Isocyanide-Promoted Ylidene Transfer to Phosphorus: Rearrangement in the First-Generation Grubbs Complex

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Summary: Carbon monoxide or an aryl isocyanide promotes a benzylidene carbene transfer from ruthenium to tricyclohexylphosphine in the first-generation Grubbs carbene complex. The resulting ruthenium(II) complexes have been isolated and structurally characterized by X-ray crystal structure analysis; a probable mechanism for the ligand-promoted transformation is also discussed.

Decomposition and carbene insertion processes in the Grubbs ruthenium carbene complexes are of great interest.[1] We recently reported a method to quench the Grubbs carbenes in order to easily purify organic products obtained from olefin metathesis reactions.[2] The procedure offers a very practical solution to a common problem in metathesis chemistry: removing the ruthenium-containing byproducts. The isocyanides **3** and **4** (or carbon monoxide) promoted a Buchner cyclopropanation/ring expansion process into an aromatic ring of the N-heterocyclic carbene ligand (NHC), as depicted in eq 1 (Scheme 1).[1e] The aromatic ring of the NHC is found in the second-generation Grubbs complex **1**. The isocyanide-promoted ligand insertion process using **4** gave the polar ruthenium(II) complex **2** (L = $CNCH_2CO_2K$), which proved to be easy to remove. Interestingly, the first-generation Grubbs complex also gave a polar product that was conveniently separated from the organic reaction products.[3] Since the first-generation Grubbs complex has no aromatic rings to give the Buchner reaction, we were interested to learn what was happening in this system. In the presence of strongly coordinating ligands (such as CO), apical coordination to the open binding site on ruthenium and ligand displacement appear to be the most likely available reaction pathways. In this report, we have identified the product of ligand-promoted rearrangement in the Grubbs first-generation carbene complex using carbon monoxide or isocyanides. The transformation is a ligand-promoted ylidene transfer from the coordination sphere of the metal to the phosphorus atom of tricyclohexylphosphine (Scheme 1, eqs 2 and 3).

Reaction of the Grubbs first-generation carbene complex with carbon monoxide gave a ruthenium complex that showed loss of the benzylidene fragment from the metal. Treatment of a benzene solution of **5** with carbon monoxide (60 psig) for 15 min resulted in a color change from purple to dark yellow. Slow diffusion of pentanes overnight resulted in precipitation of yellow crystals of complex **6**. The pure material gave a CH_2 resonance as a doublet in the ^1H NMR at δ 4.12 ppm, with J_{HP} = 14.0 Hz. The coupling suggested that this methylene was attached to phosphorus directly. The downfield chemical shift also suggested that it was deshielded, possibly bound to a phosphonium species. The ^{31}P NMR spectrum of complex **6** revealed two phosphorus atoms at δ 29.5 and 16.6 ppm. The ^{31}P resonance at δ 29.5 ppm correlated with the proton CH_2 resonance at δ 4.12 ppm by $^1H-^{31}P$ HETCOR analysis. The remaining ^{31}P signal found at δ 16.6 ppm correlated with a CH at δ 2.9 ppm. The crystals of complex **6** proved suitable for X-ray crystal structure determination, which revealed the solid-state structure depicted in Figure 1. The carbon monoxide reaction produced the salt **6** in 27% yield (based on **5**). The solid -state structure shows that two molecules of CO added to ruthenium, which bears three chloride ligands. Two different tervalent phosphorus atoms can be found in the salt **6**. Interestingly, this ruthenium(II) species is anionic and is paired with a phosphonium counterion.

