

# Cu-Catalyzed Synthesis of Symmetric Group 6 (Fischer) Bis-carbene Complexes

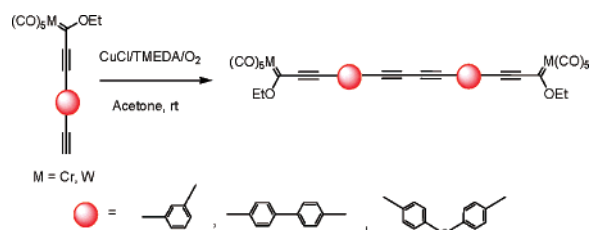
María P. López-Alberca, María J. Mancheño,\* Israel Fernández, Mar Gómez-Gallego, and Miguel A. Sierra\*

Departamento de Química Orgánica, Facultad de Química, Universidad Complutense, 28040 Madrid, Spain

mjmreal@quim.ucm.es; sierraor@quim.ucm.es

Received October 10, 2007

## ABSTRACT



The efficient copper oxidative homocoupling (CuCl/TMEDA/O<sub>2</sub>) of alkyne Fischer carbene complexes yields bis-carbene complexes having  $\pi$ -tethers. The bimetallic complexes are exceptional templates to prepare diverse organic symmetric structures connected by  $\pi$ -extended fragments.

The chemistry of Fischer-type carbene complexes has steadily developed during the last 40 years.<sup>1</sup> However, to date, most of the synthetic applications of Fischer carbenes in organic synthesis have been restricted to monocarbene complexes.<sup>2</sup> The first examples of the use of polymetallic carbene complexes were reported just 15 years ago,<sup>3</sup> and

(1) Selected reviews on different aspects of metal carbene chemistry: (a) Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissel, R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1983. (b) Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, p 1065. (c) Wulff, W. D. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, p 470. (d) Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271. (e) Aumann, R.; Nienaber, H. *Adv. Organomet. Chem.* **1997**, *41*, 163. (f) de Meijere, A.; Schirmer, H.; Duetsch, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3964. (g) Barluenga, J.; Flórez, J.; Fañanás, F. J. *J. Organomet. Chem.* **2001**, *624*, 5.

(2) For recent examples of some natural products synthesized using Fischer carbenes, see: (a) Huang, J.; Wu, C.; Wulff, W. D. *J. Am. Chem. Soc.* **2007**, *129*, 13366. (b) Eastham, S. A.; Ingham, S. P.; Hallet, M. R.; Herbert, J.; Quayle, P.; Raftery, J. *Tetrahedron Lett.* **2006**, *47*, 2299. (c) Camacho-Dávila, A.; Herndorn, J. W. *J. Org. Chem.* **2006**, *71*, 6682. (d) Minatti, A.; Dötz, K. H. *J. Org. Chem.* **2005**, *70*, 3745. (e) Gupta, A.; Sen, S.; Harmata, M. *J. Org. Chem.* **2005**, *70*, 7422. See, also (f) Barluenga, J.; Santamaría, J.; Tomás, M. *Chem. Rev.* **2004**, *104*, 2259.

even after the recognition of the usefulness of bi- and polymetallic reagents as catalysts for organic synthesis, the full potential of these complexes is yet to be discovered. The drawback with respect to monocarbene complexes originates in the difficulties to access and elaborate bi- and polymetallic carbene structures. Most synthetic routes to these bis-carbene complexes use the original method of Fischer,<sup>4</sup> consisting of the addition of organolithium compounds to M(CO)<sub>6</sub> (M = Cr or W) and subsequent capture of the intermediate acylate complex with powerful electrophile agents.<sup>5</sup> Other approaches to these compounds are the double Aumann reaction between a dialdehyde and a monocarbene complex

(3) For a review in the synthesis and synthetic applications of bi- and polymetallic carbenes, see: Sierra, M. A. *Chem. Rev.* **2000**, *100*, 3591.

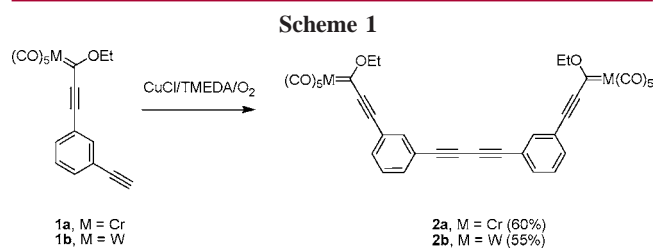
(4) Fischer, E. O.; Maasbol, A. *Angew. Chem., Int. Ed.* **1964**, *3*, 580.

