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Highly Efficient Redox Isomerization of Allylic Alcohols and Transfer Hydrogenation of Ketones and Aldehydes Catalyzed by Ruthenium Complexes

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Abstract: A dicationic dichloro-bipyridine-ruthenium complex shows very high catalytic activity in redox isomerization of allylic alcohols but a relatively low one in transfer hydrogenation of ketones; surprisingly, the analogous dimethyl-bipyridine-ruthenium complex shows reverse catalytic activities in the two reactions.

Keywords: aldehydes; isomerization; ketones; reduction; ruthenium

The catalytic redox isomerization of allylic alcohols into the corresponding saturated carbonyl compounds represents an atom-economic and elegant shortcut to valuable carbonyl compounds. Conventionally, the transformation involves a two-step sequential oxidation and reduction process.[1] In the last few decades, various transition metal complexes of Rh, Co, Ni, Mo, Ir, Fe, Os, Pd and Pt have been explored as catalysts for this isomerization[1] and, in particular, ruthenium complexes have been described as the most efficient catalysts.[2–6] However, most of these catalytic systems have limited substrate scopes, and harsh reaction conditions and high catalytic loadings are usually required for the catalytic processes. Recently, bis(allyl)-ruthenium(IV) complexes have been disclosed by Gimeno et al as the most efficient catalysts for the redox isomerization of allylic alcohols.[2,3] The redox isomerization catalyzed by the Ru(IV) complexes demonstrated turnover frequency (TOF) values in the range of 1–3000 h^{-1} for most substrates when 0.2 mol% catalyst was used.[3]

The ruthenium-mediated transfer hydrogenation (TH) of carbonyl compounds under basic conditions employing *i*-PrOH or other hydrogen donor solvents has attracted increasing interest in organometallic chemistry as well as organic synthesis methodology,[7] due to its practical simplicity and potential use at ambient pressure. Although a range of structurally diverse ruthenium complexes have been reported as catalysts for TH, the precatalysts featuring a Ru–NH linkage offer high levels of activity and selectivity.[7,8] To date, exploration of highly effective catalysts without ancillary N–H functionality is still in demand.[9]

Reported herein is our study on the highly efficient redox isomerization of allylic alcohols and the TH of ketones and aldehydes catalyzed by the dicationic bipy-ruthenium(II) complexes.

The dicationic ruthenium complexes containing bipyridine (bipy) ligands such as *cis*-[Ru(6,6′-Cl_2bipy)$_2$(H_2O)$_2$] ($OTf)_2$ (**1**) and *cis*-[Ru(6,6′-Me_2bipy)$_2$(H_2O)$_2$] ($OTf)_2$ (**2**) (Figure 1) have been known for decades, but their applications as catalysts for organic reactions are still very limited.[10] We first studied the catalytic isomerization of 1-butene-3-ol (**3a**) with the dichloro-

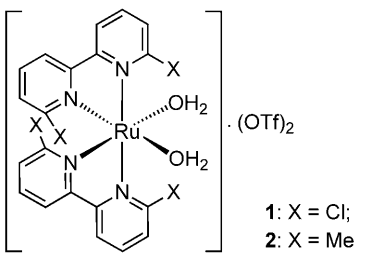


Figure 1. Structures of complexes **1** and **2**.

Table 1. Isomerization of 3-butene-2-ol (**3a**) catalyzed by bipy-ruthenium(II) complexes.[a]

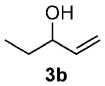
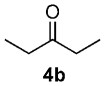
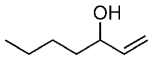
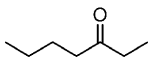
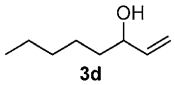
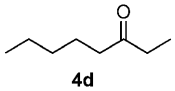
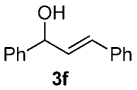
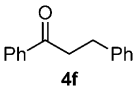
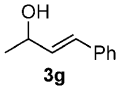
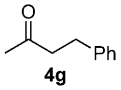
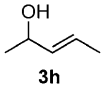
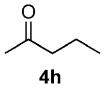
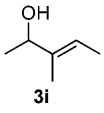
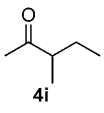
Entry	Catalyst	S/C	Solvent	Time	Temp. [°C]	Conv. [%][b]
1	**1**	1000	Neat	10 min	80	100
2	**1**	1000	THF	10 min	72	100
3	**1**	1000	DCE	10 min	50	100
4	**1**	1000	acetone	10 min	reflux	91
5[c]	**1**	1000	H_2O	4 h	90	72
6	**1**	5000	THF	10 min	72	100
7	**1**	5000	Neat	10 min	80	<5
8	**1**	5000	DCE	10 min	50	16
9[c]	**1**	5000	THF	10 min	72	98
10[d]	**1**	5000	THF	10 min	72	25
11	**1**	10000	THF	20 min	72	69
12	**2**	1000	THF	20 min	72	38