The formation of the anionic ruthenium complex requires further comment. First, salt **6** comprised only 27% of the ruthenium mass. Overall, about 60% of the ruthenium mass could be accounted for by ^{31}P NMR spectroscopy of the crude reaction mixture. In addition to complex **6**, the two complexes *ttt*-$Ru(CO)_2(Cl)_2(PCy_3)_2$ and *cct*-$Ru(CO)_2(Cl)_2(PCy_3)_2$ were identified in the crude reaction mixture, on the basis of their ^{31}P chemical shifts at δ 27.5 and 27.2 ppm, as compared to the shifts for authentically prepared samples. Complex **6** shows that the benzylidene fragment was transferred from ruthenium to Cy_3P to make the phosphonium salt. A simple ligand displacement mechanism would produce a phosphorus ylide. Loss of $CH_2{=}PPh_3$ in decomposition of the second-generation Grubbs methylidene $(H_2IMes)(Cy_3P)Cl_2Ru{=}CH_2$ has been reported by Grubbs.[1h] Though ylidene transfer would result in formation of a phosphorus ylide, an ylide was not detected in the crude reaction mixture (on the basis of comparison to an authentic sample) and the product **6** observed requires that the ylide obtained a proton. The proton source has not been identified. It is plausible that the ylide deprotonated a CO adduct of carbene

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(1) Ruthenium carbene decomposition studies: (a) Ulman, M.; Grubbs, R. H. *J. Org. Chem.* **1999**, *64*, 7202–7207. (b) Dinger, M. B.; Mol, J. C. *Organometallics* **2003**, *22*, 1089–1095. Bond insertion: (c) Trnka, T. M.; Morgan, J. P.; Sanford, M. S.; Wilhelm, T. E.; Scholl, M.; Choi, T.-L.; Ding, S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 2546–2558. (d) Jazzar, R. F. R.; Macgregor, S. A.; Mahon, M. F.; Richards, S. P.; Whittlesey, M. K. *J. Am. Chem. Soc.* **2002**, *124*, 4944–4945. (e) Galan, B. R.; Gembicky, M.; Dominiak, P. M.; Keister, J. B.; Diver, S. T. *J. Am. Chem. Soc.* **2005**, *127*, 15702–15703. (f) Hong, S. H.; Chlenov, A.; Day, M. W.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 5148–5151. Methylidene decomposition: (g) Hong, S. H.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2004**, *126*, 7414–7415. (h) Hong, S. H.; Wenzel, A. G.; Salguero, T. T.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2007**, *129*, 7961–7968.

(2) Galan, B. R.; Kalbarczyk, K. P.; Szczepankiewicz, S.; Keister, J. B.; Diver, S. T. *Org. Lett.* **2007**, *9*, 1203–1206.

(3) The isocyanide treatment of crude metathesis reactions promoted by the Grubbs complex **5** effectively quenches metathesis activity.[2] Crude metathesis reactions contain several different metal carbene species.

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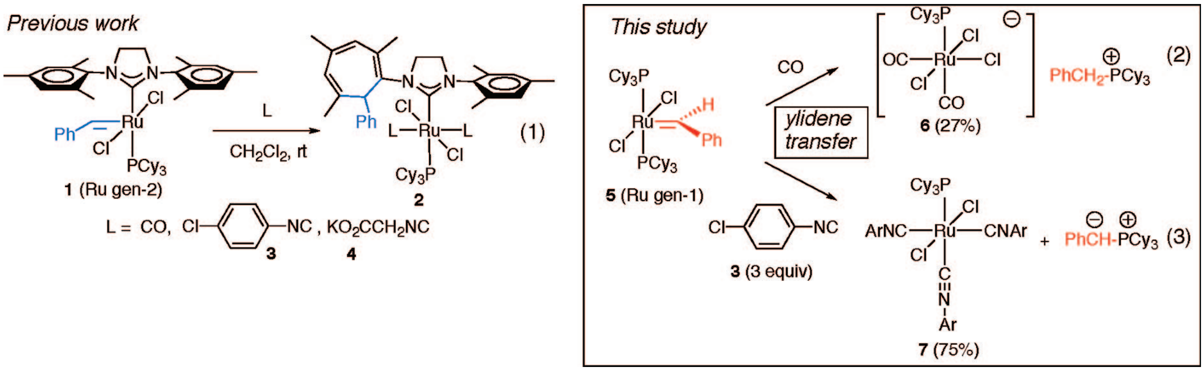
Scheme 1. Dichotomous Ligand-Promoted Insertion in the First- and Second-Generation Grubbs Carbenes



