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Reaction of 1-Iodoalkynes with Allylzirconiums: Generation of Alkylidene Carbenoid *via* Allylzirconation

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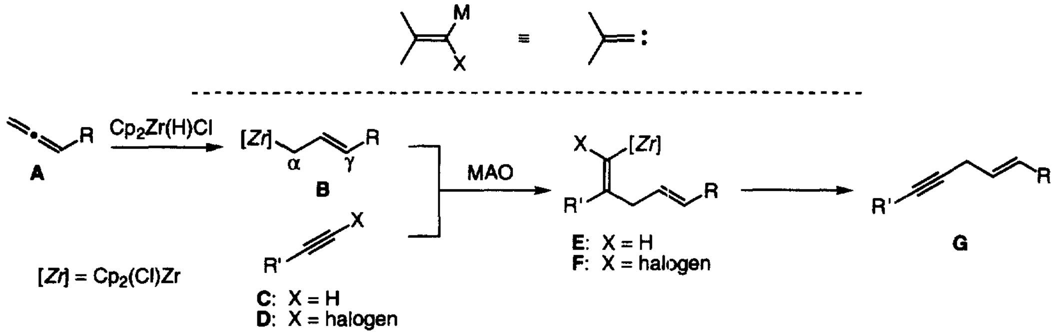
Abstract: Allylzirconium species, generated by hydrozirconation of allenes, react with 1-iodoalkynes in the presence of methylaluminoxane (MAO) to give the substitution products of the iodide by an allyl group. Labelling study for 2-(iodoethynyl)naphthalene suggested that the reaction involves allylzirconation of iodoalkynes to generate an alkylidene carbenoid that undergoes 1,2-rearrangement. © 1999 Elsevier Science Ltd. All rights reserved.

Alkylidene carbenoid is a reactive species of considerable interest, which are to be exploited in organic synthesis.[1] We became interested in a possibility to generate such a species *via* the carbometallation of 1-haloalkyne, which occurred to us during our recent study on a related system (Scheme 1):[2] The allylzirconium **B**, generated by the hydrozirconation of allene **A**,[3] adds to alkyne **C** in the presence of methylaluminoxane (MAO) to give the adduct **E**.[2,4,5] Given that the haloalkyne **D** similarly underwent such an allylzirconation reaction, an alkylidene carbenoid **F** would be generated, which may exhibit various reactivities.[1,6]



Scheme 1

In this communication, we report the outcome of the attempts along these lines:

(1) The MAO-catalyzed reaction of 1-haloalkyne **D** with allylzirconium **B** leads to a formal substitution reaction, thereby giving the alkyne **G** in good to excellent yields.

(2) The relevance of the process to the alkylidene carbenoid chemistry was suggested, as the 1,2-shift was proven to be involved in some cases.

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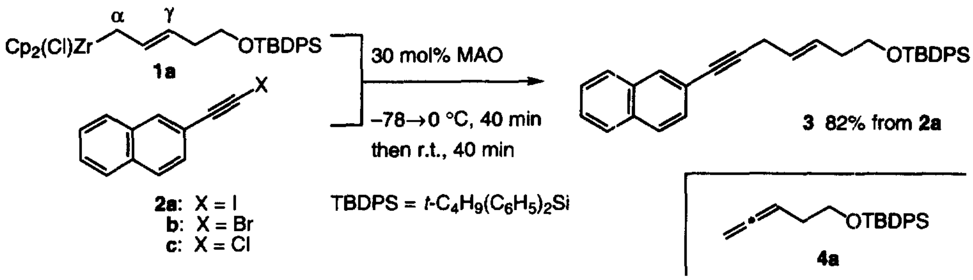
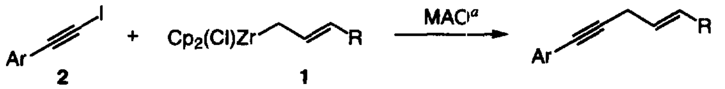
We first carried out the reaction of iodoalkyne **2a** with allylzirconium **1a**, generated by hydrozirconation of allene **4a** (eq. 1). Allene **4a** (1.7 equiv.) was subjected to hydrozirconation ($Cp_2Zr(H)Cl$, 2.0 equiv./ CH_2Cl_2, −78 °C → 25 °C),[3,7] and the resulting red solution of the allylzirconium was chilled to −78 °C, to which was added iodoalkyne **2a** (1.0 equiv.). At this point, only **2a** and the hydrolysate of **1a** were observable on TLC. After the addition of MAO (0.3 equiv., toluene soln.),[5] the reaction started to proceed: TLC assay showed the gradual consumption of iodoalkyne **2a** and the appearance of a single new spot. After stirring for 40 min at 0 °C and another 40 min at 25 °C, the reaction was quenched, and purification gave the alkyne **3** (82% yield).[8] The reaction site for **1a** was the α position, and the geometry of the double bond was *trans* (J = 15.1 Hz). Control experiments showed that, as a haloalkyne substrate, the corresponding bromo and chloro congeners led to poorer yields of **3** (70% for **2b**, 55% for **2c**).



