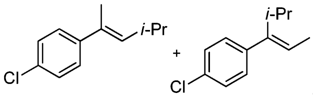
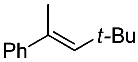
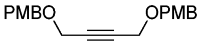
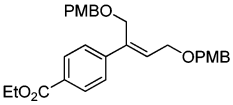
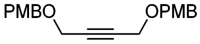
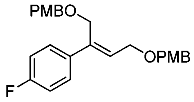
Entry	ArZnBr FG	Alkyne	Product	Time (h)	Yield^a (%)
1	4-OMe **1a**	n-Bu—≡—n-Bu **2a**	 **3aa**	0.5	73
2	H **1b**	n-Bu—≡—n-Bu **2a**	 **3ba**	0.5	76
3	4-CN **1c**	n-Bu—≡—n-Bu **2a**	 **3ca**	1.5	69
4	4-EtO$_2$C **1d**	n-Bu—≡—n-Bu **2a**	 **3da**	1.25	71
5	2-F **1e**	n-Bu—≡—n-Bu **2a**	 **3ea**	24	nd
6	4-Cl **1f**	—≡—i-Pr **2b**	 **3fb+3fb’**	2	61^b
7	H **1b**	—≡—t-Bu **2c**	 **3bc**	1.5	56
8	4-EtO$_2$C **1d**	 **2d**	 **3dd**	1.5	70
9	4-F **1g**	 **2d**	 **3gd**	0.75	76

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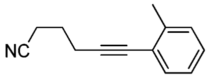
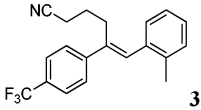
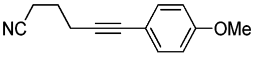
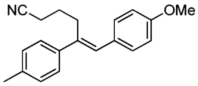
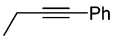
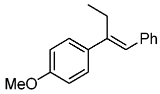
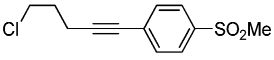
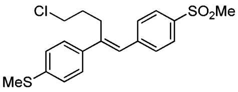
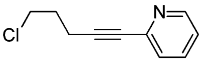
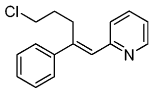
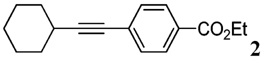
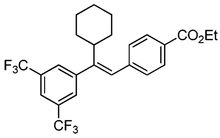
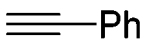
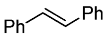
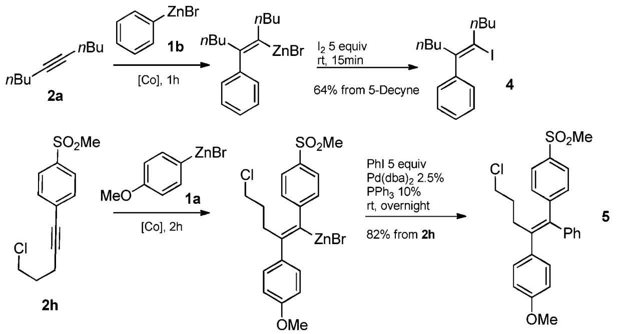
Table 2 (*continued*)

Entry	ArZnBr FG	Alkyne	Product	Time (h)	Yield[a] (%)
10	4-CF_3 **1h**	 **2e**	 **3he**	1	82
11	4-Me **1i**	 **2f**	 **3if**	1	73
12	4-OMe **1a**	 **2g**	 **3ag**	1	80
13	4-SMe **1j**	 **2h**	 **3jh**	2.5	91
14	H **1b**	 **2i**	 **3bi**	4	77
15	3,5-DiCF_3 **1k**	 **2j**	 **3kj**	5	48[c]
16	H **1b**	 **2k**	 **3bk**	0.75	63

[a] Isolated yield. In all cases the *E* : *Z* ratio was >99 : 1 in favor of the depicted isomer (only one isomer detected by GC and ^{1}H NMR). [b] Regioselectivity: 6 : 4 (**3fb**/**3fb′**). [c] Reaction at 50 °C.



Scheme 3 Post-functionalisation of the vinylzinc.

tight temperature control, distilled solvents, or any other particular precautions, making this methodology an interesting tool for the selective synthesis of alkenes. Further investigations are being conducted in our laboratory as to the characteristics and use of the $CoBr_2$(bipy) complex for arylzinc synthesis and reactivity, as well as other reactions.

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