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Activation of Mononuclear Arene Ruthenium Complexes for Catalytic Propargylation Directly with Propargyl Alcohols

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Abstract: Mononuclear complexes of the type [(*p*-cymene)RuX(CO)(PR_3)][OTf] (R = Ph, Cy; X = Cl, OTf) promote the direct catalytic propargylation of furan with propargyl alcohols. These precursors are generated *in situ* from [(*p*-cymene)RuCl(OTf)(PR_3)] by activation of the propargylic alcohol, leading to the carbonyl ligand formation *via* allenylidene and alkenyl-hydroxycarbene intermediates. The generation of the catalytically active species requires a short initial thermal activation to induce decoordination of the *p*-cymene ligand. The *in situ* generated catalyst has been applied to catalytic transformations of alkynes and propargylic alcohols: propargylation of furans, propargyl ether synthesis from internal and terminal propargylic alcohols with propargyl, homopropargyl and allyl alcohols, selective dimerization of phenylacetylene into *E*-enyne, and propargyl alcohol rearrangement into α,β-unsaturated aldehydes and ketones *via* the Meyer–Schuster rearrangement. The propargylation of propargylic alcohols containing internal C≡C bonds suggests an activation *via* the Nicholas-type intermediate, the metal-stabilized propargyl cation.

Keywords: arene complexes; diynes; furans; propargylation; propargylic alcohols; ruthenium catalyst

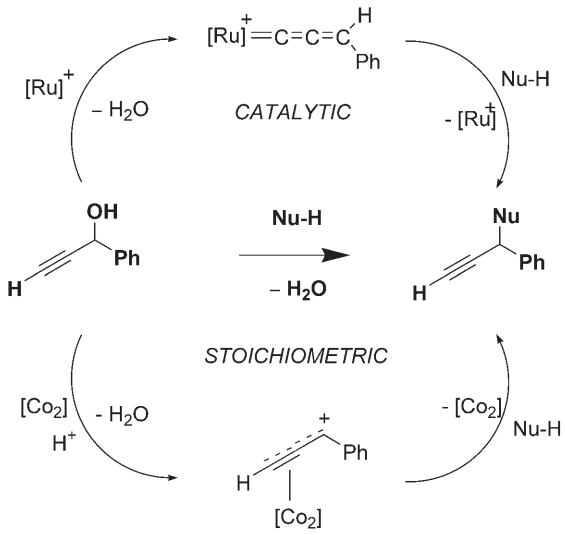
Introduction

Modern catalysis aims at the discovery of new reactions to selectively produce useful added-value products from simple and cheap materials.[1] The understanding of the catalytic cycle, based on the identification of the catalytically active species, should lead to the design of catalysts with an increased efficiency and selectivity from the most appropriate precursors. As an example, the sequential use of allenylidene, alkenylcarbyne and indenylidene derivatives of the [(*p*-cymene)RuCl(PCy_3)]$^+$ fragment, has recently allowed the generation of a series of olefin metathesis catalysts with successively increased activity.[2]

Propargyl alcohols are simple organic species easily available by addition of acetylenes to aldehydes and ketones. They represent an important group of chemical intermediates for organic synthesis. Their selective catalytic transformations with ruthenium catalysts have recently led to the production of, for example, tetrahydrofuran and tetrahydropyrans by tandem cyclization-reconstitutive addition of propargyl and allyl alcohols, aldehydes by hydration of propargyl alcohols, alkenes by alkynol carbon-carbon triple bond cleavage, alkylidenecyclobutenes through head-to-head propargyl alcohol dimerization, and others.[3] The direct propargylic substitution of propargyl alcohols would constitute a straightforward method for the synthesis of functional alkynes. In spite of its potential, the catalytic version of this reaction has been much less studied than the related allylic substitution.

Of particular relevance is the ruthenium-catalyzed propargylic substitution of propargyl alcohols with a variety of heteroatom- and carbon-centered nucleophiles, recently developed by Nishibayashi et al. (Scheme 1).[4–7] A nucleophilic addition on the electrophilic γ-carbon in allenylidene metal intermediates seems to be the key step. This innovative transformation represents a catalytic alternative to the Nicholas reaction, which requires a stoichiometric amount of cobalt complex to stabilize the propargyl cation intermediate.[8] However, the Nicholas reaction has the advantage of being applicable to propargyl alcohols bearing internal alkynes, unable to give allenylidene.

Nishibayashi's catalysis requires a thiolate-bridged diruthenium complex. The search for alternative mon-



Scheme 1.

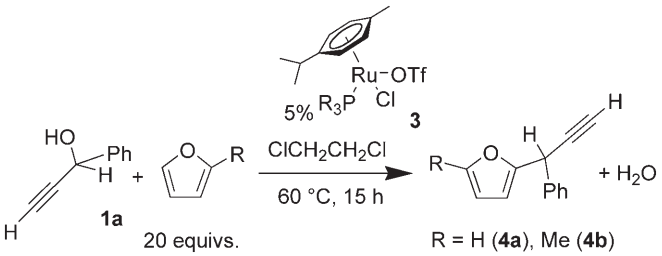
onuclear ruthenium catalysts able to promote this innovative process has been a challenge. However, most mononuclear ruthenium complexes are not active catalysts for this reaction, and particularly ruthenium semi-sandwich complexes, in spite of their well-known reactivity with propargyl alcohols to give allenylidene species, which are proposed as key intermediates for this reaction.[4]

The first examples of mononuclear ruthenium catalysts were simultaneously reported by Gimeno et al.[9] and the Rennes group.[10,11] The catalyst precursors [Ru(η^3-2-C_3H_4Me)(CO)(dppf)] and [(*p*-cymene)RuCl-(PR_3)][OTf] are able to catalyze the propargylic substitution reaction with alcohols and heterocycles, respectively. Several recent reports have showed the rising interest in this propargylation reaction. Rhenium complexes (dppm)$ReOCl_3$),[12] gold salts ($NaAuCl_4 \cdot 2H_2O$),[13] and organic acids (i.e., *p*-toluenesulfonic acid),[14] have been employed as catalysts with variable results depending on the use of terminal or internal alkynols, and on the particular nucleophiles (alcohols, thiols, heterocyclic and aromatic compounds, etc). Rhenium and gold catalysts are restricted to internal propargyl alcohols and they seem to proceed through stabilized carbonium intermediates.

In this paper we report the enhanced catalytic activity of the mononuclear ruthenium precatalyst [(*p*-cymene)Ru(OTf)(CO)(PR_3)][OTf] and the rationale of its formation from [(*p*-cymene)Ru(OTf)(PR_3)] [OTf] and propargyl alcohol, for the catalytic propargylic substitution of propargylic alcohols. We show how the catalyst activity can be further improved by *in situ* thermal preactivation, and orientated towards the Meyer–Schuster selective catalytic reaction, the catalytic coupling of heterocycles with ketones, and extended to propargyl ether synthesis from propargyl alcohols.

