Extended Enyne Structures

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Chromium(0) Alkynylcarbene Complexes as C_β-Electrophilic Carbene Equivalents: Regioselective Access to Dienynes and Dienediynes**

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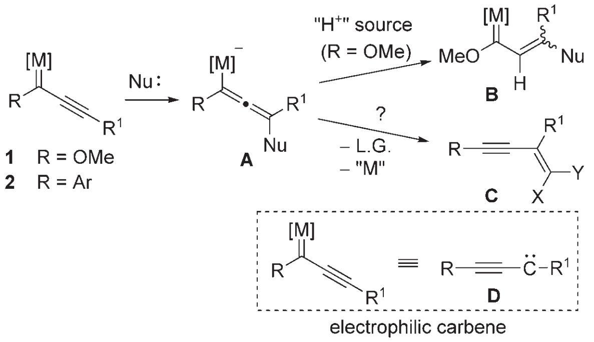
The evolution of organic chemistry has been marked by the incorporation of novel transformations and the development of new synthetic tools, many of which are based on the potential of transition metals in carbon–carbon and carbon–heteroatom bond-forming reactions. A number of these synthetic processes mediated by heteroatom-stabilized carbene complexes—particularly chromium and tungsten complexes—have been reported in the last two decades.[1] For instance, the reactivity of unsaturated carbene complexes such as the alkynyl(alkoxy)carbene complexes **1** is determined by the strong electron-acceptor nature of the metal–carbene functionality, which makes these metal species useful substrates for cycloaddition reactions as well as for 1,2- and 1,4-nucleophilic addition reactions. Recent advances in this area have shown that the novel nonstabilized alkynylcarbene complexes **2** are also readily available,[2] thus making studies of their reactivity possible.

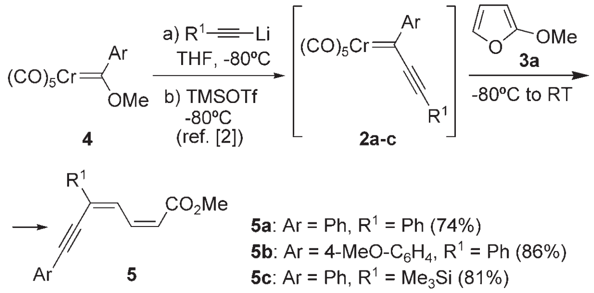
It is well known that the metal alkynyl(alkoxy)carbenes **1** (Scheme 1) readily undergo conjugate nucleophilic addition to form substituted alkenyl(alkoxy)carbenes **B** via the allenylmetalate species **A**,[3] and that intermediates containing a metal–carbon single bond, such as metalates, have a high tendency to expel a neutral metal pentacarbonyl fragment.[4] This observation led us to suppose that if a leaving group is adequately placed within the nucleophile moiety, the allenylmetalate **A** might evolve to enynes **C** in an overall process that would involve olefination of an sp-hybridized carbon and subsequent carbene rearrangement.



Scheme 1. Nucleophilic addition to metal alkynylcarbene complexes: the fate of intermediate **A**. L.G. = leaving group.

We report herein that alkynylcarbene complexes **1** and **2** behave as synthetic equivalents of the electrophilic propargylcarbene species **D** (Scheme 1) in their reaction with 2-oxyfurans **3** (2-methoxyfuran (MeOF; **3a**) and 2-trimethylsilyloxyfuran (TMSOF; **3b**)). Although 2-oxyfurans are known to add to electron-poor alkenes, addition to an alkyne functionality has not been reported previously as far as we are aware.[5–7]

We initiated this study by using nonstabilized, highly reactive alkynylcarbene complexes **2**. These complexes, which were generated at −80 °C from **4** as described previously,[2] gave the dienyne adducts **5a–c** in good yields upon treatment with MeOF (**3a**; 1.6 equiv) and warming the reaction mixture to room temperature (Scheme 2).[8] This novel olefination of an alkynylcarbene is stereoselective and involves a formal 1,2-migration of the C-C triple bond that leads to an overall regioselective olefination at C_β of the alkynylcarbene.



