CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200700477

Efficient Tandem Process for the Catalytic Deprotection of N-Allyl Amides and Lactams in Aqueous Media: A Novel Application of the Bis(allyl)–Ruthenium(IV) Catalysts $[Ru(\eta^3:\eta^2:\eta^3\text{-}C_{12}H_{18})Cl_2]$ and $[\{Ru(\eta^3:\eta^3\text{-}C_{10}H_{16})(\mu\text{-}Cl)Cl\}_2]$**

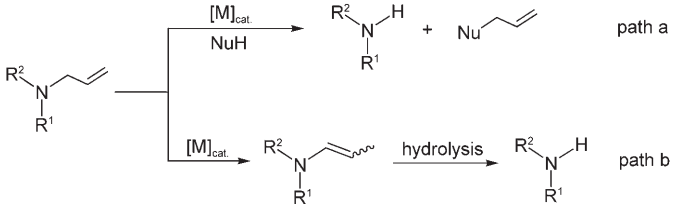
Victorio Cadierno,* José Gimeno,* and Noel Nebra[a]

Abstract: An operationally simple and highly efficient methodology for the removal of the allyl protecting group in amides and lactams has been developed by using the commercially available bis(allyl)–ruthenium(IV) catalysts $[Ru(\eta^3:\eta^2:\eta^3\text{-}C_{12}H_{18})Cl_2]$ ($C_{12}H_{18}$ = dodeca-2,6,10-triene-1,12-diyl) and $[\{Ru(\eta^3:\eta^3\text{-}C_{10}H_{16})(\mu\text{-}Cl)Cl\}_2]$ ($C_{10}H_{16}$ = 2,7-dimethylocta-2,6-diene-1,8-diyl). The tandem process, which takes place in aqueous media and proceeds in a one-pot manner, involves the initial isomerization of the C=C bond of the allyl unit and subsequent oxidative cleavage of the resulting enamide.

Keywords: allylic compounds · amides · aqueous-phase catalysis · lactams · protecting groups · ruthenium

Introduction

Neither the continuous improvements in selectivity nor the invention of new reactions have abated the dependence of synthetic organic chemists on protecting groups.[1] So, the proper selection of efficient protecting groups, as well as the search of selective deprotection methodologies, still remain crucial issues in modern organic chemistry. In particular, among the plethora of alternatives, the use of allyl moieties for the protection of amines is becoming more and more popular as, in contrast to classical protecting groups (for example, BOC (*tert*-butoxycarbonyl), FMOC (9-fluorenylmethyl carbamate), tosylamide, etc.), they remain inert under both acidic and basic conditions.[1] Moreover, due to the presence of an orthogonal π bond, the final N–C bond cleavage step can be easily achieved in the presence of transition-metals via appropriate coordination.[1,2] Thus, except for a few miscellaneous methods, transition-metal-catalyzed reactions are currently the most efficient and selective strategies for the deprotection of N-allylamines.[1,2] These metal-mediated methodologies can be roughly classified into two groups according to their mechanistic features: 1) those based on a nucleophilic substitution reaction, in which the amine unit becomes a leaving group (Scheme 1; path a) and



Scheme 1. Strategies used for the catalytic deprotection of N-allylamines.

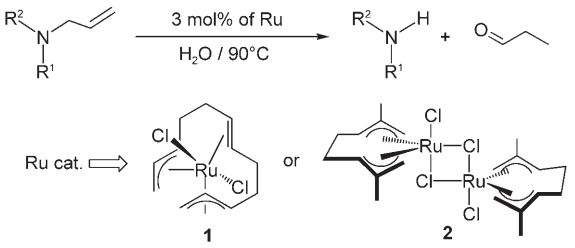
2) those based on the isomerization of the allylamine into an enamine which is subsequently cleaved upon acidic hydrolysis (Scheme 1; path b). While the former involves the intermediate formation of a π-allyl complex (Pd catalysts), the catalytically active species in the latter are usually hydride complexes able to promote the isomerization of the allylic C=C double bond (Ru and Rh catalysts).[1,2]

