Synthesis of new polymetallic carbene complexes: Uracil analogs

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Abstract

The easy cycloaddition of ureas with alkynyl alkoxy biscarbene complexes afforded, in fairly good yields, new biscarbene uracil analogs. X-ray structural data is reported for the dimethyluracil biscarbene complex. By changing the reaction conditions, a new non symmetric complex was obtained whose reaction with ethylenediamine afforded a new tetrakis amino carbene complex.
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1. Introduction

The presence of organometallic moieties in macromolecular, supramolecular and dendrimer chemistry [1] has acquired a growing importance in the last years. In this way, the use of metal (Cr, W)–carbene (Fischer type) complexes could represent an interesting entry to these macromolecular compounds [2] and, as has been previously described [3] electronic and steric effects could be allowed to the presence of the metal–carbene moiety.

The study of the reactivity and properties of the alkynyl alkoxy carbene complexes was started by us some time ago, and our work was directed to the study of the addition [4] and cycloaddition reactions [5] taking advantage of the activation induced by the presence of metal carbene moiety into the triple bond. In these complexes is pointed out, in accordance with Fischer and Kalder [6] and Aumann et al. [7] studies, the existence of two activated electrophilic sites able to react in very mild conditions (from −78 °C to rt.) [8].

On the way to the synthesis of more complex multiple metalloorganic systems we present here a study on the synthesis and properties of new biscarbene complexes. These complexes could by classified in two modes [9] depending on the junction (through a carbon chain **A** or through the heteroatom **B**) as it is shown in Fig. 1.

The general synthesis of both types of complexes are shown in Scheme 1 and has been previously described [9].

The compounds studied here represent a particular case of bioorganometallic molecules [10] having an analog of the uracil structure conjugated to a metal pentacarbonyl system. The aim of the present work is to gain insight in the synthesis and further reactivity of these new biscarbene complexes and also to explore the possibility to build macrostructures with polyorganometallic carbene moieties. A similar approach has been developed in the field of metal-conjugated peptide nucleic acids (PNAs) by the group of Maiorana [2].

2. Reaction of alkoxy alkynyl biscarbene complexes of W(0) with disubstituted ureas

In the first part of our work, the reactivity of bis alkynyl alkoxy carbene **1** (type **A**) was studied in front of different

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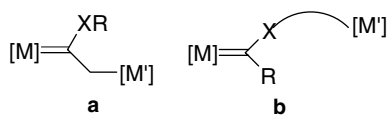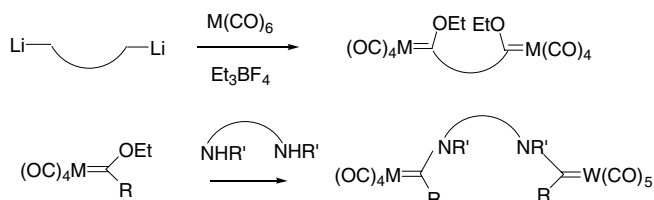 *E-mail address:* ricart@icmab.es (S. Ricart).

Fig. 1. Junction modes for biscarbene complexes.

Scheme 1.

Scheme 2.

ureas and thioureas using the previously described reaction for the synthesis of uracils [5]. The results obtained are shown in Table 1.

A similar reaction with the monocarbene **2** (Scheme 2) took place in 4 h while the presence of the DBU enhanced the rate but, lowering the yield.

Studies focused on the reactivity of the triple bond of the complex **5a**, obtained in good yield from the monocarbene **2**, are in progress in our laboratory.

