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First Transfer of Chirality in the Fritsch-Buttenberg-Wiechell Rearrangement, via Zinc Carbenoids : A Migration with Retention of Configuration

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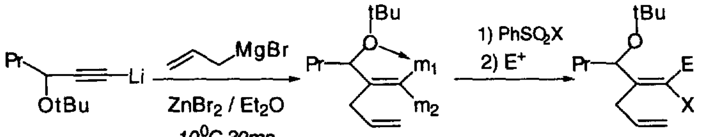
Abstract : Carbozincation of a metallated propargylic ether can lead to a gem bismetallic reagent with a good 1,3-diastereoselection. This latter can be relayed to a 1,4-diastereoselection, when the gembismetallic thus formed is monohalogenated to give a carbenoid which rearranges at room temperature.

Keywords :Zinc reagents ;rearrangements ;diastereoselection.

We have recently described a synthetically useful procedure for the stereoselective synthesis of polysubstituted olefins via the reaction of sp^2 organogembismetallics[1]. These 1,1-dianions can be used as a source of stereodefined polyhalogenated double bonds by sequential reaction with two different halogenating agents[2].



X = Cl, Br, CN, SPh
E = Br, I, D
1 X =Cl E = I

Scheme 1

A second possible reaction pathway of alkylidene carbenoids (or carbenes) has been known in the litterature since 1894, namely the Fritsch-Buttenberg-Wiechell[3] (FBW)[4] rearrangement. This rearrangement is known to be an efficient approach for alkyne synthesis[5] when the migrating group (R_1 or R_2) is a hydrogen[6a,b], an heteroatom [6c,d] or an aryl moiety [6e-i] (Scheme 2). The elegant labeling studies of Bothner-By[7a] and Curtin[7b] established that the rearrangement of a β,β-diarylvinyl halide with base is stereospecifically *trans* to the leaving group, thereby ruling out the involvement of the free carbene or carbenoid (Scheme 2). However, when R_1 and R_2 are alkyl groups, the yields in alkynes *are very low* (<10%) due to the competitive C-H insertion reaction to form cyclopentenes[8].

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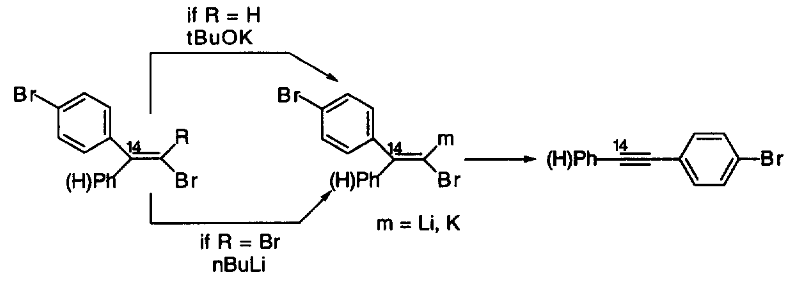
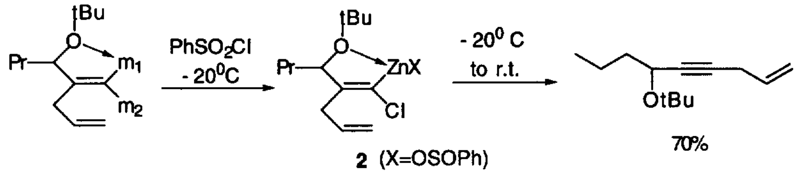


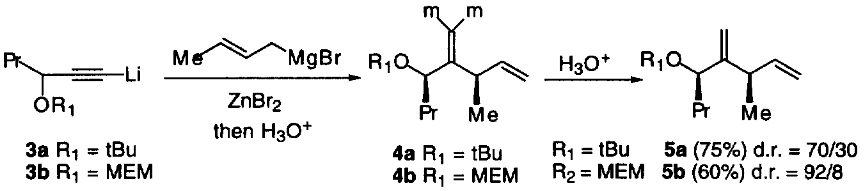
Scheme 2

During our studies on the reactivity of alkylidene zinc carbenoids **2**, we found that they are much more stable than their lithio[9], sodio or potassio analogs. Even more, their thermal decomposition above room temperature generates a clean rearrangement, which, to our knowledge, is the first FBW rearrangement of a zincated species to give the disubstituted alkyne in 70% yield (Scheme 3). The use of the zinc organometallic is compulsory for the obtention of good chemical yield in the FBW rearrangement. Indeed, when the same reaction is performed with the lithium carbenoid (generated from an iodine-lithium exchange on **1**, (Scheme 1, X = Cl, E = I), we obtained a complex mixture of products in which the alkyne is present *in less* than 10%.



