

Communications

Polymer-Bound Fischer Tungsten Carbene Complexes: Synthesis and Reactivity

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Summary: The solid-phase synthesis of polymer-bound tungsten Fischer carbene complexes of the types **8** and **16** is described. Starting with isocyanide ligands **5** and **14**, readily available from the Merrifield resin **1**, the pentacarbonyl(isocyanide)tungsten complexes **7** and **15** are efficiently formed. The synthesis of the corresponding methoxycarbene complexes **8a,b** and **16a,b** (**a**, R = Me; **b**, R = Ph) is undertaken under standard Fischer conditions. The solid-phase amination, methyl acrylate cyclopropanation, and C–H insertion arise as preliminary studies related to their reactivity.

The important role that the solid-phase chemistry has acquired during the last decades in the development of organic synthesis is well recognized, particularly within the area of combinatorial chemistry.¹ Moreover, increasing efforts have been made also to extend such a strategy to organic synthesis mediated or catalyzed by transition metals.² On the other hand, group 6 Fischer carbene complexes have been envisaged as a powerful tool for selective synthesis of an array of carbocycles and heterocycles as well as open-chain molecules.³ A major limitation of these systems lies in the fact that stoichiometric amounts of metal complexes are required, the metal unit being routinely discarded. Although it seems clear that application of the polymer-supported reagents

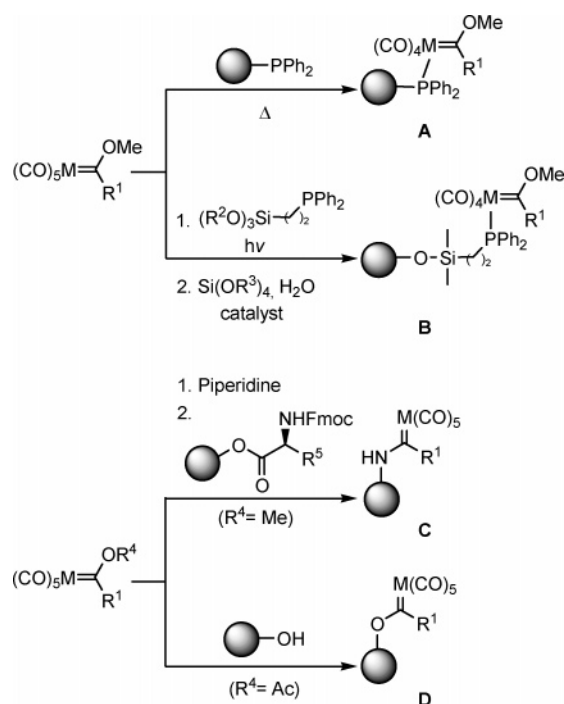


Figure 1. Polymer-bound Fischer carbene complexes.

strategy⁴ would be an attractive approach to face this problem, few reports in this sense have been released (Figure 1). The pioneering work is due to Maiorana et al., who prepared polymer-bound Fischer chromium carbene complexes **A** from the corresponding (pentacarbonyl)carbene complexes via polymer-supported diphenylphosphine/carbon monoxide ligand exchange.⁵ Following the same strategy, Dötz et al. were also able to immobilize pentacarbonyl[phenyl(methoxy)carbene]chromium in a silica matrix by formation of complexes **B**.⁶ Fischer (amino)carbene⁵ and (alkoxy)carbene⁷ complexes, **C** and **D**, bound to the polymer support through

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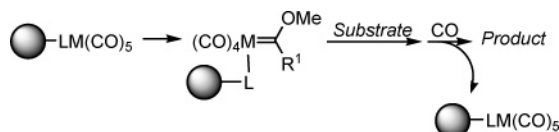


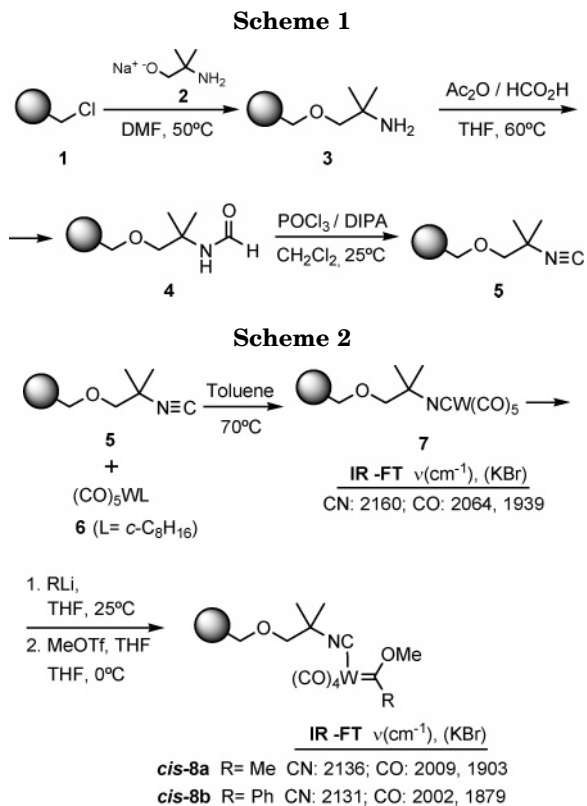
Figure 2. Schematic approach for the synthesis and use of polymer-bound Fischer carbene complexes.