Results and Discussion

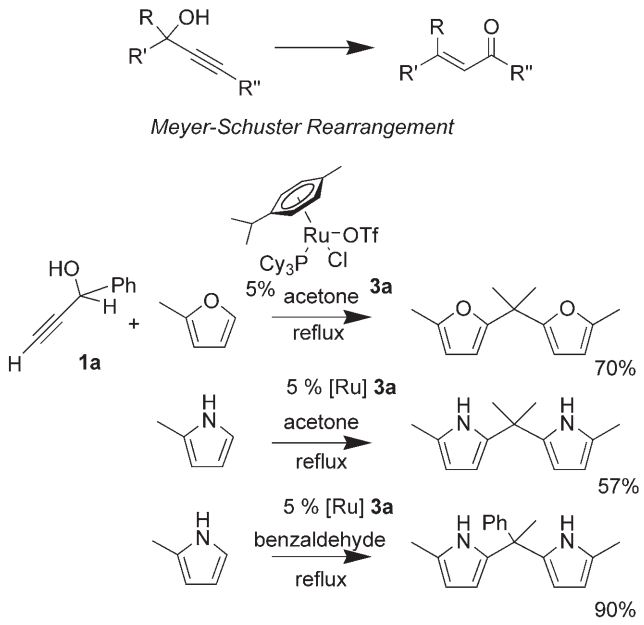
After Selegue's discovery of a general method for the synthesis of allenylidene metal complexes from propargylic alcohols,[15] semi-sandwich arene ruthenium compounds of the type [(arene)$RuCl_2(PR_3)$] are among the first reported complexes able to activate propargylic alcohols to give allenylidene species.[16] Therefore, [(*p*-cymene)$RuCl_2(PR_3)$] complexes have first been evaluated as mononuclear catalyst precursors to perform the catalytic propargylation of different substrates. 1-Phenyl-2-propynol (**1a**) has been treated with a large excess (20 equivalents) of furan and 2-methylfuran in the presence of catalytic amounts of [(*p*-cymene)$RuCl_2(PR_3)$] [$PR_3 = PCy_3$ (**2a**), PPh_3 (**2b**)] in 1,2-dichloroethane. A low conversion took place and small amounts of the propargylated product were detected (yield < 5%) (Scheme 2).



Scheme 2.

In order to enhance the interaction between the alkynol and the ruthenium complex, [(*p*-cymene)RuCl-(PR_3)][OTf] [$PR_3 = PCy_3$ (**3a**), PPh_3 (**3b**)] complexes were prepared from **2a** and **2b** by chloride abstraction with AgOTf in CH_2Cl_2. The reaction of alkynol **1a** and furan (or 2-methylfuran) in the presence of 5% of **3a**/**3b** leads to the complete conversion of the propargyl alcohol, but the propargylated heterocycles HC≡CCHPh(Nu) [Nu = 2-furanyl (**4a**), 5-methyl-2-furanyl (**4b**)] were obtained in low yields (yield < 10%).[17]

The analysis of the by-products shows the presence of aldehydes and polymeric materials. It is noteworthy that α,β-unsaturated aldehydes and ketones can be obtained by propargyl alcohol isomerization. The Meyer–Schuster rearrangement (Scheme 3)[18] is usually catalyzed by strong acids, but also ruthenium complexes are able to catalyze the isomerization of propargyl alcohols to α,β-unsaturated aldehydes through vinylidene and allenylidene intermediates.[19] More recently, Gimeno and co-workers have reported the Ru-catalyzed propargylic substitution of 1,1-di-



Scheme 3.

phenyl-2-propynol with alcohols[9] and the alternative formation of α,β-unsaturated aldehydes *via* isomerization in the absence of alcohol.[20]

This isomerization process is expected to be responsible for the low yields observed in the first tests. Complexes **3a** and **3b** behave as efficient catalysts for Meyer–Schuster rearrangement and the subsequent heterocyclic addition to the resulting α,β-unsaturated ketones. This behaviour is revealed when the catalytic reaction is carried out in acetone instead of 1,2-dichloroethane. The double addition of 2-methylfuran to acetone occurs in almost quantitative yield (Scheme 3). Furthermore, substituted dipyrans are obtained by reaction of acetone or benzaldehyde with 2-methylpyrrole in the presence of a catalytic amount of the arene ruthenium complexes **3a** or **3b** (Scheme 3).

In view of this, substantial modifications of the catalyst to avoid as much as possible undesirable side-reactions seemed mandatory and among a variety of additives it was observed that the addition of small amounts of water to the reaction mixture afforded an increased of yield of 25–30% for the products **4a**/**4b** (Table 1, entries 1 and 2).

Stoichiometric low temperature NMR experiments provided valuable information and an accurate explanation of the water effect: Two complexes resulting from the activation of alkynol **1a** by [(*p*-cymene)RuCl(OTf)(PR_3)] [R = Cy (**3a**), Ph (**3b**)] were detected by $^{31}P\{^1H\}$ NMR at −60 °C, and identified as allenylidene intermediate and alkenyl-hydroxycarbene species, showing singlets at $\delta = 58.1$ and 39.0 ppm respectively. When the temperature is raised to 0 °C, the second signal ($\delta = 39.0$ ppm) increases while the other completely disappears ($\delta = 58.1$ ppm). (Scheme 4). The remaining species ($\delta = 39.0$ ppm) was identified by NMR as a hydroxycarbene complex. Its main spectroscopic data are signals at $\delta = 14.18$ ppm [=C(O*H*)] and 287.5 ppm [Ru=*C*(OH)] in the ^1H and $^{13}C\{^1H\}$ NMR spectra respectively, which were analyzed by COSY, HMBC and HMQC bidimensional experiments. The low-field signal at $\delta = 14.18$ ppm does not correlate with any carbon atom in the HMQC bidimensional experiment (one-bond C–H couplings). However, the signal shows a correlation with the carbon atom appearing at $\delta = 287.5$ ppm in the HMBC experiment (two- and three-bond couplings). Both low-field signals are characteristic of metal-carbene species and consistent with the proposed hydroxycarbene complex **5a**/**5b**, thus arising by addition of the released H_2O to the allenylidene-ruthenium intermediate (Scheme 4).

