ORGANOMETALLICS

Volume 17, Number 11, May 25, 1998

Communications

Reaction of Alkynyl Alkoxy Metal (Cr, W) Carbene Complexes with 1,3-Dinitrogen Systems. A Direct Entry to the Pyrimidine Skeleton

Rolando Polo, Josep M. Moretó, Ute Schick,† and Susagna Ricart*

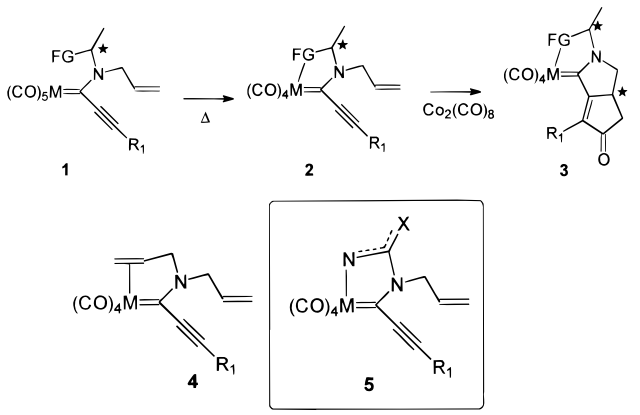
Departament de Química Orgànica Biològica, CID (CSIC), c/J. Girona 18-26, 08934-Barcelona, Spain

Received October 14, 1997

Summary: The reaction of alkynyl alkoxy metal (Cr, W) carbene complexes with 1,3-dinitrogen systems (amidines, guanidines, ureas) is described. In all cases, the main product obtained corresponds to the cycloadduct whose cyclic structure may be related to a pyrimidinic ring arising from a formal [3 + 3] cycloaddition between the metal carbene complexes and the dinitrogen systems.

The importance of the presence of the pyrimidine moiety in compounds having a broad range of applications in biochemistry (cytosine, thymine, and uracil as components of nucleic acids,[1] agrochemicals,[2] pharmacological compounds[3]) and supramolecular and materials chemistry is well-known.[4] In this context, the search for more efficient ways of preparing pyrimidine derivatives constitutes an area of permanent attention in organic synthesis.[5]

Scheme 1



In this communication, we present a straightforward and versatile synthesis of pyrimidine derivatives consisting of a formal [3 + 3] cycloaddition involving both alkynylmetal (Cr, W) carbene complexes and 1,3-dinitrogen systems.

In our studies on the Pauson−Khand cycloaddition on allylamino alkynyl carbene complexes **1**,[6] the possible use of the chelation of the *Z* branch of the heteroatom

† Present address: Kekulé-Institute für Organische Chemie und Biochemie der Universität Bonn, Germany.

(1) Wamhoff, H.; Dzenis, J.; Hirota, K. *Adv. Heterocyclic Chem.* **1992**, *55*, 130−237 and references therein.

(2) Akbar, A. *Ger. Offen.* DE 3319843 A1, 1964; *Chem. Abstr. 102*, 95667j.

(3) Kulilowski, T. *Pharm. World Sci.* **1994**, *16*, 127.

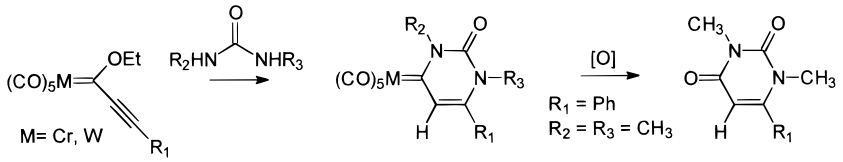
(4) (a) Kelly, S. M.; Funfschilling, J. *J. Mater. Chem.* **1993**, *3*, 953. (b) Beijer, F. H.; Sijbesma, R. P.; Vekemans, J. A. J. M.; Meijer, E. W.; Kooijman, H.; Spek, A. L. *J. Org. Chem.* **1996**, *61*, 6371−6380.

(5) (a) Undheim, K.; Benneche, T. in *Comprehensive Heterocyclic Chemistry II*; Katrizky, A. R., Ed.; Pergamon: New York, **1996**; Vol. 6, p 93. (b) Zaschke, H. *J. Prakt.Chem.* **1975**, *317*, 617.

(6) (a) Jordi, L.; Viñas, J. M.; Ricart, S.; Moretó, J. M. *Organometallics* **1997**, *16*, 2808−2818. (b) Schick, U.; Jordi, L.; Ricart, S; Veciana, J.; Dötz, K. H.; Moretó, J. M. *J. Am. Chem. Soc.* **1998**, *120*, 2283−2289.