As is has been stated before [8,11] some kind of interaction between the metal centers during the reaction could be expected. In our case we have observed an enhancement of the reaction rate (compare entry 1, Table 1 and Scheme 2). The cycloaddition takes place easily with very good yields and the reaction times were, in all the cases, shorter than the observed for the monocarbene systems in the same conditions [5].
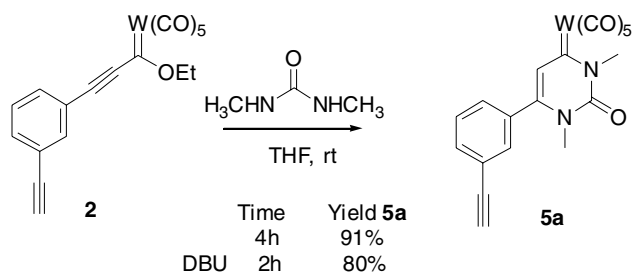
The existence of steric effects due to the substituents on the starting urea, was already observed in a previous work with monocarbene complexes [8]. In the present study with biscarbene complexes this effect is emphasized, as pointed out by the decreasing yields and increasing reaction times in the sequence Me > Et > allyl. The reaction with dimethylthiourea merits a special comment because in this case, the existence of concurrent products arising from sulfur reactivity (of difficult characterization) cause a decrease in yield of the expected product **3d**, even in the presence of a catalytic amount of DBU [12].

We tried also the reaction of complex **1** with only 1 equivalent of dimethylurea (entry 2). In this case the non symmetric complex **4a** was mainly obtained, albeit in moderate yield. In this way, it is shown here a nice example of a biscarbene complex with a different reactivity on the two carbene moieties (Fig. 2). The existence of the alkynyl alkoxy system gives the possibility to perform further reactions (amine additions or other type of cycloadditions) to attain more complex structures. To our

Table 1
Reaction of bis alkynyl alkoxy carbene complexes in front of ureas and thioureas
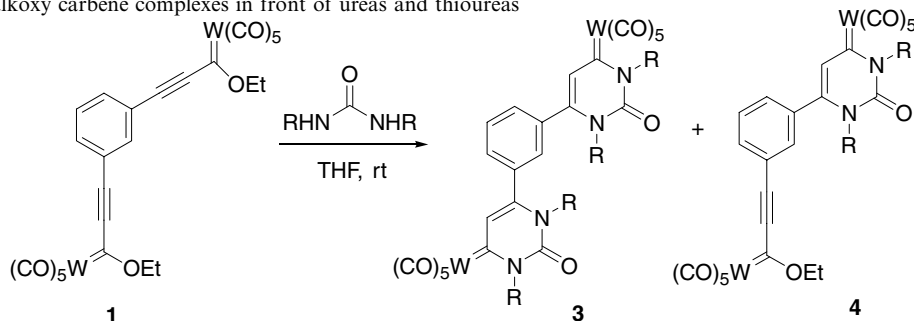
Entry	Carbene	Urea (equiv)	Additive (DBU) mmol	Reaction Time (h)	Product(yield %)
1	**1**[a]	R = Me (4)	–	1	**3a** (87)
2	**1**	R = Me (1)	–	2.5	**3a** (15)
					4a (33)
					1 (16)
3	**1**	R = Et (4)	–	4	**3b** (63)
4	**1**	R = allyl (4)	–	26	**3c** (34)
					4c (9)
5	**1**	R = allyl (4)	0.025	22	**3c** (53)
					4c (22)
6	**1**	Dimethylthiourea (4)	–	0.25	**3d** (35)

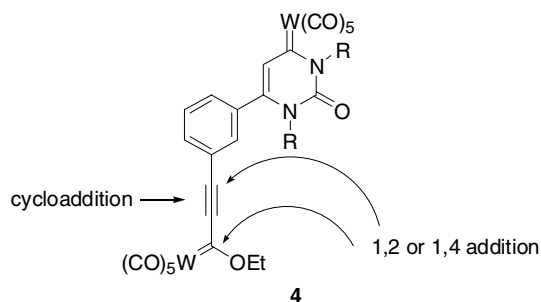[a] Reaction conditions, 0.09 M in THF, room temperature.

Fig. 2. Biscarbene complex with different reactivity on the two carbene moieties.

knowledge, there are not many examples of such type of unsymmetrical complexes [13].

3. Reaction of 4a with ethylenediamine

As an example of this diverse reactivity the reaction of ethylenediamine with the biscarbene complex **4a** was performed using previously described conditions [8] (-78 °C, 0.5 M in THF) for the synthesis of biscarbene complexes with a bridgehead heteroatom. The tetracarbene complex **6** was readily obtained in 82% yield after 2 min, in a reaction able to be followed by the color change (from dark brown to light yellow) of the reaction mixture.