[a] *Reaction conditions:* **3a** (2 mmol), catalyst:KOBu-*t* = 1:2, solvent (1 mL), unless otherwise noted.
[b] Determined by ^{1}H NMR spectroscopy.
[c] Using KOH as the base.
[d] Using K_2CO_3 as the base.

substituted bipy-Ru(II) complex **1**. It can be seen from Table 1 that with a substrate/catalyst (S/C) ratio of 1000, quantitative conversions were obtained when the reactions were carried out neat (80 °C) and in refluxing THF and DCE solutions (entries 1–5). The reaction also proceeds, but at a much slower rate, in aqueous solution (entry 5). However, with a higher S/C ratio (5000), THF stands out as the solvent of choice (entries 6–8). It should be pointed out that base is required for the catalytic isomerization reactions; it seems that the weak base K_2CO_3 is inferior to the stronger ones, KOBu-*t* and KOH (entries 6, 9 and 10). Interestingly, the complex containing the 6,6′-dimethylbipyridine ligand *cis*-[Ru(6,6′-Me_2bipy)$_2$(H_2O)$_2$]($OTf)_2$ (**2**) exhibits much lower activity (TOF = 1200 h^{-1}) in comparison to complex **1** (entry 12).

Subsequently, the catalytic redox isomerization of allylic alcohols in THF was examined for more substrates at 72 °C in the presence of **1**/KOBu-*t*, and the results are listed in Table 2. Monosubstituted secondary aliphatic allylic alcohols [RCH(OH)CH=CH_2] **3a–d** exhibit high reactivity (TOF = 12,000–49,000 h^{-1})

Table 2. Redox isomerization of allylic alcohols catalyzed by complex **1**.[a]

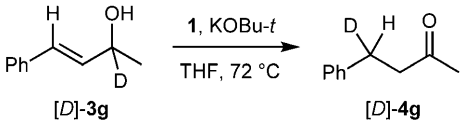
Entry	Substrate	Product	S/C	Time	Conversion [%][b]	TOF [h^{-1}][c]
1	 **3a**	 **4a**	5000	10 min	>99	49,000 (5 min)
2	 **3b**	 **4b**	5000	10 min	>99	30,000 (10 min)
3	 **3c**	 **4c**	5000	20 min	>99	39,000 (10 min)
4	 **3d**	 **4d**	1000	10 min	>99	12,000 (5 min)
5	 **3e**	 **4e**	1000	60 min	>99	1,200 (30 min)
6	 **3f**	 **4f**	20	30 min	78	31 (30 min)
7	 **3g**	 **4g**	20	2 h	>99	19 (30 min)
8	 **3h**	 **4h**	20	23 h	72	13 (0.5 h)
9	 **3i**	 **4i**	20	48 h	74	0.5 (24 h)

[a] *Reaction conditions:* substrate (2 mmol), **1**:KOBu-*t* = 1:2, THF (1 mL), 72 °C.
[b] Determined by ^{1}H NMR spectroscopy.
[c] TOF values were determined according to the conversions at the time noted in parentheses.

with 0.02–0.1 mol% catalyst and the conversions (>99%) are quantitative within 10–20 min (entries 1–4). The results previously reported for the isomerization of **3a**–**3d** were 100% conversion after 15–20 min (TOF = 1,000–2000 h^{-1}) when 0.2 mol% of Ru(IV) catalyst was used.[3] The isomerization of **3e** to ketone **4e** was also effective and >99% conversion was achieved after 1 hour with a high TOF (1220 h^{-1}, entry 5). For this reaction, TOF values of 600–1200 h^{-1} have been reported using ruthenium complexes,[5c,11] and even 2400 h^{-1} was achieved when a rhodium complex was used.[12] When allylic alcohols with internal C=C bonds (**3f–h)** were used as substrates, a higher catalyst loading (5 mol%) was needed for high conversions, and the TOF values decreased to 13–31 h^{-1} (entries 6–8). The strong dependence of catalytic reactivity upon the substitution of the C=C bonds of the allylic alcohols has been previously observed with other catalytic systems.[3,5b] When the trisubstituted substrate **3i** was used as the substrate, 74% conversion was also obtained after 48 h (entry 9). If the trisubstituted allylic alcohol 4-methyl-3-penten-2-ol was applied in this isomerization, no isomerized product could be detected after 48 h, which indicated the disubstitution at the teminal carbon of the C=C bond prohibited the isomerization due to the steric hindrance.

