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First [4 + 3] Annulation of Alkynyl Fischer Carbene Complexes and Azadienes. X-ray Structure of a Metalated Zwitterionic Intermediate

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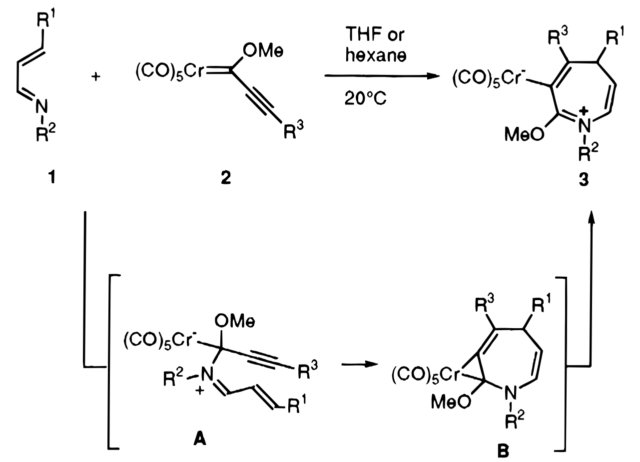
Recently, α,β-unsaturated Fischer carbene complexes have been recognized to play an important role in transition-metal-mediated organic synthesis.[1] Although alkynyl Fischer carbene complexes are less versatile intermediates than their alkenyl counterparts, a number of useful reactions have been reported; for instance, 1,2- and 1,4-nucleophilic additions[2] as well as [2 + 2],[3] [3 + 2],[4] [3 + 3],[5] [4 + 2][6] and Pauson−Khand type[7] cyclization reactions. On the other hand, the [4 + 3] cycloaddition of alkenyl carbenes with electron-rich dienes, which may involve a tandem cyclopropanation/Cope rearrangement, has recently emerged as an attractive entry into seven-membered carbocycles;[8] in contrast, no examples of this type of process involving alkynyl complexes are known, perhaps because of the required involvement of a strained cumulene ring.[9] In an extension of this reaction we found that activated 1-azadienes, like 4-amino-1-azadienes and *N*-hydroxy-1-azadienes, readily undergo [4 + 3] annulation with alkenyl Fischer carbene complexes leading to the azepine ring; interestingly, NMR studies proved that the cycloaddition involves nucleophilic addition of the imine nitrogen to the carbene carbon and cyclization rather than consecutive [2 + 1] cycloaddition and [3,3] rearrangement.[10]

Scheme 1



On working with alkynyl carbene complexes and nitrogen-containing substrates one can anticipate that either 1,4- or 1,2-addition might take place and therefore different reaction pathways should be observed.[11] Reported here is the achievement of a [4 + 3] cycloaddition reaction of alkynyl Fischer carbene complexes with α,β-unsaturated imines as well as the isolation of an η^1-azepine chromium complex intermediate.[12]

The reaction of azadienes **1** with pentacarbonyl methoxy (phenylethynyl)chromium carbene complex **2** (R^3 = Ph) in hexane at 20 °C was complete in 3 h affording a precipitate that consisted essentially of the [4 + 3] cycloadducts **3a**−**c** (Scheme 1, Table 1, entries 1−3). When chromium alkynyl complexes **2** having bulky groups at the β-carbon (R^3 = $SiMe_3$, *tert*-Bu; entries 4−6) were employed, the cyclization became much more sluggish and therefore required the reaction to be

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(13) Running the reaction of azadiene **1** (R^1 = Ph; R^2 = *n*-Pr) with carbene **2** (R^3 = Ph) in THF at 20 °C resulted in the formation of **3a** (55%) along with a second compound (28%) resulting from the [4 + 2] cycloaddition of the azadiene to the alkynyl function of the carbene complex. Unpublished results.

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Table 1. Azepines **3** and **4** Prepared from 1-Azadienes **1** and Carbene Complexes **2**

entry	R^1	R^2	R^3	*T*, °C (*t*, h)	compd	yield,[a] %	compd	yield,[b] %
1	Ph	nPr	Ph	20 (3)	**3a**	90	**4a**	93[c]
2	Ph	Bn	Ph	20 (3)	**3b**	80	**4b**	87[c]
3	Ph	iPr	Ph	20 (3)	**3c**	85	**4c**	90[c]
4	Me	nPr	SiMe3	20 (24)	**3d**	60	**4d**	85[c] (75)[d]
5	Ph	nPr	SiMe3	20 (3)			**4e**	64
6	Ph	nPr	tBu	50 (36)			**4f**	57

[a] Isolated yields (not optimized) after column chromatography (deactivated SiO_2, 2:1 hexane−ethyl acetate). [b] Isolated yields (not optimized) after column chromatography (SiO_2, 2:1 hexane−ethyl acetate). [c] Refers to heating compounds **3** at 50 °C. [d] Yield obtained by reacting azadiene **1** and carbene **2** at 50 °C for 3 h.

carried out in THF, instead of hexane, at 20−50 °C. Thus, **3d** was obtained in moderate yield, while cycloadducts **3e**,**f** underwent further transformation into their metal-free derivatives **4e**,**f** under the reaction conditions.[13]

The unprecedented 1,2-migration of the pentacarbonylmetal portion is rather intriguing,[14] although it is well established that the [1,3] shift of the pentacarbonylchromium and -tungsten groups does take place when nitrogen-containing substrates are involved.[15] The formation of heterocycles **3** is thought to occur by nucleophilic addition of the imine nitrogen of **1** to the carbene carbon of **2** to form the zwitterionic species **A** followed probably by cyclization to the η^2-chromium-cumulene azepine **B**;[16] finally, metallacyclopropane ring opening on complex **B** would provide the isolated η^1-complexes **3**.

