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Hydrogen Autotransfer and Related Dehydrogenative Coupling Reactions using a Rhenium(I) Pincer Catalyst

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A novel rhenium complex¹ bearing a non-innocent PNP pincer ligand was prepared. This novel catalyst is active in hydrogen autotransfer reactions to form new C-C and C-N bonds. More specifically, valuable alkylations of ketones and sulfonamides with primary alcohols are herein presented. In addition, the first examples of rhenium-catalysed synthesis of pyrroles are described by dehydrogenative coupling of diols, amines and ketones.

Compared to other transition metals, molecularly defined rhenium complexes remained largely unexplored in catalysis.² Selected examples for reductive processes and C-C bond formation include the dehydration of alcohols,³ hydrosilylation reactions,⁴ as well as coupling of propargylic alcohols.⁵ Most recently, some rhenium-pincer complexes have been also described for the stoichiometric activation of nitrogen.⁶ In addition, several rhenium catalysts were applied for the dehydrogenative coupling of carbonyl compounds with alcohols,⁷ as well as the alkylation of primary amines with the same substrates, in the latter case to give the corresponding imines⁸ or secondary amines.⁹

Transition metal-catalyzed hydrogen autotransfer (also called borrowing hydrogen) of alcohols are atom economical, operational simple and eco-friendly methodologies where water is formed as the only stoichiometric residue.¹⁰ Mechanistically, readily available alcohols are initially dehydrogenated to afford more reactive carbonyl compounds. Further condensation with an appropriate nucleophile provides the corresponding unsaturated intermediates, which are finally reduced with the hydrogen extracted in the first step, regenerating the active species. This strategy has been widely used to form new C-C and C-N bonds. More specifically, the alkylation of amines or ketones with non-activated, cheap and abundant alcohols continues to be challenging. Furthermore, a plethora of relevant heterocyclic compounds can be synthesised using such methodologies or related dehydrogenative coupling processes.¹¹ So far, such protocols are mainly performed using ruthenium and iridium complexes, although recently significant attention has been paid to use alternative metals. For example, a variety of complexes bearing PNP pincer ligands have been developed using several metals such as ruthenium,¹² iron,¹³ cobalt¹⁴ and lately manganese (Scheme 1).¹⁵



Scheme 1. Ruthenium, iron and manganese PNP pincer complexes. Synthesis of cationic rhenium(I) pincer complex 5.

All these complexes showed reactivity in hydrogenation and dehydrogenation reactions, as well as hydrogen autotransfer processes. Notably, the reactivity for individual catalytic steps can be tuned by varying the metal centre and not the ligand scaffold. Hence, we are interested in the preparation of novel related complexes. Following our previous experience on this topic, we herein describe the synthesis of a rhenium-based pincer complex and its application in hydrogen autotransfer reactions, which are barely known in the presence of rhenium. Initially, the reaction of Re(CO)₅Br with the PNP pincer ligand in toluene at 100 °C overnight, provided the cationic complex 5 quantitatively (Scheme 1). Crystallisation from chloroform/heptane provided the X-ray molecular structure shown in Figure 1. To our delight, 5 showed a good reactivity in the $\alpha\text{-alkylation}$ of ketones with alcohols, $^{15d,\ 16}$ a greener alternative for the carbon-carbon formation compared to classical enolate procedures.

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Figure 1. X-ray molecular structure of rhenium complex 5 (ellipsoids correspond to 30% probability. Hydrogen atoms except the NH-proton and solvent molecules are omitted for clarity. There are two molecules in the asymmetric unit of which one is shown).

More specifically, we optimised the reaction of acetophenone **6a** with benzyl alcohol **7a** to form 3-phenylpropiophenone (**8a**) (Table 1). By testing different bases (Table 1, entries 1-4), we found Cs_2CO_3 to be the most effective one for this transformation. Lowering the amount of catalyst led to a slight drop in yield while a higher amount does not improve the reaction (Table 1, entries 6-7).

