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Mononuclear Biscarbene Complexes by Direct Nucleophile Addition to a CO Ligand of Fischer Arylcarbene Complexes

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Mononuclear Group 6 Fischer biscarbene complexes **I**, which are organometallic compounds that have two carbene ligands bonded to the same transition-metal atom, have been much less investigated than the corresponding Fischer monocarbene complexes **II** (Figure 1).[1] Only very few examples of this class of compounds **I** have been reported and characterized by reactivity and/or X-ray studies, and their synthetic potential remains to be explored. In addition, there is a lack of a general method to produce such complexes.

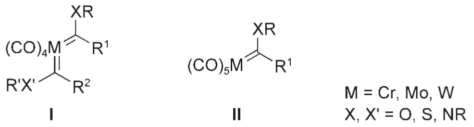

Figure 1. General structure of mononuclear Fischer biscarbene complexes **I** and monocarbene complexes **II**.

The classical Fischer synthesis (successive treatment of a Group 6 hexacarbonylmetal with an organolithium (2 equiv) and then a strong electrophile) is limited to only particular types of both cyclic[2] and acyclic mononuclear *cis*-biscarbene complexes,[3] and typically affords low product yields. In addition, these complexes have been prepared by thermal reaction of tetraaminoalkenes with the corresponding Group 6 $M(CO)_6$ complex,[4,5] and a single tungsten biscarbene derivative was synthesized from an (amino)-(alkenyl)monocarbene complex and a phenyl isocyanide under photochemical conditions.[6]

The synthesis of a mononuclear biscarbene complex by direct reaction of a Fischer monocarbene complex with a nucleophile has been reported to succeed only in the case of cyclic diaminocarbene complexes which after successive treatment with an organolithium (MeLi or PhLi) and a strong electrophile ($MeSO_3F$ or Et_3OBF_4) provided mixed *cis*-biscarbene complexes.[4] The addition of a nucleophile to a pentacarbonylcarbene complex such as **II** usually takes place at the carbene carbon atom, which has a strong electrophilic character, and not at one of the CO ligands.[7] Nevertheless, organolithium addition at a coordinated CO occurred when nucleophilic attack at the carbene carbon has been suppressed by a previous enolization-type reaction;[8] and an intramolecular addition of a heteronucleophile to a CO ligand of a neutral alkoxymonocarbene complex has been referred to explain the formation of a reaction product.[9]

On the other hand, mononuclear biscarbene complexes of Group 6 have been proposed as intermediates in the thermal carbene–carbene coupling reactions of either Fischer mononuclear monocarbene complexes[10] or dinuclear biscarbene complexes.[11] These carbene ligand coupling processes, that produced alkenes, have also been reported to occur at room temperature in the presence of a palladium(0)[12] or a copper(I)[13] catalyst.

In the context of our ongoing studies of the reactivity of Fischer carbene complexes with nucleophiles,[14] we have found that in the case of (menthyloxy)(aryl)monocarbene complexes the site of nucleophile addition is strongly depending on the nature of the organolithium compound. While butyllithium and alkynyllithiums react with the carbene carbon atom,[15a,16] and more substituted alkyllithiums (such as *s*BuLi or *t*BuLi) and phenyllithium undergo conju-

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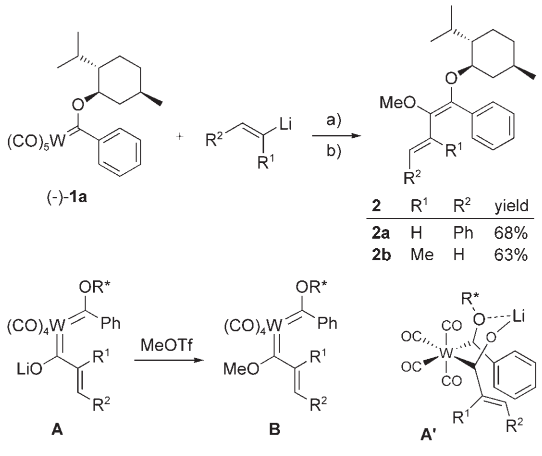
gate addition to the aromatic ring,[15] alkenyllithiums exhibit clean addition to a CO ligand. Herein, we describe a general method for the preparation of different types of mononuclear biscarbene complexes of chromium and tungsten which involves the unusual attack of a nucleophile on a CO ligand of the corresponding Fischer arylcarbene complex.