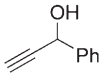
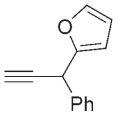
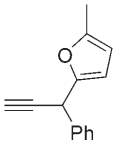
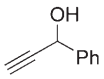
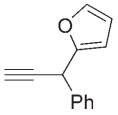
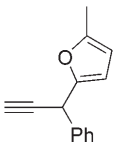
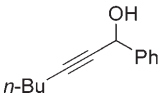
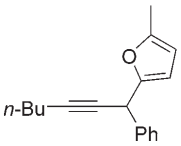
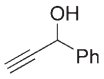
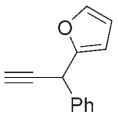
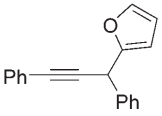
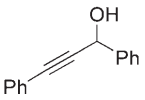
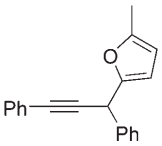
The addition of 100 μL of water to a CD_2Cl_2 solution of complex **3a/3b** and the alkynol **1a** in an NMR tube at −60 °C, gave directly the hydroxycarbene complex **5a/5b** as the only observed reaction product. At above 50 °C this complex slowly disappears, giving rise to a new derivative identified as [(*p*-cymene)RuCl(PR_3)(CO)]$^+$ (**6a/6b**) and to the release of free styrene, observed by NMR and GC-MS (Scheme 4).

The presence of additional water accelerates the formation of the hydroxycarbene complex [(*p*-cymene)RuCl(PCy_3){=C(OH)CH=CHPh}]$^+$ (**5a**). Compound **5a** slowly disappears at above 50 °C, giving rise to the carbonyl complex [(*p*-cymene)RuCl(PCy_3)(CO)]$^+$ (**6a**) and free styrene, as detected by NMR and GC-MS (Scheme 4). The analogous PPh_3 complexes [(*p*-cymene)RuCl(PPh_3){=C(OH)CH=CHPh}]$^+$ (**5b**) and [(*p*-cymene)RuCl(PPh_3)(CO)]$^+$ (**6b**) are also observed starting from complex **3b**.

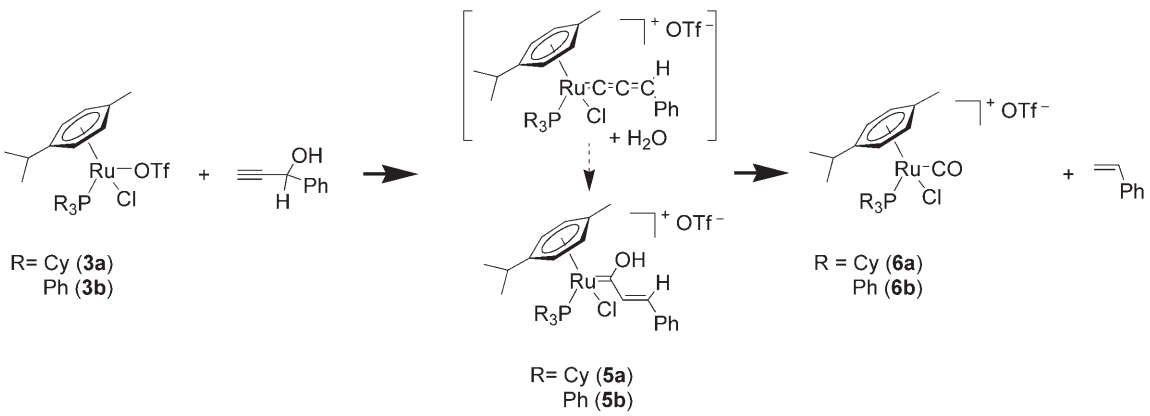
Werner et al. have reported similar mixed phosphine-carbonyl arene ruthenium complexes.[21] In fact, **6a**/**6b** are more readily prepared from the parent complexes **3a**/**3b** on addition of carbon monoxide. The question is whether these saturated complexes could be related or not to the catalytically active species. Surprisingly, **6a** and **6b** also catalyze the propargylation of furan and 2-methylfuran by alkynol **1a** with a remarkably shorter reaction time than **3a** and **3b**. Under similar conditions (1,2-dichloroethane, 60 °C) the catalytic reaction was completed in 2 h. Therefore, the addition of water to the allenylidene intermediate favours the hydroxycarbene and thus the carbonyl complex formation, which acts as an improved catalyst precursor.

Complexes **6a** and **6b** provide similar catalytic results. The catalyst of choice was the complex [(*p*-cymene)RuCl(CO)(PPh_3)][OTf] (**6b**), which can be prepared with high yield in a three-step synthesis from readily available reagents [$RuCl_2$(*p*-cymene)]$_2$

Table 1. Ruthenium-catalyzed propargylation of furans by propargyl alcohols.

Entry	Catalyst	A	B	Time[a]	Product	Yield [%][b]
1	**3a/3b** + 100 μL H_2O	 **1a**		15 h	 **4a**	25
2	**3a/3b** + 100 μL H_2O				 **4b**	30
3	**6b**	 **1a**		2 h	 **4a**	25
4	**6b**				 **4b**	30
5	**6b**	 **1d**			 **4c**	45
6	**7a**					27
7	**7a***	 **1a**		2 h	 **4a**	42
8	**7a***				 **4d**	31
9	**7a***	 **1e**		2 h	 **4e**	25

[a] *Reaction conditions:* 1,2-dichloroethane, 60 °C, 5% catalyst loading.
[b] Isolated yield.



Scheme 4.

and PPh_3. A catalyst loading of 5% of **6b** affords propargylated furan and 2-methylfuran in moderate yields (Table 2, entries 3 and 4).

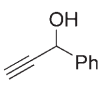
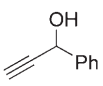
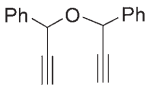
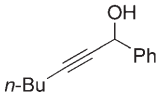
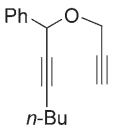
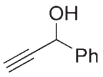
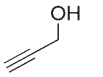
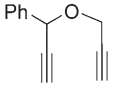
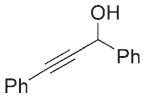
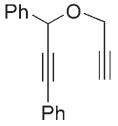
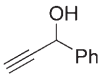
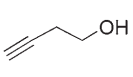
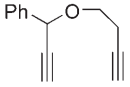
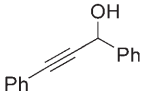
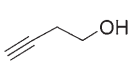
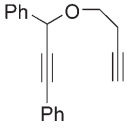
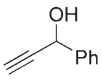
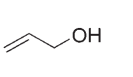
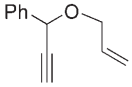
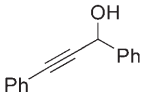
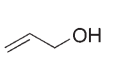
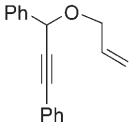
Since the catalyst precursors **6a** and **6b** are saturated 18-electron complexes, the release of one ligand is required to allow alkyne coordination prior to allenylidene or propargyl cation formation. As a working hypothesis, the release of *p*-cymene during the initial catalytic step would generate a coordinatively unsaturated, and thus very reactive, electrophilic species "[RuCl(CO)(PR_3)(solvent)$^+$]". This is supported by the observation (NMR and GC-MS) of free *p*-cymene besides the catalysis product.