the heteroatom have also been reported. From a practical point of view, the carbenes **A** and **B** are more attractive, but they seemingly suffer from two major drawbacks: (i) replacing a CO ligand with a phosphine lowers the metal-carbene reactivity to a noticeable extent;⁸ (ii) since the supported metal carbene is made from the pentacarbonylcarbene precursor itself, the polymer-supported carbene complex could not eventually be recycled after the carbene ligand is transferred to the substrate.⁹

Within this scenario we were highly interested in devising a new protocol that would allow the synthesis of the polymer-bound Fischer carbene complex from the corresponding polymer-bound (pentacarbonyl)metal complex according to the Fischer procedure.¹⁰ This would allow recovering and reusing the starting supported reagent by simply passing a stream of CO at the end of the reaction (Figure 2). Moreover, taking into account its electronic properties as a π -acceptor ligand, we selected the isocyanide functionality, rather than σ -donating phosphine ligands, as the metal-resin connecting link. On the basis of Figure 2, we present here the preparation of new polymer-bound Fischer carbene complexes of tungsten using isocyanides as the supported ligands,¹¹ as well as some preliminary studies on their reactivity.

Group 6 pentacarbonyl(isocyanide)metal complexes are readily available in solution from $(\text{CO})_5\text{M}-\text{L}$ ($\text{M} = \text{Cr}, \text{W}$; $\text{L} = \text{THF}, \text{cyclooctene}^{12}$). Moreover, while $(\text{CO})_5\text{Cr}(\text{CNCH}_2\text{Ph})$ has been reported to undergo nucleophilic addition of RLi onto the isocyanide ligand to form the amino carbene complex $(\text{CO})_5\text{Cr}=\text{C}(\text{NHCH}_2\text{Ph})\text{R}$,¹³ the use of bulky isocyanide ligands results in the selective addition to a carbonyl ligand, giving rise to the corresponding tetracarbonyl(alkoxy)carbene complexes $(\text{CO})_4(\text{R}^1\text{NC})\text{M}=\text{C}(\text{OMe})\text{R}^2$.¹⁴

First, the solid-phase synthesis of the isocyanide-linked resin **5** was accomplished from the Merrifield resin **1** (loading 1.06 mmol/g), as shown in Scheme 1. Thus, a suspension of the resin **1** (18.9 g, 20 mmol) in DMF (60 mL) was treated at 50 °C with the aminoalkoxide **2** (100 mmol). The resulting mixture was filtered and washed first with water (2×20 mL) and methanol (3×20 mL) and then with 20 mL of methyl-



ene chloride followed by 20 mL of diethyl ether (three times), to give 19.9 g of the amine-linked resin **3**. This resin **3** (19.9 g, 20 mmol) was suspended in 200 mL of THF and reacted at 60 °C with a mixture of acetic anhydride (57.2 mL, 600 mmol) and formic acid (22.6 mL, 600 mmol). After filtration, the solid was washed in a similar way as **3** to give 20.7 g of the polymer-bound amide **4**. Finally, 20.7 g (20 mmol) of the amide-linked resin **4** in 200 mL of methylene chloride was dehydrated at room temperature with a mixture of 42.1 mL (300 mmol) of diisopropylamine (DIPA) and 9.3 mL (100 mmol) of phosphorus oxychloride to form, after filtration and successive washes, the isocyanide resin **5**.

The complexation of the newly formed isocyanide ligand to metal was effected by heating a mixture of the complex precursor $(\text{CO})_5\text{W}(\text{cyclooctene})$ **6** (18.3 g, 42 mmol) and isocyanide polymer **5** (10.6 g, 10.5 mmol based on the loading of the starting resin **1**) in toluene at 70 °C (Scheme 2). The resulting pentacarbonyl(isocyanide)tungsten complex **7** was filtered and purified by consecutive washings with 20 mL of methylene chloride and 20 mL of diethyl ether (three times). At this point, the corresponding metal carbenes were generated following the standard procedure disclosed by Fischer.¹⁰ Thus, a suspension of complex **7** in THF was treated with an excess of methyl lithium or phenyllithium (5 equiv as referred to the initial resin loading) at 25 °C for 30 min, followed by quenching with 10 equiv of methyl triflate (0 °C, 30 min). The solid was filtered, and the residue was washed consecutively with methylene chloride, water, methanol, and then with methylene chloride followed by diethyl ether (three times). The resulting solid was dried, and the polymer-bound Fischer carbene complexes **8a** and **8b** were isolated.¹⁵ In all cases, the *cis*-isomer is selectively formed as deduced from the $\nu(\text{CO})$ absorptions, which are in complete

