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New Allene Synthesis via Carbocupration–Zinc Carbenoid Homologation and β-Elimination Sequence

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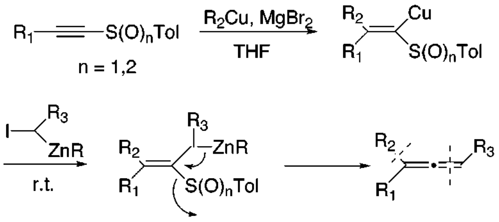
ABSTRACT



Polysubstituted propadienes are obtained in good to excellent yields by the consecutive carbocupration–homologation–β-elimination reactions on the easily accessible alkynyl sulfoxides or sulfones. This one-pot reaction also allows the preparation of functionalized allenes.

One of the most popular methods for the synthesis of allenes is the reaction of propargylic derivatives with organometallic reagents, especially organocopper reagents.[1] Since the first report by Crabbe et al.,[2] many authors have used modified organocopper reagents, with stoichiometric or catalytic amounts of copper salt.[3] The propargylic substrate itself varies from ethers[4] and epoxides[5] to various esters of more or less reactivity.[6] The stereochemistry of the formal 1,3-substitution reaction depends on the organometallic reagent (and also on its halide),[7] on the solvent, and on the type of leaving group.[8] However, in many cases, the synthesis of substituted allenes has proven difficult and these previously cited methods can lead to mixtures of desired allenes

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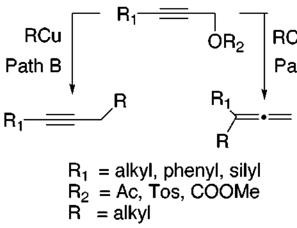
contaminated with the corresponding acetylenes. For example, the unequivocal preparation of 1,1-disubstituted propadienes[9] (terminal allenes) still remains difficult since the reaction of organocopper species can proceed either via an S_N2 (Scheme 1, path B) or an S_N2' process (Scheme 1, path A).[10] Several factors can influence this distribution,[11] and as a consequence, a mixture of isomers is generally formed, which leads to some tedious separations.

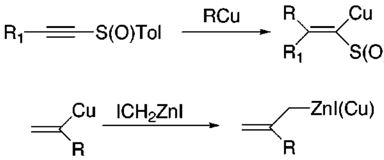
Scheme 1



In this Letter, we would like to report a fundamentally different approach for the synthesis of polysubstituted allenes (including terminal allenes) which avoids the possible formation of alkynes (via the S_N2 process, path B, Scheme 1).

When monoalkylcopper reagents are added to α,*β*-acetylenic sulfoxides, the *β*-alkylated α,*β*-ethylenic sulfoxides are formed with an exclusive *cis* stereoselectivity and in quantitative yields (Scheme 2).[12] It is also known that the homologation reactions of alkenyl copper with (iodomethyl)zinc iodide[13] ($(ICH_2)ZnI$) or bis(iodomethyl)zinc ($(ICH_2)_2Zn$, **1)**[14] represent a powerful tool for the conversion of alkenyl copper derivatives into allylic-zinc or -copper compounds (Scheme 2).[15]

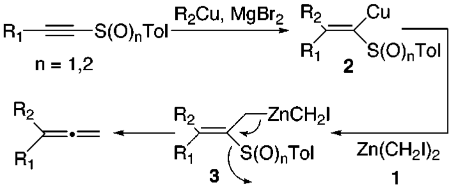
Scheme 2



However, this reaction has to be performed in the presence of an electrophile such as an aldehyde since the allylic species would undergo a further reaction with the carbenoid leading to a doubly homologated product. Interestingly, the corresponding reaction with secondary zinc carbenoid is not known, and except for the cyclopropanation of alkenes,[16] the use of secondary zinc carbenoid in organic synthesis is still in its infancy.

Therefore, we reasoned that the combined reaction—carbocupration of alkynyl sulfoxide and then homologation of the resulting vinyl copper with zinc carbenoid—can result in the formation of an allyl zinc derivative which will undergo *β*-elimination[17] to furnish a substituted allene as described in Scheme 3. We first tested this new strategy by using the well-known bis(iodomethyl)zinc derivative **1** for the synthesis of 1,1-disubstituted propadienes.

Scheme 3



We indeed found that organocopper reagent (generated by the addition of 1 equiv of RMgBr to 1 equiv of CuBr in THF) added quantitatively to the alkynyl sulfoxide ($n = 1$, Scheme 3) to give the vinyl organocopper derivative **2**. Upon addition of bis(iodomethyl)zinc derivative **1**, prepared by the treatment of Et_2Zn with CH_2I_2 in THF at 0 °C for 0.5 h, vinyl copper derivative **2** underwent homologation followed by spontaneous *β*-elimination[18] in less than 10 min at room temperature. The scope of this reaction is broad as described in Table 1. Primary (Me, Bu, and Oct, entries 1, 2, and 6) as well as secondary (entry 3) and even tertiary alkyl groups (entry 4) add cleanly to alkynyl sulfoxides and then lead to

Table 1. Synthesis of 1,1-Disubstituted Propadienes

entries	R_1	R_2	*n*	allenes	yield,[a] %
1	Hex	Me	1	**4**	75
2	Hex	Bu	1	**5**	80
3	Hex	i-Pr	1	**6**	65
4	Hex	t-Bu	1	**7**	50
5	Hex	Ph	1	**8**	95
6	Bu	Oct	1	**9**	80
7	Bu	Oct	2	**9**	85

[a] Isolated yield after purification on silica gel.