As an attempt to provide a higher stability to the catalytic intermediates, the complex [(*p*-cymene)Ru(OTf)(CO)(PCy_3)][OTf] (**7a**) has been prepared by abstraction of the two chlorides with 2 equivalents of AgOTf from [(*p*-cymene)$RuCl_2$(PCy_3)] (**2a**), followed by CO bubbling. This complex should benefit from the different coordination modes of the triflate ligand, which can act as a counterion or be bonded in mono- or bidentate modes. High-resolution mass spectrometry of **7a** confirms the expected $m/z =$ 693.1936 (calcd. for $[C_{30}H_{47}O_4F_3PS^{102}Ru]^+$: 693.1928), corresponding to a mononuclear monocationic complex with one coordinated triflate ligand and one triflate counterion.

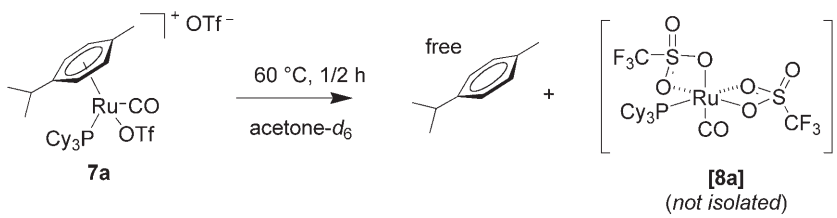
An acetone-d_6 solution of complex **7a** has been monitored by ^1H and $^{31}P\{^1H\}$ NMR. The release of *p*-cymene at room temperature is slow, but at 60 °C all the arene ligand is completely removed after 20 min, as shown by the characteristic free *p*-cymene signals in the ^1H NMR spectrum. The $^{31}P\{^1H\}$ NMR signal for complex **7a** (at $\delta = 58.9$ ppm) is replaced by another one at $\delta = 54.7$ ppm, which should correspond to an unsaturated complex such as "[Ru($OTf)_2$(CO)(PCy_3)]" [**8a**]. The proposed structure (Scheme 5) would exhibit two bidentate triflate ligands to complete 18 valence electrons, although the coordination of an acetone molecule can also be considered. Attempts to isolate [**8a**] as a solid were unsuccessful, showing the low stability of this reactive species.

Arene decoordination by treatment of [(η^6-toluene)Ru{κ^2(*Si,Si*)-xantsil}(CO)] [xantsil = bis(dimethylsilyl) chelating ligand] with PCy_3 has been recently reported to generate a highly unsaturated rutheni-

Table 2. Ruthenium-catalyzed propargyl ether synthesis.

A	B	Product[a]	Yield [%][b]	A	B	Product[a]	Yield [%][b]
 **1a**		 **10**	61	 **1d**		 **11b**	31
 **1a**		 **11a**	35	 **1e**		 **11c**	41
 **1a**		 **12a**	51	 **1e**		 **12b**	43
 **1a**		 **13a**	15	 **1e**		 **13b**	28

[a] *Reaction conditions:* acetone, 60 °C, 5% catalyst loading.
[b] Isolated yield.

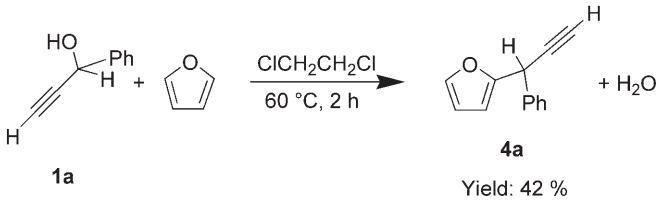


Scheme 5. Generation and possible structure of catalyst **8a**.

um complex [Ru{κ³(*Si,Si,O*)-xantsil}(PCy_3)(CO)],[22] considered as a 14-electron synthetic equivalent. The release of the arene ligand is also described in analogous ruthenium complexes of type [(η^6-*p*-cymene)-RuX_2L] (L = PR_3, NHC),[23] and it is proposed as the initial step towards the generation of the olefin metathesis catalytically active species from [(η^6-*p*-cymene)RuCl(PCy_3)(=CHR)]$^+$ complexes.[2]

The analogous complex [(*p*-cymene)Ru(OTf)(CO)-(PPh_3)][OTf] (**7b**) exhibits a similar behaviour [$^{31}P\{^1H\}$ NMR changes from 38.6 ppm to 47.8 ppm when heated] but the corresponding activated species [**8b**] shows a lower stability.

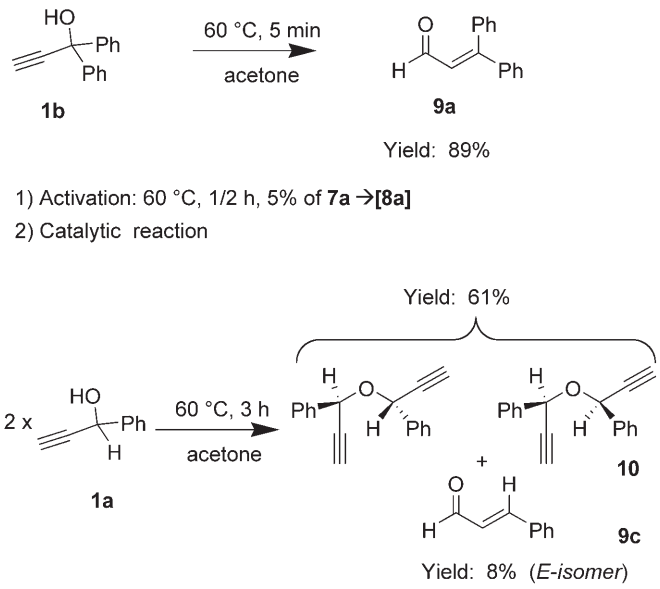
The 18-electron complex [(*p*-cymene)Ru(OTf)-(PCy_3)(CO)][OTf] (**7a**) has been tested as precatalyst. The best yield for the furan propargylation with catalyst **6b** was 25% (Table 1, entry 3). The yield is analogous with that of the precatalyst **7a** (27%, entry 6). However, it is noteworthy that a preactivation of the catalyst by heating **7a** at 60 °C for 30 min before the addition of the catalysis substrates, significantly increases the yield to 42% (Scheme 6, Table 1, entry 7). These results clearly indicate that the actual catalytic active species is related to the complex [**8a**], generated *in situ* from **7a**.



Scheme 6.

The aforementioned preactivation of the catalyst has also been employed to extend the propargylic substitution reaction to other propargyl alcohols. Nishibayashi's catalyst shows a marked preference for secondary propargyl alcohols [HC≡CCH(OH)Ar] as substrate for the propargylic substitution. Gimeno's catalyst is limited to the tertiary 1,1-diphenyl-2-propynol, HC≡CC(OH)Ph_2 (**1b**).[9] In our case, the preactivated catalyst appears as an excellent Meyer–Schuster catalyst with tertiary alkynols. When **1b** is treated with 5% of **7a** (preactivated at 60 °C, thus **7a**→[**8a**]), the Meyer–Schuster rearrangement takes place in just 5 min to give 3,3-diphenylacrylaldehyde (**9a**) in 89% isolated yield (Scheme 7).