In the mechanism investigations for the ruthenium-catalyzed redox isomerization of allylic alcohols,[3,5] a mechanism for a half-sandwich ruthenium complex-catalyzed redox isomerization of allylic alcohols was suggested and substantiated by Bäckvall and co-workers.[6] It was proposed that the catalytic reaction involves the intermediacy of a ketohydride species, generated *via* β-elimination of the alkoxide species. The hydride can be added to the carbonyl group (1,2-addition) to reform the alkoxide or alternatively to the double bond of the keto ligand (1,4-addition) to form the metal enolate; the overall rate of the isomerization reaction is dependent on the relative rates of the two addition steps. The isomerization of [*D*]-**3g** catalyzed by the complex **1** was performed and [*D*]-**4g** was obtained (Scheme 1), which confirmed a Bäckvall-type reaction pathway in the complex **1**-catalyzed isomerization of allylic alcohols.[6]

It can be seen from Table 1 that the 6,6′-dimethyl-bipy-ruthenium complex **2** is a much less active catalyst than its dichloro analogue **1** for the isomerization reaction (entry 12, Table 1); and since the crucial step in the well-known transfer hydrogenation (TH) of ketones and aldehydes is the 1,2-addition of hydride to the carbonyl carbon,[13] we are therefore interested to study and compare the catalytic activities of **1** and **2** toward the TH reactions.



[*D*]-**3g** [*D*]-**4g**

Scheme 1. The isomerization of [*D*]-**3g** catalyzed by complex **1**.

Interestingly, it was found that **1** exhibits low catalytic activity in the TH of acetophenone while the dimethyl analogue **2** is highly active for the reduction reaction (TOF: 130 *vs.* 150,000 h^{-1}, entries 1 and 2, Table 3). Acetophenones, the analogous acetonaphthone, and benzophenone show very high reactivities (entries 2–6, 9). Steric hindrance seems to play a role in reducing the reactivity of the substrate (entries 7 and 8). In the TH of the cyclic ketone **5i**, excellent yields and TOF are observed with complex **2** as the catalyst; and complexes **1** also demonstrates low catalytic activity (TOF: 140,000 *vs.* 510 h^{-1}, entries 10 and 11). The TH of cyclohexanone provides good yield although the TOF is much lower (entry 12). Aliphatic ketones are reduced with high yields, however, much longer reaction times are required (entries 13 and 14). The catalytic reduction of aldehydes to primary alcohols,[14] which is still uncommon by use of the TH reaction, is found to be successful with complex **2** as the catalyst. For aromatic benzaldehyde, the reaction was completed after 1 min and very high reactivity (TOF = 92,000 h^{-1}) was observed (entry 15). For the reduction of aliphatic octanal, quantitative yield was obtained in 20 seconds, although higher catalyst loading was required (2 mol%, entry 16). Note that all the transfer hydrogenation reactions were quenched at the indicated reaction time by adding 1 M aqueous HCl to the reaction, which then could not proceed any more under reflux conditions.

In summary, we have found that the electrophilic dichloro-bipy ruthenium complex **1** is highly efficient for the redox isomerization of allylic alcohols but shows low activity for TH of ketones. It is, however, very interesting to learn that, with respect to **1**, complex **2** shows reverse catalytic activities in the redox isomerization and TH reactions. A preliminary mechanistic study on the **1**-catalyzed isomerization of allylic alcohol indicates that the reaction probably proceeds *via* the intermediacy of a ketohydride species. Our work reported here shows that a subtle modification of the electronic properties of the metal centers in similar complexes could lead to very different catalytic properties. It is definitely worth spending much effort, in terms of experimental and theoretical studies, to gain more understandings and to provide explanations for this phenomenon. Such mechanism investigations are in progress in our laboratories.