(1)

Some combinations of *aryl*iodoacetylenes and allylzirconiums were subjected to the same reaction conditions as above. Irrespective of the structural variation of the aromatic moiety in the iodoalkyne substrate **2** and the substituent (R) in the allylzirconium **1**, consistently high yields were attained to give the corresponding alkynes (**5**–**10**; Table 1).

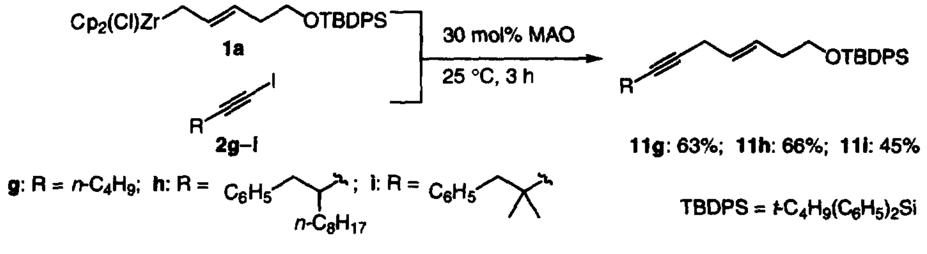
Table 1



run	Ar in iodoalkyne		R in allylzirconium[b]		product	yield/%
1	C_6H_5-	(**2d**)	TBDPSO$(CH_2)_2$-	(**1a**)	**5**	92
2	*m*-$CH_3OC_6H_4$-	(**2e**)	**1a**		**6**	84
3	*p*-$CH_3OC_6H_4$-	(**2f**)	**1a**		**7**	81
4	2-naphthyl	(**2a**)	*n*-C_7H_{15}-	(**1b**)	**8**	85
5	**2a**		*cyclo*-C_6H_{11}-	(**1c**)	**9**	84
6	**2a**		TBDPSO$CH_2(CH_3)$CH-	(**1d**)	**10**	86

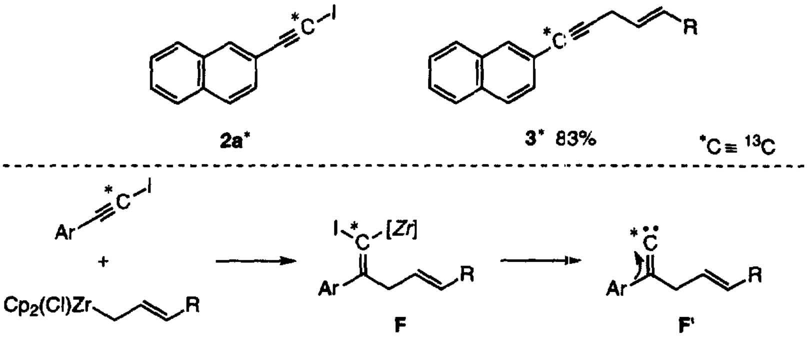
[a] 30 mol%; [b] TBDPS = *t*-$C_4H_9(C_6H_5)_2$Si

On the other hand, the iodoacetylenes with an *alkyl* substituent reacted more slowly. Longer reaction period was required (3 h, 25 °C) in order to obtain reasonable yields of the enyne products (eq. 2). Attempts to improve the yield by prolonged reaction or the use of stoichiometric MAO were unfruitful. Although such a tendency was especially the case for **2i** with a *t*-alkyl substituent, it became apparent that the inferior reactivity could not be simply due to the steric demand of the substituent but to the changeover of the mechanism (vide infra).



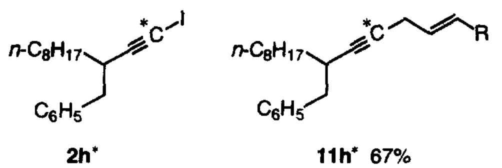
(2)

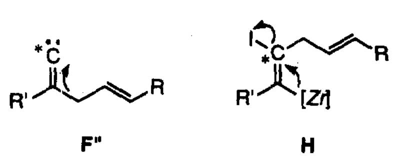
Labelling experiments clearly showed the difference in the reaction paths for *aryl* and *alkyl* iodoalkyne substrates.[9] Notably, when the ^{13}C-labelled alkyne **2a*** was employed in the reaction shown in eq. 1, the alkyne **3*** had the ^{13}C directly connected to the 2-naphthyl group (^{13}C NMR, 100 MHz). Thus, two *sp* carbons completely switched their positions during the reaction, which is consistent with the intermediacy of an alkylidene carbenoid **F** that undergoes *1,2-shift* of the 2-naphthyl group (as represented by the arrow in "carbene" **F'**, eq. 3).