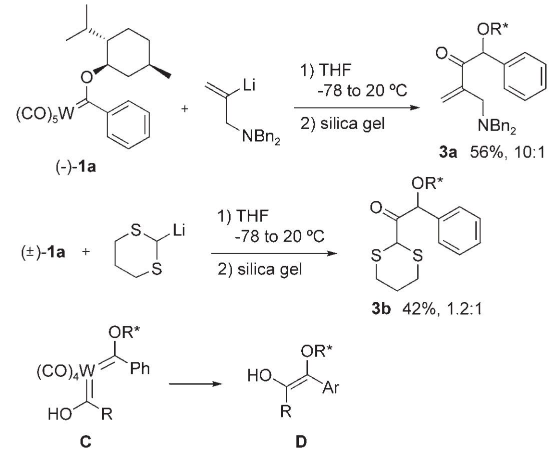
In the initial experiments we observed that the successive treatment of tungsten (menthyloxy)(phenyl)carbene complex (−)-**1a**[17] with an alkenyllithium [(*E*)-2-phenylethenyllithium or 1-methylethenyllithium] and then with methyl triflate under the reaction conditions shown in Scheme 1, provided, after silica gel column chromatography, *cis*-1,2-dialkoxy-1,3-dienes **2a**,**b**, each one as a single diastereoisomer. The selective formation of compounds **2** can be understood assuming an addition of the alkenyllithium to a CO ligand of complex (−)-**1a** to give lithioxy intermediate **A** and after treatment with MeOTf (alkoxyaryl)(methoxyalkenyl)biscarbene complexes **B**, which would undergo a spontaneous carbene–carbene coupling reaction. Presumably, biscarbene complexes **B** have the two carbene ligands in the thermodynamically more stable *cis* orientation[18] and with a disposition of the alkoxy groups to the same side of the molecule what could be controlled by intramolecular coordination of the lithium cation to the menthyloxy group oxygen as depicted in model **A'** (Scheme 1). This model accounts for the selective formation of diastereoisomers **2** with a *Z* configuration of the 1,2-dialkoxy substituted C=C bond. The stereochemistry was ascertained on the bases of a NOE difference experiment performed with compound **2a**.



2	R1	R2	yield
2a	H	Ph	68%
2b	Me	H	63%

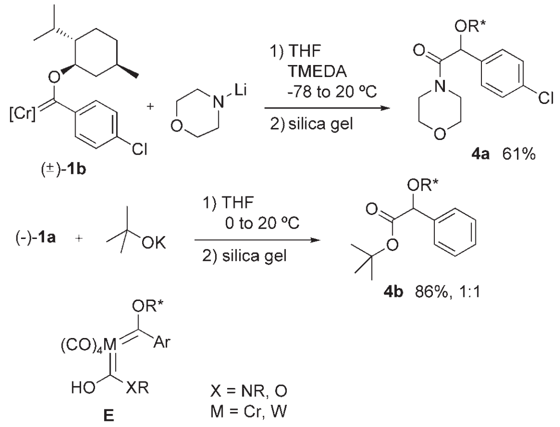
Scheme 1. Two-heteroatom-stabilized mononuclear (alkoxy)(alkoxy)biscarbene complexes **B**. a) THF, −78 to 20°C; b) MeOTf, Et$_2$O, 0 to 20°C. R*OH = (−)-menthol.

Analogous reactions carried out with carbene complex **1a** and functionalized organolithium compounds but quenched with silica gel instead of MeOTf afforded functionalized α-alkoxyketones **3** (Scheme 2). The addition of 1-(dibenzylaminomethyl)ethenyllithium to (−)-**1a** provided enone **3a**[19] as a 10:1 mixture of diastereoisomers while combination of 2-lithio-1,3-dithiane (a stabilized alkyllithium) with (±)-**1a** furnished **3b** as a roughly equimolecular mixture of isomers. Accordingly, these reactions would involve formation of (alkoxy)(hydroxy)biscarbene complexes **C** and, after intramolecular carbene–carbene coupling, 2-menthyloxy substituted enols **D** (Scheme 2).



Scheme 2. Two-heteroatom-stabilized mononuclear (alkoxy)(hydroxy)-biscarbene complexes **C**. R*OH = (−)-menthol or (±)-menthol. Bn = CH$_2$Ph.