[a] Dr. V. Cadierno, Prof. J. Gimeno, Dipl.-Chem. N. Nebra
Departamento de Química Orgánica e Inorgánica
Instituto Universitario de Química Organometálica
"Enrique Moles" (Unidad Asociada al CSIC)
Universidad de Oviedo, Julián Clavería 8
E-33006 Oviedo (Spain)
Fax: (+34) 98-510-3446
E-mail: vcm@uniovi.es
jgh@uniovi.es

[**] $C_{12}H_{18}$ = dodeca-2,6,10-triene-1,12-diyl and $C_{10}H_{16}$ = 2,7-dimethylocta-2,6-diene-1,8-diyl.

Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author.

An important drawback of the π-allyl–palladium methodology (path a) is the requirement of stoichiometric amounts of a nucleophilic compound, which acts as the allyl group scavenger.[2,3] Therefore, although they involve two steps, the isomerization-based methodologies (path b) are undoubtedly more convenient.[2,4] In this context, we have recently described a catalytic one-pot procedure for the removal of the allyl protecting group in amines (Scheme 2),[5]



Scheme 2. Deprotection of N-allylamines catalyzed by the Ru^{IV} complexes **1** and **2**.

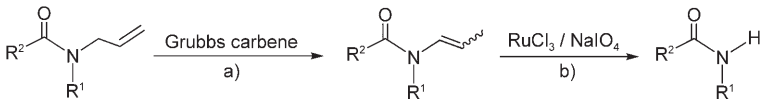
which is based on the ability of the commercially available bis(allyl)–ruthenium(IV) complexes $[Ru(\eta^3:\eta^2:\eta^3\text{-}C_{12}H_{18})Cl_2]$ ($C_{12}H_{18}$ = dodeca-2,6,10-triene-1,12-diyl) (**1**) and $[\{Ru(\eta^3:\eta^3\text{-}C_{10}H_{16})(\mu\text{-}Cl)Cl\}_2]$ ($C_{10}H_{16}$ = 2,7-dimethylocta-2,6-diene-1,8-diyl) (**2**) to promote C=C migrations in water,[6,7] allowing the direct hydrolysis of the initially formed enamines. Remarkably, this is the first synthetic procedure for the removal of the allyl protecting group in amines which can be performed in pure aqueous media, organic solvents being up till now required for the initial isomerization step (path b). Although a wide range of N-allylamines could be efficiently and selectively deprotected by using this methodology,[5] one important limitation was encountered when N-allylic amides and lactams were used as substrates. In these cases, only the isomerization of the C=C bond was observed as the higher stability of enamides compared with enamines prevented the hydrolytic (CO)N–allyl cleavage.

In this paper, we would like to report that such a limitation can be easily overcome by introducing a stoichiometric amount of KIO_4 in the reaction media. Under these conditions, oxidative cleavage of the initially formed enamide readily takes place leading to the clean formation of the desired NH amide or lactam. Herein, we present a novel catalytic procedure which represents a simple, general, and more convenient alternative to previously known methods for the deprotection of (CO)N–allyl units[8–13] as: 1) it is performed in a one-pot manner, 2) it takes place for the first time in an environmental benign and inexpensive solvent (water),[14] and 3) it is applicable to the deprotection of N,N-diallylamides for which no catalytic methodologies are known.

Results and Discussion

Despite its great synthetic interest,[15] the deprotection of allylic amides and lactams has been scarcely documented,[8–13] only one general procedure being presently available.[8] It consists of a two-step process involving: 1) the initial catalytic isomerization of the allyl unit, promoted by the Grubbs carbene $[Ru(=CHPh)Cl_2(PCy_3)_2]$ in refluxing toluene,[16] to give enamides and 2) the subsequent scission of the internal C=C bond of the isolated enamides by the system $RuCl_3$/$NaIO_4$ in a 1,2-dichloroethane/water mixture (Scheme 3). In the latter step, $RuCl_3$ catalyzes the oxidative cleavage of the C=C bond to generate a N-formyl amide or lactam which decarboxylates in aqueous media.

