DOI: 10.1002/adsc.200800508

A Practical and Effective Ruthenium Trichloride-Based Protocol for the Regio- and Stereoselective Catalytic Hydroamidation of Terminal Alkynes

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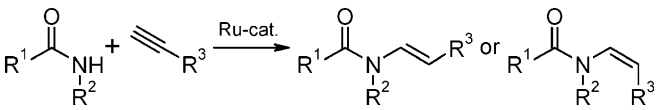
Received: August 14, 2008; Published online: November 19, 2008

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.200800508.

Abstract: A rational catalyst development based on mechanistic and spectroscopic investigations led to the discovery of a new protocol for catalytic hydroamidation reactions that draws on easily available ruthenium trichloride trihydrate ($RuCl_3 \cdot 3H_2O$) as the catalyst precursor instead of the previously employed, expensive bis(2-methylallyl)(1,5-cyclooctadiene)ruthenium(II). This practical and easy-to-use protocol dramatically improves the synthetic applicability of Ru-catalyzed hydroamidations. The catalyst, generated *in situ* from ruthenium(III) chloride hydrate, tri-*n*-butylphosphine, 4-(dimethylamino)-pyridine and potassium carbonate, effectively promotes the addition of secondary amides, lactams and carbamates to terminal alkynes under formation of (*E*)-*anti*-Markovnikov enamides. The scope of the new protocol is demonstrated by the synthesis of 24 functionalized enamide derivatives, among them valuable intermediates for organic synthesis.

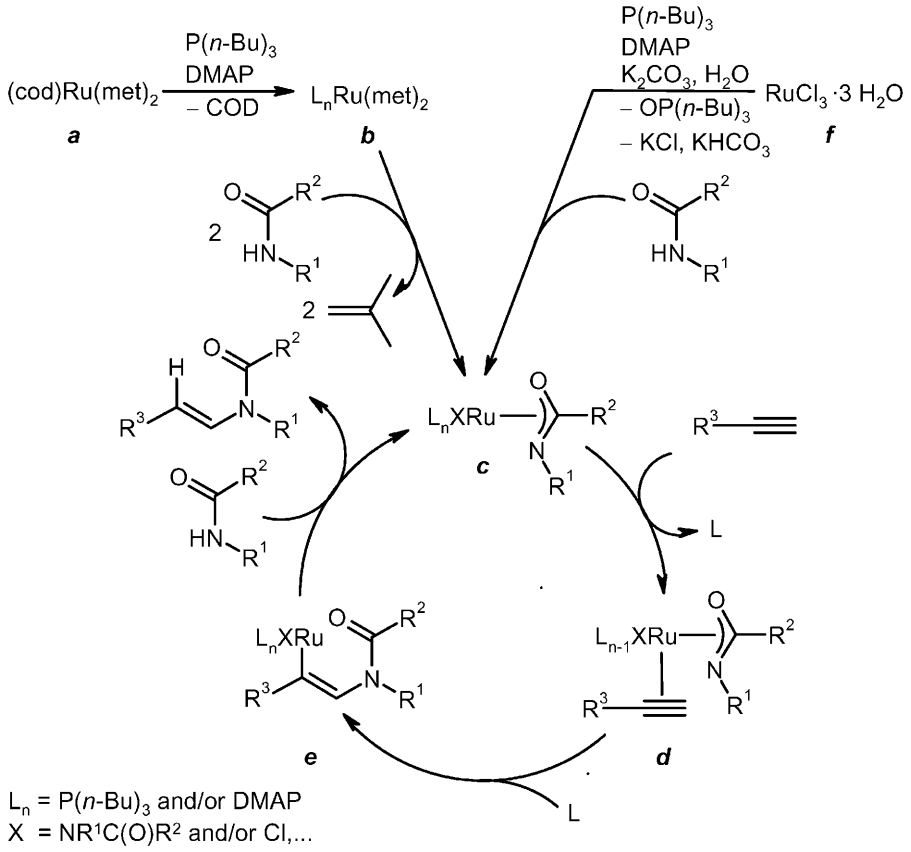
Keywords: addition reactions; enamides; homogeneous catalysis; hydroamidation; ruthenium

In recent years, the addition of nucleophiles across carbon-carbon triple bonds has evolved to become a versatile tool, for example, for the atom-economic synthesis of enol esters,[1] aldehydes,[2] (en)amines,[3] and imines,[3a,4] as well as enamides and their derivatives.[5] Our own contribution to this field was the development of effective Ru-catalysts that, for the first time, allowed the addition of various amide derivatives, such as amides, imides, carbamates, lactams, and ureas, to terminal alkynes.[5a–c] These hydroamidations are highly *anti*-Markovnikov-selective, while their stereochemistry is controlled by the ligands and either auxiliary bases or Lewis acids (Scheme 1). They promise to be valuable alternatives to traditional syntheses, for example, from carbonyl compounds and amides[6] or from hydroxylamines and carboxylic anhydrides,[7] that usually require harsh conditions and give (*E*/*Z*)-mixtures, and to metal-catalyzed coupling reactions of amides with vinyl halides, pseudohalides[8] or ethers,[9] which suffer from limited substrate availability.



