Research Repository UCD

Title	Oxidations and Oxidative Couplings Catalyzed by Triazolylidene Ruthenium Complexes
Authors(s)	Prades, Amparo, Peris, Eduardo, Albrecht, Martin
Publication date	2011-02
Publication information	Prades, Amparo, Eduardo Peris, and Martin Albrecht. "Oxidations and Oxidative Couplings Catalyzed by Triazolylidene Ruthenium Complexes." American Chemical Society, February 2011. https://doi.org/10.1021/om101145y.
Publisher	American Chemical Society
Item record/more information	http://hdl.handle.net/10197/6572
Publisher's statement	This document is the unedited author's version of a Submitted Work that was subsequently accepted for publication in Organometallics, copyright © American Chemical Society after peer review. To access the final edited and published work, see http://pubs.acs.org/doi/abs/10.1021/om101145y.
Publisher's version (DOI)	10.1021/om101145y

Downloaded 2026-05-01 23:36:21

The UCD community has made this article openly available. Please share how this access benefits you. Your story matters! (@ucd_oa)

© Some rights reserved. For more information

Oxidations and Oxidative Couplings Catalyzed by Triazolylidene Ruthenium Complexes

Amparo Prades,[†,‡] *Eduardo Peris**[‡] *and Martin Albrecht**[‡]

[†] Dpto. de Química Inorgánica y Orgánica, Universitat Jaume I, Avda. Vicente Sos Baynat s/n, 12071 Castellón, Spain (eperis@qio.uji.es)

[‡] School of Chemistry & Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland (martin.albrecht@ucd.ie)

* To whom correspondence should be addressed: eperis@qio.uji.es, martin.albrecht@ucd.ie

ABSTRACT. A series of '$Ru^{II}(\eta^6$-arene)' complexes with 1,2,3-triazolylidene ligands have been prepared and fully characterized. The molecular structure of one of the new complexes has been determined by means of X-ray diffractrometry. The new complexes have been tested in a set of catalytic reactions involving alcohols and amines as substrates, including: i) base-free oxidation of benzylic alcohols to benzaldehydes, ii) homocoupling of amines to imines, and iii) oxidative coupling of amines and alcohols to amides. The results show the high versatility of the catalysts used and illustrate the application potential of 1,2,3-triazolylidene ligands in the design of effective homogeneous catalysts.

Introduction

The formation of carbon-nitrogen bonds is one of the most important transformations in organic

chemistry.[1] Homogeneous catalysis has provided effective methodologies to allow for the alkylation of amines by hydrogen-borrowing strategies.[2,3-4,5] In addition, great efforts have been devoted to the development of oxidative cross-coupling reactions between alcohols and amines to selectively form imines[6-7] or amides,[8-9,10-13] because these types of carbon-nitrogen compounds are key functional groups of peptides (amides),[14] and also because of their versatile applicability in laboratory and industrial synthetic processes (amides and imines).[15] Although the principles governing the oxidation processes are common to alcohols and imines, versatile homogeneous catalysts capable of reacting with both types of substrates are rare, with Shvo's catalyst being one of the most representative examples in terms of high efficiency and versatility.[16,17]

In the formation of amides by direct coupling between alcohols and amines, N-heterocyclic-carbene (NHC) ruthenium-based catalysts have recently played an important role.[8,11-13,18] Notably, simple well-defined '(η^6-arene)Ru(NHC)' complexes are among the best catalysts for this transformation, which can be performed using a wide variety of amines and alcohols.[11] The use of NHC-based ligands seems to bring a series of advantages to the development of this catalytic reaction, because NHCs combine a number of attractive features.[19] Firstly, the azolium ligand precursor is stable towards oxidation.[20] Secondly, the number of possible coordination modes of the carbene to the metal, paired with the large library of NHC-type ligands, may allow the electronic properties of the metal to be fine-tuned, with obvious implications for catalytic outcomes. And thirdly, the carbene ligand displays a pronounced mesoionic character,[21,22] thus accommodating positive and negative partial charges in the same heterocycle. These latter properties may be key for coordinating metal centers in different oxidation states.[23] Low-valent electron-rich centers may be stabilized by an increased carbene-type neutral resonance contribution, whereas the mesoionic contribution may prevail when coordinated to an electron-poor metal in high oxidation state, resulting from a carbanionic metal binding site that is charge-compensated intramolecularly by an iminium fragment. Indeed, a number of applications have been disclosed, predominantly in transfer hydrogenation under basic conditions, which involves the

oxidation of a sacrificial hydrogen donor.[3,24]

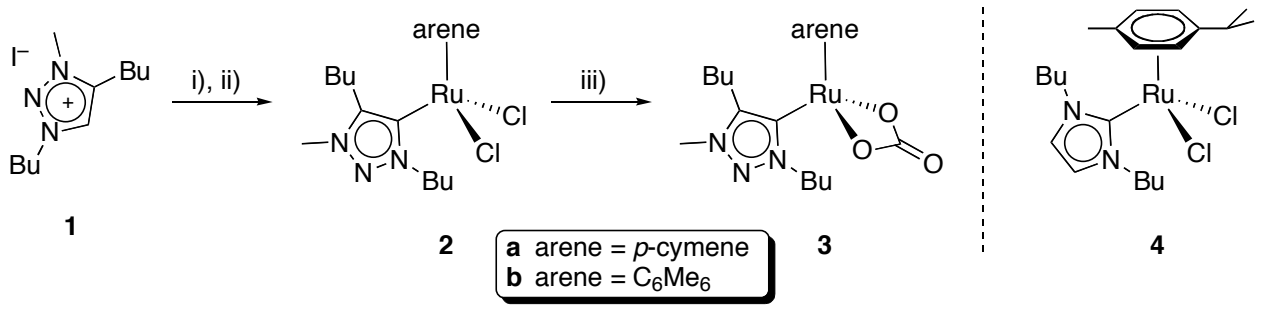
Aiming to expand the family of abnormal N-heterocyclic carbene ligands,[25] we recently reported the preparation of 1,4-substituted 1,2,3-triazolium salts, which provided versatile ligand precursors for the synthesis of new 1,2,3-triazolylidene metal complexes.[26] The new ligands were coordinated to a wide set of metals, such as Ag, Rh, Ir, Ru and Pd, and their donor properties were estimated to compare well with the most basic 2-imidazolylidenes, although being slightly less basic than other abnormal carbenes.[27] In a very recent report, Bertrand and co-workers were able to isolate and determine the X-ray molecular structure of one of such 1,2,3-triazolylidenes,[22] and these authors signaled its potential application in nucleophilic organocatalysis. We thought that the new ligand may have great potential for the development of new catalysts with unprecedented ligand-induced reactivity patterns, a largely underdeveloped area.[10,28] Based on our experience in employing several 'Ru(η^6-arene)(NHC)'-derived catalysts for the coupling of alcohols and amines,[5] and because of the extraordinary industrial interest in these reactions, we investigated the potential of such abnormal carbenes as spectator ligands for oxidation catalysts using alcohol and amine substrates. Here we report on a first proof of principle of this approach by using ruthenium(II) complexes comprising a 1,2,3-triazolium-derived carbene ligand as catalyst for the selective oxidation of benzylic alcohols, amines, and for the oxidative coupling of alcohols and amines to amides.