Inspired by these results, we decided to explore the ability of the bis(allyl)–ruthenium(IV) complexes $[Ru(\eta^3:\eta^2:\eta^3\text{-}C_{12}H_{18})Cl_2]$ (**1**) and $[\{Ru(\eta^3:\eta^3\text{-}C_{10}H_{16})(\mu\text{-}Cl)Cl\}_2]$ (**2**) to promote the removal of the allyl unit of amides under oxidative conditions through a tandem allyl group isomerization/enamide C=C cleavage process. The deprotection of N-allyl benzamide (**3a**) was used as a model reaction. Thus, we

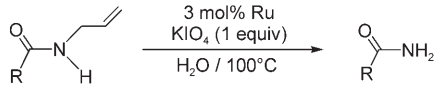


Scheme 3. General procedure for the (CO)N–allyl cleavage. Conditions: a) 5 mol% $[Ru(=CHPh)Cl_2(PCy_3)_2]$, toluene, reflux; b) 3.5 mol% $RuCl_3$, $NaIO_4$ (2 equiv), 1,2-dichloroethane/water (1:1 v/v), RT, aqueous workup under basic conditions, see reference [8].

have found that, under optimized conditions (3 mol% of Ru; 0.1 M solution of the substrate in water, 100 °C), both complexes are efficient catalysts for this transformation if one equivalent of KIO_4 is present in the reaction media, affording deallylated benzamide in >97% yield after approximately 3 h (entry 1 in Table 1).[17] The use of lower temperatures and/or catalyst loadings slows down the reaction considerably. For example, by using a catalyst loading of 0.1 mol% of Ru (complex **2**) 12 h are required to deprotect **3a** in 96% GC yield.

Under these optimal reaction conditions, catalysts **1** and **2** are also active in the deprotection of a large number of secondary N-allyl amides (Table 1). Thus, as observed for *N*-allyl benzamide (**3a**), its *ortho*, *meta*, and *para*-substituted derivatives undergo a fast (3 h) and quantitative removal of the allyl unit regardless of the presence of electron-withdrawing (**3b–d**, entries 2–4) or electron-donating groups (**3e–g**, entries 5–7). As shown in entries 8–11, this transformation is not restricted to aromatic amides, the deprotection of alkylic substrates **3h–k** being readily (<5 h) and efficiently (>98% GC yields) achieved under the standard reaction conditions. Close examination of the reaction mixtures shows that they are emulsions rather than homogeneous solutions, the catalytic transformation taking place probably at the interface. As previously observed in the aqueous deprotection of allylic amines,[5] no remarkable differences in ac-

Table 1. Ruthenium-catalyzed deprotection of secondary N-allyl amides in water.[a]



3a-k

Entry	Substrate	Cat.	t [h]	Yield [%][b]
1	R = Ph (**3a**)	**1**	3	97
		2	3	99
2	R = 2-C_6H_4F (**3b**)	**1**	3	99
		2	3	99
3	R = 3-C_6H_4F (**3c**)	**1**	3	99
		2	3	99
4	R = 4-C_6H_4F (**3d**)	**1**	3	99
		2	3	99
5	R = 2-C_6H_4OMe (**3e**)	**1**	2	99
		2	2	98
6	R = 3-C_6H_4OMe (**3f**)	**1**	3	98
		2	3	99
7	R = 4-C_6H_4OMe (**3g**)	**1**	3	99
		2	3	99
8	R = *n*-pent (**3h**)	**1**	2	98
		2	2	99
9	R = *n*-hept (**3i**)	**1**	5	99
		2	5	99
10	R = CH_2Bn (**3j**)	**1**	3	99
		2	3	99
11	R = $CH_2CH_2C_5H_9$ (**3k**)	**1**	5	99
		2	5	99

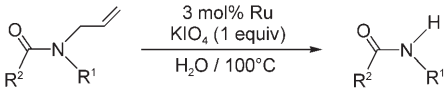
[a] Reactions were performed under a N_2 atmosphere at 100 °C by using 1.0 mmol of the corresponding N-allyl amide, 1.0 mmol of KIO_4, and 10 mL of H_2O. [b] Yields were determined by GC analysis.

tivity between the mononuclear derivative **1** and the dimeric compound **2** have been noted.