Scheme 1. Ru-catalyzed addition of amides to alkynes.

However, practical applications of this and other Ru-catalyzed additions have so far been hampered by the prohibitive price of Ru(II) complexes stabilized with labile ligands, for example, tris(acetonitrile)pentamethylcyclopentadienylruthenium(II) hexafluorophosphate (154 €/mmol), acetonitrilebis(2-diphenylphosphino-6-*tert*-butylpyridine)-cyclopentadienylruthenium(II) hexafluorophosphate (425 €/mmol), or bis-(2-methallyl)-cycloocta-1,5-diene-ruthenium(II) [(cod)Ru(met)$_2$, 68 €/mmol], that are required for generating the catalytically active species.[10] The synthetic utility of this type of addition reaction would thus vastly be improved if the catalyst could instead be generated from easily available Ru(III) salts such as $RuCl_3 \cdot 3H_2O$ (5 €/mmol). However, the complexity of this replacement of the Ru precursor becomes apparent when considering the necessity of selectively reducing Ru(III) to Ru(II) during catalyst preforma-



Scheme 2. Proposed hydroamidation mechanism starting from (cod)Ru(met)$_2$, and from $RuCl_3 \cdot 3H_2O$.

tion, and of scavenging the strongly coordinating halide ions.

In the original hydroamidation protocol, the catalyst is generated from (cod)Ru(met)$_2$ (***a***), tri-*n*-butylphosphine, 4-(dimethylamino)pyridine (DMAP), and the amide substrate (Scheme 2, left). In the preformation steps, the 1,5-cyclooctadiene (COD) ligand is displaced by the phosphine and/or DMAP ligands giving rise to intermediate ***b***, as indicated by the characteristic signals for free, unaltered COD and Ru-coordinated P(*n*-Bu$_3$) in GC-MS/NMR spectra.[5c,11] Moreover, the detection of isobutene suggests that the methallyl ligands are protonated off by the N–H acidic amides, thus leading to a Ru(II) amide complex ***c***. The alternative formation of a Ru(0) species appears less likely, as no 2,5-dimethylhexadienes were detected, that would have been indicative of a reductive dimerization of the methallyl ligands. An ESI-mass spectrum taken at this stage is dominated by two signals, which on the basis of their mass and isotope pattern can be attributed to $\{Ru[P(n\text{-}Bu)_3]_2(C_4H_6NO)(DMAP)\}^+$ and $\{Ru[P(n\text{-}Bu)_3]_3(C_4H_6NO)\}^+$ fragments. This again supports our proposed catalytic cycle that starts from $[P(n\text{-}Bu_3)]_n(DMAP)_mRu(II)$ amide complex (***c***) (see Figure 1). Initially, the alkyne adds to the Ru center, possibly displacing one of the ligands under formation of complex ***d***. The amide anion then attacks the coordinated alkyne, and the enamide product is finally released from the intermediate ***e*** by protonolysis, thus regenerating the original catalytic species ***c***.

Apparently, none of the original ligands of the elaborate Ru precursor ***a*** actually remain bound to the metal center, suggesting that simple ruthenium salts may also be utilized as precursors. In our search for a protocol that would allow the selective reduction of ruthenium chloride (***f***) to a Ru(II) species while at the same time removing the chloride ions, which can be expected to compete with the substrates for coordination sites at the ruthenium, we came across a publication by Kölle et al.[12] They describe the synthesis of di-μ-methoxo-bis[(η^5-pentamethylcyclopentadienyl)diruthenium(II) from di-μ-chloro-bis[(η^5-pentamethylcyclopentadienyl)chlororuthenium(III)] [(Cp*RuCl$_2$)$_2$] using MeOH as reductant and the mild base K_2CO_3 for the generation of the methoxide ligands as well as for precipitation of the chloride as KCl.

In order to investigate whether a related strategy would be successful also for the *in situ* generation of an effective hydroamidation catalyst (Scheme 2, right), we treated a suspension of $RuCl_3 \cdot 3H_2O$ in toluene with K_2CO_3, methanol, P(*n*-Bu)$_3$, and DMAP,