Results and discussion

Synthesis of the complexes. The new ruthenium(II) complexes **2** comprising a mesoionic triazolylidene ligand were prepared according to an established protocol from the corresponding triazolium salt **1** (Scheme 1). This salt is available from butyl azide and hexyne through Cu-mediated click chemistry and subsequent alkylation with MeI, according to a synthetic method previously reported in our group.[26] The ruthenium center was installed via a transmetallation procedure, involving a stepwise reaction of **1** with Ag_2O followed by the addition $[Ru(\eta^6\text{-arene})Cl_2]_2$ (arene = *p*-cymene,

hexamethylbenzene) to afford complexes **2**, as depicted in Scheme 1.

Scheme 1 [a]



[a] *Reagents and conditions*: i) Ag_2O, CH_2Cl_2, rt; ii) $[RuCl_2(arene)]_2$, CH_2Cl_2, rt; iii) Na_2CO_3, EtOH, rt.

Carbene-type bonding of the triazolylidene ligand was indicated by the low-field resonance in the ^{13}C NMR spectrum (δ_C 160.9 for **2a**, 165.5 for **2b**). The chemical shift difference may reflect the stronger electrondonating power of hexamethylbenzene to ruthenium as compared to *p*-cymene. Steric implications of the arene spectator ligand are evident when considering the ^1H magnetic resonances due to the α-CH_2 groups of the heterocycle substituents. In **2a,** both the NCH_2 and the carbon-bound CH_2 appear each as one multiplet, while in **2b**, the permethylated arene ring induces a splitting of these resonances in four distinct multiplets. The diastereotopicity of these protons suggests a sterically rigid conformation of the heterocycle and hindered rotation about the heterocycle–CH_2 and the C_{trz}–Ru bonds.

An X-ray diffraction analysis of single crystals of **2b** confirmed the connectivity pattern and the expected 3-legged piano-stool geometry of the complex (Fig. 1). The Ru(1)–C(1) bond is 2.093(6) Å and hence sligthly longer when compared to similar bonds in other 'Ru(η^6-arene)(NHC)' complexes.[5,29] The long bond may be a consequence of the steric constraints imposed by the hexamethylbenzene as suggested by ^1H NMR spectroscopy. The chloride ligands and the triazolylidene are occupying a regular face of the ruthenium center, with L–Ru–L' bond angles between 86.0 and 90.4°.

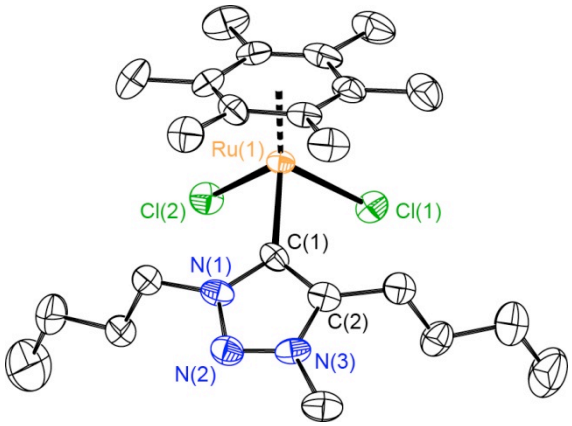


Fig. 1. ORTEP representation of **2b** (50% probability, hydrogens omitted for clarity). Selected bond lengths (Å) and angles (°): Ru(1)–C(1) 2.093(6), Ru(1)–Cl(1) 2.4386(19), Ru(1)–Cl(2) 2.4377(19), Ru(1)–C(centroid) 1.718(1), C(1)–Ru(1)–Cl(1) 87.11(19), C(1)–Ru(1)–Cl(2) 90.44(18), Cl(1)–Ru(1)–Cl(2) 86.08(7).

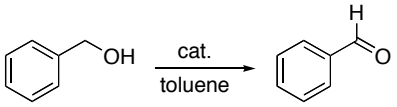
Anion metathesis with ethanolic Na_2CO_3 gave the corresponding carbonate complexes **3** as air- and moisture-stable yellow solids (Scheme 1). Direct evidence for the presence of the carbonate group was provided by the new ^{13}C NMR resonance around 170 ppm and by the strong IR absorption band at 1610 cm^{-1}, as shown for other previously reported 'Ru(η^6-arene)(NHC)(CO_3)' complexes.[30] In the ^1H NMR spectrum, an upfield shift of the NCH_2 resonance (*e.g.* from δ_H 4.61 in **2a** to δ_H 4.34 in **3a**) constitutes another evidence for successful chloride substitution. In addition, the separation of the multiplets in **3b** is considerably less pronounced than in **2b**, which may be attributed to a substantial decrease of the X–Ru–X bond angle from 86.1° in **2b** (X = Cl) to an estimated 60° in **3b**.[31] Accordingly, rotation should become less hindered and the chemical environment of the two hydrogens in each methylene group is indeed less disparate.

