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Osmium(II)/R-pybox *vs* ruthenium(II)/R-pybox complexes in the catalytic asymmetric transfer hydrogenation of arylketones

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ABSTRACT

The reaction of the complexes *trans*-[$RuCl_2(\eta^2\text{-}C_2H_4)$\{(*S*,*S*)-^{i}Pr-pybox\}] (**1a**) and *trans*-[$RuCl_2(\eta^2\text{-}C_2H_4)$\{(*R*,*R*)-Ph-pybox\}] (**1b**) with nitrogen heterocyclic ligands, provide the complexes *trans*-[$RuCl_2$(L)(R-pybox)] (L = py (**3a,b**), 3-Br-py (**4a,b**), isoquinoline (**5a,b**), pyrazine (**6a,b**), 1-methylimidazole (**7a,b**), 1-benzylimidazole (**8a,b**), pyrazole (**9a,b**), 3-methylpyrazole (**10a,b**), and 1H-1,2,4-triazole (**11a,b**)). The complexes *trans*-[$OsCl_2$(L)\{(*S*,*S*)-^{i}Pr-pybox\}] (L = py (**12**), 3-Br-py (**13**), 3-CN-py (**14**), 3-MeO-py (**15**), 3-NO_2-py (**16**), 4-CN-py (**17**), 4-MeO-py (**18**), isoquinoline (**19**), 1-methylimidazole (**20**), 1-benzylimidazole (**21**), pyrazole (**22**)) have been similarly synthesized by the substitution of ethylene from the precursor complex *trans*-[$OsCl_2(\eta^2\text{-}C_2H_4)$\{(*S*,*S*)-^{i}Pr-pybox\}] (**2**) by the corresponding N-donor ligand in refluxing toluene. Moreover, the dinuclear complexes [$(RuCl_2$\{(*S*,*S*)-^{i}Pr-pybox\}$)_2(\mu\text{-}N,N\text{-}C_4H_4N_2)$] (**23a**), [$(RuCl_2$\{(*R*,*R*)-Ph-pybox\}$)_2(\mu\text{-}N,N\text{-}C_4H_4N_2)$] (**23b**) and [$(OsCl_2$\{(*S*,*S*)-^{i}Pr-pybox\}$)_2(\mu\text{-}N,N\text{-}C_4H_4N_2)$] (**24**) have been prepared by the reaction of the complexes **1** and **2** with pyrazine (1:0.5 M ratio for **23** and 1:1.5 for **24**). The structure of the complexes **9a**, **12**, **23a** and **24** has been determined by single-crystal X-ray diffraction analysis. The ruthenium **3a,b**, **6a** and **10a,b** and osmium complexes **12–22** and **24** have been assayed as catalysts for the asymmetric transfer hydrogenation reaction. Among them, the osmium complexes **12**, **15**, **16**, **18** and **24** have proven more efficient in the reduction of a variety of aromatic ketones affording the (*R*)-benzylalcohols with very high conversion and moderate enantioselectivity up to 73% *e.e.*

1. Introduction

The asymmetric transfer hydrogenation (ATH) of prochiral ketones leading to enantiopure alcohols has been usually focused on the use of ruthenium, rhodium and iridium catalysts containing well designed chiral ligands [1], although other late transition metal complexes have also been also studied [2]. In spite that osmium catalysts have been traditionally considered less active than the ruthenium analogs due to their slower ligand exchange kinetics and, consequently, only occasionally employed [3], the Baratta's group [4] has demonstrated in the last years that osmium complexes containing Josiphos-type phosphanes [5], and substituted aminomethylpyridines show great potential in this field displaying comparable catalytic activity as related ruthenium complexes. Specifically, the complexes *in situ* generated from [$OsCl_2(PPh_3)_3$], (*S*,*R*)-Josiphos or (*S*,*R*)-Josiphos* and (pyridin-2-yl)alkanamine derivatives (R-Pyme and H-Pyme) (Chart 1, ligands A) promoted the ATH of acetophenone and methyl-arylketones to the corresponding *S*-alcohols with high TOF (up to 1.9×10^4 h^{-1}) and *e.e.* (91–96%) [6]. These results are rather similar to those reached using the corresponding ruthenium complexes [7]. This group also studied the catalytic potential of ruthenium and osmium complexes [MCl(CNN)(PP)] containing Josiphos-type ligands and anionic CNN pincer ligands derived from 1-(6-arylpyridin-2-yl)alkanamine (Chart 1, ligands B–D) [8–10], and (benzo[*h*]quinolin-2-yl)alkanamine (Chart 1, ligands E) [11]. They found that both types of metal complexes behave very efficiently for transfer hydrogenation of methylarylketones (Ru: TOF up to 1.3×10^6 h^{-1}, 81–99% *e.e.*; Os: TOF up to 4.0×10^5 h^{-1}, 91–97% *e.e.*) [8–11]. Interestingly, the nature of the enantiopure pyridine-derived and Josiphos-type ligands notably improved the reduction efficiency. In fact, the isolated complexes [MCl(CNN)\{(*R*,*S*)-Josiphos*\}] (M = Ru, Os; HCNN = (*S*)-1-(6-(2-naphtyl)pyridin-2-yl)ethanamine (Chart 1, ligand D(r)) provided the best results, in terms of rate (TOF 10^5-10^6 h^{-1}) and enantioselectivity (up to 99% *e.e.*), for the conversion of different alkylaryl ketones and methylpyridyl ketones into the corresponding alcohols [10].