Scheme 2. Formation of conjugated dienynoic acid esters **5** (yields given in brackets)

Next, we found that classic heteroatom-stabilized Fischer carbenes could also be used in this reaction; they provide an

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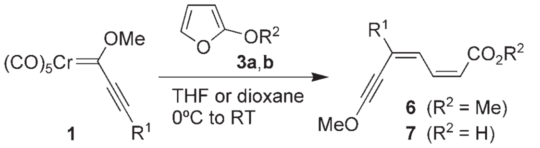
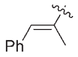
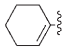
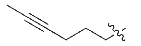
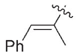
Supporting Information for this article (experimental procedures and spectroscopic data for **5a–c**, **6a–g**, **7a–d**, **9a–c**, and **11**) is available on the WWW under http://www.angewandte.org or from the author.

alkoxy functionality at the alkynyl appendage (Table 1). When chromium carbene complexes of **1a**–**g** were treated with two equivalents of **3a** (THF or 1,4-dioxane, 0 °C to room temperature, overnight) the expected 7-methoxy-2,4-heptadien-6-ynoic acid derivatives **6a**–**g** were produced in 73–97 % yield (Table 1, entries 1–7). The scope of this reaction is noteworthy as both simple and functionalized R^1 substituents are tolerated (alkyl, aryl, alkenyl, trimethylsilyl (TMS), alkynylalkyl). Moreover, the reaction of **3b** with carbene complexes **1a**,**c**,**f**,**h** under the same reaction conditions led to the corresponding polyunsaturated carboxylic acids **7a**–**d**, although in somewhat lower yield (41–56 %; Table 1, entries 8–11).

Table 1: Formation of conjugated dienynoic acid derivatives **6** and **7**.[a]

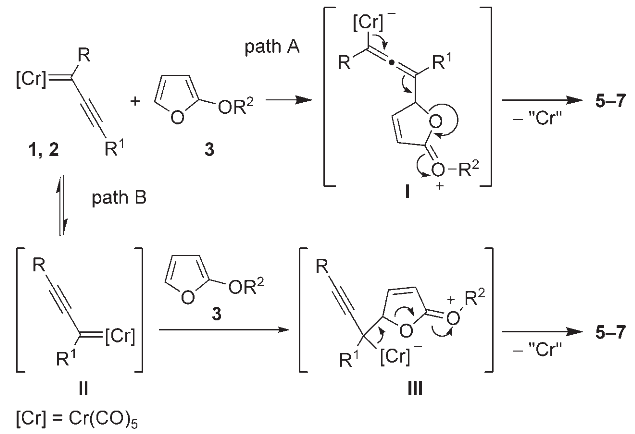


Entry	1	R^1	3	Product	Yield [%][b,c]
1	**1a**	Ph	**3a**	**6a**	83 (97)
2	**1b**	4-MeO-C_6H_4	**3a**	**6b**	91
3	**1c**		**3a**	**6c**	86 (91)
4	**1d**		**3a**	**6d**	87
5	**1e**	TMS	**3a**	**6e**	89
6	**1f**	*n*Bu	**3a**	**6f**	96
7	**1g**		**3a**	**6g**	73
8	**1a**	Ph	**3b**	**7a**	54 (55)
9	**1c**		**3b**	**7b**	44
10	**1f**	*n*Bu	**3b**	**7c**	41
11	**1h**	*t*Bu	**3b**	**7d**	56