Complex **6** represents an example of the diverse linkage between metal carbene complexes (through the carbon chain **A** or alternatively through the heteroatom chain **B**) in a single molecule. Furthermore, the molecule contains two activated triple bonds able to further react with nucleophiles or in cycloaddition reactions (see Scheme 3).

4. X-ray crystallographic study of complex 3a

Fig. 3 shows a perspective view of the complex **3a** along with selected bond lengths. The compound **3a** consists of a two staggered uracil ring analogs having the pentacarbonyltungsten moieties joined through C6 and C24 of the uracil rings, with the aromatic ring acting as a bridge between both metallorganic biomimetic moieties. The absence of planarity avoids any conjugation between the two organometallic uracil rings. The C=W bonds 2.236 and 2.239 Å, fall within the normal range for the aminocarbene tungsten complexes.
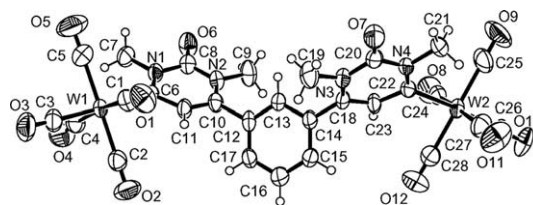

Fig. 3. Compound **3a.** Selected bond lengths (Å): W(1)–C(6) 2.236(5); N(1)–C(6) 1.373(6); N(1)–C(8) 1.417(7); N(2)–C(8) 1.372(7); W(2)–C(22) 2.239(5); N(4)–C(22) 1.377(6); N(4)–C(20) 1.387(6); N(3)–C(20) 1.389 (6); C(10)–C(12) 1.498(7); C(14)–C(18) 1.462(6).

The overall structure is oriented to maximize the distance between the two bulky organometallic moieties (see Fig. 3).

5. Conclusions

The easy cycloaddition of disubstituted ureas and bis (alkoxy)alkynyl tungsten carbene complexes afforded in good yields new bisorganometallic analogs of the uracil systems. These compounds showed to be a particular case of biscarbene complexes and the study of their reactivity is in course in our laboratories. A careful control of the reaction conditions, using a substoichiometric amount of urea, afforded new biscarbene complexes having different reactivity in the two carbene centers. This regiochemistry is showed in the reaction of **4a** with ethylenediamine . A new tetrakis amino carbene complex **6** was obtained in fairly good yield.

6. Experimental

Unless otherwise stated all common reagents and solvents were used as obtained from commercial suppliers without further purification.

^{1}H NMR and ^{13}C NMR spectra were recorded in CDCl$_3$, on a Bruker ARX 300 (300 and 75.5 MHz) spectrometer. Chemical shifts are given in ppm relative to TMS (^{1}H, 0.0 ppm) or CDCl3 (^{13}C, 77.0 ppm). IR spectra were taken on a Perkin Elmer Spectrum One FT-IR spectrometer using CH$_2$Cl$_2$ as the solvent. THF and diethyl ether were freshly distilled from sodium benzophenone under argon. Flame-dried glassware and standard Schlenck techniques were used.

Unless otherwise indicated all the reactions were performed under Ar atmosphere. Carbene complexes **1**, and **2** [9] were prepared according to the literature procedures.

7. Synthesis of 3a

General procedure. 1,3-bis {pentacarbonyl[ethoxy(phenyletynyl)carbene]}tungsten (0) 150 mg (0.17 mmol) was placed in a Schlenck with a stirring bar. The Schlenck was sealed with a rubber septum and at room temperature 2 mL of THF and 61 mg (0.68 mmol) of 1,3-dimethylurea were added under argon atmosphere. The reaction mixture was al-
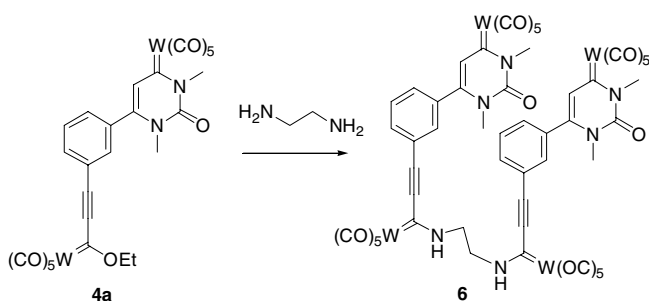
Scheme 3.

lowed to react until the disappearance of the starting carbene (1 h). The solvent was removed under reduced pressure and the dark orange residue was purified by flash column chromatography (dichloromethane as eluent) affording 143 mg (87%) of **3a** as an orange solid.