Our catalytic protocol can be extrapolated to the deprotection of tertiary N-allyl amides. Table 2 illustrates several examples in which both aliphatic (**4a–f**, entries 1–6) or aromatic (**4g–h**, entries 7–8) substituents are attached to the *N*-atom. As expected, the corresponding unprotected amides are generated in high yields (>80%) within 2–7 h.[18] Nevertheless, it should be noted that no completely clean transformations were observed in all cases (entries 2, 4, 5, 7 and 8), the formation of minor amounts of the corresponding carboxylic acid R^2CO_2H, as the result of the enamide group hydrolysis, being detected by GCMS analysis.

Remarkably, complexes **1** and **2** can also be applied to the selective deprotection of N,N-diallyl amides in marked contrast to the Grubbs carbene-based methodology (Scheme 3).[8,19] Thus, as shown in Table 3, amides **5a–l** can be completely deallylated in excellent yields (>87%) after only 1–8 h without detection by GCMS analysis of ring-closing metathesis (RCM) products in the crude reaction mixtures. It is interesting to note that, in order to achieve the complete removal of both allylic units, two equivalents of KIO_4 are required, the use of only one equivalent leading to incomplete transformations. As far as we know this is the first synthetic procedure able to perform the chemoselective deprotection of N,N-diallylic amides, allowing us to extend the use of allyl groups for the protection of $(CO)NH_2$ units.[1]

Table 2. Ruthenium-catalyzed deprotection of tertiary N-allyl amides in water.[a]

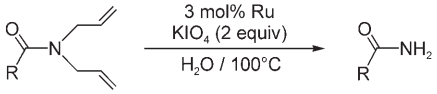


4a-h

Entry	Substrate	Cat.	t [h]	Yield [%][b]
1	R^1 = Me; R^2 = Me (**4a**)	**1**	3	95
		2	3	93
2	R^1 = Me; R^2 = *n*-pent (**4b**)	**1**	3	80
		2	3	83
3	R^1 = Me; R^2 = $CH_2CH_2C_5H_9$ (**4c**)	**1**	2	89
		2	2	92
4	R^1 = Me; R^2 = 4-C_6H_4F (**4d**)	**1**	7	84
		2	6	82
5	R^1 = Me; R^2 = 2-C_6H_4OMe (**4e**)	**1**	7	83
		2	7	85
6	R^1 = Bn; R^2 = Ph (**4f**)	**1**	20	97
		2	17	97
7	R^1 = 3-C_6H_4COMe; R^2 = Me (**4g**)	**1**	2	85
		2	2	80
8	R^1 = 2-$C_6H_4CO_2Et$; R^2 = 2-C_6H_4F (**4h**)	**1**	7	87
		2	7	93

[a] Reactions were performed under a N_2 atmosphere at 100 °C by using 1.0 mmol of the corresponding N-allyl amide, 1.0 mmol of KIO_4, and 10 mL of H_2O. [b] Yields were determined by GC analysis.

Table 3. Ruthenium-catalyzed deprotection of N,N-diallyl amides in water.[a]



