

Accepted Manuscript

Deep Eutectic Solvents (DES) as green reaction media for the redox isomerization of allylic alcohols into carbonyl compounds catalyzed by the ruthenium complex $[\text{Ru}(\eta^3\text{:}\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{benzimidazole})]$

Cristian Vidal, Francisco J. Suárez, Joaquín García-Álvarez

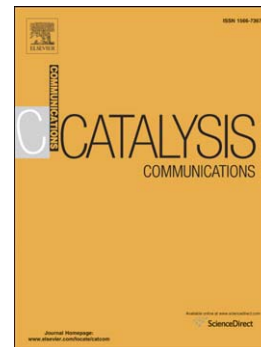
PII: S1566-7367(13)00125-8
DOI: doi: [10.1016/j.catcom.2013.04.002](https://doi.org/10.1016/j.catcom.2013.04.002)
Reference: CATCOM 3467

To appear in: *Catalysis Communications*

Received date: 28 February 2013
Revised date: 2 April 2013
Accepted date: 3 April 2013

Please cite this article as: Cristian Vidal, Francisco J. Suárez, Joaquín García-Álvarez, Deep Eutectic Solvents (DES) as green reaction media for the redox isomerization of allylic alcohols into carbonyl compounds catalyzed by the ruthenium complex $[\text{Ru}(\eta^3\text{:}\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{benzimidazole})]$, *Catalysis Communications* (2013), doi: [10.1016/j.catcom.2013.04.002](https://doi.org/10.1016/j.catcom.2013.04.002)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Deep Eutectic Solvents (DES) as green reaction media
for the redox isomerization of allylic alcohols into
carbonyl compounds catalyzed by the ruthenium
complex $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{benzimidazole})]$

*Cristian Vidal,^a Francisco J. Suárez,^a and Joaquín García-Álvarez^{*a}*

^aLaboratorio de Compuestos Organometálicos y Catálisis (Unidad Asociada al CSIC). Departamento de Química Orgánica e Inorgánica (IUQOEM), Facultad de Química, Universidad de Oviedo, E-33071, Oviedo, Spain.

*Corresponding Author

E-mail: garciajoaquin@uniovi.es

HIGHLIGHTS

- 1.- A rare example of the use of Deep Eutectic Solvents (DES) as green and renewable media in metal-catalyzed organic reactions.
- 2.- Complex $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{benzimidazole})]$ (**1c**) is a highly active and selective catalyst in the redox isomerization of monosubstituted aliphatic allylic alcohols into saturated carbonyl compounds using DES.
- 3.- Isomerization reaction takes place in the absence of base and in a large-scale experiment.
- 4.- The catalytic system was recycled up to four consecutive runs.

ABSTRACT

The bis-allyl Ru(IV) complex $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{benzimidazole})]$ (**1c**) is an active catalyst in the redox isomerization of allylic alcohols into saturated carbonyl compounds using, for the first time, Deep Eutectic Solvents (DES) as reaction media. A series of primary and secondary allylic alcohols could be isomerized into the corresponding carbonyl compounds in the absence of base. Although high activities and selectivities were reached at short reaction times and with low catalyst loadings (0.2 mol% in Ru) for monosubstituted allylic alcohols, for their disubstituted counterparts, high catalyst loading and longer reaction times were always required. It is important to note that the catalytic system: *i*) is active in a large-scale experiment, and *ii*) could be recycled up to four consecutive runs.

KEYWORDS: Deep Eutectic Solvents; Homogeneous catalysis; Allylic alcohols; Redox isomerization; Ruthenium(IV).

1. INTRODUCTION

One of the largest areas of consumption of petroleum-based chemicals in a conventional metal-catalyzed organic reaction is the solvent used as the reaction medium. However, the use of green and bio-renewable solvents still remains a lasting challenge, even when the environmental and safety problems