A similar behaviour is observed for 2-phenyl-3-butyn-2-ol, HC≡CC(OH)MePh (**1c**). After 10 min at 60 °C a mixture of (*E*)- and (*Z*)-3-phenyl-2-butenal (**9b**) is obtained in 25% yield, besides unreacted start-



Scheme 7.

ing product (40%). The propargylation of furan with **1c** always provides yields lower than 10%. As a conclusion, the fast Meyer–Schuster rearrangement prevents the propargylic substitution on tertiary alkynols. It should be noted that the Meyer–Schuster rearrangement usually requires strong acids and high temperatures in absence of metal catalysts.[24]

An unforeseen behaviour is observed for alkynol **1a** when treated with 5% of complex **7a** previously activated in acetone at 60 °C to give [**8a**]. Whereas the expected (*E*)-cinnamaldehyde (**9c**) is only obtained in 8% yield, the alkynol undergoes self-condensation and the dipropargyl ether $(HC{\equiv}CCHPh)_2O$ (**10**) is isolated as a mixture of diasteroisomers in 61% yield (Scheme 7).

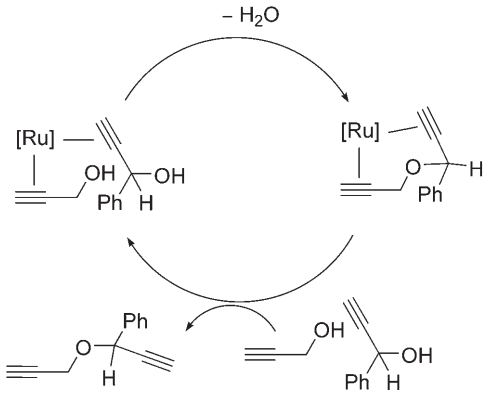
The self-condensation reaction of **1a** has not been reported for other ruthenium catalysts. Small amounts of **10** (<15%) were found as a by-product of the etherification of **1a** with EtOH catalyzed by organic acid.[14] A direct access to dipropargyl ethers is interesting, since α,ω-diynes are useful building blocks frequently employed for [2+2+2] cyclization reactions catalyzed by transition metal complexes,[25,26] and also with potential interest as monomers for the preparation of conducting polymers.[27] Propargyl ethers are also key substrates for the ruthenium-assisted retro-ene reaction and generation of alkene metathesis catalysts.[2d]

The synthesis of propargyl ethers has been extended to the condensation of propargyl alcohol **1a** with propargyl alcohol itself ($HC{\equiv}CCH_2OH$), homopro-

pargyl alcohol ($HC{\equiv}CCH_2CH_2OH$) and allyl alcohol ($H_2C{=}CHCH_2OH$) (Table 2).

The access to a series of non-conjugated enynes and diynes is motivated by their use as substrates for selective catalytic transformations into complex molecules especially promoted by platinum(II) or gold catalysts.[28] The treatment of **1a** and a slight excess of propargyl alcohol with 5 mol% of preactivated complex **7a** in acetone at 60°C for 3 h, gives the dipropargyl ether $HC{\equiv}CCH(Ph)OCH_2C{\equiv}CH$ (**11a**) in 24% isolated yield. Optimization of the catalytic conditions led to the use of an excess of the propargyl alcohol (1 mL) and a longer reaction time (overnight), increasing the yield up to 35%. It is noteworthy that a classical etherification to obtain **11a** from alkynol **1a**, propargyl bromide and a strong base provides yields around 25%.[26]

Homopropargyl alcohol condensation with **1a** is more effective and the propargyl ether derivative $HC{\equiv}CCH(Ph)OCH_2CH_2C{\equiv}CH$ (**12a**) is isolated in 51% yield under similar conditions. In sharp contract with Gimeno's and Nishibayashi's propargylation catalysts,[6,9] no reaction is observed with simple alcohols such as methanol, ethanol or 2-propanol. This suggests that the condensation process is promoted by the prior coordination of the two acetylenic substrates to the unsaturated active species [**8a**] (Scheme 8). The condensation reaction between **1a** and allyl alcohol takes places with a lower yield, furnishing the allyl propargyl ether $HC{\equiv}CCH(Ph)OCH_2CH{=}CH_2$ (**13a**) in 15% isolated yield.



Scheme 8.

In general, ruthenium catalysts are more specific for propargylic substitution of terminal propargyl alcohols and allenylidene complexes have always been proposed as key intermediates.[4,5,9] However, for Nishibayashi's catalyst very similar diruthenium complexes have been reported to be active also for the propargylic substitution of internal alkynols.[7] On the other hand, catalysts with other metals (Re,[12] Au[13]) and organic acids,[14] offer their best results with internal alkynols. In our case, experiments with internal alkynols give better results, and support the existence of propargyl cation intermediates instead of allenylidenes, whose formation is restricted to terminal alkynols.

In an attempt with catalyst **6b**, the internal propargyl alcohol 1-phenyl-2-heptyn-1-ol, *n*-$BuC{\equiv}CCH(OH)Ph$ (**1d**) and 2-methylfuran afforded *n*-$BuC{\equiv}CCH(C_4H_2O\text{-}CH_3)Ph$ (**4c**) in 45% yield (Table 1, entry 5).[10] Additionally, the internal propargyl alcohol 1,3-diphenyl-2-propynol, $PhC{\equiv}CCH(OH)Ph$ (**1e**), has been reacted with furan and 2-methylfuran at 60°C in acetone in the presence of 5 mol% of the preactivated complex **7a**(→[**8a**]), affording the corresponding propargylated product $PhC{\equiv}CCH(R)Ph$ [$R = C_4H_3O$ (**4d**), $C_4H_2O\text{-}CH_3$ (**4e**)] in 31% and 25% isolated yields, respectively (Table 1, entries 8 and 9).

The internal propargyl alcohols **1d** and **1e** are also useful for condensation reactions to give propargyl ethers in the same conditions as for alkynol **1a**. Reactions with propargyl alcohol $HC{\equiv}CCH_2OH$ provide dipropargyl ethers $RC{\equiv}CCH(Ph)OCH_2C{\equiv}CH$ [R = *n*-Bu (**11b**), Ph (**11c**)] in 31% and 41% yields, respectively (Table 2). In similar conditions, the internal alkynol **1e** reacts with homopropargyl alcohol to give the corresponding ether $PhC{\equiv}CCH(Ph)OCH_2CH_2C{\equiv}CH$ (**12b**), and with allyl alcohol to obtain the allyl propargyl ether $PhC{\equiv}CCH(Ph)OCH_2CH{=}CH_2$ (**13b**), in 43% and 28% isolated yields, respectively (Table 2). The better coordinative capability of alkynes with respect to alkenes might justify the higher condensation yields for propargyl and homopropargyl alcohols with regard to allyl alcohol (Scheme 8).