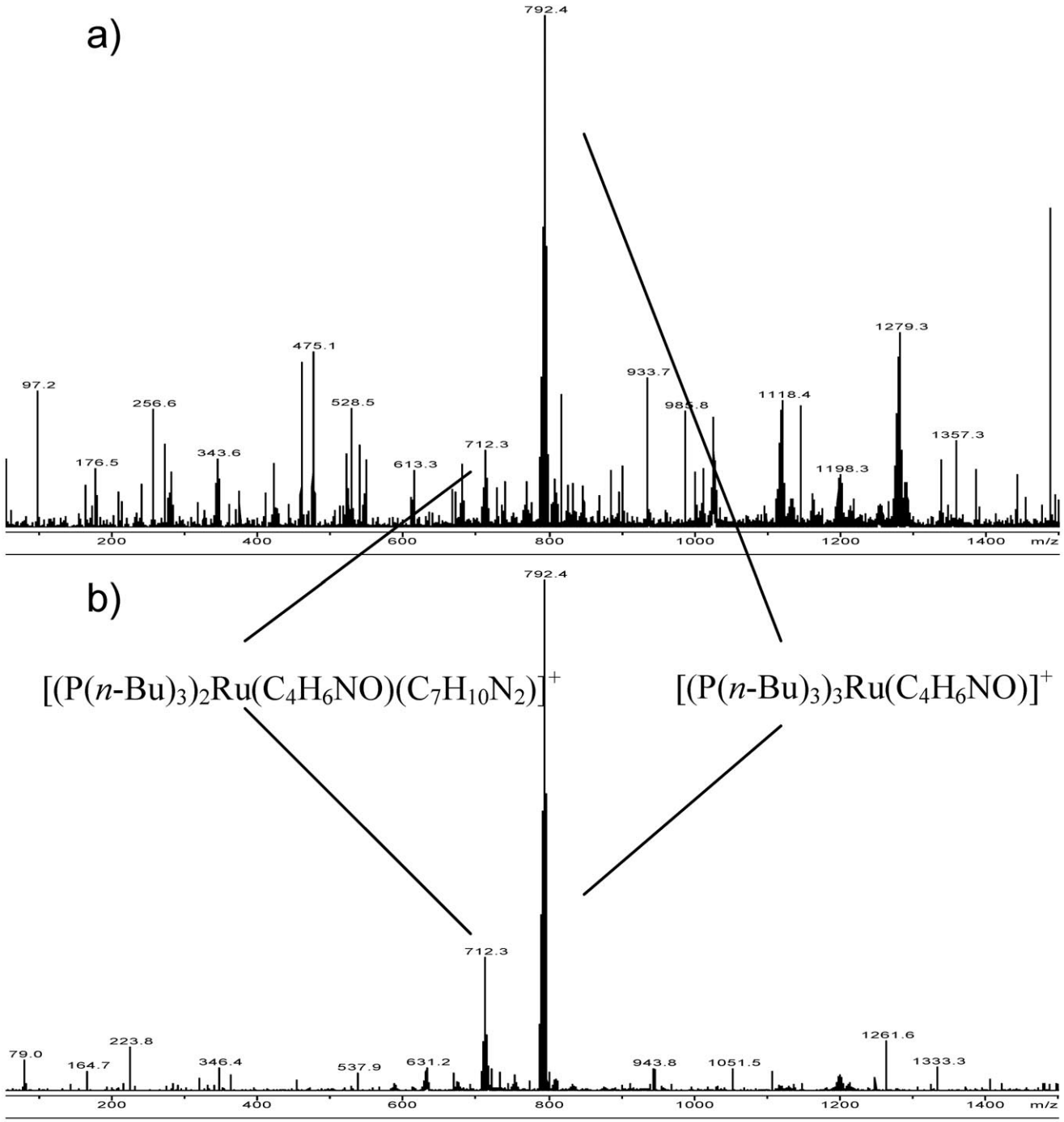
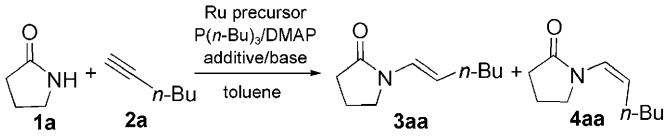


Figure 1. ESI-MS of the catalyst systems based on a) $RuCl_3$ and b) $(cod)Ru(met)_2$.

and added pyrrolidin-2-one (**1a**) and 1-hexyne (**2a**) as typical hydroamidation substrates (Table 1). We were pleased to find that after heating the reaction mixture to 100 °C overnight, the desired product (*E*)-*N*-(hex-1-enyl)pyrrolidin-2-one (**3aa**) had formed in high (*E*/*Z*)-selectivity and reasonable but varying yields (entry 2). The best results obtained with this protocol became reproducible when using amorphous $RuCl_3$ generated by dissolution of commercial $RuCl_3 \cdot 3H_2O$ in acetone followed by evaporation (entry 3).[13] The use of $(cod)RuCl_2$ gave comparable results but offered no advantage (entry 4). Systematic investigations revealed that a base, for example, potassium carbonate or hydroxide, is essential, whereas the alcohol can be replaced by water (entries 5–9). This goes along with reports in the literature that phosphines themselves can act as reducing agents for transition metals, a process assisted by water.[14]

Table 1. Optimization of the catalyst and conditions.[a]