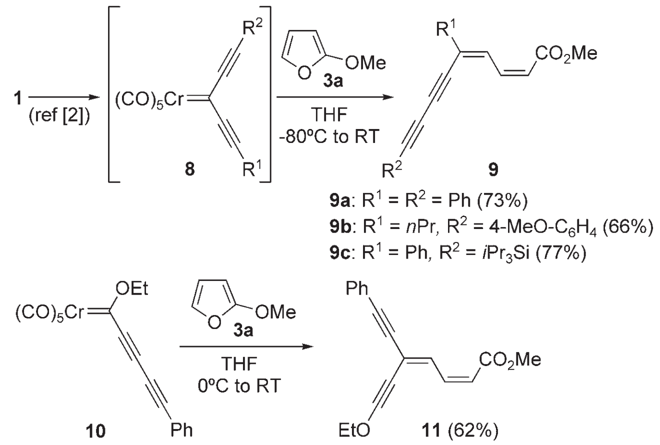
[a] All reactions were carried out with 1.0 mmol of the carbene complex and two equivalents of the corresponding 2-oxyfuran in 10 mL of THF (or 1,4-dioxane). [b] Yields of isolated product for the reaction performed in THF, based on **1**. [c] Yields for the reaction performed in 1,4-dioxane are given in brackets.

The observed results can be rationalized by Michael-type addition of **3a** to the alkynyl function of carbenes **1** and **2** to generate the zwitterionic allenyl intermediate **I** (Scheme 3, path A). Reorganization of this species by metal-elimination-induced furan ring-opening regenerates the alkyne function and provides the (*Z*)-pentadienoate moiety of adducts **5**–**7**. An alternative proposal would involve a 1,3-$Cr(CO)_5$ shift to generate the rearranged metal carbene **II**,[9] which would evolve by 1,2-addition of **3** (to form intermediate **III**) and metal elimination/ring-opening (Scheme 3, path B). However, the latter pathway can be ruled out, at least for metal carbenes **1** (R = OMe), since their equilibration into carbenes **II** is thermodynamically unfavorable.[2]

We also explored more complex substrates, such as linear and cross-conjugated diynylcarbenes (Scheme 4), and were delighted to find that the symmetrical carbene **8a** ($R^1 = R^2 =$ Ph) reacts with **3a** to form the linear diendiyne **9a** (73 % yield), whose structure was determined by X-ray diffraction analysis.[10,11] Unsymmetrical carbenes **8b** ($R^1 = n$Pr; $R^2 =$ 4-MeO-C_6H_4) and **8c** ($R^1 =$ Ph; $R^2 = i\text{Pr}_3\text{Si}$) led exclusively to single regioisomers **9b** and **9c**, respectively. These observations allowed us to estimate the ability of the R^1 group to induce the 1,3-carbene rearrangement as being in the order alkyl > aryl > trialkylsilyl.



Scheme 3. Proposed reaction pathways for the formation of **5**–**7**.



Scheme 4. Synthesis of linear- (**9**) and cross-conjugated dienynes (**11**; yields given in brackets) from cross- (**8**) and linear-conjugated diynecarbenes (**10**).

Finally, cross-conjugated dienediynes are also accessible from linear dienylcarbenes. For instance, the reaction of the chromium phenylbutadiynyl(ethoxy)carbene **10** with **3a** afforded the cross-conjugated dienediyne **11** (62 % yield), with complete chemoselectivity, as a result of initial nucleophilic attack at C_β of the diyne system.[12]

In summary, we have established a direct, flexible, and selective route to a variety of dienynes, which may be useful as building blocks for molecular scaffolding, including several dienediynes bearing different conjugation patterns and functionalities.[13] Importantly, the reaction reported herein involves isomerization of the alkynyl function of an alkynylcarbene complex and olefination at C_β.[14] Representative experiments show complete regioselectivity for the competitive alkyne isomerization for alkyl, aryl, and silyl groups. This new reactivity pattern for Group 6 metal alkynylcarbene complexes could open up the possibility of designing new reactions of the proposed propargylic-type carbene. Research aimed at performing a twofold coupling at C_β, for instance, is currently underway.

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