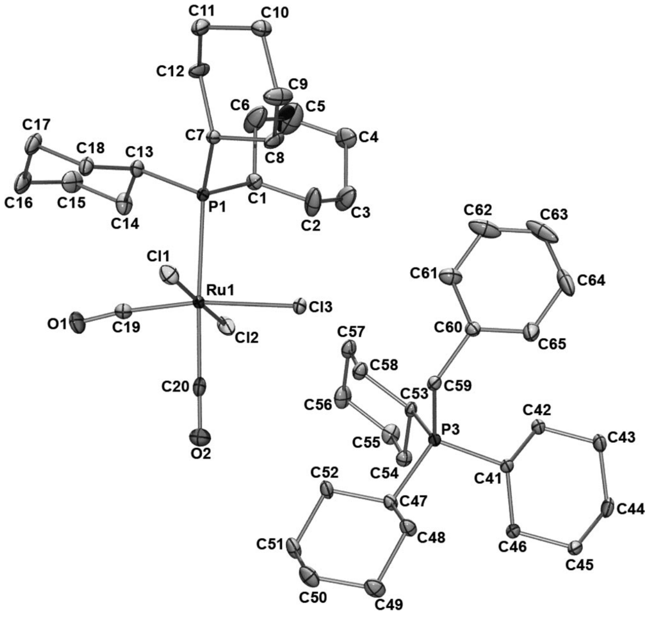


Figure 1. ORTEP drawing of $Cy_3PCH_2Ph^+[Ru(CO)_2Cl_3(PCy_3)]^-$ (**6**). Two ion pairs were found in the asymmetric unit cell, with one ion pair being shown in the figure. Thermal ellipsoids are drawn at the 50% probability level. The Supporting Information gives complete structural details.

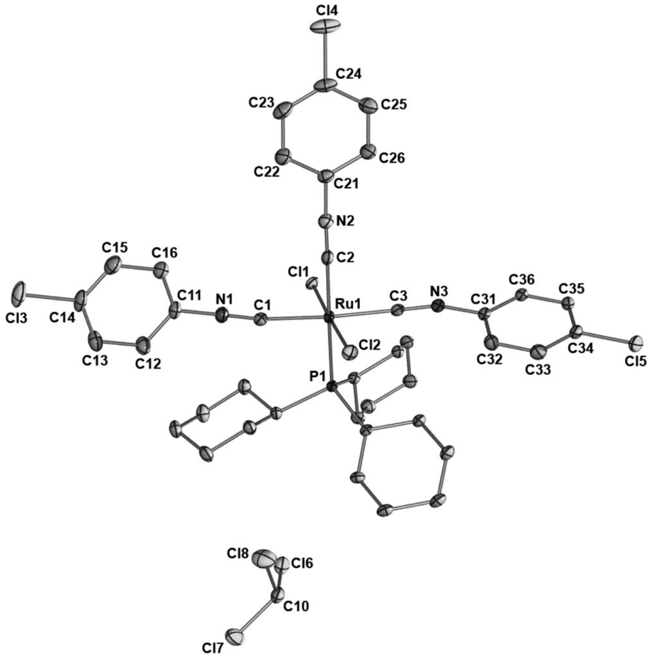


Figure 2. ORTEP drawing of the tris(isocyanide) ruthenium complex **7**. Thermal ellipsoids are drawn at the 50% probability level. One molecule of *d*-chloroform appears in the unit cell.

complex **5**.[4] For example, Schrock has shown that phosphorus ylides are sufficiently basic to deprotonate the Schrock molybdenum(IV) carbene, giving an alkylidyne.[5] Recently, Johnson found that a germylene abstraction of HCl from the Grubbs complex **5** gave a ruthenium alkylidyne.[6] So far, efforts to identify other ruthenium-containing coproducts have been unsuccessful.