Table 1. Rhenium-catalysed α -alkylation of acetophenone (6a) with benzyl alcohol (7a): Variation of reaction conditions.^[a]

0		<u>_ </u>	thenium catalyst	→	0
Ph	T HO F	Bas	e cat., solvent, T, t	Ph	Ph
6a	7a				8a
Entry	Re catalyst	Base	Solvent	T (°C)	Yield (%) ^[b]
1	Re complex 5	КОН	t-amyl alcohol	140	74
2	Re complex 5	KO <i>t</i> Bu	t-amyl alcohol	140	81
3	Re complex 5	K ₂ CO ₃	t-amyl alcohol	140	65
4	Re complex 5	Cs_2CO_3	t-amyl alcohol	140	84
5	Re(CO)₅Br	CS ₂ CO ₃	t-amyl alcohol	140	—
6 ^[c]	Re complex 5	Cs_2CO_3	t-amyl alcohol	140	81
7 ^[d]	Re complex 5	Cs_2CO_3	t-amyl alcohol	140	88
8	Re complex 5	Cs_2CO_3	1,4-dioxane	140	86
9	Re complex 5	Cs_2CO_3	toluene	140	85
10 ^[e]	Re complex 5	CS ₂ CO ₃	t-amyl alcohol	140	86
11 ^[f]	Re complex 5	CS ₂ CO ₃	t-amyl alcohol	140	86
12 ^[e]	Re complex 5	Cs_2CO_3	t-amyl alcohol	130	72
13 ^[e]	Re complex 5	Cs_2CO_3	t-amyl alcohol	150	75
14	Re complex 5	_	t-amyl alcohol	140	—
15 ^[e]	_	Cs_2CO_3	t-amyl alcohol	140	4
16 ^[e]	Ru complex 2	Cs_2CO_3	t-amyl alcohol	140	41
17 ^[e]	Fe complex 3	Cs_2CO_3	t-amyl alcohol	140	13
18 ^[e]	Mn complex 4	Cs_2CO_3	t-amyl alcohol	140	64

[a] Unless otherwise specified, all reactions were carried out with 6a (1 mmol), 7a (1.2 mmol), Re catalyst (0.02 mmol), base (0.05 mmol) in a solvent (1 mL) at indicated temperature for 22 h. [b] Isolated yields. [c] Catalyst loading: 1 mol%.
[d] Catalyst loading: 5 mol%. [e] Base: 2 mol%. [f] Base: 10 mol%.

Different solvents do not have a strong influence on the reaction (Table 1, entry 8-9). To our delight, it was possible to reduce the base loading to only 2 mol% without a significant decrease of the yield (Table 1, entry 10). This is an important improvement compared to most other catalysts known for

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such transformations. Advantageously, the reaction it takes places with only one equivalent of base with 1968 between the catalyst although the activation of the catalyst as well as the product formation require basic conditions. Finally, we chose the reaction of **6a** (1 mmol) with **7a** (1.2 mmol), rhenium complex **5** (2 mol%) and Cs₂CO₃ (2 mol%) as base in *tert*-amyl alcohol at 140°C as model system, giving the product **8a** in a good 86% yield.

 Table 2. Rhenium-catalysed reaction of ketones (6) with primary alcohols (7).^[a]



[a] Unless otherwise specified, all reactions were carried out with **6** (1 mmol), **7** (1.2 mmol), Re catalyst **5** (0.02 mmol), $C_{52}CO_3$ (0.02 mmol) in *t*-amyl alcohol (1 mL) at 140°C for 22 h. [b] Isolated yields.

With optimised conditions in hand, we compared the activity of our novel rhenium complex with previously described

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ruthenium-, iron- and manganese-pincer complexes 2-4 (Scheme 1).^{11g, 11h, 15d, 17} Reaction of acetophenone (6a) with benzyl alcohol (7a) catalyzed by 2 and 3 (2 mol%) under the same conditions provided 8a in lower yield (41 and 13%, respectively; Table 1, entries 16 and 17). Similarly, the manganese complex 4, recently reported to catalyse this alkylation of ketones,^{15d} gave the desired product in 64% yield (Table 1, entry 18). Comparing all the product yields in the presence of the different pincer complexes showed clearly the superiority of the rhenium system (86% yield). These results suggest that this catalyst is more reactive than analogous complexes bearing other metals at low concentration of base. Next, the versatility and generality of the method was studied (Table 2). Initially, differently 4-substituted acetophenones were tested in the rhenium-catalyzed reaction with benzyl synthesis alcohol. The of methoxy-, bromoand trifluoromethyl-substituted 3-phenylpropiophenones (8b-d) was possible in moderate to very good yields (53-91%, Table 2, entries 2-4). Moreover, heteroaryl derivatives such as 2acetylthiophene (6e) and 2-acetyl-N-methylpyrrol (6f) were applied affording the desired products in 88 and 40% yield, respectively (8e-f, Table 1, entries 5 and 6). Tetralone was also α -alkylated in secondary carbon to give compound 8g in a moderate 38% yield (Table 1, entry 7). On the other hand, structurally diverse alcohols 7 were assayed in the reaction with acetophenone (6a). Electron-rich 4-methoxybenzyl and electron-deficient 4-bromobenzyl alcohol were effectively used affording products 9b and 9c in good yields (80 and 72%, respectively, Table 1, entries 8 and 9). In addition, 1naphthalenemethanol and 2-thiophenemethanol were applied as alkylating agents giving the corresponding coupled products in 83 and 68% yields (Table 1, entries 10 and 11). Finally, we found that aliphatic alcohols such as *n*-butanol can also be used, obtaining the desired ketone in modest yield (Table 1, entry 12).