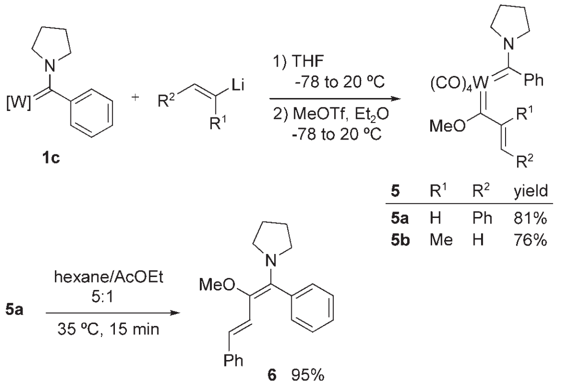
We found that heteronucleophiles as lithium amides or potassium alkoxides are also able to react with a CO ligand of complexes **1** (Scheme 3). Thus, the reaction of chromium carbene complex (±)-**1b** with the lithium amide of morpholine, which requires the presence of TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine),[20] furnished after treatment with silica gel α-menthyloxyamide **4a** as a single isomer.[21] In a similar way, addition of potassium *tert*-butoxide to complex (−)-**1a** led to α-alkoxyester **4b** (1:1 mixture of diastereoisomers).[22] These products **4a**,**b** are likewise the stable tautomeric form of 2-alkoxyenols arising from intramolecular



Scheme 3. Three-heteroatom-stabilized mononuclear (alkoxy)(alkoxyhydroxy or aminohydroxy)biscarbene complexes **E**. R*OH = (−)-menthol or (±)-menthol. [Cr] = (CO)$_5$Cr. TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.

coupling of the two carbene ligands of (alkoxy)(alkoxyhydroxy or aminohydroxy)biscarbene complexes **E** (Scheme 3).

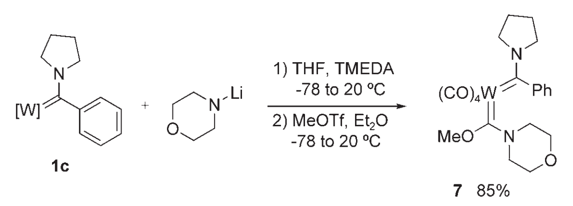
To obtain a more direct evidence of the formation of mononuclear biscarbene complexes we decided to test (amino)arylcarbene complexes, which under the above reaction sequence would produce more stable biscarbene complexes given the greater stability of the aminocarbene complexes in relation to the alkoxycarbene derivatives.[23] Gratifyingly, it was observed that aminocarbene complex **1c** reacted with an alkenyllithium and MeOTf as summarized in Scheme 4 to afford the desired (aminoaryl)(alkoxyalkenyl)biscarbene complexes **5a**,**b** each one as a single diastereoisomer. These mononuclear biscarbene complexes **5** are relatively stable derivatives at room temperature but as a preventive measure they were stored refrigerated (−3 °C) and under N_2. In fact, when a solution of biscarbene complex **5a** in hexane/ethyl acetate (5:1) was heated at 35 °C for a short time (15 min) the diastereoselective and almost quantitative formation of (1*Z*,3*E*)-1-amino-2-alkoxy-1,3-diene (**6**) was observed (Scheme 4). The stereochemistry of this carbene–carbene coupling product **6** was ascertained from a 2D NOESY experiment.[24] Biscarbene derivatives **5** represent the first examples of mononuclear biscarbene complexes stabilized by two heteroatoms and with an acyclic structure which have been isolated and characterized. The ^{13}C NMR spectra of compounds **5** show four signals between 200–220 ppm assigned to four chemical inequivalent CO ligands what reveals a *cis* relative configuration of the two carbene ligands. From the 1D and 2D NMR studies the relative arrangement of the substituents of each carbene ligand could not be established.



5	R¹	R²	yield
5a	H	Ph	81%
5b	Me	H	76%

Scheme 4. Two-heteroatom-stabilized mononuclear (amino)(alkoxy)biscarbene complexes **5**. [W] = $(CO)_5W$.