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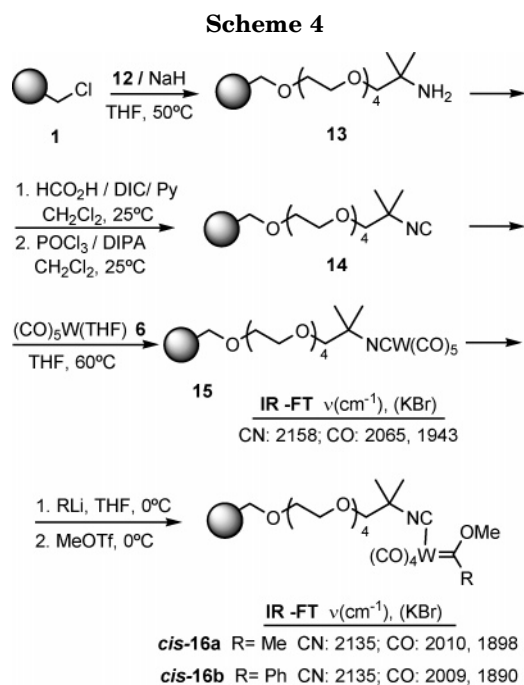
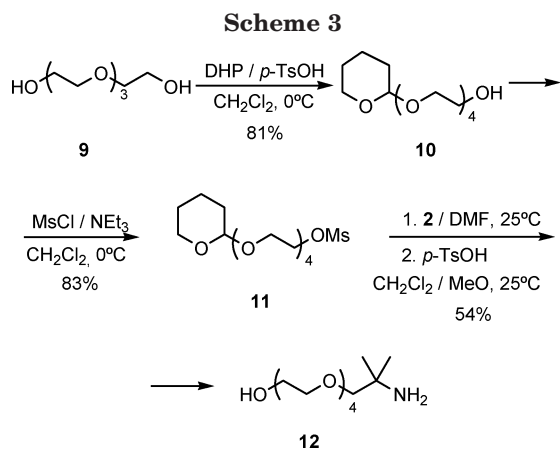
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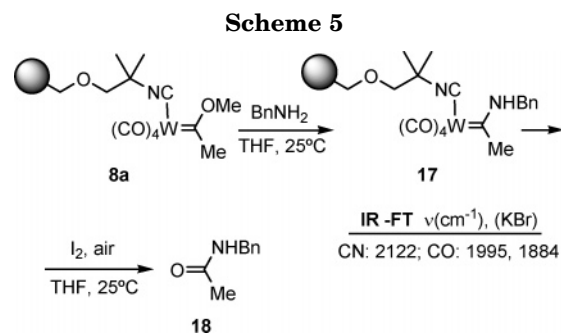
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accordance with solution studies¹⁴ and with the report by Maiorana for the resin-bound carbenes **A** (R = Me: 2008, 1888 cm^{-1} ; R = Ph: 2010, 1887 cm^{-1}).⁵

At this point, we thought it of synthetic interest to access polymer-supported carbenes of different nature, particularly in terms of swelling properties, by modifying the linker chain length. Specifically, the amino alcohol **12**, readily available from tetraethylene glycol **9**, seemed to be an adequate linker to meet this purpose (Scheme 3). The preparation of **12** was accomplished by initial monoprotection of **9** with DHP to afford **10**, which was then mesylated to yield **11**. Finally, the latter was reacted with sodium 2-methyl-2-aminopropanolate **2** to provide **12** in moderate overall yield.

Next, the linker was successively connected to the resin and to the metal pentacarbonyl complex as outlined in Scheme 4. First, a THF solution of resin **1** (2.9 g, 3.1 mmol) and the sodium alkoxide salt of **12** (3 equiv) was heated at 50 °C for 15 h. The resulting mixture was cooled, filtered, and washed first with water (2 × 20 mL) and methanol (3 × 20 mL) and then with 20 mL of methylene chloride followed by 20 mL of