Scheme 2. Rhenium-catalysed reaction of sulfonamides (10) with primary alcohols (7). Unless otherwise specified, all reactions were carried out with 10 (1 mmol), 7 (1.2 mmol), Re catalyst 5 (0.02 mmol), Cs_2CO_3 (0.02 mmol) in *t*-amyl alcohol (1 mL) at 150°C for 22 h. Isolated yields. [a] 5 mol% Cs_2CO_3 .

After studying the rhenium-catalyzed *C*-alkylation of ketones, we focused our interest on *N*-alkylation processes using hydrogen autotransfer methodology, which had been described earlier.¹⁸ In this reaction, a new carbon-nitrogen

bond is formed using simple and easily available ical cohols in as electrophiles. In this line, we found that sulforhamides can be efficiently N-functionalized using the rhenium complex 5 as catalyst (Scheme 2).^{18d, 19} Applying the aforementioned developed conditions although increasing the reaction temperature to 150°C, p-toluenesulfonamide (10a) was Nalkylated with benzyl alcohol affording N-benzyl-ptoluenesulfonamide (11a) in 84% yield. Likewise, N-benzyltert-butylsulfonamide (11b) was obtained in 79% yield, whereas 2-thiophenesulfonamide (10c) was also functionalized, albeit in lower yield. In addition, higher base concentration was required in the latter case to get a modest 30% yield. Gratifyingly, different alcohols can be used as alkylating agents in this transformation. For example, 4methoxybenzyl alcohol and 2-thiophenemethanol were applied for the alkylation of *p*-toluenesulfonamide (10a) giving the desired products 11d and 11e in 94 and 69% yield, respectively (Scheme 2). Finally, the reaction of 10a with cyclohexanemethanol gave only traces of product 11f, even in presence of higher amounts of caesium carbonate.

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Scheme 3. Rhenium-catalysed reaction of ketones 12 with amines 13 and alcohol 14. Unless otherwise specified, all reactions were carried out with 6 (0.5 mmol), 13 (1.0 mmol), 14 (5.0 mmol), Re catalyst 5 (0.01 mmol), Cs_2CO_3 (0.01 mmol) in *t*-amyl alcohol (1 mL) at 150°C for 22 h. Isolated yields.

Besides the formation of new C-C and C-N bonds, one of the most relevant applications of the hydrogen autotransfer methodology is the synthesis of heterocycles. In this case, related dehydrogenative coupling processes have been also described to obtain unsaturated heterocyclic compounds. Here, in addition to water, hydrogen gas is obtained as byproduct. As an example, the multistep ruthenium-catalysed synthesis of pyrroles from ketones, amines and diols was recently developed by our research group.^{11c, 11d} With the aim of extending the scope of the novel cationic rhenium catalyst, we also assayed such a three-component reaction (Scheme 3). Indeed, the reaction of 1,2-diphenylethanone, ethylene glycol and phenethylamine provided N-phenethyl-2,3diphenylpyrrole (15a) in 66% yield. It is worth mentioning that two C-C and one C-N bonds are sequentially formed in this domino reaction. Using hexylamine allowed to obtain the corresponding N-hexyl-2,3-diphenylpyrrole (15b, 49% yield), while the reaction with cyclohexanone as ketone gave rise to 1-phenethyl-4,5,6,7-tetrahydroindole (15c) in modest yield.

In conclusion, we have synthesised a new cationic rhenium(I) pincer complex and demonstrated for the first time that such complexes can be conveniently used in several hydrogen

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autotransfer reactions. More specifically, the α -alkylation of ketones, the *N*-functionalization of sulfonamides with nonactivated alcohols and the synthesis of pyrroles by dehydrogenative coupling of ketones, diols and amines were developed. Notably, these transformations take place in good to moderate yields in presence of very low concentrations of base. Under such conditions, the new complex has proven to be more efficient than other comparable PNP pincer complexes.