The structure of compounds **3** was determined by an X-ray crystal analysis of complex **3a** (Figure 1).[17] Although η^1-chromium complexes **3** are air-stable and withstand purification by column chromatography, the carbon−metal σ-bond was labile under thermal, hydrolytic, and electrophilic conditions (Scheme 2). Thus, heating complexes **3a**−**d** at 50 °C in either THF or benzene followed by column chromatography resulted in the formation of azepinones **4a**−**d** in high yields; compounds **4e**,**f** formed directly at 20 and 50 °C, respectively, from **1** and **2** as indicated above.[18] Compounds **4a**−**d** were also obtained in comparable yields by stirring a THF solution of **3a**−**d** with H_2O (20 °C, 24 h). In addition, **3b** produced the deuterated azepinone **5** (R^1 = Ph, R^2 = Bn; 90%) upon treatment with D_2O, whereas **3a** reacted with iodine to furnish the 3-iodo-2-azepinone **6** (55%; 93% estimated before column chromatography).[19]

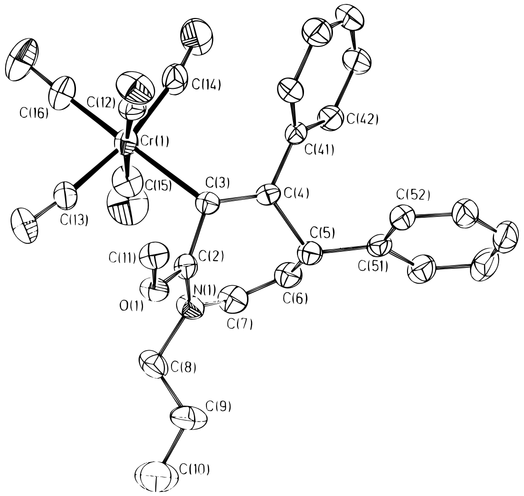
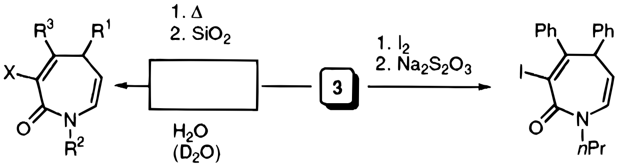


Figure 1. Crystal structure of **3a**. Selected bond lengths (Å): N(1)−C(2) 1.336, C(2)−O(1) 1.325, O(1)−C(11) 1.445, C(2)−C(3) 1.442, C(3)−C(4) 1.348, Cr−C(3) 2.233, C(4)−C(5) 1.556, C(5)−C(6) 1.498, C(6)−C(7) 1.324, C(7)−N(1) 1.419.

Scheme 2



4 (X = H)
5 (X = D)

6

In summary, we have accomplished the first [4 + 3] cycloaddition of alkynyl Fischer carbene complexes leading to σ-complexed and metal-free azepines;[20] a novel [1,2] shift of a pentacarbonylmetal moiety is demonstrated and seems to be the driving force of the cyclization. Mechanistic studies directed to gain a better understanding of the process are currently under way.[21]

Acknowledgment. This research was supported by the DGICYT (Grant PB92-1005).

Supporting Information Available: Synthetic procedures and characterization data for **3**−**6** and X-ray crystallographic data for **3a** including tables of atomic coordinates, bond lengths, and bond angles (22 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(17) Crystal data for **3a**: $C_{27}H_{23}CrNO_6$, M_r = 509.46, monoclinic, space group $P2_1/n$, $a = 12.322(7)$ Å, $b = 10.170(3)$ Å, $c = 20.820(7)$ Å, $\beta = 99.07(4)°$, $V = 2546(2)$ Å^3, $Z = 4$, $r_{calc} = 1.31$ Mg m^{-3}, $F(000) = 1056$, λ(Mo Kα) = 0.710 73 Å, $\mu = 0.484$ cm^{-1}, $T = 293$ K. Colorless crystal (0.30 × 0.30 × 0.26 mm).

(18) We have not been able yet to ascertain where the hydrogen atom replacing the metal group is coming from. In fact, heating either the 2-methoxyazepine **3b** in C_6D_6 or its 2-trideuteriomethoxy analogue in C_6H_6 did not lead to the deuterated azepinone **5**, but **4b** was the sole product detected.

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(21) Following the suggestions of one reviewer, attempts were made to tune the electronic factors governing the process. We found that amino carbene derivatives, *e.g.*, pentacarbonyl pyrrolidinyl (phenylethynyl)-chromium carbene, were unreactive, the starting materials being recovered after prolonged heating at 80 °C. Complexes $(CO)_4(PR_3)Cr(OMe)(C{\equiv}CPh)$ (R = Ph, Bu) could not be tested because we were unable to prepare them. Finally, pentacarbonyl methoxy (phenylethynyl)tungsten carbene led almost exclusively to the corresponding [4 + 2] cycloadduct.[22]

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