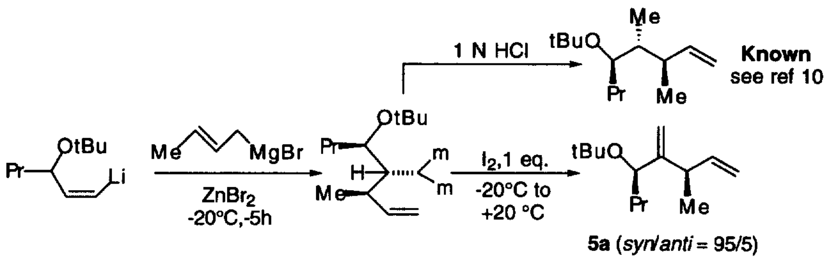
Scheme 3

Moreover, from our initial studies on the formation of sp^3 organobismetallic derivatives[10], the control of the metallotropic equilibrium of a substituted allylic organometallic[11] as well as its diastereofacial choice [11a,12] when this latter reacts with a vinyl metal can be achieved with a good diastereoselectivity. So, if we are able to control the diastereoselectivity of the carbometalation reaction of such allylmetals on the more challenging substituted *alkynyl* metal we should be able to obtain the corresponding vinyl gembismetallic reagents bearing two chiral moieties in allylic position, with a given relationship and hence, the corresponding carbenoids. The question of the fate of a chiral sp^3 carbon as a migrating group in the FBW rearrangement is then raised. In order to prepare the corresponding starting material, we considered the crotyl zincation of ethers **3a** and **3b** (Scheme 4).



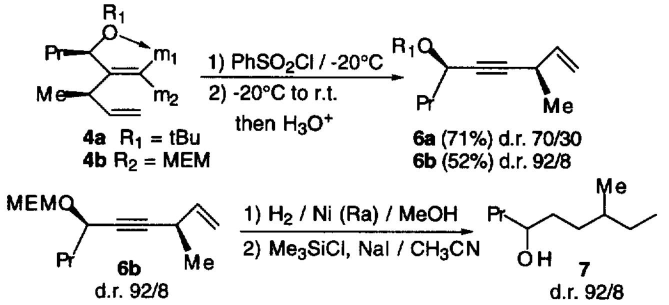
Scheme 4

Compound **3a** led to a mixture of **5a** *syn*/*anti* in a 70/30 diastereomeric ratio. The relative configuration of the major isomer **5a** was determined by comparison with authentic samples[10] as described in the following Scheme.



Scheme 5

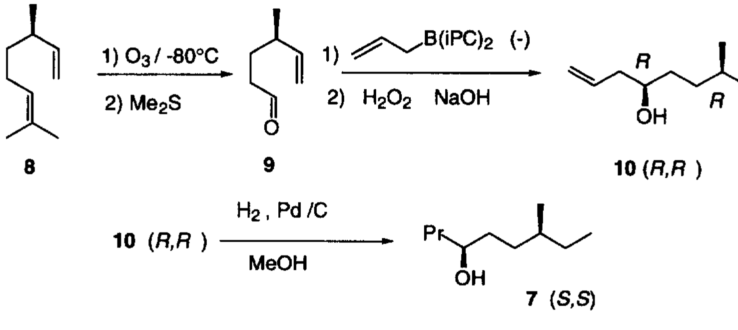
When the OtBu protection is replaced by a methoxyethoxymethyl ether (OMEM) as in **3b**, this diastereoselection is raised to 92/8 in 60% yield (Scheme 4). Now, when **4a** is treated by $PhSO_2Cl$, and then warmed from -20°C to room temperature, a clean rearrangement takes place (scheme 6) leading to enynether **6a**.



Scheme 6

The diastereomeric ratio of **6a** could not be evaluated from GLPC, ^1H or ^{13}C NMR, but its dicobalt hexacarbonyl complex[13] disclosed a 70/30 ratio of the two diastereomers : *i.e.* a ratio identical to that of **5a** *syn/anti*. Starting from **3b**, we also observed that the alcohol **7**, obtained by total hydrogenation of **6b** on Raney nickel, followed by deprotection with Me_3SiCl, NaI[14] displayed two ^{13}C NMR signals for the -CHOH-carbon corresponding to the 92/8 ratio present in diastereomers **6b**.

In order to know wether the migration had occurred with a total retention (or inversion) of configuration (whatever the migrating group is), we prepared the S,S isomer of **7** according to Scheme 7, from (R)-(-)-β citronellene **8**.



Scheme 7

Aldehyde **9** was submitted to an enantioselective allylboration reaction[15], which is known to deliver a major (R)-secondary alcohol **10** which was then hydrogenated to the S,S alcohol **7** corresponding to the major diastereomer obtained from **6b**. We can thus conclude that the FBW rearrangement occurs, via the zinc carbenoids[16], with a complete *retention of configuration* at the migrating carbon atom.

Reactions which involve a chirality transfer in alkyne synthesis and in the FBW rearrangement are unknown. The ease of preparation of the starting materials (propargylic ethers), combined with the convenience of this approach (one step-reaction for the formation of **6b** from **3b**), promises wide applicability of this new strategy. Efforts to further delineate the scope of this new chirality transfer associated with the alkyl group migration are being vigorously pursued.

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