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Notes and references

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- 1 The complex was independently reported very recently in the following publication: D. Wei, T. Roisnel, C. Darcel, E. Clot and J.-B. Sortais, *ChemCatChem*, 2017, **9**, 80-83.
- (a) G. Mao, B. Jia and C. Wang, Youji Huaxue, 2015, **35**, 284-293; (b) R. Hua and J.-L. Jiang, Curr. Org. Synth., 2007, **4**, 477-498; (c) M. C. Lipke, A. L. Liberman-Martin and T. D. Tilley, Angew. Chem. Int. Ed., 2016, DOI: 10.1002/anie.201605198.
- (a) T. J. Korstanje, E. F. de Waard, J. T. B. H. Jastrzebski and R. J. M. Klein Gebbink, ACS Catal., 2012, 2, 2173-2181; (b) T. J. Korstanje, J. T. B. H. Jastrzebski and R. J. M. Klein Gebbink, ChemSusChem, 2010, 3, 695-697.
- 4 J. J. Kennedy-Smith, K. A. Nolin, H. P. Gunterman and F. D. Toste, *J. Am. Chem. Soc.*, 2003, **125**, 4056-4057.
- 5 (a) J. J. Kennedy-Smith, L. A. Young and F. D. Toste, *Org. Lett.*, 2004, 6, 1325-1327; (b) M. R. Luzung and F. D. Toste, *J. Am. Chem. Soc.*, 2003, 125, 15760-15761; (c) Y. Kuninobu, H. Ueda and K. Takai, *Chem. Lett.*, 2008, 37, 878-879; (d) Y. Kuninobu, E. Ishii and K. Takai, *Angew. Chem. Int. Ed.*, 2007, 46, 3296-3299.
- 6 (a) I. Klopsch, M. Kinauer, M. Finger, C. Würtele and S. Schneider, *Angew. Chem. Int. Ed.*, 2016, 55, 4786-4789; (b) I. Klopsch, M. Finger, C. Würtele, B. Milde, D. B. Werz and S. Schneider, *J. Am. Chem. Soc.*, 2014, 136, 6881-6883; (c) M. J. Bezdek and P. J. Chirik, *Angew. Chem. Int. Ed.*, 2016, 55, 7892-7896.
- 7 (a) P. P. M. Schleker, R. Honeker, J. Klankermayer and W. Leitner, *ChemCatChem*, 2013, 5, 1762-1764; (b) H. Jin, J. Xie, C. Pan, Z. Zhu, Y. Cheng and C. Zhu, *ACS Catal.*, 2013, 3, 2195-2198.
- M. Vogt, A. Nerush, M. A. Iron, G. Leitus, Y. Diskin-Posner, L. J. W. Shimon, Y. Ben-David and D. Milstein, J. Am. Chem. Soc., 2013, 135, 17004-17018.
- 9 A. Abdukader, H. Jin, Y. Cheng and C. Zhu, *Tetrahedron Lett.*, 2014, **55**, 4172-4174.
- 10 (a) A. J. A. Watson and J. M. J. Williams, *Science*, 2010, 329, 635-636; (b) S. Bähn, S. Imm, L. Neubert, M. Zhang, H. Neumann and M. Beller, *ChemCatChem*, 2011, 3, 1853-1864; (c) C. Gunanathan and D. Milstein, *Science*, 2013, 341; (d) Y. Obora, *ACS Catal.*, 2014, 4, 3972-3981; (e) Q. Yang, Q. Wang and Z. Yu, *Chem. Soc. Rev.*, 2015, 44, 2305-2329; (f) F. Huang, Z. Liu and Z. Yu, *Angew. Chem. Int. Ed.*, 2016, 55, 862-875; (g) J. Leonard, A. J. Blacker, S. P. Marsden, M. F. Jones, K. R. Mulholland and R. Newton, *Org. Process Res. Dev.*, 2015, 19, 1400-1410.