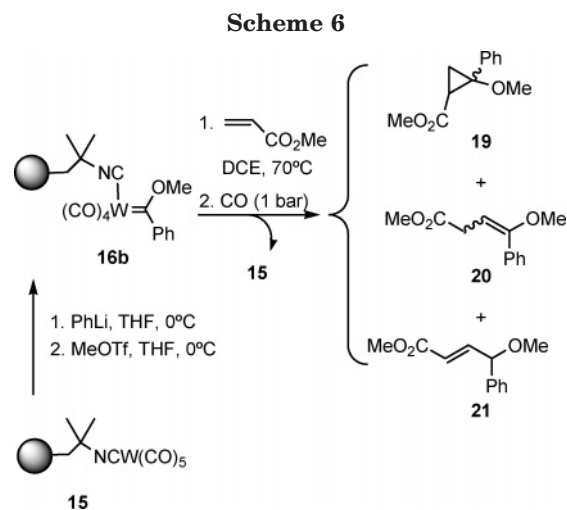


diethyl ether (three times) to afford the amine resin **13**. Further formylation (formic acid/1,3-diisopropylcarbodiimide/pyridine; 25 °C) and dehydration (phosphorus oxychloride/diisopropylamine; 25 °C) produced the supported isocyanide ligand **14**, which was complexed to tungsten, yielding the tungstenpentacarbonyl complex **15**. The synthesis of the Fischer carbene complexes **16a** and **16b** was undertaken by reacting a THF solution of **15** with methyllithium (3 equiv) or phenyllithium (5 equiv) at 0 °C for 60 min, followed by quenching with methyl triflate (2 equiv vs RLi, 1 min, 0 °C). The mixture thus obtained was filtered and the residue washed. Complexes **16** were isolated as the *cis*-isomers on the basis of the IR data (see complexes **8**, Scheme 2). Representative HR-MAS NMR resonances (CDCl_3 , δ) for carbene complex **16a**: ¹H NMR, 1.45 (2 CH₃), 3.36 (CH₃), 3.5–3.9 (OCH₂), 3.7 (OCH₃) ppm; ¹³C NMR, 27 (CH₃), 59 (CH₃), 70–73 (OCH₂), 75 (OCH₃) ppm.

The initial experiments to check the reactivity of this type of supported Fischer carbene complexes were directed to the solid-phase aminolysis reaction. For instance, the methyl(methoxy)carbene complex **8a** reacted with benzylamine (9 equiv) in THF at room temperature to provide the corresponding polymer-bound aminocarbene complex **17** (Scheme 5). The isocyanide and carbonyl IR absorptions reflect clearly the bathochromic effect due to the presence of a stronger donating group (amino vs alkoxy). The facile oxidation with I₂/air to the amide **18** provides a mild method for delivering the aminocarbene ligand.

The long-term-studied cyclopropanation reaction with Fischer carbene complexes was also considered. Although, the solid-phase reaction of carbene **8a** with methyl acrylate in 1,2-dichloroethane (DCE) at 70 °C was rather sluggish, the preliminary studies with carbene **16b** under solution-phase conditions were more promising (Scheme 6). Thus, heating a mixture of **16b** and methyl acrylate (20 equiv) in 1,2-dichloroethane (DCE) at 70 °C resulted in the disappearance of the IR absorptions of **16b** after 3.5 h. The mixture was cooled to 25 °C, saturated with CO, and stirred for 10 min. The suspension was filtered, and the residue was washed thoroughly with tetrahydrofuran, methylene chloride, and diethyl ether. The solution consisted of a mixture of cyclopropanes **19** and the C–H insertion products **20** and **21**, the yield amounting to ca. 40% from the alkoxy carbene complex **16b**.¹⁵ On the other hand, the polymer-supported pentacarbonyltungsten complex **15** was recovered from the solid phase and re-elaborated into the Fischer carbene **16b**. The recycled pentacarbonyl and carbene complexes **15** and **16b** provided IR spectra of excellent quality, thus indicating good efficiency for the recovering step. Then, **16b** was subjected

(15) A rough IR estimation points out that around 15% of the pentacarbonylmetal units remain unreacted.



again to react with methyl acrylate, affording the resulting products **19–21** in ca. 20% yield.

In conclusion, we have been successful in achieving the first synthesis of alkoxy carbene complexes on solid support following the standard Fischer procedure.¹⁰ This is particularly advantageous in terms of recycling and reusing the metal reagent. Compared with the use of donor phosphine ligands as resin-metal connector, the use of a π -acceptor ligand, such as isocyanide, should result in increasing reactivity in the metal carbene

functionality.¹⁶ The method seems to be flexible, as polymer-bound carbene complexes of different nature would be accessible by using diverse linking connectors. Regarding their reactivity, the solid-phase exchange reaction of the carbene complex **8a** with benzylamine leads efficiently to the corresponding polymer-bound aminocarbene complex **17**, while the carbene complex **16b** undergoes with moderate efficiency solid-phase reaction toward methyl acrylate, yielding cyclopropanes and C–H insertion products. From these preliminary results it might be realized that a new perspective is open in the chemistry of group 6 carbene complexes, although it is anticipated that further efforts to increase the efficiency of this procedure are of need.

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Supporting Information Available: This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(16) Phosphinecarbene complexes **A** and **B** have just been reported to be reactive toward primary amines.