5a-l

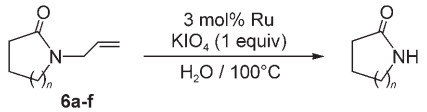
Entry	Substrate	Cat.	t [h]	Yield [%][b]
1	R = Ph (**5a**)	**1**	5	99
		2	5	99
2	R = 2-C_6H_4F (**5b**)	**1**	4	99
		2	4	99
3	R = 3-C_6H_4F (**5c**)	**1**	5	99
		2	5	96
4	R = 4-C_6H_4F (**5d**)	**1**	4	99
		2	4	99
5	R = 2-C_6H_4OMe (**5e**)	**1**	2	99
		2	3	99
6	R = 3-C_6H_4OMe (**5f**)	**1**	5	99
		2	5	99
7	R = 4-C_6H_4OMe (**5g**)	**1**	3	96
		2	3	98
8	R = *n*Pr (**5h**)	**1**	8	87
		2	8	92
9	R = *n*-pent (**5i**)	**1**	3	96
		2	3	97
10	R = *n*-hept (**5j**)	**1**	5	89
		2	5	92
11	R = $CHCl_2$ (**5k**)	**1**	3	99
		2	3	99
12	R = CF_3 (**5l**)	**1**	1	95
		2	1	96

[a] Reactions were performed under a N_2 atmosphere at 100 °C by using 1.0 mmol of the corresponding N,N-diallyl amide, 2.0 mmol of KIO_4, and 10 mL of H_2O. [b] Yields were determined by GC analysis.

Concerning the tolerance of functional groups, as clearly shown in Tables 1, 2, and 3, this methodology is compatible with the presence in the substrates of halide (**3b–d**, **4d**,**h**, and **5b–d**,**k**,**l**), alkoxy (**3e–g**, **4e**, and **5e–g**), ketone (**4g**), and ester (**4h**) substituents. In addition, as stated in the Experimental Section, the reactions can be performed on a preparative scale, the isolation of the final unprotected amides being easily achieved by simple extraction from the aqueous phase and subsequent flash chromatography. All these facts confer to catalysts **1** and **2** genuine potential for practical application in synthetic organic chemistry.

Once we had confirmed the generality of this catalytic transformation with acyclic N-allyl and N,N-diallyl amides, we decided to check the ability of complexes **1** and **2** to catalyze the allyl-group removal in lactams. The catalytic performances shown in Table 4 clearly demonstrate that our experimental protocol using complexes **1** and **2** is also efficient for the N-allyl deprotection of lactams. Thus, regardless of

Table 4. Ruthenium-catalyzed deprotection of N-allyl lactams in water.[a]



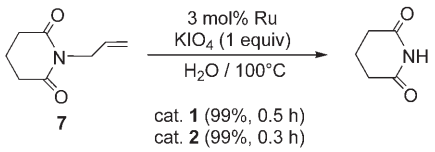
6a-f

Entry	Substrate	Cat.	*t* [h]	Yield [%][b]
1	*n*=1 (**6a**)	**1**	4.5	99
		2	5.3	95
2	*n*=2 (**6b**)	**1**	0.3	98
		2	0.5	97
3	*n*=3 (**6c**)	**1**	0.3	99
		2	0.3	99
4	*n*=4 (**6d**)	**1**	0.5	97
		2	0.5	99
5	*n*=5 (**6e**)	**1**	0.5	99
		2	0.5	99
6	*n*=9 (**6f**)	**1**	4.0	96
		2	4.0	95

[a] Reactions were performed under a N_2 atmosphere at 100 °C by using 1.0 mmol of the corresponding N-allyl lactam, 1.0 mmol of KIO_4, and 10 mL of H_2O. [b] Yields were determined by GC analysis.

the ring size, clean and selective transformations (>98% GC yields) were observed in all cases within 0.3–5.3 h under the standard reaction conditions.

Finally, it is also interesting to note that systems containing an extra carbonyl unit attached to the nitrogen atom can also be deprotected by using **1** and **2**. As a representative example, treatment of an aqueous suspension of N-allyl glutarimide (**7**) with a catalytic amount of complex **1** or **2** (3 mol% of Ru) in the presence of KIO_4, quantitatively liberates glutarimide in approximately 30 min (Scheme 4).



7

Scheme 4. Deprotection of N-allyl glutarimide by using catalysts **1** and **2**.