- (a) S. Michlik and R. Kempe, *Nature Chem.*, 2013, **5**, 140-144;
 (b) D. Srimani, Y. Ben-David and D. Milstein. *Angewe Chemore* Online
 (b) D. Srimani, Y. Ben-David and D. Milstein. *Angewe Chemore Int. Ed.*, 2013, **52**, 4012-4015;
 (c) M. Zhang, X. Fang, H. Neumann and M. Beller, *J. Am. Chem. Soc.*, 2013, **135**, 11384-11388;
 (d) M. Zhang, H. Neumann and M. Beller, *Angew. Chem. Int. Ed.*, 2013, **52**, 597-601;
 (e) A. Monney, M. Peña-López and M. Beller, *Chimia*, 2014, **68**, 231-234;
 (f) M. Peña-López, H. Neumann and M. Beller, *Chem. Eur. J.*, 2014, **20**, 1818-1824;
 (g) M. Peña-López, H. Neumann and M. Beller, *Chem. ChemCatChem*, 2015, **7**, 865-871;
 (h) M. Peña-López, H. Neumann and M. Beller, *Angew. Chem. Int. Ed.*, 2016, **55**, 7826-7830.
- (a) W. Kuriyama, T. Matsumoto, O. Ogata, Y. Ino, K. Aoki, S. Tanaka, K. Ishida, T. Kobayashi, N. Sayo and T. Saito, Org. Process Res. Dev., 2012, 16, 166-171; (b) J. Neumann, C. Bornschein, H. Jiao, K. Junge and M. Beller, Eur. J. Org. Chem., 2015, 2015, 5944-5948; (c) A. Monney, E. Barsch, P. Sponholz, H. Junge, R. Ludwig and M. Beller, Chem. Commun., 2014, 50, 707-709; (d) M. Nielsen, H. Junge, A. Kammer and M. Beller, Angew. Chem. Int. Ed., 2012, 51, 5711-5713.
- E. Alberico, P. Sponholz, C. Cordes, M. Nielsen, H.-J. Drexler, W. Baumann, H. Junge and M. Beller, *Angew. Chem. Int. Ed.*, 2013, **52**, 14162-14166.
- 14 (a) G. Zhang, K. V. Vasudevan, B. L. Scott and S. K. Hanson, J. Am. Chem. Soc., 2013, 135, 8668-8681; (b) G. Zhang, B. L. Scott and S. K. Hanson, Angew. Chem. Int. Ed., 2012, 51, 12102-12106.
- (a) S. Elangovan, M. Garbe, H. Jiao, A. Spannenberg, K. Junge and M. Beller, *Angew. Chem. Int. Ed.*, 2016, **55**, 15364-15368; (b) S. Elangovan, C. Topf, S. Fischer, H. Jiao, A. Spannenberg, W. Baumann, R. Ludwig, K. Junge and M. Beller, *J. Am. Chem. Soc.*, 2016, **138**, 8809-8814; (c) A. Mukherjee, A. Nerush, G. Leitus, L. J. W. Shimon, Y. Ben-David, N.-A. Espinosa-Jalapa and D. Milstein, *J. Am. Chem. Soc.*, 2016, **138**, 4298-4301; (d) M. Peña-López, P. Piehl, S. Elangovan, H. Neumann and M. Beller, *Angew. Chem. Int. Ed.*, 2016, **55**, 14967-14971.
- 16 (a) R. Martínez, D. J. Ramón and M. Yus, *Tetrahedron*, 2006,
 62, 8988-9001; (b) S. Elangovan, J.-B. Sortais, M. Beller and C. Darcel, *Angew. Chem. Int. Ed.*, 2015, 54, 14483-14486.
- 17 N. J. Oldenhuis, V. M. Dong and Z. Guan, J. Am. Chem. Soc., 2014, **136**, 12548-12551.
- (a) S. Bähn, S. Imm, K. Mevius, L. Neubert, A. Tillack, J. M. J. Williams and M. Beller, *Chem. Eur. J.*, 2010, **16**, 3590-3593;
 (b) K.-I. Fujita, A. Komatsubara and R. Yamaguchi, *Tetrahedron*, 2009, **65**, 3624-3628;
 (c) C. Gunanathan and D. Milstein, *Angew. Chem. Int. Ed.*, 2008, **47**, 8661-8664;
 (d) M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson and J. M. J. Williams, *J. Am. Chem. Soc.*, 2009, **131**, 1766-1774;
 (e) A. Tillack, D. Hollmann, K. Mevius, D. Michalik, S. Bähn and M. Beller, *Eur. J. Org. Chem.*, 2008, **2008**, 4745-4750;
 (f) T. Yan, B. L. Feringa and K. Barta, *Nat. Commun.*, 2014, **5**, 5602.
- 19 (a) A. Martínez-Asencio, D. J. Ramón and M. Yus, *Tetrahedron Lett.*, 2010, **51**, 325-327; (b) A. Martínez-Asencio, D. J. Ramón and M. Yus, *Tetrahedron*, 2011, **67**, 3140-3149; (c) A. J. A. Watson, A. C. Maxwell and J. M. J. Williams, *J. Org. Chem.*, 2011, **76**, 2328-2331.