Table 3. TH of ketones and aldehydes catalyzed by ruthenium complex **2**.[a]

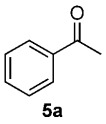
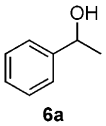
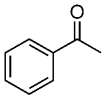
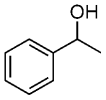
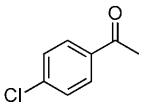
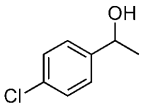
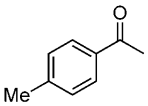
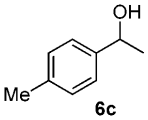
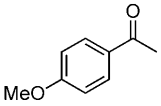
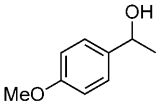
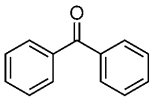
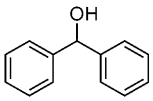
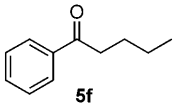
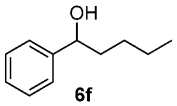
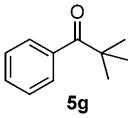
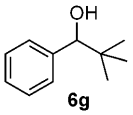
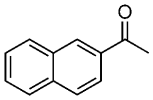
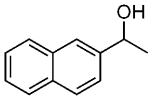
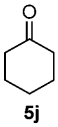
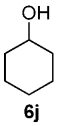
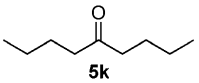
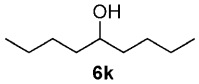
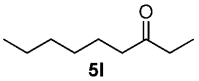
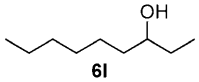
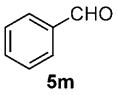
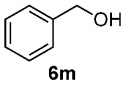
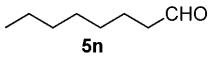
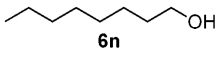
Entry	Substrate	Product	Time	Conversion [%][b]	TOF [h^{-1}][c]
1[d]	 **5a**	 **6a**	3 h	40	130 (3 h)
2	 **5a**	 **6a**	1 min	93	150,000 (20 s)
3	 **5b**	 **6b**	1 min	96	170,000 (20 s)
4	 **5c**	 **6c**	1 min	84	100,000 (20 s)
5	 **5d**	 **6d**	1 min	68	83,000 (20 s)
6	 **5e**	 **6e**	1 min	95	130,000 (20 s)
7	 **5f**	 **6f**	20 min	94	13,000 (3 min)
8	 **5g**	 **6g**	18 h	94	300 (1.5 h)
9	 **5h**	 **6h**	1 min	92	110,000 (20 s)
10	 **5i**	 **6i**	1 min	94	140,000 (20 s)
11[d]	 **5i**	 **6i**	3 h	89	510 (1 h)
12	 **5j**	 **6j**	20 min	99	8,800 (3 min)
13	 **5k**	 **6k**	14 h	92	800 (0.5 h)
14	 **5l**	 **6l**	14 h	94	840 (0.5 h)

Table 3. (Continued)

Entry	Substrate	Product	Time	Conversion [%][b]	TOF [h^{-1}][c]
15	 **5m**	 **6m**	1 min	98	92,000 (20 s)
16[e]	 **5n**	 **6n**	20 s	99	8,900 (20 s)

[a] *Reaction conditions:* substrate (1.5 mmol), substrate:**2**:KOBu-*t* = 1000:1:25, 0.5 M solution of substrate in *i*-PrOH, 85 °C, unless otherwise noted.
[b] Determined by GC-FID.
[c] TOF values were determined according to the conversions at the time noted in parentheses.
[d] Complex **1** used as catalyst.
[e] Substrate:**2**:KOBu-*t* = 50:1:25 was used.

Experimental Section

Typical Procedure for the Isomerization of Allylic Alcohols Catalyzed by Complex 1

A THF (1 mL) solution of **1** (0.0004 mmol), allylic alcohol (2.0 mmol), and KOBu-*t* (0.0008 mmol) was stirred in a test-tube sealed with a rubber septum at 72 °C under N_2 for the designated time. The course of the reaction was monitored by regular sampling and the conversion was determined by ^{1}H NMR spectroscopy.

Typical Procedure for the Transfer Hydrogenation of Ketones and Aldehydes Catalyzed by Complex 2

A solution of **2** (0.0015 mmol) and KOBu-*t* (0.038 mmol) in *i*-PrOH (3.0 mL) in a test-tube sealed with a rubber septum was heated at 85 °C under N_2 for 30 min. The substrate (1.5 mmol) was added and the resulting solution was heated in a sealed tube at 85 °C for the required period of time. The reaction was then quenched by adding 1 M aqueous HCl (80 μL) to the reaction mixture. The course of the reaction was monitored by regular sampling and the conversion was determined by GC-FID. Before GC analysis, the sample was passed through a short collum throgh silica gel (eluent: diethyl ether) to remove the ruthenium complex.

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