IR (CH$_2$Cl$_2$) cm^{-1}: 2925, 2061, 1969, 1906, 1694. ^{1}H NMR (300 MHz, CDCl$_3$ δ (ppm): 3.41 (s, 6H, 2 CH$_3$), 4.20 (s, 6H, 2 CH$_3$), 7.41 (s, 2H, 2 CH=), 7.45–7.83 (m, 4H, Ph). ^{13}C NMR (75.5 MHz, CDCl$_3$) δ (ppm): 36.0 (q), 48.0 (q), 126.7 (d), 127.4 (d), 130.6 (d), 133.1 (d), 144.1 (s), 149.3 (s), 198.3 (s), 203.6 (s), 240.1 (s).

8. X-ray diffraction structure resolution of 3a

The experiment was done on an Enraf-Nonius CAD4 diffractometer using graphite-monochromated Mo Kα radiation. The structure was solved by direct methods using SIR2002 after applying Lorentz, polarization, and absorption (empirical PSI-scan) corrections. Full-matrix least squares refinement (SHELXL-97) with anisotropic thermal parameters for non-H atoms and riding thermal parameters for H-atoms (positioned at calculated positions, methyl groups allowed to rotate along the ternary axis) converged to a R factor of 0.0330 (calculated for the reflections with $I > 2\sigma(I)$). Crystal data: C$_{28}$H$_{18}$-N$_4$O$_{12}$W$_2$, triclinic, space group $P\bar{1}$, $a = 10.8934(10)$ Å, $b = 10.9352(10)$ Å, $c = 13.4684(10)$ Å, $\alpha = 82.881(5)°$, $\beta = 78.933(6)°$, $\gamma = 82.671(4)°$, $V = 1553.5$ (2) Å^3, $Z = 2$, μ(Mo Kα) = 7.467 mm^{-1}, $D_c = 2.074$ g/cm^3. Approximate dimensions: $0.26 \times 0.22 \times 0.09$ mm^3. Data collection was up to a resolution of $2\theta = 60.84°$ producing 9709 reflections. Largest peak and hole at the final difference Fourier synthesis were 0.975 and -1.344 e Å^{-3}. Calculations were done using the WINGX package [14].

3b. IR (CH$_2$Cl$_2$) cm^{-1}: 2924, 2853, 2062, 1900 ^{1}H NMR (CDCl$_3$) δ 1.43 (t, 3H, $J = 6.9$ Hz, CH$_3$), 1.52 (t, 3H, $J = 6.9$ Hz, CH$_3$), 3.84 (q, 2H, $J = 6.9$ Hz, CH$_2$), 4.75 (q, 2H, $J = 6.9$ Hz, CH$_2$, 7.36 (s, 1H, CH), 7.45–7.80 (m, 4H, Ph). ^{13}C NMR δ 13.6 (2q), 43.7 (t), 56.4 (t), 126.9 (d), 127.2 (d), 129.9 (d), 130.4 (d), 133.0 (s), 144.2 (s), 147.7 (s), 198.2 (s), 203.2 (s), 238.3 (s).

3c. IR (CH$_2$Cl$_2$)cm^{-1}: 2924, 2854, 2062, 1971, 1913 ^{1}H NMR (CDCl$_3$) δ 4.40 (m, 2H, CH$_2$), 4.99 (d, 2H, $J = 17.1$ Hz, CH$_2$) 5.29–5.40 (m, 2H, CH), 5.78–5.91 (m, 2H, CH), 5.99–6.10 (m, 2H, CH), . ^{13}C NMR δ 50.2 (t), 62.5 (t), 118.5 (t), 119.1 (t), 127,1 (d), 127.4 (d), 129.9 (d), 130.3 (d), 130.5 (d) 131.3 (d), 132.5 (s), 144.1 (s), 147.8 (s), 198.1 (s), 203.0 (s), 241.3 (s).