Entry	Ru precursor	Additive	Base	Yields [%]	Ratio **3aa**/**4aa**
1	$(cod)Ru(met)_2$	–	–	>99	19:1
2	$RuCl_3{\cdot}3H_2O$	MeOH	K_2CO_3	30–99	5–25:1
3	$RuCl_3{\cdot}3H_2O$[b]	MeOH	K_2CO_3	>99	18:1
4	$(cod)RuCl_2$	MeOH	K_2CO_3	>99	24:1
5	$RuCl_3{\cdot}3H_2O$[b]	MeOH	–	7	3:2
6	$RuCl_3{\cdot}3H_2O$[b]	–	K_2CO_3	95	14:1
7	$RuCl_3{\cdot}3H_2O$[b]	EtOH	K_2CO_3	>99	23:1
9	$RuCl_3{\cdot}3H_2O$[b]	H_2O	K_2CO_3	>99	24:1
10[c]	$RuCl_3{\cdot}3H_2O$[b]	H_2O	K_2CO_3	>99	31:1
11[d]	$RuCl_3{\cdot}3H_2O$[b]	H_2O	K_2CO_3	94	31:1
12[e]	$RuCl_3{\cdot}3H_2O$[b]	H_2O	K_2CO_3	>99	25:1
13[f]	$RuCl_3{\cdot}3H_2O$[b]	MeOH	K_2CO_3	>99	22:1

[a] *Reaction conditions*: 1.00 mmol pyrrolidin-2-one, 2.00 mmol 1-hexyne, 2 mol% Ru precursor, 6 mol% P(*n*-Bu)$_3$, 4 mol% DMAP, 10 mol% base, 0.30 mmol additive, 3 mL toluene, 100 °C, 15 h; yields and selectivities determined by GC using *n*-tetradecane as internal standard.

[b] The catalyst was injected as a stock solution of $RuCl_3{\cdot}3H_2O$ (0.02 mmol) in acetone (1 mL) *via* syringe. The solvent was removed under vacuum before any liquid compound was added.

[c] At 80 °C.

[d] At 70 °C.

[e] 1 mol% $RuCl_3{\cdot}3H_2O$, 3 mol% P(*n*-Bu)$_3$, 2 mol% DMAP.

[f] $[HP(n\text{-}Bu)_3]^+ BF_4^-$ instead of P(*n*-Bu)$_3$

At a temperature of 80 °C, an optimal balance between reaction rate and selectivity was achieved (entries 9–11), leading to near quantitative yields and (*E*/*Z*)-selectivities in excess of 30:1 with a catalyst loading of 2 mol%. Similar results were obtained with 1 mol% of $RuCl_3{\cdot}3H_2O$ (entry 12), and when replacing the air-sensitive, liquid P(*n*-Bu)$_3$ by its tetrafluoroborate salt, which is air- and water-stable, and advantageous especially for large-scale applications (entry 13).

The performance of this simple system in the model reaction matches that of the expensive $(cod)Ru(met)_2$-derived catalyst, which supports our hypothesis that the same type of catalytically active Ru(II) species is generated with either method (Scheme 2). Moreover, ESI-MS measurements of a sample taken from a toluene solution of $RuCl_3{\cdot}3H_2O$, P(*n*-Bu)$_3$, DMAP, K_2CO_3, water, and pyrrolidin-2-one (Figure 1) again display the distinct signals corresponding to $\{Ru[P(n\text{-}Bu)_3]_2(C_4H_6NO)(DMAP)\}^+$ and $\{Ru[P(n\text{-}Bu)_3]_3(C_4H_6NO)\}^+$, but also contains small signals for potassium adducts and, for example, chloride-bridged polynuclear ruthenium species.[15]

We next tested the generality of the new protocol by applying it to the synthesis of enamide derivatives from various *N*-nucleophiles and alkynes. As can be seen from Table 2, linear and branched aliphatic as well as aromatic terminal alkynes bearing a range of functional groups were smoothly and selectively converted with pyrrolidin-2-one in yields that were sometimes even in excess of those obtained with the first-generation catalyst. Moreover, various *N*-nucleophiles could be added to 1-hexyne, including amides, lactams, bislactams, oxazolidinones, and even thioamide substrates that with $(cod)Ru(met)_2$ required a customized set of ligand and additive.[16] The yields and selectivities were usually high, but for acyclic amides do not quite reach those of the original protocol, which we attribute to the competition of remaining halide ions for coordination sites at the ruthenium giving rise to less active Ru species (Scheme 2, X = Cl). The protocol could easily be scaled up to gram quantities without any losses in yield or selectivity.