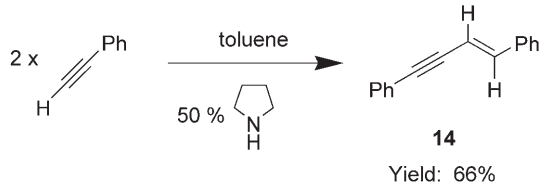
By contrast to **1a**, the internal propargyl alcohol **1e** does not undergo the self-condensation reaction, likely because of the higher steric requirements, hindering the prior coordination of a second alkyne molecule before condensation. Instead, a mixture of (*Z*)- and (*E*)-chalcone $PhCOCH{=}CHPh$ (**9d**) is obtained in 49% isolated yield, as a result of the Meyer–Schuster rearrangement.

The propargylic substitution of internal propargylic alcohols cannot involve allenylidene intermediates, which require an initial acetylenic C–H activation. Although different pathways could be operative for terminal or internal alkynols, it seems more plausible to propose a common mechanism analogous to that of Nicholas reaction, including temporary coordination of the triple bond and assistance to OH elimination by stabilization of the resulting propargyl cation (Scheme 1).

The proposed initial coordination of two alkyne molecules is further supported by the ability of the *in situ* generated catalyst [**8a**] to promote the catalytic phenylacetylene dimerization, which mechanism occurs either *via* alkynyl/vinylidene M(C≡CR)(=C=

CHR) or alkynyl/π-alkyne M(C≡CR)(η²-HC≡CR) coupling, by insertion into the σ Ru–C bond.[29]

Due to the difficulty of isolating the catalytically active species, the phenylacetylene dimerization reaction is carried out by heating a solution of the catalyst **7a** (2.5%) at 60°C during 30 min (**7a**→[**8a**]) and then adding phenylacetylene. The mixture is heated overnight. Removal of the solvent gives a white solid corresponding exclusively to the (*E*)-1,3-enyne product (**14**, Scheme 9).



1) Activation: 60°C, 1/2 h, 2.5% of **7a** → **[8a]**

2) Catalytic reaction

Scheme 9.

This reaction is very solvent-dependent, and whereas THF and 1,2-dichloroethane give low yield, acetone, DMF and toluene provide 52%, 50% and 66% isolated yields, respectively. The presence of a base such as pyrrolidine is also required (1:2 ratio with regard to phenylacetylene), likely to generate the essential alkynyl intermediate by deprotonation of vinylidene or π-alkyne ligands.[29]

Conclusions

This study has revealed the existence of alternative mononuclear ruthenium catalysts for the propargyl substitution reaction, and how to find out the appropriate modifications of the initial arene ruthenium complex [(*p*-cymene)$RuCl_2(PR_3)$] on the basis of stoichiometric key experiments. Low temperature NMR analysis allowed us to characterize a hydroxycarbene intermediate, leading to [(*p*-cymene)$RuCl(CO)(PR_3)$][OTf] (R = Ph, Cy) complexes, which offer an improved catalytic efficiency and provide a better understanding of the catalytic steps.

The thermal preactivation of [(*p*-cymene)Ru(OTf)(CO)(PCy_3)][OTf] generates the most active species likely by loss of the *p*-cymene ligand. The catalysis activity has been tested for the propargylation of furan derivatives, the formation of propargyl ethers and non-conjugated enynes, and the Meyer–Schuster reaction, with internal and terminal propargyl alcohols, as well as the selective dimerization of phenylacetylene.

Despite the moderate yields obtained with respect to the Nishibayashi catalyst, this study reveals a family of readily available mononuclear ruthenium precursors for selective catalytic propargylation with propargylic alcohols. The Meyer–Schuster rearrangement constitutes a competitive process, which has been used to prepare α,β-unsaturated aldehydes and ketones in good yields. The alternative self-condensation of secondary propargyl alcohols has been applied to the formation of non-conjugated diynes and enynes.

Experimental Section

General Remarks

All catalytic reactions were carried out under an inert atmosphere in Schlenk tubes. Chemicals were obtained commercially and used as supplied, except for the alkynols **1d** and **1e**.[30] Complexes **2a** and **2b**,[21] and **3a** and **3b**,[31] were prepared according to reported methods. Complexes **6a** and **6b** were obtained as described by Werner et al.,[21] but using AgOTf as chloride abstractor. The formation of compounds **5a**, **5b**, **6a** and **6b**, observed by low temperature ^1H, $^{31}P\{^1H\}$ NMR and bidimensional experiments (COSY, HMQC, HMBC) was described in the Experimental Section of the previous communication.[10] NMR spectra were recorded on Bruker AM 3000 WB and DPX 200 spectrometers in deuterated solvents. Elemental analysis and high resolution mass spectrometry were performed by the Centre Régional de Mesures Physiques de l'Ouest, Université de Rennes 1. IR spectra were recorded on a Bruker IFS28 spectrometer. Solvents were distilled before use from the appropriate drying agents. A Büchi GKR-51 oven was used for distillation.

General Procedure for the Catalytic Propargylation of Furan Derivatives

Catalyst **7a** (42 mg,0.05 mmol) was dissolved in 2 mL of 1,2-dichloroethane (DCE) and heated at 60°C for 30 min. Then 1 mmol of the corresponding propargyl alcohol (132 mg of **1a**, 188 mg of **1d**, 208 mg of **1e**) and the corresponding heterocycle (10 mmol of furan, 1 mmol of 2-methylfuran) were added. After heating for 2 h at 60°C, the solvent was removed under vacuum and the residue extracted with 2× 5 mL of Et_2O. Purification of the product was carried out by distillation under reduced pressure, giving a pale yellow oil. NMR, IR and analysis data for 2-(1-phenyl-2-propynyl)furan (**4a**), 2-methyl-5-(1-phenyl-2-propynyl)furan (**4b**), 2-methyl-5-(1-phenyl-2-heptynyl)furan (**4c**), 2-(1,3-diphenylprop-2-ynyl)furan (**4d**) and 2-(1,3-diphenylprop-2-ynyl)-5-methylfuran (**4e**) match well with those previously reported.[5] See yields in Table 1.

General Procedure for Catalytic Propargylic Ether Synthesis

Catalyst **7a** (42 mg, 0.05 mmol) was dissolved in 5 mL of acetone and heated at 60°C for 30 min. Then 1 mmol of the

corresponding propargyl alcohol (132 mg of **1a**, 188 mg of **1d**, 208 mg of **1e**) and 1 mL of 2-propyn-1-ol, 3-butyn-1-ol or 2-propen-1-ol were added. After heating overnight at 60 °C, the solvent was removed under vacuum and the residue extracted with 2×5 mL of Et_2O. Purification of the product was carried out by column chromatography (silica, pentane), giving the corresponding propargyl ether as yellow oils. Characterization data are provided as Supporting Material. See yields in Table 2.