Catalytic oxidation of alcohols. Complexes **2** and **3** together with the known NHC ruthenium complex **4**,[32] were evaluated as catalyst precursor in the base- and oxidant-free oxidation of alcohols. We decided to evaluate the catalytic properties of compound **4** because of its steric similarity to **2a** (*cf* Scheme 1). Hence, catalytic differences can be attributed predominantly to the distinct electronic

properties imparted by the two different types of carbene ligands. The homogeneously catalyzed base-free dehydrogenation of alcohols is a highly attractive process for the synthesis of reactive carbonyl species from readily accessible alcohol substrates, constituting a much more benign methodology than (typically used) Cr-mediated oxidations.[29] Moreover, this process generates molecular hydrogen as most useful side product.[17,33]

Oxidation reactions were carried out in refluxing toluene under base-free conditions, using a catalyst loading of 5 mol%. An initial test using BnOH as model substrate revealed highest activity for complex **2a** (Table 1). Full conversion to benzaldehyde was observed within 16 h, while the C_6Me_6 analogue **2b** performed considerably worse. Substitution of the chlorides in the catalyst precursor for carbonate had diverging effects. While in **3a**, the activity was reduced as compared to **2a**, a significant increase from 55% to 85% conversion was noted for the hexamethylbenzene analogue **3b**. Lowering the temperature to 70 ºC still provided high conversion, though increased catalyst loading (10 mol%) and reaction times were required (compare entries 7 and 8).

Table 1. Catalyst screening in the oxidation of benzylalcohol[a]

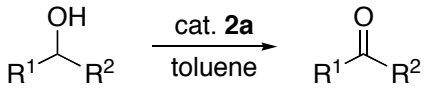


Entry	catalyst	t (h)	yield (%)[b]
1	---	20	< 2
2	**2a**	16	> 95
3	**2b**	20	55
4	**3a**	16	82
5	**3b**	16	85
6	**4**	20	60
7	**2a**[c]	24	32
8	**2a**[d]	24	95

[a] General conditions: benzylalcohol (0.2 mmol), catalyst (0.01 mmol) in toluene (2 mL) at reflux. [b]Yields determined by ^{1}H NMR (C_6Me_6 as internal standard). [c]At 70ºC. [d]At 70ºC using 10 mol% of catalyst.

Variation of the substrate revealed the scope and limitations of the best catalyst **2a** (Table 2). Both primary and secondary benzylic alcohols were oxidized readily into benzaldehyde and acetophenone, respectively, with good conversions (entries 1, 2). Aliphatic alcohols such as 2-phenylethanol or 1-octanol were not oxidized (entries 3, 4). The electronic nature of the aryl group plays an important role. Electron-withdrawing substituents reduced the activity of the catalyst although the conversions to the final benzylic alcohols were still high (entries 5–7), while neutral or electron-donating substituents gave conversions of 90% or higher (entries 8–10).

Table 2. Oxidation of different alcohols using **2a**[a]



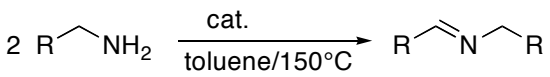
Entry	R^1	R^2	T (h)	yield (%)[b]
1	C_6H_5	H	16	> 95
2	C_6H_5	CH_3	24	> 95
3	CH_2-C_6H_5	H	20	< 5
4	C_7H_{15}	H	20	< 5
5	4-C_6H_4-NO_2	H	22	65
6	4-C_6H_4-Cl	H	22	68
7	2-C_6H_4-Cl	H	22	70
8	4-C_6H_4-Br	H	16	91
9	4-C_6H_4-CH_3	H	16	> 95
10	4-C_6H_4-OCH_3	H	16	90

[a] General conditions: alcohol (0.2 mmol), catalyst (0.01 mmol) in toluene (2 mL) at reflux. [b]Yields determined by ^{1}H NMR (C_6Me_6 as internal standard).

Catalytic oxidation of primary amines. In recent years considerable attention has been devoted to the oxidation of amines to imines.[34,35] Extensive efforts have been made in particular to develop catalytic systems that use green oxidants for the synthesis of imines from primary amines. Due to the promising catalytic behavior of complexes **2–4** in the oxidation of alcohols, we were interested in seeing if an extension of the catalytic activity to amines under oxidant-free conditions was accessible, hence

contributing to the development of greener methods for imine production. Our results are summarized in Table 3. At 150 ºC, with a catalyst loading of 5 mol%, and in the absence of an auxiliary base, oxidative homocoupling of amines was observed, cleanly affording the corresponding imines. The normal NHC complex **4** was more active than the triazolylidene-based complex **2** and reached full conversion after 12 h (*cf* 20 h for complexes **2**, entries 2–6). In contrast, the carbonate-containing complexes were inactive (entries 4, 5), maybe because the exchange of the carbonate ligand by an amine is thermodynamically unfavored. Aliphatic amines were also effectively oxidized, albeit at a lower rate (entries 7, 8). The somewhat harsher conditions in amine oxidation as compared to alcohol oxidation may be a consequence of the stronger bonding of imines as opposed to ketones to the ruthenium(II) center, thus insinuating that product release from the metal coordination sphere could be rate-limiting.

Table 3 Oxidative homocoupling of amines to imines[a]

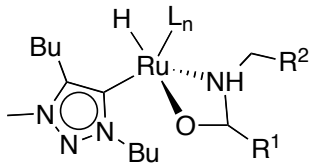


Entry	catalyst	R	t (h)	yield (%)[b]
1	---	C_6H_5	20	< 2
2	**2a**	C_6H_5	20	> 95
3	**2b**	C_6H_5	20	> 95
4	**3a**	C_6H_5	20	< 5
5	**3b**	C_6H_5	20	< 5
6	**4**	C_6H_5	12	> 95
7	**4**	C_5H_{11}	22	70
8	**4**	C_3H_7	22	62
9	**4**	4-C_6H_4-Cl	22	90

[a] General conditions: amine (0.2 mmol), catalyst (0.01 mmol) in toluene (2 mL) at 150 °C. [b]Yields determined by ^{1}H NMR (decane as internal standard).

Catalytic amide formation. As a consequence of the catalytic activity of the complexes in both alcohol and amine oxidative dehydrogenation, a combination of these two processes conceivably provides a convenient protocol for amide synthesis.[10–13] Indeed, reaction of benzyl alcohol or 2-