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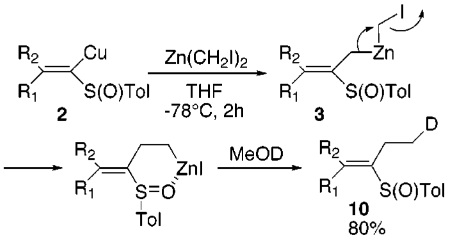
the expected allenes in good yields (the yield is slightly decreasing when the substitution of the organocopper is increasing). When the homologation described in entry 6 was performed with iodomethylzinc iodide instead of bis(iodomethyl)zinc, **1**, the yield of **9** is slightly lower (70%). Arylcopper also reacted to give the corresponding allene in excellent yield (entry 5).

It is interesting to note that although methyl and phenyl copper are known to be sluggish in the carbocupration reaction of alkyne, the activation of the sulfoxide moiety allowed these additions in excellent yields.

In all cases, no trace of any isomeric product was detected (no other nonpolar products), which leads to a very easy final purification. Even alkynyl sulfones furnished allenes in excellent yield by the carbocupration−homologation−β-elimination sequence (entry 7, Table 1). Although alkynyl sulfides[19] and alkynyl phosphonates[20] also underwent the carbocupration reaction, no homologated—or allene—products were detected.

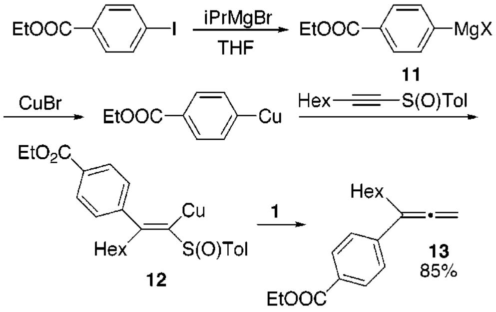
The homologation step (**2** to **3**, Scheme 3) has to be performed at room temperature since at lower temperature the allylic organometallic **3** underwent a second homologation reaction with the carbenoid **1** according to Scheme 4.[21]

Scheme 4



The presence of an organometallic derivative was proved by the isolation of **10** after the reaction was quenched with MeOD. The recently reported iodine−magnesium exchange reaction for the preparation of functionalized magnesium reagent[22] also enhances the scope of the synthesis of 1,1-disubstituted propadiene. Indeed, treatment of ethyl 4-iodobenzoate with *i*-PrMgBr leads to the corresponding functionalized arylmagnesium halide **11**. By a transmetalation reaction with copper salt, the organocopper was formed and added to the alkynyl sulfoxide as described in Scheme 5.

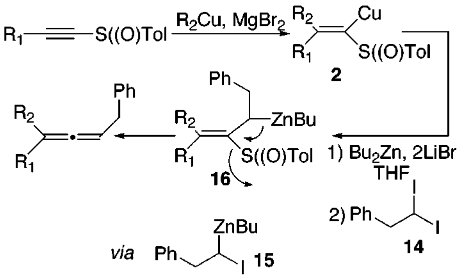
Scheme 5



This is the first example of a carbocupration reaction of an alkyne with a functionalized aryl derivative, which occurred quantitatively.[23]

Then, by addition of **1** at room temperature to the functionalized organocopper reagent **12**, the homologation−β-elimination occurred to give the expected allene **13** in 85% isolated yield (yield based on the starting ethyl 4-iodobenzoate after five consecutive steps, Scheme 5). Then, we wanted to apply our new strategy to the synthesis of 1,1,3-trisubstituted propadiene.[24] To do so, it was necessary to perform the homologation reaction with a secondary zinc carbenoid. However, as discussed previously, their uses in organic synthesis are mainly limited[25] to their in situ preparations for cyclopropanation reactions. Therefore, our strategy was designed in such a way that as soon as the secondary zinc carbenoid is formed in situ, it should react with the vinyl copper **2**. Indeed, we found that the successive addition of dibutylzinc—prepared by the reaction of ^{n}BuLi with $ZnBr_2$—followed by the addition of bisiodo alkane **14**[26] into the vinyl copper solution **2** at 20 °C gave the expected 1,1,3-trisubstituted allenes in excellent yield within 30 min as described in Scheme 6 , and the results are reported in Table 2.

Scheme 6



The plausible mechanism for this reaction is shown in Scheme 6. The in situ formed secondary carbenoid **15**—generated by the reaction between Bu_2Zn, 2LiBr, and **14**—reacted with the vinyl copper **2** to give the homologated

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Table 2. Synthesis of 1,1,3-Trisubstituted Propadienes

entries	R_1	R_2	allenes	yield,[a] %
1	Hex	Et	**17**	90
2	Hex	Ph	**18**	84
3	Hex	Bu	**19**	85
4	Bu	Et	**20**	80

[a] Isolated yield after purification on silica gel.

product **16**, as an unstable intermediate, which underwent an instantaneous β-elimination to furnish the corresponding allenes.

In conclusion, polysubstituted allenes were obtained in good to excellent yield by the consecutive carbocupration–zinc carbenoid homologation and finally β-elimination reactions on the easily accessible alkynyl sulfoxides or sulfones. This strategy also allowed for the preparation of functionalized allenes in a one-pot procedure.

Synthetic applications of the present methodology as well as new developments are in progress in our laboratory.

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Supporting Information Available: Experimental details and ^1H NMR and ^{13}C NMR spectra for compounds **4**–**10**, **13**, and **17**–**20**. This material is available free of charge via the Internet at http://pubs.acs.org.

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