associated with conventional hazardous volatile organic solvents (VOC's) are well established [1]. Thus, within the framework of "Green Chemistry", solvents occupy a strategic place [2,3]. Up to now, the number of available green solvents is rather limited. In this sense, some of these new "Green Solvents" include supercritical fluids [4], ionic liquids [5,6], water [7,8] and perfluorinated compounds [9]; and have received growing interest over the last two decades [1]. Supercritical fluids like $scCO_2$ are beneficial because they are non-toxic, relatively inert, easily removable and recyclable; however a widespread application in research and development is hampered by the demand for expensive advanced apparatus [4]. Ionic liquids currently receive much attention because of their thermal stability, negligible vapor pressure, non-flammability and catalytic effect on many types of reactions [5,6]. However, the wider use of ILs has to be evaluated as many reports pointed the hazardous toxicity and the very poor biodegradability of most ILs [10]. Water can be considered an ideal solvent, because it is non-toxic, cheap and easily available [7,8], although limitations arise when hydrolysis reactions of both the catalyst and the organic products can take place. To overcome these limitations a new generation of solvents is strongly needed. In this sense, Deep Eutectic Solvents (DES, generally composed of two or three cheap and safe components which are capable of associating with each other through hydrogen bond interaction to form an eutectic mixture) have been used as environmentally-friendly solvents in a variety of applications including biologic transformations, metal deposition, metal-oxide dissolutions, purification of bio-diesel, synthetic processes and material chemistry [11-14]. However, and as far as we are aware, the ability of DES to serve as eco-friendly and renewable solvents in the field of homogeneous catalysis has been barely noticed [15-17].



Scheme 1 Metal-catalyzed isomerization of allylic alcohols.

On the other hand, the search for organic reactions proceeding with efficiency, selectivity and atom economy, has emerged as a major goal in synthetic chemistry [18-20]. Isomerization reactions are

typical examples of atom economic processes as no by-products are generated. In this sense, the redox isomerization of readily accessible allylic alcohols is a useful and straightforward synthetic route to saturated carbonyl compounds, which are very valuable raw materials in organic chemistry (Scheme 1) [21-26]. During the past few years, the development of the redox isomerization of allylic alcohols catalyzed by ruthenium(IV) complexes (*i.e.*, $[\{\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})(\mu\text{-Cl})\text{Cl}_2\}]$ (**1a**), Figure 1), which proceeded in excellent yields and under mild reaction condition, has received growing interest [27-30]. In this sense, some of us have recently described that a new family of monomeric ruthenium(IV) complexes (namely $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{L})]$), containing imidazole based ligands (**1b-c**, Figure 1), are highly active catalysts for this isomerization reaction in water [31-33].

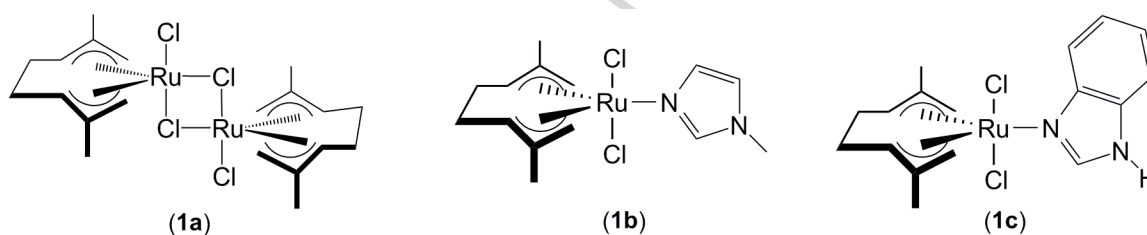


Figure 1 Ruthenium(IV) catalysts **1a-c** active in the isomerization of allylic alcohols in water.

Thus, following our interest in studying the catalytic activity of ruthenium complexes in organic processes using non-conventional solvents (water and ionic liquids) as reaction media [34], herein we report, for the first time, the catalytic activity of the ruthenium(IV) complex $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{benzimidazole})]$ (**1c**) in the selective isomerization of both primary and secondary allylic alcohols into carbonyl compounds using DES as green and bio-renewable solvents. For the isomerization of monosubstituted aliphatic allylic alcohols, the catalytic process displays: *i*) high efficiency for the isomerization reaction in DES [mixtures of non-toxic quaternary ammonium salt (ChCl) with a safe and renewable hydrogen donor, Figure 2], *ii*) high activity under mild reaction conditions and low catalyst loadings, *iii*) high yields in the absence of base, and *iv*) recyclability for four consecutive runs.