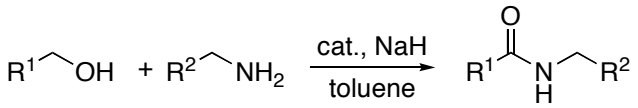
phenylethanol with benzylamine or *n*-hexylamine in the presence of catalytic amounts of **2** or **4** and NaH gave the corresponding amide (Table 4, entries 1–3). When using complex **4** as catalyst precursor, aliphatic and benzylic substrates (both as amine or alcohol) were successfully converted (entries 4, 5). Interestingly, 2-phenylethanol behaves as an excellent substrate for this type of coupling, contrary to what may be suggested by the results shown in Table 2, where the same substrate is inert toward oxidation under base-free conditions. The difference in behavior in this coupling reaction is probably due to the presence of base, which obviously facilitates the oxidation of the primary alcohol to the aldehyde in the step preceeding the coupling to the amine. Yields for the different catalyst precursors seem to correlate with the activity in amine oxidation (*cf* Table 3) and compare well with recent studies using related Ru(NHC) catalyst precursors.[11,13] The absence of any imine in the product mixture indicates efficient suppression of H_2O elimination from the postulated hemiaminal intermediate. Presumably, the hemiaminal displays an enhanced stability when bound to the ruthenium carbene unit, *viz*. intermediate **A** (Fig. 2), which is reminiscent of the carbonate complexes **3**. Subsequent β-hydrogen elimination to produce the amide in the metal coordination sphere is apparently more favorable than ligand dissociation, which would complete the Schiff'base reaction and would result in imine formation via water elimination. Hydrogen migration from the carbon in intermediate **A** to ruthenium is surmised to subsequently yield a ruthenium dihydride species that has been proposed as a further intermediate very recently by Hong and coworkers in the same context.[11-12]



A

Fig. 2. Schematic representation of the ruthenium-bound hemiaminal as intermediate in thesynthesis of amides catalyzed by **2**.

Table 4. Amide formation from alcohols and amines[a]



Entry	catalyst	R^1	R^2	t (h)	yield (%)[b]
1	**2a**	CH_2-C_6H_5	C_6H_5	15	68

2	**2b**	CH_2-C_6H_5	C_6H_5	15	40
3	**4**	CH_2-C_6H_5	C_6H_5	15	> 95
4	**4**	C_6H_5	C_6H_5	20	> 95
5	**4**	C_6H_5	C_5H_{11}	20	> 95

[a] General conditions: alcohol (0.2 mmol), amine (0.8 mmol), NaH (0.04 mmol), catalyst (0.01 mmol) in toluene (2 mL) at reflux. [b]Yields determined by ^{1}H NMR (C_6Me_6 as internal standard).

Conclusions

We have explored the catalytic properties of a series of 'Ru(η^6-arene)(NHC)' (NHC = 1,2,3-triazolylidene, imidazolylidene) complexes in various oxidations of alcohols and amines. The results demonstrate the catalytic potential of 1,2,3-triazolylidene-based metal complexes, and complement our previus studies on the coordination ability of this type of abnormal NHC ligands. The catalytic activity of the triazolylidene-based Ru complexes **2** and **3** has been compared with that shown by the isostructural imidazolylidene analogue **4**. The triazolylidene complexes are more effective than the imidazolylidene systems in the base-free oxidation of alcohols, while this trend is inverted for the oxidative homocoupling of amines and the coupling of amines and alcohols to amides. This work thus illustrates how subtle changes in the electron-donating properties of spectator ligands may affect the catalytic activity of Ru(η^6-arene)(NHC) scaffolds. These changes may not have the same effect in different although related transformations, as seen here in the catalytic dehydrogneation of alcohols and amines. Most significantly, the catalytic oxidations take place in the absence of base and oxidants. Only few catalysts have shown appreciable activity under such mild conditions for the oxidation of alcohols, and we are unaware of similar behavior towards amines.

Experimental section

General procedures. The metal complexes $[RuCl_2(p\text{-cymene})]_2$,[36] $[RuCl_2(CMe)_6]_2$,[37] complex **4**,[32] and 1,4-dibutyl-1,2,3-triazole[26] were prepared according to literature procedures. All other reagents were commercially available and used without further purification. NMR spectra were recorded on Varian

Innova 300 MHz and 400 MHz spectrometers at 298 K. Chemical shifts (δ) were referenced to the residual protiated solvent signals and are reported downfield of $SiMe_4$. Electrospray mass spectra (ESI-MS) were recorded on a Micromass Quatro LC instrument; nitrogen was employed as drying and nebulizing gas. Elemental analyses were carried out on a EuroEA3000 Eurovector Analyser.

Synthesis of (1,4-dibutyl-3-methyl-1,2,3-triazolium iodide) 1. To a solution of 1,4-dibutyl-1,2,3-triazole (1 g, 5.5 mmol) in acetonitrile (7 mL) was added iodomethane (3.5 mL, 55 mmol) and the mixture was stirred under microwave irradiation for 5 hours at 90 °C. The solvent was removed in vacuo. The oil residue was washed with diethyl ether several times and dried to afford the triazolium salt **1.** Yield: 1.5 g (85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.14 (s, 1H, CH_{trz}), 4.74 (t, ^3J(H,H) = 6.00 Hz, 2H, $NCH_{2\ n\text{-Bu}}$), 4.34 (s, 3H, NCH_3), 2.98 (t, $^3J_{HH}$ = 6.00 Hz, 2H, C_{trz}–$CH_{2\ n\text{-Bu}}$), 2.06 (m, 2H, $CH_{2\ n\text{-Bu}}$), 1.80 (m, 2H, $CH_{2\ n\text{-Bu}}$), 1.47 (m, 2H, $CH_{2\ n\text{-Bu}}$) 0.99 (t, $^3J_{HH}$ = 6.00 Hz, 6H, $CH_{3\ n\text{-Bu}}$). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 144.6 (C_{trz}–Bu), 129.2 (CH_{trz}), 54.0 ($NCH_{2\ n\text{-Bu}}$), 38.8 (CH_3), 31.3, 39.0, 23.7, 22.2, 19.4 (5 x $CH_{2\ n\text{-Bu}}$), 13.6, 13.3 (2 × $CH_{3\ n\text{-Bu}}$). Electrospray MS (30 V): m/z: 196.3 $[M–I]^+$. Anal. Calcd for $C_{11}H_{22}IN_3(H_2O)$: (341.10): C, 38.72; H, 7.09; N, 12.31. Found: C, 38.59; H, 7.17; N, 12.10.