In this context we have recently reported on the capability of the

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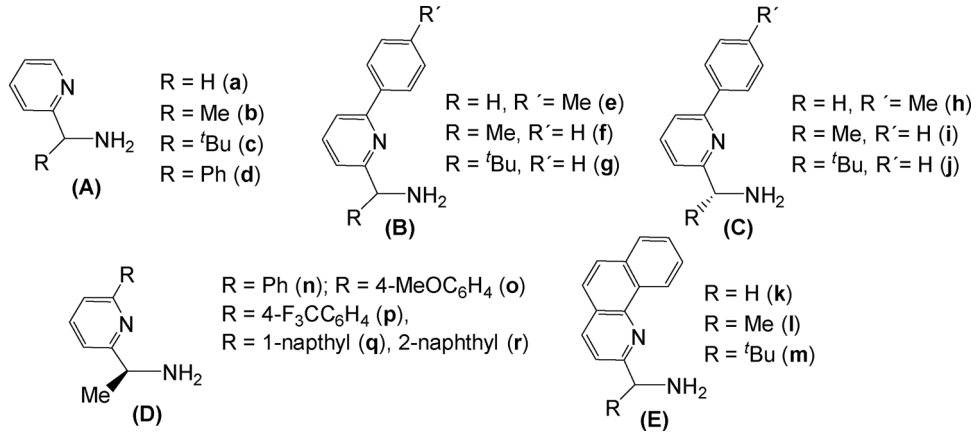

Chart 1. (pyridine-2-yl)alkanamine, 1-[6-arylpyridin-2-yl)alkanamine and (benzo[*h*]quinolin-2-yl)alkanamine ligands.

osmium and ruthenium complexes *cis*-[$RuCl_2$(L){(*R*,*R*)-Ph-pybox}] (L = PPh_3, P^iPr_3) [12] and *trans*-[$OsCl_2$(L){(*S*,*S*)-^{i}Pr-pybox)] (L = P$(OR)_3$) [13] towards the asymmetric transfer hydrogenation of aryl ketones. In all cases, both catalysts behave similarly affording more than 95% of conversion and up to 95% of *e.e.* Moreover, it constitutes the first application of an osmium catalyst bearing an aprotic nitrogen ligand as the chiral asymmetric inductor in the ATH of ketones. On the other hand, it was found that the nature of the achiral ligand has notable influence on the efficiency of these catalysts [12,13]. After these promising results, it seems therefore apparent to undertake further studies by choosing ligands with electronic/steric demand properties different than those of the mentioned phosphorous ligands.

Accordingly, we report herein the synthesis of new ruthenium *trans*-[$RuCl_2$(L)(R-pybox)] (R-pybox = (*S*,*S*)-^{i}Pr-pybox, (*R*,*R*)-Ph-pybox)) and osmium complexes *trans*-[$OsCl_2$(L){(*S*,*S*)-^{i}Pr-pybox}] containing achiral N-donor ligands, specifically five- and six-membered aromatic nitrogen heterocycles, which feature very different electronic properties than the P-donor ligands (phosphanes and phosphites) already reported. Moreover, the catalytic activity of some of these complexes towards the AHT of ketones is explored.

2. Results and discussion

*2.1. Synthesis of the complexes trans-[$RuCl_2$(L)(R-pybox)] [R-pybox = (S,S)-^{i}Pr-pybox = 2,6-bis[4'-(S)-isopropyloxazolin-2´-yl]pyridine, L = py (**3a**), 3-Br-py (**4a**), isoquinoline (**5a**), pyrazine (**6a**); R-pybox = (R,R)-Ph-pybox = 2,6-bis[4'-(R)-phenyloxazolin-2´-yl]pyridine, L = py (**3b**), 3-Br-py (**4b**), isoquinoline (**5b**), pyrazine (**6b**)]*

We have firstly carried out the preparation of ruthenium complexes wherein the metal is coordinated to six-membered nitrogen heterocycles, *e.g.* pyridine, isoquinoline, and pyrazine (complexes **3**,**4**,**5**,**6**, respectively). Thus, the complexes *trans*-[$RuCl_2$(η^2-C_2H_4)(R-pybox)] **1** (**1a**: R^1 = ^{i}Pr, R^2 = H; **1b**: R^1 = H, R^2 = Ph**)** were reacted with the *N*-donor ligands pyridine, 3-Br-pyridine, isoquinoline and pyrazine in dichloromethane (**1a**: reflux, 1:1.5 M ratio; **1b**: 60 °C, sealed tube, 1:2 M ratio) giving rise stereoselectively to the formation of the *trans*-complexes **3–6** in moderate to very high yield (**3a**-**6a**: 87–98 %; **3b**-**6b**: 58–81%) by ethylene/*N*-donor ligand exchange (Scheme 1; see Experimental Section for details).