Conclusion

An operationally simple and highly efficient procedure for the catalytic removal of the allyl protecting group in amides and lactams has been developed by using the commercially available bis(allyl)–ruthenium(IV) complexes $[Ru(\eta^3{:}\eta^2{:}\eta^3\text{-}C_{12}H_{18})Cl_2]$ ($C_{12}H_{18}$ = dodeca-2,6,10-triene-1,12-diyl) (**1**) and $[\{Ru(\eta^3{:}\eta^3\text{-}C_{10}H_{16})(\mu\text{-}Cl)Cl\}_2]$ ($C_{10}H_{16}$ = 2,7-dimethylocta-2,6-diene-1,8-diyl) (**2**). The process, which takes place in the presence of KIO_4, consists of a Ru-catalyzed tandem process involving the initial isomerization of the allyl unit and subsequent oxidative C=C bond cleavage of the resulting enamide.[20] The (CO)N–allyl cleavage protocol presented herein represents an appealing and competitive alternative to previously known catalytic procedures as: 1) in contrast to the Grubbs carbene/$RuCl_3$ two-step methodology, it is performed in a one-pot manner by using a single ruthenium source, 2) it takes place for the first time in an environmental benign and inexpensive solvent (water), and 3) it can be applied to the deprotection of N,N-diallylamides for which no precedents have been till now reported. In addition, as lactams usually present pharmacologic activity, serving also as crucial intermediates for the preparation of a large variety of natural products, the development of efficient procedures for the protection/deprotection of their N–H unit presents a particular synthetic interest. We are confident that the simplicity, selectivity, and efficiency of the catalytic method reported in this paper will be of interest to a wide range of synthetic organic chemists, who may include its use in their future research programs.

Experimental Section

General procedure for the catalytic deallylation reactions: Under a nitrogen atmosphere, the corresponding N-allylic substrate (1 mmol), the ruthenium catalyst precursor **1** or **2** (3 mol% of Ru), KIO_4 (1 or 2 mmol), and water (10 mL) were introduced into a sealed tube and the reaction mixture was stirred at 100 °C for the indicated time. The course of the reaction was monitored by regular sampling and analysis by gas chromatography. The identity of the resulting deallylated products was assessed by comparison with commercially available (Aldrich Chemical or Acros Organics), or independently synthesized (following reported procedures), pure samples and by their fragmentation in GCMS analysis. We note that all these reactions can be performed in a preparative scale.

Representative example: Under a nitrogen atmosphere, N-allyl benzamide (**3a**) (2.1 g, 13 mmol), complex **1** (0.130 g, 0.39 mmol), KIO_4 (3.0 g, 13 mmol), and water (80 mL) were introduced into a sealed tube and the reaction mixture was stirred at 100 °C for 3.5 h (96% GC yield). The aqueous phase was then saturated with NaCl and extracted with dichloromethane (4×25 mL). The combined organic extracts were then dried over $MgSO_4$, concentrated, and purified by column chromatography over silica gel by using a 10% ethyl acetate/hexanes mixture as eluent to give 1.369 g (11.3 mmol) of analytically pure benzamide (87% yield).

Acknowledgements

We are indebted to the Ministerio de Educación y Ciencia (MEC) of Spain (project CTQ2006–08485/BQU) and the Gobierno del Principado

de Asturias (FICYT project IB05–035) for financial support. N.N. and V.C. thank the MEC and the European Social Fund for the award of a PhD grant and a "Ramón y Cajal" contract, respectively.

[1] a) P. J. Kocienski, *Protecting Groups*, 3rd ed., Thieme Verlag, Stuttgart, **2003**; b) P. G. M. Wuts, T. W. Greene, *Greene's Protective Groups in Organic Synthesis*, 4th ed., Wiley-Interscience, New York, **2006**.

[2] For specific reviews dealing with the removal of allylic protecting groups see: a) F. Guibé, *Tetrahedron* **1998**, *54*, 2967–3042; b) S. Escoubet, S. Gastaldi, M. Bertrand, *Eur. J. Org. Chem.* **2005**, 3855–3873.