Synthesis of 2a. Silver oxide (107 mg, 0.46 mmol) was added to a solution of **1** (150 mg, 0.46 mmol) in CH_2Cl_2 (20 mL). The suspension was stirred at room temperature for 2 h under the exclusion of light. The suspension was filtered through Celite and $[Ru(p\text{-cymene})Cl_2]_2$ (140 mg, 0.23 mmol) was added. The mixture was stirred at room temperature for 3 h. The suspension was filtered through Celite and the solvent was evaporated. The crude solid was purified by column chromatography. Elution with a mixture of CH_2Cl_2/Acetone (9:1) induced the separation of **2** as an orange band containing. Addition of cold Et_2O induced the precipitation of **2** as an orange solid **(**164 mg, 71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.35, 5.03 (2 × d, $^3J_{HH}$ = 6.0 Hz, 2H, $CH_{p\text{-cym}}$), 4.61 (m, 2H, $NCH_{2\ n\text{-Bu}}$), 3.97 (s, 3H, NCH_3), 2.98 (m, 2H, C_{trz}-$CH_{2\ n\text{-Bu}}$), 2.94 (m, 1H, $CH_{iso\ p\text{-cym}}$), 2.03 (s, 3H, $CH_{3\ p\text{-cym}}$), 1.99 (m, 2H, $CH_{2\ n\text{-Bu}}$), 1.56 (m, 2H, $CH_{2\ n\text{-Bu}}$), 1.48 (m, 4H, $CH_{2\ n\text{-Bu}}$), 1.29 (d, $^3J_{HH}$ = 6.0 Hz, 6H, $CH_{3\ iso\ p\text{-cym}}$), 0.98 (m, 6H,

$CH_{3\ n\text{-Bu}}$). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 160.9 (C_{trz}–Ru), 147.2 (C_{trz}–Bu), 106.9, 97.1 (2 × $C_{p\text{-cym}}$), 84.9, 82.7 (2 × $CH_{p\text{-cym}}$), 54.4 ($NCH_{2\ n\text{-Bu}}$), 36.3 (NCH_3), 33.0 ($CH_{iso\ p\text{cym}}$) 32.0, 30.7, 26.0, 23.1 (4 × $CH_{2\ n\text{-Bu}}$), 22.7($CH_{3\ iso\ p\text{-cym}}$), 20.2 ($CH_{2\ n\text{-Bu}}$), 18.7 ($CH_{3\ p\text{-cym}}$), 13.9, 13.8 (2 × $CH_{3\ n\text{-Bu}}$). Electrospray MS (30 V): m/z: 466.1 $[M–Cl]^+$. Anal. Calcd for $RuCl_2C_{21}H_{35}N_3$: (501.50): C, 50.29; H, 7.03; N, 8.38. Found: C, 50.08; H, 7.13; N, 8.11.

Synthesis of 2b. Following the same procedure as described for **2a**, reaction of **1** (150 mg, 0.46 mmol) with Ag_2O (107 mg, 0.46 mmol) in CH_2Cl_2 (20 mL) and subsequently with $[Ru(C_6Me_6)Cl_2]_2$ (140 mg, 0.23 mmol) yielded **2b** as an orange solid **(**149 mg, 62%). ^1H NMR (300 MHz, $CDCl_3$): δ 4.75 (m, 1H, $NCH_{2\ n\text{-Bu}}$), 4.06 (m, 1H, $NCH_{2\ n\text{-Bu}}$), 3.96 (s, 3H, NCH_3), 2.96 (m, 1H, C_{trz}–$CH_{2\ n\text{-Bu}}$), 2.51 (m, 1H, C_{trz}–$CH_{2\ n\text{-Bu}}$), 2.05 (m, 1H, $CH_{2\ n\text{-Bu}}$), 1,95 (s, 18H, C_{ar}–CH_3), 1.87 (m, 1H, $CH_{2\ n\text{-Bu}}$), 1.47 (m, 4H, $CH_{2\ n\text{-Bu}}$), 0.96 (m, 6H, $CH_{3\ n\text{-Bu}}$). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.5 (C_{trz}–Ru), 146.7 (C_{trz}–Bu), 92.8 (C_{ar}–Me), 54.3 ($NCH_{2\ n\text{-Bu}}$), 36.5 (NCH_3), 33.2, 31.5, 26.5, 23.4, 20.6 (5 × $CH_{2\ n\text{-Bu}}$), 15.6 (C_{ar}–CH_3), 14.1, 14.0 (2 × $CH_{3\ n\text{-Bu}}$). Electrospray MS (30 V): m/z: 494.1 $[M–Cl]^+$. Anal. Calcd for $RuCl_2C_{23}H_{39}N_3$: (529.55): C, 52.17; H, 7.42; N, 7.94. Found: C, 52.15; H, 7.70; N, 7.99.

Synthesis of 3a. Sodium Carbonate (42.6 mg, 0.4 mmol) was added to a solution of **2a** (40 mg, 0.08 mmol) in EtOH (15 mL). The suspension was stirred at room temperature for 3 h. The yellow solution was filtered through Celite and the solvent was removed. The solid was redissolved in CH_2Cl_2 (10mL) and filtered again. Concentration of the solution and subsequent precipitation with cold Et_2O gave **3a** as a yellow solid (18 mg, 45%). ^1H NMR (400 MHz, $CDCl_3$): δ 5.42, 5.06 (2 × d, $^3J_{HH}$ = 8.0 Hz, 2H, $CH_{p\text{-cym}}$), 4.34 (t, $^3J_{HH}$ = 8.0 Hz, 2H, $NCH_{2\ n\text{-Bu}}$), 3.96 (s, 3H, NCH_3), 2.80 (m, 1H, C_{trz}–$CH_{2\ n\text{-Bu}}$), 2.74 (m, 1H, $CH_{iso\ p\text{-cym}}$), 2.64 (m, 1H, C_{trz}–$CH_{2\ n\text{-Bu}}$), 2.07 (s, 3H, $CH_{3\ p\text{-cym}}$), 2.03 (m, 1H, $CH_{2\ n\text{-Bu}}$), 1.91 (m, 2H, $CH_{2\ n\text{-Bu}}$), 1.73 (m, 1H, $CH_{2\ n\text{-Bu}}$), 1.46 (m, 4H, $CH_{2\ n\text{-Bu}}$), 1.32 (d, $^3J_{HH}$ = 8.0 Hz, 6H, $CH_{3\ iso\ p\text{-cym}}$), 1.00 (m, 6H, $CH_{3\ n\text{-Bu}}$). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.7 (CO_3), 165.1 (C_{trz}–Ru), 146.5 (C_{trz}–Bu), 105.6, 94.3 (2 × $C_{p\text{-cym}}$), 82.7, 80.4 (2 × $CH_{p\text{-cym}}$), 53.8 ($NCH_{2\ n\text{-Bu}}$), 36.1 (NCH_3), 32.2 ($CH_{iso\ p\text{cym}}$)

31.9, 31.8, 25.4, 23.1 (4 × $CH_{2\ n\text{-Bu}}$), 22.9 ($CH_{3\ \text{iso}\ p\text{-cym}}$), 20.2 ($CH_{2\ n\text{-Bu}}$), 19.1 ($CH_{3\ p\text{-cym}}$), 13.8, 13.7 (2 × $CH_{3\ n\text{-Bu}}$). IR (KBr): ν = 1611 cm^{-1} (s; C=O). Electrospray MS (30 V): m/z: 448.2 $[M–CO_3+OH]^+$, 492.2 $[M+H]^+$. Anal. Calcd for $RuC_{22}H_{35}N_3O_3$: (490.60): C, 53.86; H, 7.19; N, 8.57. Found: C, 53.61; H, 7.16; N, 8.48.