The reaction of Grubbs' complex **5** with the aryl isocyanide *p*-ClC_6H_4NC (eq 3, Scheme 1) showed similar loss of the benzylidene from the metal. This reaction proved to be high-yielding and was much cleaner than the CO reaction described above. Reaction of **5** with 3.3 equiv of *p*-ClC_6H_4NC in benzene gave complex **7**. The isolated complex **7** showed a single ^{31}P resonance at δ 23.9 ppm. The ^{13}C NMR spectrum showed the presence of two isocyanide sp carbons as doublets coupled to phosphorus (see the Supporting Information); similarly, IR showed two isocyanide absorptions at 2168 and 2106 cm^{-1}. The isocyanide complex **7** was crystallized from $CDCl_3$ by slow diffusion of pentanes, to give yellow crystals (75% yield). The crystals proved suitable for an X-ray crystal structure determination, yielding the structure shown in Figure 2. The structure shows that the benzylidene fragment was lost from the metal and three isocyanides added to the metal center in a *mer* arrangement. The isocyanide carbon atoms are located 1.96−1.99 Å from the ruthenium atom, whereas the phosphorus is located 2.45 Å away. Some deformation of the linear isocyanides is seen, as a result of steric compression against the tricyclohexylphosphine ligand and crystal packing forces.

We posited that a phosphorus ylide could explain the loss of the benzylidene fragment, similar to the observation in the CO-promoted reaction above. To test this hypothesis, repetition of the reaction with isocyanide **3** using freshly distilled C_6D_6 resulted in the appearance of three peaks in the ^{31}P NMR spectrum at δ 29.5, 22.0, and 9.8 ppm, assigned to complex **7**, $PhCH{=}PCy_3$, and free Cy_3P, respectively. The chemical shift of the phosphorus ylide was determined by comparison to an authentically prepared sample and by a spiking experiment (see

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[4] In a control experiment, the phosphorus ylide $Cy_3P{=}CHPh$ did not react with the Grubbs complex **5** in the absence of CO. In the presence of CO, it is possible that the 18-electron CO complex could serve as a Brønsted acid, though further experiments are needed and will be reported in the full paper.

[5] Tonzetich, Z. J.; Schrock, R. R.; Mueller, P. *Organometallics* **2006**, *25*, 4301–4306.

[6] Caskey, S. R.; Stewart, M. H.; Ahn, Y. J.; Johnson, M. J. A.; Rowsell, J. L. C.; Kampf, J. W. *Organometallics* **2007**, *26*, 1912–1923.

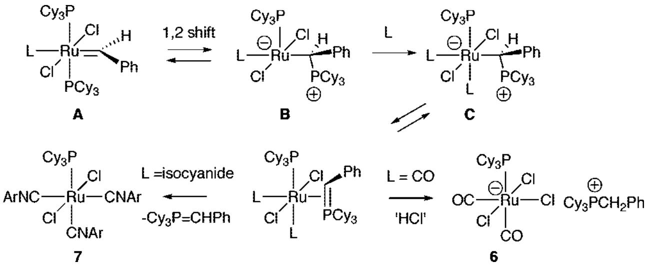
the Supporting Information). We repeated the reaction in the presence of a protic solvent ($CDCl_3$, undegassed) and observed the crude reaction mixture by ^{31}P NMR spectroscopy. In the ^{31}P NMR, three resonances were seen at δ 50.0, 29.3, and 29.0 ppm. The downfield resonance was assigned to $Cy_3P{=}O$,[7] and that at δ 29.3 ppm was due to the isocyanide complex **7**. The new resonance observed at δ 29.0 ppm was assigned to $[Cy_3PCH_2Ph]^+$, on the basis of comparison to an authentic sample.

The mechanism of ylidene transfer could be intermolecular or intramolecular. The first isocyanide binds trans to the benzylidene to give **A**. Presumably, the π-acceptor properties of the ligand serve to increase the electrophilic character of the carbene center, setting the stage for nucleophilic attack by the phosphine. In the first case, the ylide formation in eq 3 of Scheme 1 could involve ligand-promoted dissociation of Cy_3P (to solution) and subsequent capture of the benzylidene by free Cy_3P (intermolecular ylidene transfer). In this case, a second ligand binding would prevent Cy_3P from rebinding to the metal. As a result, the displaced phosphine attacks the electrophilic carbene center. Alternatively, apical donor ligand binding to give **A** may cause the Cy_3P to migrate *intra*molecularly by a 1,2-shift (intramolecular ylidene transfer) to give the intermediate **B**. This would be provoked by a combination of enhanced electrophilicity of the carbene and would alleviate ligand−ligand crowding in complex **A**. A second ligand binding would prevent the phosphine from returning to the metal, giving intermediate **C**, ultimately suffering elimination of the ylide to give the observed products **6** and **7**.