(5) Examples: (a) Fischer, E. O.; Röhl, W.; Huy, N. H. T.; Ackermann, K. *Chem. Ber.* **1982**, *115*, 2951. (b) Huy, N. H. T.; Lefloch, P.; Robert, F.; Jeannin, Y. *J. Organomet. Chem.* **1987**, *327*, 211. (c) Dötz, K. H.; Tomuschat, P.; Nieger, M. *Chem. Ber.* **1997**, *130*, 1605. (d) Albrecht, T.; Sauer, J.; Nöth, H. *Tetrahedron Lett.* **1994**, *35*, 561. (e) Neidlein, R.; Gürtler, S.; Krieger, C. *Helv. Chim. Acta* **1994**, *77*, 2303. (f) Anderson, D. M.; Bristow, G. S.; Hitchcock, P. B.; Jasim, H. A.; Lappert, M. F.; Skelton, B. W. *J. Chem. Soc., Dalton Trans.* **1987**, 2843. (g) Berke, H.; Härter, P.; Huttner, G.; v. Seyerl, J. *J. Organomet. Chem.* **1981**, *219*, 317.

having  $\alpha$ -hydrogens,<sup>6</sup> the alkylation of alkyl dihalides with monocarbene anions,<sup>7</sup> the reaction of highly reduced pentacarbonylmetalates with bis-amides,<sup>8</sup> and the reductive coupling of alkenyl carbenes.<sup>9</sup> All of these methods usually lead to low yields of the desired complex or are even unable to produce it.

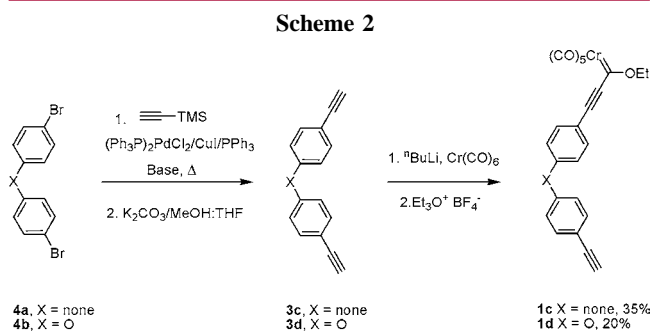
Modification of a mononuclear metal–carbene complex by using a transition-metal-catalyzed reaction would be a simple answer to obtain elaborated bi- and polymetallic structures. Nevertheless, the use of transition-metal catalysts to effect transformations in group 6 metal carbene complexes is often hampered by the transmetalation reaction of the metal carbene to the catalysts.<sup>10</sup> Our ongoing project directed to prepare new macrocyclic structures based on a bi- and polymetallic macrocyclic Fischer carbene scaffolds<sup>11</sup> required an easy and efficient route to alkynyl tethered bis-carbene complexes. The oxidative coupling of terminal acetylenes was an attractive way to access these structures. However, the reactivity of the catalyst in the alkyne coupling had to be preferred to the transmetalation reaction. For this reason and based on our experience with catalytic reactions of Fischer carbene complexes,<sup>10</sup> the Hay<sup>12</sup> modification of the original Glaser coupling reaction was chosen. Reported herein is the successful implementation of this idea to obtain new bis-carbene complexes as building blocks for the design of new polymetallic structures and the application of these scaffolds to the preparation of bis-uracils and bis-imidazoles as examples of the versatility of these structures in organic synthesis.

First, assays to achieve the dimerization reaction were effected on monocarbene **1a**, which was prepared from 1,3-diethynylbenzene following our previously reported procedure.<sup>11,13</sup> Reaction of complex **1a** with an excess of CuCl–TMEDA/air in acetone yielded after 90 min bis-carbene **2a** in good yield (60%).<sup>14</sup> The same process with the tungsten carbene **1b** was also efficient. The reaction was completed within 1 h, yielding carbene **2b** in 55% yield (Scheme 1).



Therefore, no systematic differences were observed between isostructural chromium and tungsten complexes toward this process.

This coupling reaction was extended to other alkynylcarbene complexes. Thus, dialkynes **3** were obtained in good yields by Sonogashira coupling of dibromo derivatives **4** with trimethylsilylacetylene and further desilylation in the presence of base. The dialkynes **3** were monolithiated with *n*-BuLi and reacted with Cr(CO)<sub>6</sub>, and finally, the “ate” complex thus formed was reacted with Et<sub>3</sub>OBF<sub>4</sub> to give monocarbene complexes **1c,d** in 35% and 20% yield, respectively (Scheme 2).