Synthesis of 3b. According to the procedure described for **3a**, complex **3b** was obtained from **2b** (53 mg, 0.1 mmol) and Na_2CO_3 (42.6 mg, 0.4 mmol) in EtOH (15 mL) as a yellow solid (39 mg, 75%). ^1H NMR (400 MHz, $CDCl_3$): δ 4.25 (m, 1H, $NCH_{2\ n\text{-Bu}}$), 4.15 (m, 1H, $NCH_{2\ n\text{-Bu}}$), 3.95 (s, 3H, NCH_3), 2.62 (m, 2H, C_{trz}–$CH_{2\ n\text{-Bu}}$), 2.09 (s, 18H, C_{ar}–CH_3), 1.84, 1.77 (2 × m, 1H, $CH_{2\ n\text{-Bu}}$), 1.45 (m, 4H, $CH_{2\ n\text{-Bu}}$), 0.97 (m, 6H, $CH_{3\ n\text{-Bu}}$). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.0 (CO_3), 166.8 (C_{trz}–Ru), 146.2 (C_{trz}–Bu), 91.6 (C_{ar}–Me), 53.8 ($NCH_{2\ n\text{-Bu}}$), 36.3 (NCH_3), 32.0, 31.2, 25.5, 23.3, 20.4 (5 × $CH_{2\ n\text{-Bu}}$), 16.0 (C_{ar}–CH_3), 13.9, 13.8 (2 × $CH_{3\ n\text{-Bu}}$). IR (KBr): ν = 1602 cm^{-1} (s; C=O). Electrospray MS (30 V): m/z: 476.2 $[M-CO_3+OH]^+$, 520.2 $[M+H]^+$. Anal. Calcd for $RuC_{24}H_{39}N_3O_3$ (518.6): C, 55.38; H, 7.58; N, 8.10. Found: C, 55.12; H, 7.70; N, 7.97.

General procedure for alcohol oxidations. A mixture of alcohol (0.2 mmol) and the ruthenium complex (0.01 mmol) was refluxed in toluene (2 mL) for the time indicated in Table 1 or 2. The reaction mixture was analyzed by ^1H NMR spectroscopy. Hexamethylbenzene (0.033 mmol) was used in all cases as internal standard in order to determine conversions and yields. Products were identified according to commercially available samples (benzaldehyde, acetophenone, phenylacetaldehyde, octanal, 4-nitrobenzaldehyde, 4-chlorobenzaldehyde, 2-chlorobenzaldehyde, 4-bromobenzaldehyde, *p*-tolualdehyde and 4-methoxybenzaldehyde).

General procedure for amine oxidations. A mixture of amine (0.2 mmol) and the ruthenium complex (0.01 mmol) was heated in toluene (2 mL) to 150 ºC in a thick-walled glass tube fitted with a Teflon cap. The reaction mixture was analyzed by ^1H NMR spectroscopy using decane (0.2 mmol) as internal standard. Products were identified according to commercially available samples (N-benzylidenbenzylamine) or previously reported spectroscopic data (N-hexylidenhexylamine,[6] N-

butylidenbutylamine[38] and N-(4-chlorobenzylidene)-4-chlorobenzylamine).[35]

General procedure for the formation of amides. A mixture of alcohol (0.2 mmol), amine (0.8 mmol), NaH (0.04 mmol), and the ruthenium complex (0.01 mmol) was refluxed in toluene (2 mL). The reaction mixture was analyzed by ^{1}H NMR spectroscopy using hexamethylbenzene (0.033 mmol) as internal standard. Products were identified according to previously reported spectroscopic data (N-benzylphenylacetamide, N-benzylbenzamide and N-hexylbenzamide).

X-Ray Diffraction Studies. Single crystals of **2b** were mounted on a glass fiber in a random orientation. Data collection was performed at room temperature on a Siemens Smart CCD diffractometer using graphite monochromated Mo-Kα radiation (λ=0.71073 Å) with a nominal crystal to detector distance of 4.0 cm. Space group assignment was based on systematic absences, E statistics and successful refinement of the structures. The structure was solved by direct methods with the aid of successive difference Fourier maps and were refined using the SHELXTL 6.1 software package.[39] All non-hydrogen were refined anisotropically. Hydrogen atoms were assigned to ideal positions and refined using a riding model. The diffraction frames were integrated using the SAINT package.[40] Further crystallographic details are compiled in the Supporting Information. CCDC 803583 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgments

We thank H. Müller-Bunz for assistance with the crystal structure determination. We thank the financial support from the MCINN of Spain (CTQ2008-04460), Bancaixa (P1.1B2007-04), and the European Research Council (StG 208561). We also thank the MICINN for a fellowship (A. Prades). The authors are grateful to the Serveis Centrals d'Instrumentació Científica (SCIC) of the Universitat Jaume I for providing us with X-ray facilities.

Supporting Information Available. Crystallographic information files for complex **2b** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Shafir, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 8742. (b) Djakovitch, L.; Dufaud, V.; Zaidi, R. *Adv. Synth. Catal.* **2006**, *348*, 715. (c) Balraju, V.; Iqbal, J. *J. Org. Chem.* **2006**, *71*, 8954. (d) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873. (e) Buchwald, S. L.; Mauger, C.; Mignani, G.; Scholz, U. *Adv. Synth. Catal.* **2006**, *348*, 23.

(2) (a) Dobereiner, G. E.; Crabtree, R. H. *Chem. Rev.* **2010**, *110*, 681. (b) Guillena, G.; Ramon, D. J.; Yus, M. *Chem. Rev.* **2010**, *110*, 1611.

(3) Hamid, M.; Slatford, P. A.; Williams, J. M. J. *Adv. Synth. Catal.* **2007**, *349*, 1555.