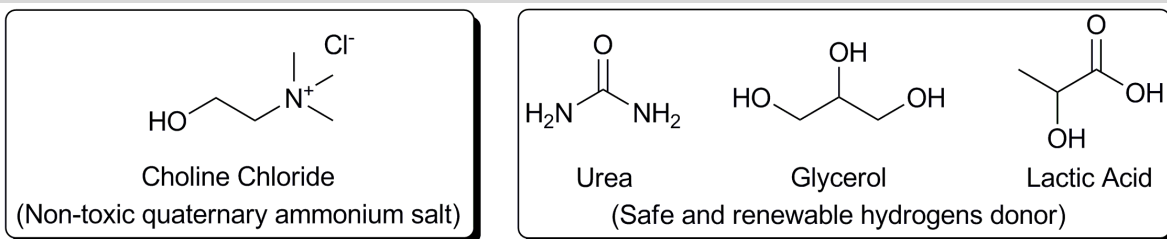


Figure 2 Components used in the synthesis of the DES employed as solvent in this communication.

2. EXPERIMENTAL

General procedure for the catalytic isomerization of allylic alcohols into carbonyl compounds.

The corresponding allylic alcohol (1 mmol) and the DES solvent (1 g) were introduced into a sealed tube under a nitrogen atmosphere. Complex **1c** (0.2-10 mol%) was then introduced at room temperature, and the resulting solution was heated at 75 °C for the indicated time. The course of the reaction was monitored by regular sampling and analysis by GC. The validity of this method has been confirmed by analyzing mixtures of the corresponding allylic alcohol / carbonyl compound in known proportions under the same conditions. To evaluate the recyclability of complex **1c**, the addition of successive amounts of 1-octen-3-ol to the reaction mixture at regular times was tested.

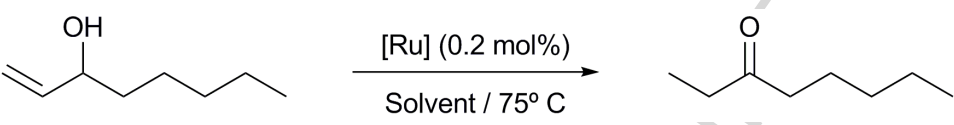
3. RESULTS AND DISCUSSION

We have investigated the catalytic activity of the dinuclear ruthenium(IV) complex [$\{\text{Ru}(\eta^3\text{-C}_{10}\text{H}_{16})(\mu\text{-Cl})\text{Cl}_2\}$] (**1a**) and the monomeric complexes [$\text{Ru}(\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{L})$] (L = *N*-methylimidazole (**1b**), benzimidazole (**1c**)) in the isomerization of allylic alcohols into saturated carbonyl compounds in different DES using as a model reaction the isomerization of 1-octen-3-ol (**2a**) into 3-octanone (**3a**). The course of the reaction was monitored by gas chromatography and the results obtained are summarized in Table 1. Firstly, we checked the isomerization reaction in a 1:2 mixture of choline chloride and glycerol (entries 1-3, Table 1) [35]. To our satisfaction, the three complexes tested (**1a-c**) were found to be active and selective catalysts at 75 °C, using only a 0.2 mol% metal loading, affording 3-octanone (**3a**) as the unique reaction product. It is important to note that in no case, the addition of a base to the catalytic system was required, in contrast to most of the known organometallic

catalysts active in this isomerization process [21-26]. This experimental evidence is in accordance with the fact that previously studied bis-allyl Ru(IV) complexes are also active catalyst in this transformation in the absence of base in water or ionic liquids [27-34]. Thus, we found that complex **1c** (entry 3, Table 1) displays much higher catalytic activity than complexes **1a** or **1b** (entries 1-2, Table 1), leading to quantitative transformation in only ten minutes ($\text{TOF} = 2970 \text{ h}^{-1}$, isolated yield for **3a** 98%). This fact can be probably attributed to the cooperative effect established by a hydrogen-bond network within the DES solvent and the benzimidazole ligand present in complex **1c** [11-14], which cannot be formed with complexes **1a,b**. This idea is also in accordance with the lower activity found for complex **1c** in traditional ionic liquids ($[\text{BMIM}][\text{BF}_4]$), which also contain both anions and cations and display similar electrostatic solvation properties to DES (entry 4), but is unable to establish the proposed hydrogen-bonds networks. It should be noticed that, although a higher catalytic activity has been previously described for complex **1c** in water ($\text{TOF} = 60.000 \text{ h}^{-1}$) [33], the activity found for **1c** in the DES (entry 3) is higher than those observed in pure organic solvents (entry 5) or ILs (entry 4). All these facts seem to indicate that the activity of complex **1c** can be enhanced by using hydrogen-donor solvents (water or DES). The presence of catalytic amounts of complex **1c** was found to be essential for the reaction outcome, as in the absence of the catalyst the reaction did not generate any product (entry 6). The nature of the DES was also crucial, as the efficiency of the reaction was remarkably lower when: *i*) different ratios of choline chloride and glycerol (entry 7), *ii*) other mixture of components in DES (1ChCl/2Urea, entry 8; 1ChCl/2Lactic Acid, entry 9), or *iii*) pure glycerol (entry 10), were used as solvents. Also, it is important to note that the catalyst **1c** is inactive in neat conditions (entry 11), disclosing a new example of an accelerated organic reaction in non-conventional solvents [1]. Finally, we found that the use of lower temperatures slowed down the reaction considerably; as an example, for quantitative formation of the carbonyl compound **3a** (98%) by using 0.2 mol% of complex **1c** in the DES 1ChCl/2Gly at 35 °C, 27 hours of reaction were required (after 10 min of reaction no appreciable formation of **3a** was observed). The method is also amenable to scaling-up, and the preparation of **3a** in a large scale is a