(3)

In sharp contrast, the reaction of the *alkyl*iodoacetylene **2h*** (see eq. 2) gave the product **11h***, where no, if any, positional exchange was observed.[10]





The latter outcome could be formally rationalized in two ways. One rationale is based on the intermediacy of the carbenoid **F** as above, in which, however, the allyl group, rather than the alkyl group (a poor migrator), undergoes 1,2-shift (see **F''**). Another possibility is the changeover of the regiochemistry of the initial carbometallation, for some unknown reasons, to generate the intermediate **H**, which undergoes β-elimination to form the alkyne product.[11]

In summary, we have described that the alkyne is obtained by the MAO-catalyzed reaction of 1-haloalkyne with allylzirconium,[12] where the intermediacy of an alkylidene carbenoid was suggested. It is noted that the products derived from other possible reactivities of carbenoids (C–H insertion reaction[1] or nucleophilic substitution[1,6]) were not observed in all reactions mentioned above. Further work to extend the scope of the present reaction is underway in our laboratory.

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References and Notes

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5. Modified MAO, hydrolysate of Me_3Al–*i*-Bu_3Al (2:1), Al = 6 wt% in toluene, mw = 1200, used for this reaction was kindly donated from Tosoh Akzo Co.
6. For nucleophilic substitution of alkylidene carbenoids, see: (a) Kasai, K.; Liu, Y.; Hara, R.; Takahashi, T. *Chem. Commun.* **1998**, 1989. (b) Kasatkin, A.; Whitby, R. J. *Tetrahedron Lett.* **1997**, *38*, 4857. (c) Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, *62*, 1933. (d) Negishi, E.; Akiyoshi, K.; O'Conner, B.; Takagi, K.; Wu, G. J. *J. Am. Chem. Soc.* **1989**, *111*, 3089. (e) Miller, J. A. *J. Org. Chem.* **1989**, *54*, 998. (f) Harada, T.; Hara, D.; Hattori, K.; Oku, A. *Tetrahedron Lett.* **1988**, *29*, 3821. (g) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086.
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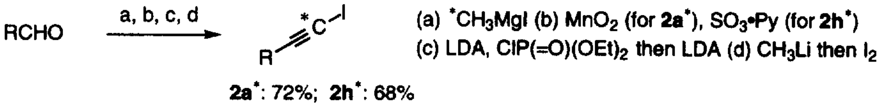
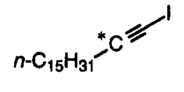
8. All new compounds were fully characterized by ^1H and ^{13}C NMR, IR, and high-resolution MS and/or combustion analysis.
9. ^{13}C-Labelled iodoalkynes **2a***and **2h*** (>99 atom% ^{13}C) were prepared from the corresponding aldehydes and the $^{13}CH_3I$ (Aldrich, 99.5 atom% ^{13}C).



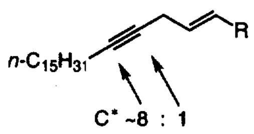
(a) $^*CH_3MgI$ (b) MnO_2 (for **2a***), SO_3•Py (for **2h***)
(c) LDA, ClP(=O)(OEt)$_2$ then LDA (d) CH_3Li then I_2

2a*: 72%; **2h***: 68%

10. In contrast to the results for **2a***and **2h***, the reaction of *prim*-alkyliodoacetylene **2j*** with **1a** gave **11j*** (56% yield) with a partially scrambled ^{13}C distribution (retained:switched = 8:1). Note that, **2j***, which was prepared by a different method (from palmitic-1-^{13}C acid, Aldrich, 99 atom% ^{13}C), has the labelled carbon at the inner position (cf. **2a***, **2h***).



2j*



11j* 56%

11. All attempts to quench the reaction in various periods failed to give the hydrolysate of the assumed intermediates **F** or **H**.
12. Copper-catalyzed coupling of alkenylzirconocenes with alkynyl halides has been reported, see: Hara, R.; Liu, Y.; Sun, W.-H.; Takahashi, T. *Tetrahedron Lett.* **1997**, *38*, 4103. see also ref. 6a.