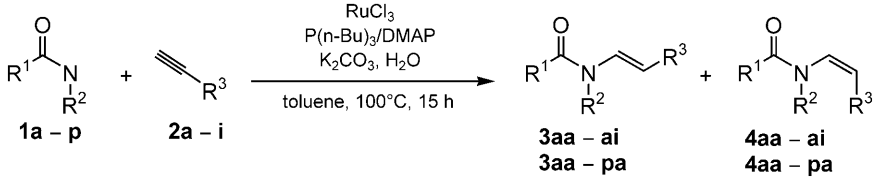
In summary, a practical protocol for hydroamidation reactions has been discovered in which the catalyst is generated *in situ* from inexpensive ruthenium(III) chloride hydrate, tri-*n*-butylphosphine or its HBF_4 adduct, 4-(dimethylamino)pyridine and potassium carbonate. The catalyst system effectively promotes the addition of secondary amides, thioamides, lactams and carbamates to terminal alkynes under formation of (*E*)-*anti*-Markovnikov enamides in yields that often match or even exceed those of the costly first-generation catalyst, thus greatly extending the synthetic utility of hydroamidation reactions.

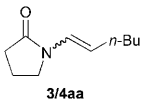
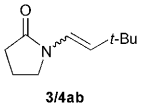
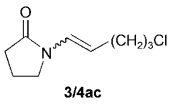
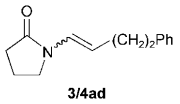
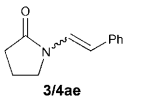
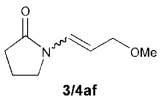
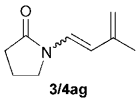
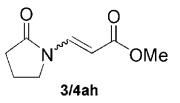
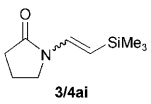
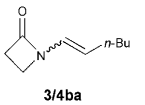
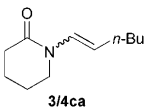
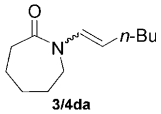
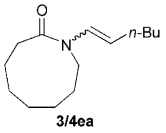
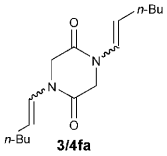
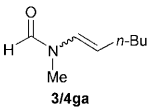
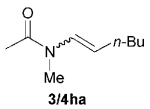
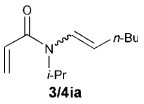
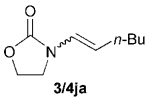
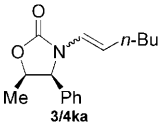
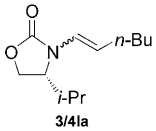
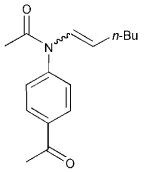
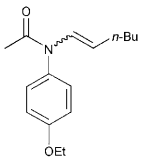
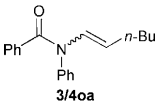
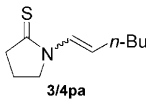
Experimental Section

General Methods

Reactions were performed in oven-dried glassware under a nitrogen atmosphere containing a Teflon-coated stirrer bar and dry septum, unless otherwise specified. Solvents were purified by standard procedures prior to use. All reactions were monitored by GC using *n*-tetradecane as an internal standard. Response factors of the products with regard to *n*-tetradecane were obtained experimentally by analyzing known quantities of the substances. GC analyses were carried out using an HP-5 capillary column (Phenyl Methyl Siloxane 30 m × 320 × 0.25, 100/2.3–30–300/3) and a time program beginning with 2 min at 60 °C followed by 30 °C min^{-1} ramp to 300 °C, then 3 min at this temperature. Column chromatography was performed using a Combi Flash Companion-Chromatography-System (Isco-Systems) and RediSep packed columns (12 g). NMR spectra were obtained on Bruker DPX 400 or on Bruker Avance 600 systems using $CDCl_3$ or toluene-d_8 as solvent, with proton, carbon and phosphorus resonances at 400/600 MHz, 101/151 MHz and 162/243 MHz, respectively. Mass spectral data were acquired

Table 2. Substrate scope of the $RuCl_3$-catalyzed hydroamidation.



Product	Yield [%] (ratio **3**/**4**)	Product	Yield [%] (ratio **3**/**4**)	Product	Yield [%] (ratio **3**/**4**)	Product	Yield [%] (ratio **3**/**4**)
 **3/4aa**	99 (32:1)	 **3/4ab**	99 (40:1)[b]	 **3/4ac**	99 (33:1)	 **3/4ad**	96 (25:1)[b]
 **3/4ae**	97 (22:1)[b]	 **3/4af**	99 (24:1)	 **3/4ag**	97 (8:1)[b]	 **3/4ah**	96 (40:1)[b]
 **3/4ai**	90 (2:1)[b]	 **3/4ba**	35 (1:1)	 **3/4ca**	91 (40:1)	 **3/4da**	99 (40:1)
 **3/4ea**	30 (40:1)	 **3/4fa**	71 (40:1)[c]	 **3/4ga**	35 (3:1)[b]	 **3/4ha**	10 (2.4:1)[b]
 **3/4ia**	49 (40:1)[b]	 **3/4ja**	88 (30:1)	 **3/4ka**	94 (21:1)	 **3/4la**	94 (22:1)
 **3/4ma**	20 (40:1)[b]	 **3/4na**	93 (40:1)[b]	 **3/4oa**	20 (40:1)[b]	 **3/4pa**	80 (3:1)[b]

[a] *Reaction conditions*: 1.00 mmol N-nucleophile (**1a–p**), 2.00 mmol alkyne (**2a–i**), 3 mol% $RuCl_3 \cdot 3H_2O$, 9 mol% P(*n*-Bu)$_3$, 9 mol% DMAP, 15 mol% K_2CO_3, 0.40 mmol H_2O, 3 mL toluene, 15 h, 100 °C, isolated yields, selectivities determined by GC.