General Procedure for Meyer–Schuster Rearrangement

Catalyst **7a** (42 mg, 0.05 mmol) was dissolved in 5 mL of acetone and heated at 60 °C for 30 min. Then 1 mmol of the corresponding propargyl alcohol (132 mg of **1a**, 208 mg of **1b**, 146 mg of **1c**, 188 mg of **1d**, 208 mg of **1e**) were added. After heating at 60 °C overnight, the corresponding aldehyde or ketone was isolated by column chromatography (silica, 5% Et_2O/pentane). 3,3-Diphenylacrylaldehyde (**9a**) was obtained as the major product (89% yield) in 5 min. 3-Phenyl-2-butenal (**9b**) in 25% yield as a mixture of (*E*)- and (*Z*)-isomers, besides unreacted alkynol were also obtained. (*E*)-Cinnamaldehyde (**9c**) was isolated in 8% yield as a by-product of dipropargyl ether **10**. With alkynol **1e** a mixture of (*Z*)- and (*E*)-chalcone (**9d**) was isolated in 49% yield as the main product. NMR data match well with those previously reported.[32]

Catalytic Dimerization of Phenylacetylene

Catalyst **7a** (42 mg, 0.05 mmol, 2.5 mol%) were dissolved in 5 mL of acetone and heated at 60 °C for 30 min. Then 102 mg of phenylacetylene (1 mmol) and 36 mg of pyrrolidine (0.5 mmol) were added. The mixture was heated overnight at 60 °C. After removal of the solvent under vacuum and column chromatography of the residue (silica, pentane), a white solid was isolated, corresponding to the (*E*)-enyne **14**. Spectroscopic data match well with those previously reported.[33] ^1H and $^{13}C\{^1H\}$ NMR are provided in the Supporting Information.

Preparation of the Catalyst [(*p*-Cymene)Ru(CO)(OTf)(PCy_3)][OTf] (7a)

In a Schlenk tube were placed 584 mg (1 mmol) of [(*p*-cymene)$RuCl_2(PCy_3)$] (**2a**), 414 mg of AgOTf (2 mmol) and 30 mL of CH_2Cl_2. The mixture, sheltered from light, was stirred for one hour at room temperature and then filtered through celite to remove the silver salts. Then, the solution was concentrated to 10 mL. After addition of 5 mL of pentane and stirring for 15 min, the mixture was filtered a second time through Celite. The removal of the solvent under vacuum gave an orange solid, which was dissolved in CH_2Cl_2. CO was bubbled through the solution for 5 min at room temperature. A fast colour change was observed from red to light brown. The solvent was removed under reduced pressure, leaving a yellow-orange solid in 83% overall yield. ^1H NMR (300 MHz, acetone-d_6): $\delta = 1.22$ [d, 6H, $J = 6.78$ Hz, $CH(CH_3)_2$], 2.28 (s, 3H, CH_3), 1.72, 1.89, 2.55 (m, 33H, PCy_3), 2.86 [sept, 1H, $CH(CH_3)_2$], 7.02, 7.10, 7.59 and 7.72 (four d, 1H each, $J = 6.78$ Hz, C_6H_4); $^{31}P\{^1H\}$ NMR (121 MHz, acetone-d_6): $\delta = 58.9$ (s, PCy_3); IR (nujol): $\nu =$ 1974, 2032 cm^{-1}.; ESI-MS: $m/z = 693.1936$ [C^+], calcd. for $C_{30}H_{47}O_4F_3PS^{102}Ru$: 693.1928.

Supporting Information

Characterization data for compounds **10–14**.

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References

[1] a) C. Bruneau, P. H. Dixneuf, (Eds.), *Ruthenium catalysts in Fine Chemistry*, in: *Topics in Organometallic Chemistry*, Springer-Verlag, Heidelberg, **2004**, Vol. 11, pp 1–336; b) C. Bruneau, P. H. Dixneuf, *Angew. Chem. Int. Ed.* **2006**, *45*, 2176–2203; c) M. Mendez, V. Hamane, A. Fürstner, *Chemtracts: Org. Chem.* **2003**, *16*, 397–425; d) T. M. Tmka, R. H. Grubbs, *Acc. Chem. Res.* **2002**, *34*, 18–29; e) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem. Int. Ed.* **2005**, *44*, 4490–4527; f) B. M. Trost, F. D. Toste, A. B. Pinkerton, *Chem. Rev.* **2001**, *101*, 2067–2096; g) T. J. J. Müller (Ed.), in: *Metal catalyzed cascade reactions*, Springer, Berlin, **2006**, Vol 19.

[2] a) R. Castarlenas, C. Vovard, C. Fischmeister, P. H. Dixneuf, *J. Am. Chem. Soc.* **2006**, *128*, 4079–4089; b) R. Castarlenas, P. H. Dixneuf, *Angew. Chem. Int. Ed.* **2003**, *42*, 4524–4527; c) R. Castarlenas, D. Sémeril, A. Demonceau, A. F. Noels, P. H. Dixneuf, *J. Organomet. Chem.* **2002**, *663*, 235–238; d) R. Castarlenas, M. Eckert, P. H. Dixneuf, *Angew. Chem. Int. Ed.* **2005**, 2476–2479.

[3] a) B. M. Trost, J. A. Flygare, *J. Am. Chem. Soc.* **1992**, *114*, 5476–5477; b) P. Alvarez, M. Bassetti, J. Gimeno, G. Mancini, *Tetrahedron Lett.* **2001**, *42*, 8467–8470; c) S. Datta, C.-L. Chang, K.-L. Yeh, R.-S. Liu, *J. Am. Chem. Soc.* **2003**, *125*, 9294–9295; d) J. Le Paih, S. Derien, B. Demerseman, C. Bruneau, P. H. Dixneuf, L. Toupet, G. Dazinger, K. Kirchner, *Chem. Eur. J.* **2005**, *11*, 1312–1324; e) C. Bruneau, P. H. Dixneuf, *Angew. Chem. Int. Ed.* **2006**, *45*, 2176–2203.

[4] Y. Nishibayashi, S. Uemura, *Curr. Org. Chem.* **2006**, *10*, 135–150, and references cited therein.

[5] a) Y. Nishibayashi, M. Yoshikawa, Y. Inada, M. Hidai, S. Uemura, *J. Am. Chem. Soc.* **2002**, *124*, 11846–11847; b) Y. Nishibayashi, H. Imajima, G. Onodera, M. Hidai, S. Uemura, *Organometallics* **2004**, *23*, 26–30; c) Y. Inada, M. Yoshikawa, M. D. Milton, Y. Nishibayashi, S. Uemura, *Eur. J. Org. Chem.* **2006**, 881–890.