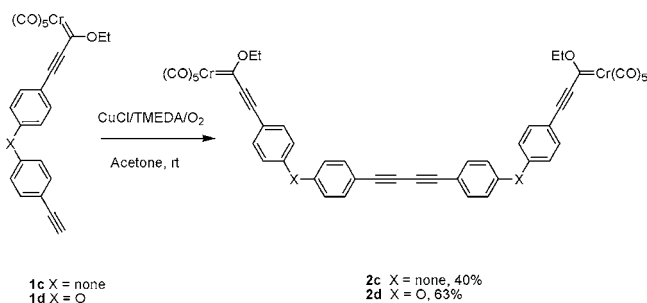
Monocarbenes **1c** and **1d** were reacted under standard Hay conditions leading to the corresponding homocoupling products **2c** and **2d**, which were isolated in 40% and 63% yield, respectively (Scheme 3). The lower yield of carbene **2c** is due to partial decomposition of the product during the isolation procedure.

All of the coupling reactions tested yielded the desired bis-carbenes exclusively. Products derived from transmetalation to the metal carbene moiety process were not observed. We have recently shown<sup>10b</sup> that transmetalation from chro-

(14) The synthesis of complex **2a** is representative: The Hay catalyst was prepared according to the literature (see ref 12). To the resulting catalyst was added dropwise a solution of the monocarbene in dry acetone. The mixture was stirred until the disappearance of monocarbene (checked by TLC). The reaction was quenched with water and filtered to eliminate the salts formed. The filtrate was extracted with diethyl ether. The combined organic phases were washed with HCl (5%) and water, dried over MgSO<sub>4</sub>, and filtered. The solvent was eliminated and purification by column chromatography on silica gel afforded pure compound: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  = 7.71–7.43 (m, 8H), 4.77 (q, *J* = 7.1 Hz, 4H), 1.60 (t, *J* = 7.1 Hz, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  = 313.7, 225.7, 216.1, 135.8, 135.0, 133.2, 129.2, 122.6, 121.7, 91.4, 80.5, 76.0, 75.0, 15.0; IR (CHCl<sub>3</sub>)  $\nu$  2062, 1954, 1217, 775 cm<sup>-1</sup>. Anal. Calcd for C<sub>36</sub>H<sub>18</sub>O<sub>12</sub>Cr<sub>2</sub>: C, 57.92; H, 2.43. Found: C, 57.78; H, 2.21.

(6) Aumann, R. *Eur. J. Org. Chem.* **2000**, 17.  
 (7) (a) Macomber, D. W.; Madhukar, P. J. *Organomet. Chem.* **1992**, 433, 279. (b) Macomber, D. W.; Hung, M.-H.; Verma, A. G.; Rogers, R. D. *Organometallics* **1988**, 7, 2072. (c) Macomber, D. W.; Hung, M.-H.; Madhukar, P.; Liang, M.; Rogers, R. D. *Organometallics* **1991**, 10, 737. (d) Macomber, D. W.; Madhukar, P.; Rogers, R. D. *Organometallics* **1991**, 10, 2121.  
 (8) (a) Wynn, T.; Hegedus, L. S. *J. Am. Chem. Soc.* **2000**, 122, 5034. (b) Puntener, K.; Hellman, M. D.; Kuester, E.; Hegedus, L. S. *J. Org. Chem.* **2000**, 65, 8301. (c) Kuester, E.; Hegedus, L. S. *Organometallics* **1999**, 18, 5318. (d) Dumas, S.; Lastra, E.; Hegedus, L. S. *J. Am. Chem. Soc.* **1995**, 117, 3368. (e) Hsiao, Y.; Hegedus, L. S. *J. Org. Chem.* **1997**, 62, 3586.  
 (9) (a) Ramírez-López, P.; Gómez-Gallego, M.; Sierra, M. A.; Lejon, T.; Mancheño, M. J. *Angew. Chem., Int. Ed.* **2002**, 41, 3442. (b) Sierra, M. A.; Martínez-Alvarez, R.; Gómez-Gallego, M. *Chem. Eur. J.* **2007**, 13, 736 and pertinent references therein.  
 (10) (a) Gómez-Gallego, M.; Mancheño, M. J.; Sierra, M. A. *Acc. Chem. Res.* **2005**, 38, 44. (b) López-Alberca, M. P.; Mancheño, M. J.; Fernández, I.; Gómez-Gallego, M.; Sierra, M. A.; Torres, R. *Org. Lett.* **2007**, 9, 1757.  
 (11) (a) Fernández, I.; Mancheño, M. J.; Gómez-Gallego, M.; Sierra, M. A. *Org. Lett.* **2003**, 5, 1237. (b) Fernández, I.; Sierra, M. A.; Mancheño, M. J.; Gómez-Gallego, M.; Ricart, S. *Organometallics* **2001**, 20, 4304.  
 (12) Hay, A. S. *J. Org. Chem.* **1962**, 27, 3320.  
 (13) (a) Llordes, A.; Sierra, M. A.; López-Alberca, M. P.; Molins, E.; Ricart, S. *J. Organomet. Chem.* **2005**, 690, 6096. (b) Della Sala, G.; Artillo, A.; Ricart, S.; Spinella, A. *J. Organomet. Chem.* **2007**, 692, 1623. (c) Artillo, A.; Della Sala, G.; De Santis, M.; Llordes, A.; Ricart, S.; Spinella, A. *J. Organomet. Chem.* **2007**, 692, 1277.