[b] Selectivities determined by ^{1}H NMR.

[c] 4.00 mmol alkyne, selectivity determined by ^{1}H NMR.

on a GC-MS Saturn 2100 T (Varian). Electrospray ionization mass spectrometry (ESI-MS) was performed with a Bruker Esquire 3000plus ion trap instrument. The ion source was used in positive electrospray ionization mode. Scan speed was 1650 *m*/*z*/s in maximum resolution scan mode (0.3 FWHM/*m*/*z*), scan range was 50 to 1500 *m*/*z*. All spectra were accumulated for at least five minutes. Sample solutions in toluene at concentrations of 0.007 M were filtered through a PVDF filter (0.45 μm–13 mm) and continuously infused into the ESI chamber at a flow rate of 4 μL min^{-1} using a syringe pump. Nitrogen was used as drying gas with flow rate of 3.0 L min^{-1} at 300 °C. The solutions were sprayed at a nebulizer pressure of 4 psi and the electrospray needle was typically held at 4.5 kV. The instrument was controlled by Bruker Esquire Control 5.3 software and data analysis was performed using Bruker Data Analysis 3.4 software.

Catalytic Hydroamidation as Exemplified by the Synthesis of (*E*)-*N*-(Hex-1-enyl)pyrrolidin-2-one (3aa)

An oven-dried flask was charged with potassium carbonate (276.0 mg, 2.00 mmol), 4-(dimethylamino)pyridine (97.7 mg, 0.80 mmol) and a stock solution of ruthenium(III) chloride hydrate (100.5 mg, 0.40 mmol) in acetone (20.00 mL). The solvent was removed under vacuum, and after purging the flask with alternating vacuum and nitrogen cycles, dry toluene (50.00 mL), water (108 μL, 6.00 mmol), pyrrolidin-2-one (**1a**, 1.54 mL, 20.00 mmol), tri-*n*-butylphosphine (300 μL, 1.20 mmol), and 1-hexyne (**2a**, 4.63 mL, 40.00 mmol) were added *via* syringe. The reaction solution was monitored

using GC. After full conversion (2 h), it was diluted with ethyl acetate (250 mL) and aqueous sodium bicarbonate (2 N, 150 mL). The resulting mixture was extracted repeatedly with 50 mL portions of ethyl acetate, the combined organic layers were washed with water and brine, dried over magnesium sulfate, filtered, and the solvent was removed under vacuum. The residue was pre-adsorbed on a pad of silica gel (10 g), layered over additional silica gel (20 g), non-polar impurities, for example, alkyne oligomers, were washed off with hexane (200 mL) and the product was eluted with an ethyl acetate/hexane mixture (3:7, 200 mL). The solvent was removed under vacuum and the residue was purified by vacuum distillation (150 °C/3×10^{-2} bar) affording **3aa** as a yellowish oil; yield: 3.30 g (99%). Its spectroscopic data matched those reported in the literature [CAS: 863709–29–9].

NMR Studies of the Catalyst Preformation

The *in situ* formation of the catalyst from (cod)Ru(met)$_2$ was investigated by a series of ^{1}H and ^{31}P NMR experiments:

A 5-mm NMR tube was charged with (cod)Ru(met)$_2$ (12.8 mg, 0.04 mmol) and DMAP (9.8 mg, 0.08 mmol). The tube was sealed with a rubber septum and purged with alternating vacuum and nitrogen cycles. Tri-*n*-butylphosphine (30 μL, 0.012 mmol) and toluene-d_8 (1 mL) were added *via* syringe and placed in an ultrasonic bath for 3 min to give a clear yellow solution.

The ^{1}H NMR spectrum taken at this point, prior to catalyst preformation, shows clear singlets at δ = 3.47 (2 H), 2.80 (2 H), 1.69 (6 H), 1.53 (2 H), and 0.15 (2 H) ppm for two ruthenium-bound methallyl ligands, and multiplets at δ = 3.87–3.92, 2.82–2.91, 2.68–2.75, 1.86–1.97 ppm (2 H each), 1.55–1.63 and 1.09–1.16 ppm (2 H each, overlapping with signals of the phosphine ligands) for the ruthenium-bound COD ligand. Doublets at δ = 8.34 and 6.07 ppm (2 H each) and a singlet at δ = 2.28 (6 H) ppm indicate the presence of free DMAP ligands. The ^{31}P NMR spectrum at 25 °C shows a minor signal at δ = 20.8 ppm for metal-coordinated tri-*n*-butylphosphine and a strong signal at δ = −31.1 ppm for uncoordinated phosphine.