(4) (a) Nixon, T. D.; Whittlesey, M. K.; Williams, J. M. J. *Dalton Trans.* **2009**, 753. (b) Tillack, A.; Hollmann, D.; Michalik, D.; Beller, M. *Tetrahedron Lett.* **2006**, *47*, 8881. (c) Fujita, K. I.; Enoki, Y.; Yamaguchi, R. *Tetrahedron* **2008**, *64*, 1943. (d) Prades, A.; Corberan, R.; Poyatos, M.; Peris, E. *Chem.-Eur. J.* **2008**, *14*, 11474. (e) da Costa, A. P.; Sanau, M.; Peris, E.; Royo, B. *Dalton Trans.* **2009**, 6960. (f) da Costa, A. P.; Viciano, M.; Sanau, M.; Merino, S.; Tejeda, J.; Peris, E.; Royo, B. *Organometallics* **2008**, *27*, 1305.

(5) Prades, A.; Viciano, M.; Sanau, M.; Peris, E. *Organometallics* **2008**, *27*, 4254.

(6) Gnanaprakasam, B.; Zhang, J.; Milstein, D. *Angew. Chem.-Int. Ed.* **2010**, *49*, 1468.

(7) (a) Gunanathan, C.; Gnanaprakasam, B.; Iron, M. A.; Shimon, L. J. W.; Milstein, D. *J. Am. Chem. Soc.* **2010**, *132*, 14763. (b) Kwon, M. S.; Kim, S.; Park, S.; Bosco, W.; Chidrala, R. K.; Park, J. *J. Org. Chem.* **2009**, *74*, 2877. (c) Kim, J. W.; He, J.; Yamaguchi, K.; Mizuno, N. *Chem. Lett.* **2009**, *38*, 920. (d) Blackburn, L.; Taylor, R. J. K. *Org. Lett.* **2001**, *3*, 1637. (e) Zanardi, A.; Mata, J. A.; Peris, E. *Chem.-Eur. J.* **2010**, *16*, 10502.

(8) Ghosh, S. C.; Muthaiah, S.; Zhang, Y.; Xu, X. Y.; Hong, S. H. *Adv. Synth. Catal.* **2009**, *351*, 2643.

(9) (a) Watson, A. J. A.; Maxwell, A. C.; Williams, J. M. J. *Org. Lett.* **2009**, *11*, 2667. (b) Nordstrom, L. U.; Vogt, H.; Madsen, R. *J. Am. Chem. Soc.* **2008**, *130*, 17672. (c) Naota, T.; Murahashi, S. I. *Synlett* **1991**, 693.

(10) (a) Gunanathan, C.; Ben-David, Y.; Milstein, D. *Science* **2007**, *317*, 790. (b) Zweifel, T.; Naubron, J. V.; Grutzmacher, H. *Angew. Chem.-Int. Ed.* **2009**, *48*, 559.

(11) Zhang, Y.; Chen, C.; Ghosh, S. C.; Li, Y. X.; Hong, S. H. *Organometallics* **2010**, *29*, 1374.

(12) Muthaiah, S.; Ghosh, S. C.; Jee, J. E.; Chen, C.; Zhang, J.; Hong, S. H. *J. Org. Chem.* **2010**, *75*, 3002.

(13) Dam, J. H.; Osztrovszky, G.; Nordstrom, L. U.; Madsen, R. *Chem.-Eur. J.* **2010**, *16*, 6820.

(14) (a) Valeur, E.; Bradley, M. *Chem. Soc. Rev.* **2009**, *38*, 606. (b) Cupido, T.; Tulla-Puche, J.; Spengler, J.; Albericio, F. *Current Opinion in Drug Discovery & Development* **2007**, *10*, 768. (c) Humphrey, J. M.; Chamberlin, A. R. *Chem. Rev.* **1997**, *97*, 2243.

(15) (a) Gawronski, J.; Wascinska, N.; Gajewy, J. *Chem. Rev.* **2008**, *108*, 5227. (b) Luo, Y. C.; Zhang, H. H.; Wang, Y.; Xu, P. F. *Acc. Chem. Res.* **2010**, *43*, 1317. (c) Adams, J. P. *J. Chem. Soc.-Perkin Trans. 1* **2000**, 125.

(16) (a) Hollmann, D.; Bahn, S.; Tillack, A.; Beller, M. *Chem. Commun.* **2008**, 3199. (b) Hollmann, D.; Bahn, S.; Tillack, A.; Beller, M. *Angew. Chem.-Int. Ed.* **2007**, *46*, 8291. (c) Hollmann, D.; Tillack, A.; Michalik, D.; Jackstell, R.; Beller, M. *Chem.-Asian J.* **2007**, *2*, 403. (d) Shvo, Y.; Czarkie, D.; Rahamim, Y.; Chodosh, D. F. *J. Am. Chem. Soc.* **1986**, *108*, 7400. (e) Shvo, Y.; Czarkie, D. *J. Organomet. Chem.* **1986**, *315*, C25.

(17) Blum, Y.; Czarkie, D.; Rahamim, Y.; Shvo, Y. *Organometallics* **1985**, *4*, 1459.

(18) Ghosh, S. C.; Hong, S. H. *Eur. J. Org. Chem.* **2010**, 4266.

(19) (a) Herrmann, W. A.; Elison, M.; Fischer, J.; Kocher, C.; Artus, G. R. J. *Angew. Chem.-Int. Ed. Engl.* **1995**, *34*, 2371. (b) Herrmann, W. A.; Kocher, C. *Angew. Chem.-Int. Ed.* **1997**, *36*, 2163. (c) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39. (d) Hahn, F. E. *Angew. Chem.-Int. Ed.* **2006**, *45*, 1348.

(20) (a) Semeril, D.; Bruneau, C.; Dixneuf, P. H. *Adv. Synth. Catal.* **2002**, *344*, 585. (b) Dupont, J.; Spencer, J. *Angew. Chem.-Int. Ed.* **2004**, *43*, 5296.

(21) (a) Iglesias, M.; Albrecht, M. *Dalton Trans.* **2010**, *39*, 5213. (b) Araki, S.; Yokoi, K.; Sato, R.; Hirashita, T.; Setsune, J. *J. Heterocycl. Chem.* **2009**, *46*, 164.

(22) Guisado-Barrios, G.; Bouffard, J.; Donnadieu, B.; Bertrand, G. *Angew. Chem.-Int. Ed.* **2010**, *49*, 4759.