The *trans* stereochemistry of the complexes **3–6** has been readily determined on the basis of the ^{1}H and ^{13}C{^{1}H} NMR spectra that are fully consistent with the presence of a C_2 symmetry axis. Thus, the ^{13}C{^{1}H} NMR spectra of the complexes **3–6** show single resonance signals for the C-2´ (OCN), C-4´ (CHR) and C-5´ (CH_2) carbon atoms of both pybox-oxazoline rings and for the C-3/C-5 and C-2/C-6 carbon atoms of the pybox pyridine ring.

*2.2. Synthesis of the complexes trans-[$RuCl_2$(L)(R-pybox)] [R-pybox = (S,S)-^{i}Pr-pybox, L = 1-methylimidazole (**7a**), 1-benzylimidazole (**8a**), pyrazole (**9a**), 3-methylpyrazole (**10a**), and 1H-1,2,4-triazole (**11a**); R-pybox = (R,R)-Ph-pybox, L = 1-methylimidazole (**7b**), 1-benzylimidazole (**8b**), pyrazole (**9b**), 3-methylpyrazole (**10b**), and 1H-1,2,4-triazole (**11b**)]*

Under the same reaction conditions as described above, the corresponding ruthenium complexes having an azole ligand were then synthesized from complexes **1a**,**b** and 1-methyl and 1-benzylimidazole (**7**,**8**; 66–93% yield), pyrazole and 3-methylpyrazole (**9**,**10**; 76–97% yield) and 1*H*-1,2,4-triazole (**11**; 83–95% yield) (Scheme 2; see Experimental Section for details). The *trans* arrangement of the chlorine atoms was also confirmed by the presence of a C_2 symmetry axis (see the ^{1}H and ^{13}C{^{1}H} NMR spectra).

The structure of the complex **9a** has been confirmed by a single crystal X-ray analysis. The asymmetric unit of the complex **9a** consists of two molecules that have similar relevant structural parameters, and therefore only the data corresponding to one of them are discussed. An ORTEP-type view of one of them is shown in Fig. 1, and selected bonding data are collected in the Table *S*1 (Supporting Information). The structure exhibits a distorted octahedral geometry around the ruthenium atom which is bonded to three nitrogen atoms of ^{i}Pr-pybox ligand, the nitrogen atom N^2 of pyrazole and two chlorine atoms. The chlorine atoms and the nitrogen atoms of pyridine and pyrazole groups are located in a *trans* disposition with both angle values close to the linearity (Cl(1)-Ru(1)-Cl(2) = 176.47(3)º; N(2)–Ru(1)–N(4) = 177.14(11)º). The Ru(1)–N(1) (2.107(3) Å), Ru(1)–N(2) (1.949(3) Å) and Ru(1)–N(3) (2.066(3) Å) distances as well as the N(1)–Ru(1)–N(2) (78.50(11)º), N(1)–Ru(1)–N(3) (156.88(11)º) and N(2)–Ru(1)–N(3) (78.37(11)º) bond angles fall in the range observed for other related ruthenium(II) pybox complexes [14,15]. The Ru(1)–N(4) distance (2.117(3) Å) is also in the range found for other ruthenium(II)-pyrazole complexes [16]. It is also observed from Fig. 1 the intramolecular hydrogen bond between the H(5 N) (distance N(5)-H(5 N), 0.92 Å) and one of the equatorial chlorine ligands. The distances N(5)···Cl(2) (3.1525(1) Å) and H(5 N)···Cl(2) (2.56 Å) as well as the angle value N(5)–H(5 N)···Cl(2) (122°) are consistent with the existence of a weak hydrogen bond [17]. On the other hand, the dihedral angle (α = 19.70(3)º), formed by the planes containing Ru(1)–N(4)–N(5)–H(5N) and Cl(2)–Ru(1)–Cl(1) moieties, appears to locate the N(5)–H(5N) vector in a such a way that the intramolecular hydrogen bond is facilitated [18].

*2.3. Synthesis of the complexes trans-[$OsCl_2$(L){(S,S)-^{i}Pr-pybox}] [L = py (**12**), 3-Br-py (**13**), 3-CN-py (**14**), 3-MeO-py (**15**), 3-NO_2-py (**16**), 4-CN-py (**17**), 4-MeO-py (**18**), isoquinoline (**19**), 1-methylimidazole (**20**), 1-benzylimidazole (**21**), pyrazole (**22**)]*

The synthesis of related osmium complexes containing six- and five-nitrogen heterocycles was also undertaken by ethylene-ligand exchange