To differentiate the two mechanistic possibilities, the following competition study was conducted: 3.3 equiv of p-ClC_6H_4NC and 3 equiv of Bu_3P in $CDCl_3$ were added to a solution of Grubbs' complex **5**. A control reaction showed that the phosphine did not pre-exchange over the course of 20−30 min. Use of protic solvent served to protonate the phosphorus ylides in situ to give the corresponding phosphonium salts. The crude reaction mixture was monitored by ^{31}P NMR spectroscopy. Within minutes, the phosphonium salts Cy_3P^+CHDPh (65% of trapped benzylidene) and Bu_3P^+CHDPh (34% of trapped benzylidene) had appeared, along with complex **7**.[8] If the phosphine migration had occurred by a completely intermolecular pathway, then at least 75% trapping by Bu_3P would have been expected. Instead, a predominance of Cy_3P trapping took place, despite its lower relative abundance. This experiment suggests that the isocyanide addition results in a predominantly *intra*molecular 1,2-shift of Cy_3P to the carbene carbon, **A** to **B** (Scheme 2).

The coordination of carbon monoxide or isocyanide triggers loss of the benzylidene carbene fragment from the metal. Depending on the existing ligands in the Grubbs complex, dichotomous reactivity is observed. In the case of the second-generation Grubbs complex **1**, this coordination results in cyclopropanation of the mesityl ring of the 1,3-bis(mesityl)dihydroimidazolylidene ligand. In the present study conducted with the first-generation Grubbs complex **5**, the absence of the aromatic moiety does not permit the cyclopropanation pathway. Instead, the carbene is intercepted by the phosphine nucleophile.[9] Only ylidene transfer to phosphine was observed, despite the fact that isocyanides are capable nucleophiles.[10] The "migrations" of the metal-bound carbene fragment are different in the two ligand environments of the first- and second-generation Grubbs carbenes but are entirely consistent with the behavior of electrophilic singlet carbenes.

Scheme 2. Probable Mechanism of Isocyanide-Promoted Ylidene Transfer to Phosphorus



In summary, a ligand-promoted transfer of the benzylidene to tricyclohexylphosphine has been observed in the first-generation Grubbs carbene complex. Owing to the importance of the Grubbs catalyst in olefin metathesis, this reaction provides insight into the reactivity of the carbene moiety and shows how donor ligands can mediate the transfer of the bound carbene ligand. Each of the ligands, carbon monoxide and p-chlorophenyl isocyanide, provokes ylidene transfer. The products from each of the two ligand-promoted reactions were structurally characterized. In the isocyanide case, the phosphine migration is primarily an intramolecular process. The data presented here provides an interesting contrast to the Buchner insertion/ring expansion observed in the Grubbs second-generation complexes. Further studies on the use of different ligands to promote similar carbene insertions in both the first- and second-generation Grubbs carbene complexes are in progress and will be reported in due course.

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Supporting Information Available: Text and tables giving experimental details and characterization data and details of the X-ray structure determination and a CIF file giving X-ray structural data for **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) Some of our samples of the complex **5** showed small amounts of $Cy_3P{=}O$. Most of the oxide can be attributed to this source, rather than oxidation under the reaction conditions.

(8) Other major peaks seen included Bu_3P and $Bu_3P{=}O$. Control studies showed that there was no exchange of phosphonium salts ($R_3PR' + PR''_3$ to $R'PR''_3$) on the time scale of these experiments.

(9) Interestingly, Grubbs used phosphorus ylides to transfer the ylidene to tungsten(IV) imido complexes to form the metal carbenes; see: Johnson, L. K.; Frey, M.; Ulibarri, T. A.; Virgil, S. C.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 8167–8177.

(10) Mayr et al. showed that phosphines are approximately 10 orders of magnitude more nucleophilic than aryl isocyanides in their reactions with stabilized carbenium ions; see: Tumanov, V. V.; Tishkov, A. A.; Mayr, H. *Angew. Chem., Int. Ed.* **2007**, *46*, 3563–3566.