[6] a) Y. Nishibayashi, I. Wakiji, M. Hidai, *J. Am. Chem. Soc.* **2000**, *122*, 11019–11020; b) Y. Nishibayashi, M. D. Milton, Y. Inada, M. Yoshikawa, I. Wakiji, M. Hidai, S. Uemura, *Chem. Eur. J.* **2005**, *11*, 1433–1451.

[7] a) Y. Inada, Y. Nishibayashi, M. Hidai, S. Uemura, *J. Am. Chem. Soc.* **2002**, *124*, 15172–15173; b) Y. Nishibayashi, Y. Inada, M. Yoshikawa, M. Hidai, S. Uemura, *Angew. Chem. Int. Ed.* **2003**, *42*, 1495–1498.
[8] K. M. Nicholas, *Acc. Chem. Res.* **1987**, *20*, 207–214.
[9] V. Cadierno, J. Díez, S. E. García-Garrido, J. Gimeno, *Chem. Commun.* **2004**, 2716–2717.
[10] E. Bustelo, P. H. Dixneuf, *Adv. Synth. Catal.* **2005**, *347, 393–397.*
[11] C. Fischmeister, L. Toupet, P. H. Dixneuf, *New J. Chem.* **2005**, *29*, 765–768.
[12] a) B. D. Sherry, A. T. Radosevich, F. D. Toste, *J. Am. Chem. Soc.* **2003**, *125*, 6076–6077; b) M. R. Luzung, F. D. Toste, *J. Am. Chem. Soc.* **2003**, *125*, 15760–15761; c) J. J. Kennedy-Smith, L. A. Young, F. D. Toste, *Org. Lett.* **2004**, *6*, 1325–1327; d) R. V. Ohri, A. T. Radosevich, K. J. Hrovat, C. Musich, D. Huang, T. R. Holman, F. D. Toste, *Org. Lett.* **2005**, *7*, 2501–2504.
[13] M. Georgy, V. Boucard, J.-M. Campagne, *J. Am. Chem. Soc.* **2005**, *127*, 14180–14181.
[14] R. Sanz, A. Martínez, J. M. Álvarez-Gutiérrez, F. Rodríguez, *Eur. J. Org. Chem.* **2006**, 1383–1386.
[15] J. P. Selegue, *Organometallics* **1982**, *1*, 217–218.
[16] D. Pilette, K. Ouzzine, H. Le Bozec, P. H. Dixneuf, C. E. F. Rickard, W. R. Roper, *Organometallics* **1992**, *11*, 809–817.
[17] Reaction with other heteroaromatic compound such as pyrrole has also been tested and gave similar results. However, improvement of the catalyst and yield has been focused on the reaction with furan and 2-methylfuran.
[18] K. H. Meyer, K. Schuster, *Ber. dtsch. chem. Ges.* **1922**, *55*, 819–823.
[19] a) M. Picquet, C. Bruneau, P. H. Dixneuf, *Chem. Commun.* **1997**, 1201–1202; b) M. Picquet, A. Fernández, C. Bruneau, P. H. Dixneuf, *Eur. J. Org. Chem.* **2000**, 2361–2366; c) T. Suzuki, M. Tokunaga, Y. Wakatsuki, *Tetrahedron Lett.* **2002**, *43*, 7531–7533.
[20] V. Cadierno, S. E. García-Garrido, J. Gimeno, *Adv. Synth. Catal.* **2006**, *348*, 101–110.
[21] R. Werner, H. Werner, *Chem. Ber.* **1982**, *115*, 3766–3780.
[22] M. Okazaki, N. Yamahira, J. J. G. Minglana, H. Tobita, *Organometallics* **2004**, *23*, 4531–4533.
[23] a) L. Delaude, A. Demonceau, A. F. Noels, *Chem. Commun.* **2001**, 986–987; b) A. Hafner, A. Mühlebach, P. A. van der Schaaf, *Angew. Chem. Int. Ed. Engl.* **199**7, 36, 2121–2124.
[24] a) S. Swaminathan, K. V. Narayanan, *Chem. Rev.* **1971**, *71*, 429–438; b) C. Y. Lorber, J. A. Osborn, *Tetrahedron Lett.* **1996**, *37*, 853–856; c) J. An, L. Bagnell, T. Cablewski, C. R. Strauss, R. W. Trainor, *J. Org. Chem.* **1997**, *62,* 2505–2511.
[25] a) Y. Yamamoto, T. Arakawa, R. Ogawa, K. Itoh, *J. Am. Chem. Soc.* **2003**, *125*, 12143–12160; b) T. Shibata, T. Fujimoto, K. Yokota, K. Takagi, *J. Am. Chem. Soc.* **2004**, *126*, 8382–8383; c) B. Trost, M. T. Rudd, M. G. Costa, P. I. Lee, A. E. Pomerantz, *Org. Lett.* **2004**, *23*, 4235–4238; d) Y. Yamamoto, K. Kinpara, T. Saigoku, H. Takagishi, S. Okuda, H. Nishiyama, K. Itoh, *J. Am. Chem. Soc.* **2005**, *127*, 605–613; e) J.-C. Hsieh, C.-H. Cheng, *Chem. Commun.* **2005**, 2459–2461.
[26] C. P. Casey, T. L. Dzwiniel, S. Kraft, I. A. Guzei, *Organometallics* **2003**, *22*, 3915–3920.
[27] S. -H, Jin, S.-W. Kang, (Samsung Display Devices Co., Ltd., S. Korea), *US Patent* 5,616,669, **1996**
[28] For reviews, see: a) C. Bruneau, *Angew. Chem. Int. Ed. Engl.* **2005**, *44*, 2328–2334; b) C. Nieto-Oberthur, S. Lopez, E. Jimenez-Munez, A. M. Echavarren, *Chem. Eur. J.* **2006**, *12*, 5916–5923; c) C. Aubert, O. Buisine, M. Malacria, *Chem. Rev.* **2002**, *102*, 813–834.
[29] E. Bustelo, P. H. Dixneuf, in: *Handbook of CH Bond Transformation*, (Ed.: G. Dycker), Wiley-VCH, Weinheim, **2005**, Vol. 1, pp 62–72.
[30] B. Jiang, Y.-G. Si, *Tetrahedron Lett.* **2002**, *43*, 8323–8325.
[31] A. Fürstner, M. Liebl, C. W. Lehman, M. Picquet, R. Kunz, C. Bruneau, D. Touchard, P. H. Dixneuf, *Chem. Eur. J.* **2000**, *6*, 1847–1857.
[32] NMR spectra from the SDBS Web : http://www.aist.go.jp/RIODB/SDBS/(National Institute of Advanced Industrial Science and Technology).
[33] C. S. Yi, N. Liu, A. L. Rheingold, L. M. Liable-Sands, *Organometallics* **1997**, *16*, 3910–3913.