[3] Representative examples: a) F. Garro-Helion, A. Merzouk, F. Guibé, *J. Org. Chem.* **1993**, *58*, 6109–6113; b) S. Lemaire-Audoire, M. Savignac, J. P. Genêt, J.-M. Bernard, *Tetrahedron Lett.* **1995**, *36*, 1267–1270; c) S. Lemaire-Audoire, M. Savignac, C. Dupuis, J. P. Genêt, *Bull. Soc. Chim. Fr.* **1995**, *132*, 1157–1166; d) M. Honda, H. Morita, I. Nagakura, *J. Org. Chem.* **1997**, *62*, 8932–8936; e) H. Tsukamoto, T. Suzuki, Y. Kondo, *Synlett* **2003**, 1105–1108; f) J. González-Sabín, V. Gotor, F. Rebolledo, *J. Org. Chem.* **2007**, *72*, 1309–1314.

[4] Representative examples: a) B. C. Laguzza, B. Ganem, *Tetrahedron Lett.* **1981**, *22*, 1483–1486; b) R. J. Sundberg, G. S. Hamilton, J. P. Laurino, *J. Org. Chem.* **1988**, *53*, 976–983; c) B. Alcaide, P. Almendros, J. M. Alonso, M. F. Aly, *Org. Lett.* **2001**, *3*, 3781–3784; d) C. Cadot, P. I. Dalko, J. Cossy, *Tetrahedron Lett.* **2002**, *43*, 1839–1841; e) B. Alcaide, P. Almendros, J. M. Alonso, *Chem. Eur. J.* **2003**, *9*, 5793–5799; f) M. Sato, Y. Gunji, T. Ikeno, T. Yamada, *Synthesis* **2004**, 1434–1438; g) B. Alcaide, P. Almendros, J. M. Alonso, A. Luna, *Synthesis* **2005**, 668–672; h) F. Aznar, A.-B. García, M.-P. Cabal, *Adv. Synth. Catal.* **2006**, *348*, 2443–2448.

[5] V. Cadierno, S. E. García-Garrido, J. Gimeno, N. Nebra, *Chem. Commun.* **2005**, 4086–4088.

[6] Complexes **1** and **2** are efficient catalysts for the redox isomerization of allylic alcohols into carbonyl compounds in both organic and aqueous media: a) V. Cadierno, S. E. García-Garrido, J. Gimeno, *Chem. Commun.* **2004**, 232–233; b) V. Cadierno, S. E. García-Garrido, J. Gimeno, A. Varela-Álvarez, J. A. Sordo, *J. Am. Chem. Soc.* **2006**, *128*, 1360–1370.

[7] For a general review on the stoichiometric reactivity and catalytic applications of complexes **1** and **2** see: V. Cadierno, P. Crochet, S. E. García-Garrido, J. Gimeno, *Curr. Org. Chem.* **2006**, *10*, 165–183.

[8] a) B. Alcaide, P. Almendros, J. M. Alonso, *Tetrahedron Lett.* **2003**, *44*, 8693–8695; b) B. Alcaide, P. Almendros, J. M. Alonso, *Chem. Eur. J.* **2006**, *12*, 2874–2879.

[9] Deprotection of tertiary N-allyl amides by $AlMe_3$ in the presence of catalytic amounts of [$NiCl_2$(dppp)] (dppp = 1,3-bis(diphenylphosphanyl)propane) has been described: T. Taniguchi, K. Ogasawara, *Tetrahedron Lett.* **1998**, *39*, 4679–4682.

[10] The N-allyl cleavage of a 3-amino-β-lactam and a 2-hydroxy-γ-lactam, induced by $RhCl_3$ followed by $KMnO_4$ or acidic treatments, has been also reported: a) G. Cainelli, M. DaCol, P. Gelletti, D. Giacomini, *Synlett* **1997**, 923–924; b) O. Kanno, M. Miyauchi, I. Kawamoto, *Heterocycles* **2000**, *53*, 173–181.

[11] The N-allyl bond of $AcN(R)CH_2CH{=}CH_2$ (R = Bn, CH_2Bn) has been cleaved in the presence of a catalytic amount of $Pd(OAc)_2$ and a stoichiometric amount of $Cu(OAc)_2$, LiCl, and water: M. Mori, Y. Ban, *Chem. Pharm. Bull.* **1976**, *24*, 1992–1999.