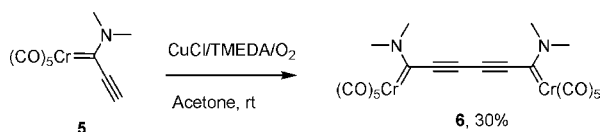
Scheme 3



mium or tungsten carbene complexes to Pd catalysts occurs preferably with Pd(II) salts, while Pd(0) species show a bias for oxidative addition instead of transmetalation. The results reported above are consistent with this behavior. The use of the bidentate ligand *N,N,N',N'*-tetramethylene diamine complex (TMEDA)–Cu(I) should enhance the oxidative coupling at the expense of the Cu–Cr or Cu–W transmetalation.

Aminocarbene **5** is also susceptible to coupling. Complex **5** was prepared following Wulff's procedure<sup>15</sup> and submitted to standard CuCl/TMEDA/O<sub>2</sub> coupling conditions. The reaction was instantaneously completed, and product **6** was isolated in 30% yield (Scheme 4). The yield was moderate,

Scheme 4



but the method constitutes a straightforward synthesis compared to the procedure developed by Fischer for the preparation of analogous complexes.<sup>16</sup>

The carbene complexes isolated throughout this work were relatively stable and could be purified by SiO<sub>2</sub> chromatography. All of them present similar spectroscopic features. Thus, the <sup>13</sup>C NMR spectra of chromium complexes **1c**, **1d**, **2a**, **2c**, and **2d** exhibit a signal in the range of 313.7–312.6 ppm characteristic of an alkoxy carbene moiety. In the same way, tungsten carbene **2b** shows the corresponding signal at 285.9 ppm. All of them also present the signals assignable to the C–C triple bond in the range 92.6–73.9 ppm.

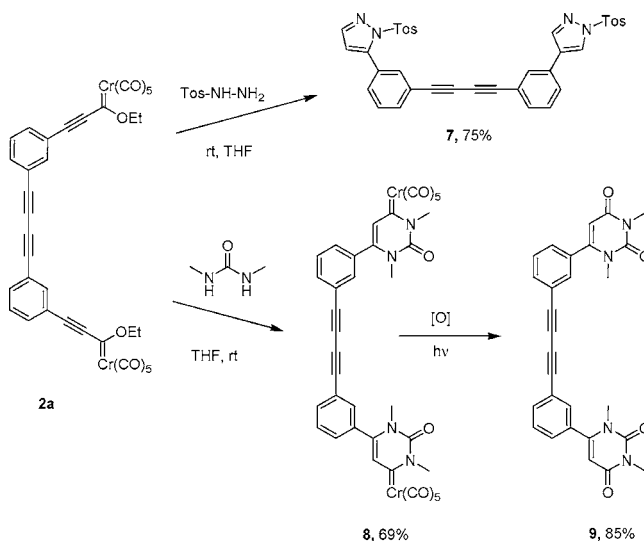
The synthesis of the compounds **2a–d** and **6** is a simple entry to new oligoenyne structures. These compounds may

(15) Rahm, A.; Wulff, W. D.; Rheingold, A. L. *Organometallics* **1993**, *12*, 597.