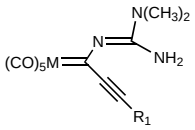
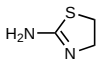
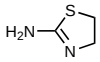
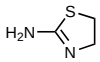
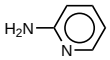
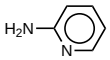
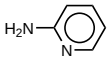
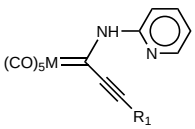
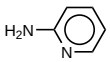
S0276-7333(97)00894-7 CCC: $15.00
Publication on Web 05/06/1998

Scheme 2



6 **7** **9** (70%)

Table 1. Reaction of 1,3-Diamino Systems with Alkynyl Carbene Complexes 6

entry	**6** (M = W) R_1	amine	*T* (°C)	time	products (%)	
1	Ph	$H_2NC(Ph)=NH$	−78	6 h	**7a** (45)	
2	Ph	$H_2NC(Ph)=NH$	room temperature	4 h	**7a** (52)	
3	t-Bu	$H_2NC(Ph)=NH$	−78	5 min	**7b** (49)	
4	t-Bu	$H_2NC(Ph)=NH$	room temperature	5 min	**7b** (47)	
5	Ph	$H_2NC(NH)N(CH_3)_2$	−78	4 h	**7c** (20)	 **8a** (21)
6	Ph		−78	5 min	**7d** (53)	
7	Ph		room temperature	5 min	**7d** (84)	
8	$Si(CH_3)_3$		room temperature	30 min	**7e** (25)	
9	Ph		−78	1h 30 min	**7f** (74)[a] (5/2)	
10	Ph		room temperature	30 min	**7f** (68)[a] (1/2)	
11	t-Bu		−78	60 min	**7g** (57)[a] (2/1)	 **8b** (9)
12	t-Bu		room temperature	45 min	**7g** (58)[a] (10/1)	**8b** (17)

[a] Obtained as a mixture of two cyclic regioisomers.

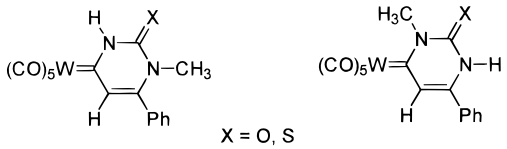
onto the metal as an element for obtaining some degree of stereocontrol in the formation of the stereogenic center in the cycloadduct **3** was envisaged (Scheme 1).

Hopefully, this bond would give extra rigidity to the system leading to the preferential formation of one of the two possible stereoisomers in the final cycloadduct. Thus, the study of the strength of this bond for different chelating groups was undertaken.

The preparation and study of compounds of type **4** has been carried out in previous work.[7] The availability of 1,3-dinitrogen systems, such as amidines, guanidines, aminothiazoles, and aminopyridines, prompted us to attempt the synthesis of systems related to **5**.

For this purpose, we reacted alkynyl alkoxy carbene complexes of tungsten and chromium **6** with different amino systems having a second nitrogen atom in a 1,3-relative position.[8] However, in all cases, the major product obtained corresponded to a cyclic compound **7**[9] and only minor amounts of the previously expected aminolysis product **8** were obtained in some cases. The results obtained are collected in Table 1. The standard reaction conditions are as follows: To a 0.05 M solution

Scheme 3



A B

	Temp. °C	A/B
7k	r.t.	3/4
7m	-78	4/1
7m	r.t.	1/4

(7) Sabaté, R.; Schick, U.; Moretó, J. M.; Ricart, S. *Organometallics*, **1996**, *15*, 3611−3615.

(8) There was a precedent of this strategy in (a) Dötz, K. H.; Rau, A.; Harms, K.; *Chem. Ber.* **1992**, *125*, 2134−2137. (b) Dötz, K. H.; Kroll, F.; Harms, K. *J. Organomet. Chem.* **1993**, 459, 169−176.

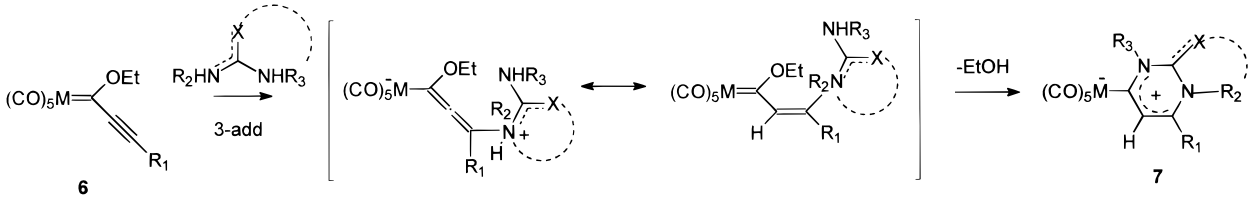
(9) **7d.** IR (CCl_4): ν 3688, 2399, 2056, 1971, 1922 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 3.38 (t, J = 7.5 Hz, 2H, NCH_2), 4.33 (t, J = 7.5 Hz, 2H, CH_2), 7.33−7.56 (m, 5H, Ph), 7.85 (s, 1H, C*H*). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.1 (t), 54.2 (t), 128.0 (d), 129.7 (d), 131.4 (s), 131.6 (d), 136.3 (d), 141.2 (s), 158.0 (s), 200.3 (s), 206.8 (s), 256.5 (C=W). Anal. Calcd for $C_{17}H_{10}N_2O_5SW$: C, 37.94; H, 1.87; N, 5.21. Found, C, 38.04; H, 2.05; N, 5.24. X-ray structure is available.