3d. IR (CH$_2$Cl$_2$) cm^{-1}: 2924, 2854, 2063, 1926. ^{1}H NMR (CDCl$_3$) δ 3.75 (s, 3H), 4.64 (s, 3H), 7.47 (s, 1H), 7.62–7.87 (m, 4H). ^{13}C NMR δ 127.1 (d), 130.5 (d), 130.8 (d), 134.1 (s), 141.7 (s), 174.3 (s).

4a. IR (CH$_2$Cl$_2$) cm^{-1}: 2159, 2068, 2062, 1908, 1696. ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 1.63 (t, $J = 6.9$ Hz, 3H, CH$_3$); 3.38 (s, 3H, CH$_3$), 4.21 (s, 3H, CH$_3$), 4.77 (q, $J = 6.9$ Hz, 2H, CH$_2$); 7.42 (s, 1H, CH), 7.45–7.83 (m, 4H, Ph). ^{13}C

NMR (75.5 MHz, CDCl$_3$) δ (ppm): 14.8 (q); 35.9 (q), 47.9 (q), 78.0 (bt); 97.8 (s); 122.9 (s); 126.6 (d); 130.1 (d), 131.5 (d); 132.7 (s), 134.3 (d), 144.3 (s); 149.4 (s); 197.2 (s); 198.3 (s); 203.5 (s); 205.4 (s); 239.8 (s).

4c. IR (CH$_2$Cl$_2$) cm^{-1}: 2925, 2855, 2159, 2062, 1906 ^{1}H NMR (CDCl$_3$) δ 1.63 (t, 3H, $J = 6.9$ Hz), 4.19 (m, 2H), 4.43 (m, 2H), 4.73 (q, 2H, $J = 6.9$ Hz), 5.08 (d, 2H $J = 17.1$ Hz), 5.32 (m, 2H), 5.82-6.09 (m, 2H), 6.09 (s, 1H), 7.38–7.50 (m, 4H).

5a. IR (CH$_2$Cl$_2$) cm^{-1}: 3299, 2061, 1971, 1916, 1688. ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 3.23 (s,1H, CH); 3.35 (s, 3H, CH$_3$), 4.19 (s, 3H, CH$_3$), 7.37 (s, 1H, CH), 7.39–7.80 (m, 4H, Ph). ^{13}C NMR (75.5 MHz, CDCl$_3$) δ (ppm): 35.9 (q), 47.9 (q), 79.6 (d); 81.8 (s); 123.7 (s); 126.6 (d); 128.0 (d); 130.1 (d), 129.5 (d); 131.72 (d), 132.0 (s); 134.4 (d), 145.2 (s); 149.4 (s); 198.4 (s); 203.5 (s); 239.s(s).

Synthesis of 6. To a stirred solution of the 0.100 g (0.1 mmol) of carbene **4a** in 1 mL of dry THF at −78 °C, 1 equiv. of the diamine was added. The reaction course was monitored by thin layer chromatography. After the starting carbene complex had completely disappeared, the solvent was removed and the residue passed through a flash chromatography column affording 0.075 g (82%) of the complex **6** as a wax orange solid.

IR (CH$_2$Cl$_2$) cm^{-1}: 2174, 2062, 1976, 1902, 1693. ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 3.34 (s, 3H, CH$_3$), 4.11 (bs, 4H, CH$_2$); 4.18 (s, 3H, CH$_3$), 7.39 (s, 1H, CH=), 7.40–7.80 (m, 4H, Ph); 9.24 (bs, 2H, NH) . ^{13}C NMR (75.5 MHz, CDCl$_3$) δ (ppm): 35.8 (q), 47.9 (q), 51.3 (t); 92.2 (s); 122.6 (s); 126.6 (d); 129.9 (d), 130.0 (d), 131.5 (d); 132.6 (s); 134.1 (s), 144.4(s); 149.3 (s); 197.9 (s); 198.4 (s); 202.8 (s); 203.5 (s); 236.7 (s); 239.5 (s).

Acknowledgements

Appendix A. Supplementary data

Tables of X-ray data for compound **5a**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2005.08.011.

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