representative example [10 mmol of **2a** were isomerized into **3a** using 10 g of DES at 75 °C and with a 0.2 mol% catalyst loading (99% yield in 24 h)].

Table 1. Isomerization of 1-octen-3-ol (**2a**) into 3-octanone (**3a**) catalyzed by complexes **1a-c** in different DES.^a



entry	[Ru]	Solvent	Time	Yield (%) ^b	TOF (h ⁻¹) ^c
1	1a	1ChCl/2Gly	20 min	99	1485
2	1b	1ChCl/2Gly	1 h	99	495
3	1c	1ChCl/2Gly	10 min	99	2970
4	1c	[BMIM][BF ₄]	24 h	76	16
5	1c	THF	3 h	95	159
6	-	1ChCl/2Gly	90 min	0	0
7	1c	1ChCl/1Gly	6 h	30	25
8	1c	1ChCl/2Urea	3 h	83	138
9	1c	1ChCl/2Lactic Acid	8 h	3	<1
10	1c	Glycerol (Gly)	45 min	98	653
11	1c	Neat	8 h	12	<1

^a General Conditions: reactions performed under N₂ atmosphere at 75 °C using 1 mmol of the allylic alcohol **2a** in 1g of solvent. ^b Yields determined by GC. ^c Turnover frequencies ((mol product/mol Ru)/time) were calculated at the time indicated in each case.

The high efficiency showed by complex **1c** in the isomerization of the allylic alcohol **2a** into compound **3a** in DES (1ChCl/2Gly), prompted us to extend the study to a variety of allylic alcohols, to prove the scope of this catalytic transformation (Table 2). For other monosubstituted secondary allylic alcohols (TOF 1455-2970 h⁻¹, entries 2-5), quantitative formation of the saturated carbonyl compound was achieved in less than 20 minutes. However, for the other substrates in Table 2, high catalyst loading

(1-10 mol%) and longer reaction times (8-24 h) were always required (entries 6-10). In this sense, for the transformation of the allylic alcohol into propanal (entry 6) longer reaction time (12 h) and higher catalyst loading (1 mol%) were required to achieve quantitative yields (99%). As far as the allylic alcohol is concerned, there is a strong dependence upon the substitution of the carbon-carbon double bond as we have previously observed for other Ru(IV) catalysts in water and ionic liquids [34]. Thus, when 1,1- and 1,2-disubstituted allylic alcohols are used (entries 8-10), longer reaction times and higher catalyst loadings (5-10 mol%) are required. No transformation was observed when trisubstituted allylic alcohols such as 3-methyl-2-buten-1-ol were used as substrates. It should be mentioned that although these results compared well with those reported by us in ILs [34], higher catalytic activities have been previously described for the isomerization of substituted allylic alcohols using complex **1c** in water [33]. The lifetime of a catalytic system and its level of reusability are very important factors [36]. Thus, we have found that under the aforementioned catalytic conditions (Table 2) and using as a model reaction the isomerization of the allylic alcohol **2a** into compound **3a**, complex **1c** could be recycled up to 4 consecutive runs [1st cycle: 10 min (99%); 2nd cycle: 45 min (99%); 3rd cycle: 4 h (97%); 4th cycle: 18 h (97%)]. Thus, while only partial loss of activity occurs in DES during the two first consecutive runs (10-45 minutes), the efficiency of the catalytic system decreases considerably after the second cycle, 18 hours of heating being required in the 4th cycle to obtain **3a** in a 97% yield.