(23) Lalrempuia, R.; McDaniel, N. D.; Müller-Bunz, H.; Bernhard, S.; Albrecht, M. *Angew. Chem. Int. Ed.* **2010**, *49*, 9765.

(24) (a) Samec, J. S. M.; Backvall, J. E.; Andersson, P. G.; Brandt, P. *Chem. Soc. Rev.* **2006**, *35*, 237. (b) Albrecht, M.; Miecznikowski, J. R.; Samuel, A.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2002**, *21*, 3596. (c) Corberan, R.; Mas-Marza, E.; Peris, E. *Eur. J. Inorg. Chem.* **2009**, 1700. (d) Normand, A. T.; Cavell, K. J. *Eur. J. Inorg. Chem.* **2008**, 2781.

(25) (a) Albrecht, M. *Chem. Commun.* **2008**, 3601. (b) Schuster, O.; Yang, L.; Raubenheimer, H. G.;

Albrecht, M. *Chem. Rev.* **2009**, *109*, 3445.

(26) Mathew, P.; Neels, A.; Albrecht, M. *J. Am. Chem. Soc.* **2008**, *130*, 13534.

(27) (a) Chianese, A. R.; Li, X. W.; Janzen, M. C.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2003**, *22*, 1663. (b) Heckenroth, M.; Neels, A.; Garnier, M. G.; Aebi, P.; Ehlers, A. W.; Albrecht, M. *Chem.-Eur. J.* **2009**, *15*, 9375.

(28) Grutzmacher, H. *Angew. Chem.-Int. Ed.* **2008**, *47*, 1814.

(29) (a) Poyatos, M.; Mas-Marza, E.; Sanau, M.; Peris, E. *Inorg. Chem.* **2004**, *43*, 1793. (b) Cariou, R.; Fischmeister, C.; Toupet, L.; Dixneuf, P. H. *Organometallics* **2006**, *25*, 2126. (c) Ozdemir, I.; Demir, S.; Cetinkaya, B.; Toupet, L.; Castarlenas, R.; Fischmeister, C.; Dixneuf, P. H. *Eur. J. Inorg. Chem.* **2007**, 2862. (d) Herrmann, W. A.; Elison, M.; Fischer, J.; Kocher, C.; Artus, G. R. J. *Chem.-Eur. J.* **1996**, *2*, 772.

(30) (a) Azua, A.; Sanz, S.; Peris, E. *Organometallics* **2010**, *29*, 3661. (b) Demerseman, B.; Mbaye, M. D.; Semeril, D.; Toupet, L.; Bruneau, C.; Dixneuf, P. H. *Eur. J. Inorg. Chem.* **2006**, 1174.

(31) Lee, D. W.; Jensen, C. M.; Morales-Morales, D. *Organometallics* **2003**, *22*, 4744.

(32) Mercs, L.; Neels, A.; Albrecht, M. *Dalton Trans.* **2008**, 5570.

(33) (a) Choi, J. H.; Kim, N.; Shin, Y. J.; Park, J. H.; Park, J. *Tetrahedron Lett.* **2004**, *45*, 4607. (b) Junge, H.; Loges, B.; Beller, M. *Chem. Commun.* **2007**, 522. (c) Sieffert, N.; Buhl, M. *J. Am. Chem. Soc.* **2010**, *132*, 8056. (d) Friedrich, A.; Schneider, S. *ChemCatChem* **2009**, *1*, 72.

(34) (a) Chu, G. B.; Li, C. B. *Org. Bio. Chem.* **2010**, *8*, 4716. (b) Landge, S. M.; Atanassova, V.; Thimmaiah, M.; Torok, B. *Tetrahedron Lett.* **2007**, *48*, 5161. (c) Jiang, G.; Chen, J.; Huang, J. S.; Che, C. M. *Org. Lett.* **2009**, *11*, 4568.

(35) Kodama, S.; Yoshida, J.; Nomoto, A.; Ueta, Y.; Yano, S.; Ueshima, M.; Ogawa, A. *Tetrahedron Lett.* **2010**, *51*, 2450.

(36) Bennett, M. A.; Smith, A. K. *J. Chem. Soc.-Dalton Trans.* **1974**, 233.

(37) Bennett, M. A.; Huang, T. N.; Matheson, T. W.; Smith, A. K. *Inorg. Synth.* **1982**, *21*, 74.

(38) Bailey, P. S.; Carter, T. P.; Southwic.Lm *J. Org. Chem.* **1972**, *37*, 2997.

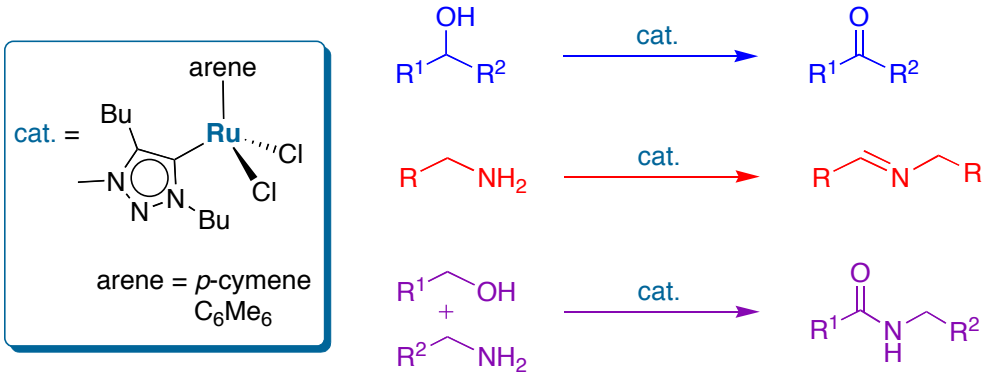
(39) Sheldrick, G. M. *SHELXTL, version 6.1, Bruker AXS, Inc* Madison, WI, 2000.

(40) *SAINT, Bruker Analytical X-ray System, version 5.0* Madison, WI, 1998.

For TOC use only

Oxidations and Oxidative Couplings Catalyzed by Triazolylidene Ruthenium Complexes

Amparo Prades, Eduardo Peris and Martin Albrecht



A series of 'Ru^{II}(η^6-arene)' complexes with 1,2,3-triazolylidene ligands have been prepared and tested in a set of catalytic reactions involving alcohols and amines as substrates, including: i) base-free oxidation of benzylic alcohols to benzaldehydes, ii) homocoupling of amines to imines, and iii) oxidative coupling of amines and alcohols to amides.