After heating the above solution to 100 °C for 5 min, the NMR spectra revealed that now, the COD ligand had completely been displaced. In the ^{1}H NMR spectrum, the signals for coordinated COD ligands have disappeared, and signals at δ = 5.43–5.57 (4 H) and 2.14–2.24 (8 H) ppm indicate free 1,5-cyclooctadiene.

Due to the ligand exchange, the signals for the methallyl ligands are shifted to higher field, making an assignment difficult. Signals for isobutene which would indicate protonolysis or decomposition of the ruthenium complex cannot be observed. A strong signal for coordinated phosphine at δ = 20.8 ppm in the ^{31}P NMR spectrum confirmed that most of the phosphine was bound to the Ru center at this point in time.

After the addition of pyrrolidin-2-one (**1a**, 6.2 μL, 0.08 mmol) *via* syringe, the methyl ligands were protonated off by the amide, and signals at δ = 4.60–4.67 and 1.61 ppm in the ^{1}H NMR spectrum gave evidence of the formation of isobutene. The α-protons of the amide were found at δ = 2.62–2.80 ppm, whereas the other ring protons being concealed among the overlapping alkyl signals of tri-*n*-butylphosphine in the range of δ = 0.0–2.5 ppm. The ^{31}P NMR spectrum now solely shows coordinated tri-*n*-butylphosphine (δ = 20.0 ppm).

ESI-MS Studies of the Catalyst Preformation

An oven-dried flask was charged with (cod)Ru(met)$_2$ (6.4 mg, 0.02 mmol) and DMAP (4.9 mg, 0.04 mmol), and flushed with nitrogen. Subsequently, dry toluene (3.0 mL), pyrrolidin-2-one (**1a**, 77 μL, 1.00 mmol), and tri-*n*-butylphosphine (15 μL, 0.06 mmol) were added *via* syringe. After stirring the resulting solution for 1 h at 100 °C, a sample of 0.5 mL was analyzed as described in the general procedure showing the fragments {Ru[P(*n*-Bu)$_3$]$_3$(C$_4$H$_6$NO)}$^+$ [*m*/*z* (% relative to peak at 792.4) = 786.4 (13), 787.5 (7), 788.4 (6), 789.4 (34), 790.4 (43), 791.4 (55), 792.4 (100), 793.4 (40), 794.4 (58), 795.4 (24), 796.3 (5); calculated: 786.5 (14), 787.5 (6), 788.6 (6), 789.5 (34), 790.5 (46), 791.5 (59), 792.5 (100), 793.5 (39), 794.5 (54), 795.5 (22), 796.5 (5)] and {Ru[P(*n*-Bu)$_3$]$_2$(C$_4$H$_6$NO)(DMAP)}$^+$ [*m*/*z* (% relative to peak at 712.3) = 706.3 (14), 707.3 (5), 708.3 (7), 709.3 (27), 710.4 (36), 711.3 (47), 712.3 (100), 713.3 (27), 714.3 (42), 715.3 (18), 716.2 (7); calculated: 706.4 (14), 707.4 (6), 708.4 (6), 709.4 (34), 710.4 (45), 711.4 (59), 712.4 (100), 713.4 (36), 714.4 (54), 715.4 (20), 716.4 (4)].

An oven-dried flask was charged with potassium carbonate (13.8 mg, 0.10 mmol), and a stock solution containing ruthenium(III) chloride hydrate (5.2 mg, 0.02 mmol), 4-(dimethylamino)pyridine (4.9 mg, 0.04 mmol), and acetone (1.0 mL). The acetone was removed under vacuum and the flask was flushed with nitrogen. Subsequently, dry toluene (3.0 mL), water (5 μL, 0.30 mmol), pyrrolidin-2-one (**1a**, 77 μL, 1.00 mmol), and tri-*n*-butylphosphine (15 μL, 0.06 mmol) were added *via* syringe. After stirring the resulting solution for 1 h at 100 °C, a sample of 0.5 mL was analyzed as described in the general procedure showing the fragments {Ru[P(*n*-Bu)$_3$]$_3$(C$_4$H$_6$NO)}$^+$ [*m*/*z* (%) = 786.4 (14), 787.4 (8), 788.4 (7), 789.4 (29), 790.4 (45), 791.4 (58), 792.4 (100), 793.4 (43), 794.4 (52), 795.4 (22), 796.3 (6)] and {Ru[P(*n*-Bu)$_3$]$_2$(C$_4$H$_6$NO)(DMAP)}$^+$ [*m*/*z* (%) = 706.4 (26), 707.3 (15), 708.4 (14), 709.3 (50), 710.2 (51), 711.3 (74), 712.3 (100), 713.3 (42), 714.3 (63), 715.2 (24), 716.1 (10)].