4. CONCLUSIONS

In summary, we have demonstrated that the complex $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{benzimidazole})]$ (**1c**), is a selective catalyst for the isomerization of secondary allylic alcohols into their corresponding saturated carbonyl derivatives using, for the first time, green and bio-renewable DES. Moreover, catalyst **1c** could be recycled up to four consecutive times with partial deactivation. Since this isomerization reaction does not involve the presence of any base and is accessible in a multi-gram scale, this methodology is an important contribution to the field of metal-catalyzed reaction in DES. Further efforts to develop new catalytic systems active and recoverable in DES are presently underway.

Table 2. Isomerization of various allylic alcohols catalyzed by complex **1c** in DES (1ChCl/2Gly).^a

entry	Substrate	Product	mol% [Ru]	Time	Yield (%) ^b	TOF (h ⁻¹) ^c
1			0.2	10 min	99	2970
2			0.2	10 min	99	2970
3			0.2	20 min	99	1485
4			0.2	20 min	97	1455
5			0.2	20 min	99	1485
6			1	12 h	99	8
7			10	24 h	95	<1
8			10	16 h	36	<1
9			5	8 h	95	<3
10			5	24 h	48	<1

^a General Conditions: Reactions performed under N₂ atmosphere at 75 °C using 1 mmol of the allylic alcohol in 1g of DES (1Ch/2Gly). ^b Yields determined by GC. ^c Turnover frequencies ((mol product/mol Ru)/time) were calculated at the time indicated in each case.

ACKNOWLEDGMENTS

We are indebted to the MICINN of Spain (CSD2007-00006 and CTQ2010-14796/BQU) for financial support. J.G.-A. thanks the MICINN and the European Social Fund for the award of a "Ramón y Cajal" contract. Authors anonymously acknowledge the reviewers of this communication who

suggested fruitful ideas for recycling improvement.

REFERENCES

- [1] P. T. Anastas (Ed.), Handbook of Green Chemistry, Vols. 4, 5 and 6, Green Solvents; Wiley-VCH: Weinheim, Germany, (2011).
- [2] P. T. Anastas, J. C. Warner in Green Chemistry: Theory and Practice, Oxford University Press, Oxford, (1998).
- [3] M. Lancaster in Green Chemistry: An Introductory Text, RSC Editions, London, (2002).
- [4] W. H. Hauthal, Chemosphere 43 (2001) 123-135.
- [5] R. Giernoth, Topics in Current Chemistry 276 (2007) 1-23.
- [6] P. Wassercheid, T. Welton (Eds.), Ionic Liquids in Synthesis, Wiley-VCH, Weinheim, Germany, vol. 1-2 (2008).
- [7] C.-J. Li, T.-H. Chan, Comprehensive Organic Reactions in Aqueous Media; 2nd Ed.; Wiley: New York, (2007).
- [8] P. H. Dixneuf, V. Cadierno (Eds.) in Metal-Catalyzed Reactions in Water, Wiley-VCH, Weinheim, Germany (2013).
- [9] I. Ryu, H. Matsubara, C. Emnet, J. A. Gladysz, S. Takeuchi, Y. Nakamura, D. P. Curran, Green Reaction Media in Organic Synthesis (2005) 59-124.
- [10] T. Welton, Green Chemistry 13 (2011) 225-225.
- [11] A. P. Abbott, R. C. Harris, K. S. Ryder, C. D'Agostino, L. F. Gladden, M. D. Mantle, Green Chemistry 13 (2011) 82-90.
- [12] D. Carriazo, M. C. Serrano, M. C. Gutiérrez, M. L. Ferrer, F. del Monte, Chemical Society Reviews 41 (2012) 4996-5014.
- [13] Q. Zhang, K. de Oliveira Vigier, S. Royer, F. Jérôme, Chemical Society Reviews 41 (2012) 7108-7146.
- [14] C. Ruß, B. König, Green Chemistry 14 (2012) 2969-2982.
- [15] G. Imperato, S. Höger, D. Lenoir, B. König, Green Chemistry 8 (2006) 1051-1055.