(16) (a) Hartbaum, C.; Mauz, E.; Roth, G.; Weissenbach, K.; Fischer, H. *Organometallics* **1999**, *18*, 2619. (b) Hartbaum, C.; Roth, G.; Fischer, H. *Chem. Ber.* **1997**, *130*, 479. (c) Hartbaum, C.; Fischer, H. *Chem. Ber.* **1997**, *130*, 1063. (d) Hartbaum, C.; Roth, G.; Fischer, H. *Inorg. Chem.* **1998**, *37*, 191. (e) Hartbaum, C.; Fischer, H. *J. Organomet. Chem.* **1999**, *578*, 186. (f) For coupling reactions in allenylidene complexes, see: Szesni, N.; Drexler, M.; Maurer, J.; Winter, R. F.; de Montigny, F.; Lapinte, C.; Steffens, S.; Heck, J.; Weibert, B.; Fischer, H. *Organometallics* **2006**, *25*, 5774.

serve as scaffolds to prepare diverse organic structures, taking advantage of the reactivity of Fischer carbene complexes. The versatility of these compounds was checked against two well-known reactions of simple Fischer carbene complexes. Thus, compound **2a** was reacted with tosylhydrazine yielding the symmetric bis-pyrazole **7**<sup>17</sup> in 75% yield, and the bimetallic bis-uracyl **8** was prepared by reacting complex **2a** with *N,N'*-dimethylurea at rt in 69% yield.<sup>13</sup> Oxidation of complex **8** gives metal free bis-uracyl **9** in excellent yield (85%)<sup>18</sup> (Scheme 5).

Scheme 5



In conclusion, a new method to prepare (poly)alkyne-tethered bis-carbene complexes is reported. The procedure is based on a copper oxidative coupling that is compatible with the metallic fragment of the starting carbene. Under the conditions employed (TMEDA)–Cu(I), Cr or W to Cu transmetalation does not occur. The procedure allows the design of new Fischer carbenes as building blocks for the synthesis of new  $\pi$ -extended polymetallic and organic compounds. Two examples of the use of these new scaffolds

(17) Aumann, R.; Jasper, B.; Frölich, R. *Organometallics* **1995**, *14*, 2447.

(18) **Compound 8**. A solution of 21 mg (0.24 mmol) of *N,N'*-dimethylurea in 20 mL of THF was added by syringe pump into a solution of 60 mg (0.08 mmol) of bis-carbene **2a** in 80 mL of THF for 12 h. Then, the mixture was stirred for an additional 24 h at room temperature. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel affording 46 mg (69%) of compound **8**: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.67–7.66 (m, 2H), 7.51–7.46 (m, 4H), 7.31–7.30 (m, 2H), 7.21 (s, 2H), 4.19 (s, 6H), 3.28 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  261.4, 223.7, 217.3, 149.4, 141.2, 134.7, 132.3, 129.7, 128.9, 124.5, 123.0, 102.8, 80.6, 75.5, 45.9, 35.7; IR (CHCl<sub>3</sub>)  $\nu$  2053, 1910, 1696, 1660 cm<sup>-1</sup>. Anal. Calcd for C<sub>38</sub>H<sub>22</sub>Cr<sub>2</sub>N<sub>4</sub>O<sub>12</sub>: C, 54.95; H, 2.67. Found: C, 55.22; H, 2.40. **Compound 9**. A solution of 50 mg (0.06 mmol) of bis-carbene **8** was stirred in a mixture of hexane/ethyl acetate 1:1 for 8 h under sunlight. The solvent was removed in vacuo and the residue dissolved in ethyl acetate and filtered through a short pad of Celite. Further chromatography on silica gel afforded 16 mg (85%) of **9**: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.61–7.57 (m, 2H), 7.47–7.39 (m, 4H), 7.29–7.28 (m, 2H), 5.62 (s, 2H), 3.33 (s, 6H), 3.14 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  162.2, 153.2, 152.5, 134.1, 133.9, 131.5, 129.3, 128.5, 122.7, 102.9, 80.7, 75.1, 34.5, 28.1; IR (CHCl<sub>3</sub>)  $\nu$  1704, 1659 cm<sup>-1</sup>. Anal. Calcd for C<sub>28</sub>H<sub>22</sub>N<sub>4</sub>O<sub>4</sub>: C, 70.18; H, 4.63. Found: C 70.32; H, 4.80.

to access to symmetric organic bis-pyrazole and bis-uracyl derivatives are reported. Efforts to explore the versatility of this method to access to other metallic complexes and organic structures are underway in our laboratories.

**Acknowledgment.** Support for this work under Grant No. CTQ2004-06250-C02-01/BQU from the Ministerio de Ciencia y Tecnología (Spain) and the CAM (CAM-UCM-910762)

is gratefully acknowledged. M.P.L.A. thanks the Ministerio de Educación y Ciencia (Spain) for a predoctoral (FPU) grant.

**Supporting Information Available:** Full experimental and characterization data for all the compounds prepared through this work. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL702464R