Acknowledgements

We thank Umicore AG for generous donations of ruthenium catalysts, the DFG, OPTIMAS and NanoKat for funding, the DAAD for scholarships for K.S.M.S and M. B., the FCI and the Studienstiftung des deutschen Volkes for scholarships for F.R., and S. Ambrus and C. Riehn for support with the ESI-MS studies.

References

[1] a) T.-A. Mitsudo, Y. Hori, Y. Watanabe, *J. Org. Chem.* **1985**, *50*, 1566–1568; b) H. Doucet, N. Derrien, Z. Kabouche, C. Bruneau, P. H. Dixneuf, *J. Organomet. Chem.* **1997**, *551*, 151–157; c) L. J. Gooßen, J. Paetzold, D. Koley, *Chem. Commun.* **2003**, 706–707.

[2] a) M. Tokunaga, T. Suzuki, N. Koga, T. Fukushima, A. Horiuchi, Y. Wakatsuki, *J. Am. Chem. Soc.* **2001**, *123*, 11917–11924; b) T. Suzuki, M. Tokunaga, Y. Wakatsuki, *Org. Lett.* **2001**, *3*, 735–737.
[3] a) F. Pohlki, S. Doye, *Chem. Soc. Rev.* **2003**, *32*, 104–114; b) T. E. Müller, K. C. Hultzsch, M. Yus, F. Foubelo, M. Tada, *Chem. Rev.* **2008**, *108*, 3795–3892.
[4] M. Beller, J. Seayad, A. Tillack, H. Jiao, *Angew. Chem.* **2004**, *116*, 3448–3479; *Angew. Chem. Int. Ed.* **2004**, *43*, 3368–3398.
[5] a) L. J. Gooßen, J. E. Rauhaus, G. Deng, *Angew. Chem.* **2005**, *117*, 4110–4113; *Angew. Chem. Int. Ed.* **2005**, *44*, 4042–4045; b) L. J. Gooßen, M. Blanchot, C. Brinkmann, K. Gooßen, R. Karch, A. Rivas-Nass, *J. Org. Chem.* **2006**, *71*, 9506–9509; c) L. J. Gooßen, K. S. M. Salih, M. Blanchot, *Angew. Chem.* **2008**, *120*, 8620–8632; *Angew. Chem. Int. Ed.* **2008**, *47*, 8492–8495; d) T. Kondo, A. Tanaka, S. Kotachi, Y. Watanabe, *J. Chem. Soc. Chem. Commun.* **1995**, 413–414; e) S. Yudha S. , Y. Kuninobu, K. Takai, *Org. Lett.* **2007**, *9*, 5609–5611.
[6] W. Adam, S. G. Bosio, N. J. Turro, B. T. Wolff, *J. Org. Chem.* **2004**, *69*, 1704–1715.
[7] M. J. Burk, G. Casy, N. B. Johnson, *J. Org. Chem.* **1998**, *63*, 6084–6085.
[8] a) X. Pan, Q. Cai, D. Ma, *Org. Lett.* **2004**, *6*, 1809–1812; b) D. J. Wallace, D. J. Klauber, C.-Y. Chen, R. P. Volante, *Org. Lett.* **2003**, *5*, 4749–4752.
[9] J. L. Brice, J. E. Meerdink, S. Stahl, *Org. Lett.* **2004**, *6*, 1845–1848.
[10] All prices quoted from Strem Chemicals for Research, Catalog No. 21, **2006–2008**.
[11] J. Powell, B. L. Shaw, *J. Chem. Soc. A* **1968**, 159–161.
[12] a) U. Koelle, J. Kossakowski, *Inorg. Syn.* **1992**, *29*, 225–228; b) U. Koelle, J. Kossakowski, *J. Organomet. Chem.* **1989**, *362*, 383–398.
[13] a) M. M. Taqui Khan, G. Ramachandraiah, R. S. Shukla, *Inorg. Chem.* **1988**, *27*, 3274–3278; b) R. Steffen, R. Schöllhorn, *Solid State Ionics* **1986**, *22*, 31–41.
[14] a) T. D. Tilley, R. H. Grubbs, J. E. Bercaw, *Organometallics* **1984**, *3*, 274–278; b) C. Amatore, A. Jutand, *Acc. Chem. Res.* **2000**, *33*, 314–321.
[15] The actual level of potassium adducts and of polynuclear species in solution should be lower than recorded since the electrospray process itself is known to enhance adduct formation and to induce precipitation. Of course, solvated $RuCl_3$ is more affected by both processes than (cod)Ru(met)$_2$. In the light of these considerations the observation of $\{Ru[P(n\text{-}Bu)_3]_3(C_4H_6NO)\}^+$ as a dominating peak and of $\{Ru[P(n\text{-}Bu)_3]_2(C_4H_6NO)$-(DMAP)$\}$ as a well detectable, although minor peak is of high significance.
[16] L. J. Gooßen, M. Blanchot, K. S. M. Salih, R. Karch, A. Rivas-Nass, *Org. Lett.* **2008**, *10*, 4497–4499.