- [16] G. Imperato, R. Vasold, B. König, *Advanced Synthesis and Catalysis* 348 (2006) 2243-2247.
- [17] F. Ilgen, B. König, *Green Chemistry* 11 (2009) 848-854.
- [18] B. M. Trost, *Science* 254 (1991) 1471-1477.
- [19] B. M. Trost, M. U. Frederiksen, M. T. Rudd, *Angewandte Chemie International Edition* 44 (2005) 6630-6666.
- [20] R. A. Sheldon, *Green Chemistry* 9 (2007) 1273-1283.
- [21] R. C. van der Drift, E. Bouwman, E. Drent, *Journal of Organometallic Chemistry* 650 (2002) 1-24.
- [22] R. Uma, C. Crévisy, R. Grée, *Chemical Reviews* 103 (2003) 27-52.
- [23] V. Cadierno, P. Crochet, S. E. García-Garrido, J. Gimeno, *Current Organic Chemistry* 10 (2006) 165-183.
- [24] V. Cadierno, P. Crochet, J. Gimeno, *Synlett* (2008) 1105-1124.
- [25] L. Mantilli, C. Mazet, *Chemistry Letters* 40 (2011) 341-344.
- [26] N. Ahlsten, A. Bartoszewicz, B. Martín-Matute, *Dalton Transactions* 41 (2012) 1660-1670.
- [27] V. Cadierno, S. E. Garcia-Garrido, J. Gimeno, *Chemical Communications* (2004) 232-233.
- [28] V. Cadierno, S. E. García-Garrido, J. Gimeno, A. Varela-Álvarez, J. A. Sordo, *Journal of the American Chemical Society* 128 (2006) 1360-1370.
- [29] V. Cadierno, J. Francos, J. Gimeno, N. Nebra, *Chemical Communications* (2007) 2536-2538.
- [30] C. Bruneau, M. Achard, *Coordination Chemistry Reviews* 256 (2012) 525-536.
- [31] J. Díez, J. Gimeno, I. Merino, E. Rubio, F. J. Suárez, *Inorganic Chemistry* 50 (2011) 4868-4881.
- [32] L. Bellarosa, J. Díez, J. Gimeno, A. Lledós, F. J. Suárez, G. Ujaque, C. Vicent, *Chemistry an European Journal* 18 (2012) 7749-7765.
- [33] J. Díez, J. Gimeno, A. Lledós, F. J. Suárez, C. Vicent, *ACS Catalysis* 2 (2012) 2087-2099.
- [34] J. García-Álvarez, J. Gimeno, F. J. Suárez, *Organometallics* 30 (2011) 2893-2896.
- [35] The DES 1ChCl/2Gly (melting point $-40\text{ }^{\circ}\text{C}$) has already been mentioned in the literature in J. T. Gorke, F. Srienc, R. J. Kazlauskas, *Chemical Communications* (2008) 1235-1237.
- [36] M. Benaglia (Ed.) *Recoverable and Recyclable Catalyst*, John Wiley & Sons, Chichester, (2009).

Graphical abstract

The bis-allyl Ru(IV) complex $[\text{Ru}(\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{benzimidazole})]$ is an efficient catalyst for the metal-mediated isomerization of allylic alcohols in their corresponding saturated carbonyl derivatives in the Deep Eutectic Solvent formed by choline chloride and glycerol in a 1:2 ratio (1ChCl/2Gly). It is important to note that this catalytic system involves no presence of any base as co-catalyst. Moreover, the catalyst could be recycled up to four consecutive times in this DES (1ChCl/2Gly) with partial deactivation.

HIGHLIGHTS

- 1.- A rare example of the use of Deep Eutectic Solvents (DES) as green and renewable media in metal-catalyzed organic reactions.
- 2.- Complex $[\text{Ru}(\eta^3:\eta^3\text{-C}_{10}\text{H}_{16})\text{Cl}_2(\text{benzimidazole})]$ (**1c**) is a highly active and selective catalyst in the redox isomerization of monosubstituted aliphatic allylic alcohols into saturated carbonyl compounds using DES.
- 3.- Isomerization reaction takes place in the absence of base and in a large-scale experiment.
- 4.- The catalytic system was recycled up to four consecutive runs.