Table 2. Reaction of Ureas and Thioureas with Alkynyl Carbenes 6

entry	metal	R_1	urea	*T* (°C)	time	products (%)
1	W	Ph	$CH_3HNCONHCH_3$	room temperature	48 h	**7h** (90)
2	Cr	Ph	$CH_3HNCONHCH_3$	room temperature	48 h	**7i** (70)
3	W	Ph	$CH_3HNCONH_2$	room temperature	48 h	**7j** (71)[a] (3/4)
4	W	Ph	$CH_3HNCSNHCH_3$	room temperature	50 min	**7k** (52)
5	W	Ph	$CH_3HNCSNH_2$	−78	1 h	**7l** (56)[a] (4/1)
6	W	Ph	$CH_3HNCSNH_2$	room temperature	45 min	**7l** (60)[a] (1/4)

[a] Obtained as a separable mixture of two cyclic regioisomers.

Scheme 4



of the corresponding complex **6** in dry THF at −78 °C (or alternatively at room temperature) and under an Ar atmosphere, the 1,3-dinitrogen systems (2 equiv) were added. The course of the reaction was monitored by TLC, and the reaction was stopped after the disappearance of the starting complex.

The extension of these reactions to ureas and thioureas was also accomplished. The reaction with dimethyl urea afforded, after 48 h at room temperature, the corresponding cyclic compound, which suffers an easy oxidation with amine *N*-oxides to give the corresponding 2,4-dioxopyrimidine system (Scheme 2).

The resulting organic product was characterized by ^{1}H and ^{13}C NMR, IR, and elemental analysis.[10]

The reaction with different ureas and thioureas always gave exclusively the cyclic product **7**. As expected,[11] the reaction with ureas was slower, yet giving similar cyclic products at −78 °C to those obtained at room temperature but with slightly lower yields and inversion of the regioselectivity (compare entries 5 and 6, Table 2).

The structures proposed for the two regioisomers obtained in entries 3, 5, and 6 are shown in Scheme 3. In principle, the formation of the cyclic products **7** could be explained by the general mechanism proposed by Aumann for a similar reaction,[12] Scheme 4.

While the regiochemistry obtained for **7l** under different temperatures might be a result of the difference in nucleophilicity toward an initial conjugate addition followed by aminolysis, the strong difference in the regioisomeric ratios obtained points to a competition between aminolysis at the carbene center (kinetic control) and conjugate addition (thermodynamic control).[13,14]

In all cases, the metal pentacarbonyl moiety remains in the final cycloadducts **7** but could be eliminated by oxidative (DMSO, CAN) or reductive (H_2, pyridine) methods, affording the corresponding organic adducts. However, the presence of the metal carbene moiety confers special reactivity to these systems, now under investigation in our laboratories.

Acknowledgment. The authors acknowledge the financial support from DGICYT (Grant No. PB-94-0084) and the HCM program (Contract No. CHRX-CT94-0501).

Supporting Information Available: Text giving spectroscopic data for compounds **7a**−**l** (4 pages). Ordering information is given on any current masthead page.

OM9708945

(10) **9.** IR (CCl_4): ν 2960, 1704, 1660, 1436 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 3.19 (s, 3H, CH_3), 3.37 (s, 3H, CH_3), 5.67 (s, 1H, C*H*), 7.28−7.33 (m, 2H, Ph), 7.45−7.49 (m, 3H, Ph). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 27.9 (q), 39.5 (q), 102.5 (d), 127.7 (d), 128.7 (d), 130.1(d), 133.3 (s), 152.6 (s), 154.5 (s), 162.4 (s). Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.95. Found: C, 66.48; H, 5.73; N, 12.52.

(11) Grotjahn, D. B.; Kroll, F. E.K; Schäfer, T.; Harms, K.; Dötz, K. H. *Organometallics* **1992**, *11*, 298−310 and references therein.

(12) Aumann, R.; Jasper, B.; Fröhlich, R. *Organometallics* **1995**, *14*, 2447−2455.

(13) (a) Fischer, E. O.; Kalder, H. J. *J. Organomet. Chem.* **1977**, *131*, 57−64. (b) Duetsch, M.; Stein, F.; Lackmann, R.; Pohl, E.; Herbst-Irmer, R; de Meijere, A. *Chem. Ber.* **1992**, *125*, 2051−2065. (c) Aumann, R.; Hinterding, P *Chem. Ber.* **1993**, *126*, 421−427. (d) Stein, F.; Duetsch, M; Pohl, E.; Herbst-Irmer, R; de Meijere, A. *Organometallics* **1993**, *12*, 2556−2564. (e) Pipoh, R.; van Eldik, R.; Henkel, G. *Organometallics* **1993**, *12*, 2236.

(14) According to Aumann et al.,[12] due to the linear geometry of the alkynyl branch conjugate addition ensuing aminolysis should be regarded as rather improbable. However, precise studies on the exact nature of these complexes in solution have not been performed as far as we know. The strong differences in the ^{13}C chemical shift of the two "acetylenic" carbon atoms might be far more than a spectroscopic rarity. Wulff, W. D.; Chan, K. S. *J Am. Chem. Soc.* **1986**, *108*, 5229−5236.