[12] Removal of the N-allyl group of a galactopyranosyl-*N*-allylacetamide has been achieved by OsO_4-catalyzed hydroxylation of the C=C bond, subsequent $NaIO_4$-mediated scission of the resulting vicinal diol, followed by repetition of this reaction sequence on the enolic form of the aldehyde intermediate: P. I. Kitov, D. R. Bundle, *Org. Lett.* **2001**, *3*, 2835–2838.

[13] Amides containing 2-arylallyl groups can be deprotected upon treatment with a stoichiometric amount of *tert*-butyllithium. The transformation involves a carbolithiation reaction of the styrenyl moiety followed by a β-elimination process: J. Barluenga, F. J. Fañanas, R. Sanz, C. Marcos, J. M. Ignacio, *Chem. Commun.* **2005**, 933–935.

[14] The development of organic transformations in aqueous media is one of the major cornerstones in modern chemistry: a) C.-J. Li, *Chem. Rev.* **1993**, *93*, 2023–2035; b) A. Lubineau, J. Augé, Y. Queneau, *Synthesis* **1994**, 741–760; c) C.-J. Li, T. H. Chan, *Organic Reactions in Aqueous Media*, Wiley, New York, **1997**; d) *Aqueous Organometallic Catalysis* (Eds.: I. T. Horváth, F. Joó), Kluwer, Dodrecht, **2001**; e) U. M. Lindström, *Chem. Rev.* **2002**, *102*, 2751–2772; f) C.-J. Li, *Chem. Rev.* **2005**, *105*, 3095–3165; g) C. K. Z. Andrade, L. M. Alves, *Curr. Org. Chem.* **2005**, *9*, 195–218; h) C.-J. Li, L. Chen, *Chem. Soc. Rev.* **2006**, *35*, 68–82.

[15] There are relatively few methods presently available for the deprotection of an amide moiety (see reference [1]), the most general involving the oxidative cleavage of an activated aryl group attached to the nitrogen atom by Ce^{IV} ammonium nitrate. See for example: D. R. Kronenthal, C. Y. Han, M. K. Taylor, *J. Org. Chem.* **1982**, *47*, 2765–2768 and references therein.

[16] The authors suggest that a ruthenium-hydride, resulting from the decomposition of the Grubbs catalyst, is the real active species in the C=C isomerization process, see references [4e,8].

[17] a) Deprotection of **3a** also takes place in the presence of other oxidizing agents (for example, $NaIO_4$, $KMnO_4$). At least one equivalent of oxidant is required, otherwise incomplete reactions are observed. b) As expected, in the absence of oxidant, a mixture of (*E*)- and (*Z*)-N-(1-propenyl)benzamide is formed (approximately a 1.2:1 ratio). c) The use of classical organic solvents (for example, toluene, THF, CH_2Cl_2) or water/organic solvent mixtures drastically reduces the efficiency of this deprotection protocol, the maximum yield attained in these cases being 30% (always in the presence of KIO_4).

[18] The presence of a benzyl substituent on the nitrogen atom leads to slower transformations, the deprotection of amide **4f** requiring at least 17 h to attain a 97% yield (Table 2, entry 6). A similar effect of the benzyl group has been previously observed by us in the deprotection of N-allylic amines promoted by complexes **1** and **2**. See reference [5].

[19] Treatment of N,N-diallyl amides with [$Ru(=CHPh)Cl_2(PCy_3)_2$] leads to the expected formation of pyrrolinyl amides through a RCM process, see for example: C. Bressy, C. Menant, O. Piva, *Synlett* **2005**, 577–582.

[20] For a review on ruthenium-catalyzed tandem processes see: C. Bruneau, S. Dérien, P. H. Dixneuf, *Top. Organomet. Chem.* **2006**, *19*, 295–326.

Received: March 27, 2007
Published online: May 22, 2007