Although compounds **5** are oil materials, a solid derivative **7** was successfully synthesized using a heteronucleophile (Scheme 5). The successive addition to complex **1c** of morpholine lithium amide and MeOTf provided diastereoselectively (amino)(aminoalkoxy)biscarbene complex **7** (yellow solid). An X-ray structure determination of a single crystal of **7**[25] confirmed the *cis* disposition of the two carbene ligands and allowed to ascertain a *syn* orientation of the pyrrolidinyl and methoxy groups (Figure 2). Biscarbene complex **7** stabilized by three heteroatoms is stable at room temperature for long periods of time even in solution (at least two days). However, heating (45 °C) solutions of this complex **7** in THF, toluene or hexane/EtOAc did not lead to the carbene–carbene coupling product, instead decomposition materials were obtained. In addition, the X-ray analysis revealed that the single crystal of **7** chosen for the study had a chiral space group ($P2_12_12_1$) while, as expected, a dichloromethane solution of compound **7** showed no optical activity. This can be explained assuming a segregation of enantiomers upon crystallization which is known as spontaneous resolution.[26] Compound **7** which is a chiral complex with exclusively achiral ligands in an octahedral environment, presumably exhibits atropisomerism (carbene ligands do not have free rotation) and condensation into crystals occurred with formation of a conglomerate[27] (each crystal is formed by only one enantiomer but the sample as a whole is racemic because it contains equal amounts of enantiomorphic



Scheme 5. Three-heteroatom-stabilized mononuclear (amino)(aminoalkoxy)biscarbene complex **7**. [W] = $(CO)_5W$. TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.

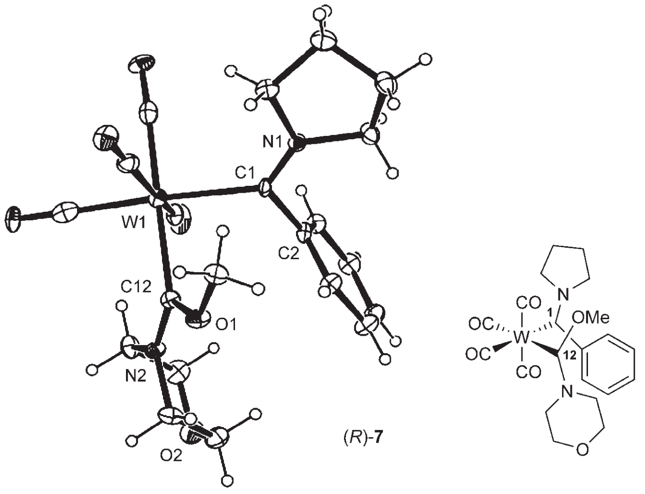


Figure 2. ORTEP representation of (*R*)-**7** in the crystal structure with thermal ellipsoids set at 30 % probability. The dihedral angle between the least squares planes through the atoms W1-C1-N1-C2 and W1-C12-N2-O1 is 69.4(1)°. Bond lengths W1−C1 2.260(6) and W1−C12 2.292(7) Å. The W coordination angles vary from 83.4(3) to 98.6(3)° indicating a distorted octahedral environment.

condensates). The enantiomer of **7** shown in Figure 2 has been designed as (*R*) [(*R*)-**7**]. This descriptor was assigned assuming a chiral axis going through the carbene carbon atoms C1 and C12 and applying the sequence rule.[28]

In summary, different types of mononuclear Fischer biscarbene complexes have been prepared by nucleophilic addition to a CO ligand of a heteroatom-stabilized arylcarbene complex. The intramolecular and diastereoselective carbene–carbene coupling is a highly favored process in these complexes that results in the formation of electron-rich 1,3-dienes including chiral derivatives.

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Keywords: diene ligands · alkenyllithiums · carbene–carbene coupling · carbenes · nucleophilic addition

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[19] The major diastereoisomer was separated by column chromatography but the absolute configuration of the stereogenic center formed in the reaction has not been determined.

[20] In the absence of TMEDA there is no reaction. Starting carbene complex (±)-**1b** was recovered.

[21] The relative configuration of the new stereogenic center formed in the reaction has not been established.

[22] These diastereoisomers were easily separated by column chromatography; the absolute configuration of the new stereogenic center has not been determined.

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[24] HMQC, HMBC, COSY and NOESY NMR spectra were measured.

[25] Crystal data for **7** [(*R*)-**7**]: $C_{21}H_{24}N_2O_6W$ $M_r = 584.27$, orthorhombic, space group $P2_12_12_1$, $a = 8.9435(1)$, $b = 14.2153(2)$, $c = 16.8631(2)$ Å, $V = 2143.88(5)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.81$ Mg m^{-3}, $Cu_{K\alpha}$ radiation (graphite crystal monochromator, $\lambda = 1.54184$ Å), $\mu = 10.35$ mm^{-1}, $F(000) = 1144$, $T = 120(2)$ K. Absolute configuration Flack parameter, −0.03(2). Final conventional $R = 0.0405$, $\omega R2 = 0.1028$ and $S = 1.033$, for 4006 "observed" reflections and 274 variables. CCDC 648590 (**7**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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