Check for updates

View Article Online
View Journal

ChemComm

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: A. H. Aboo, E. Bennett, M. Deeprose, C. M. Robertson, J. Iggo and J. Xiao, *Chem. Commun.*, 2018, DOI: 10.1039/C8CC06612D.

Volume 52 | Number 1 | 4 January 2016 | Pages 1–216

ChemComm

Chemical Communications
www.rsc.org/chemcomm

ISSN 1359-7345

COMMUNICATION
Marilyn M. Olmstead, Alan L. Balch, Josep M. Poblet, Luis Echegoyen *et al.*
Reactivity differences of $Sc_3N@C_{2n}$ (2*n* = 68 and 80). Synthesis of the first methanofullerene derivatives of $Sc_3N@D_{5h}$-C_{80}

175 YEARS

This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the author guidelines.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard Terms & Conditions and the ethical guidelines, outlined in our author and reviewer resource centre, still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.

rsc.li/chemcomm

View Article Online
DOI: 10.1039/C8CC06612D

Journal Name

COMMUNICATION

Methanol as Hydrogen Source: Transfer Hydrogenation of Aromatic Aldehydes with a Rhodacycle

Ahmed H. Aboo, Elliot L. Bennett, Mark Deeprose, Craig M. Robertson, Jonathan A. Iggo and Jianliang Xiao*

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

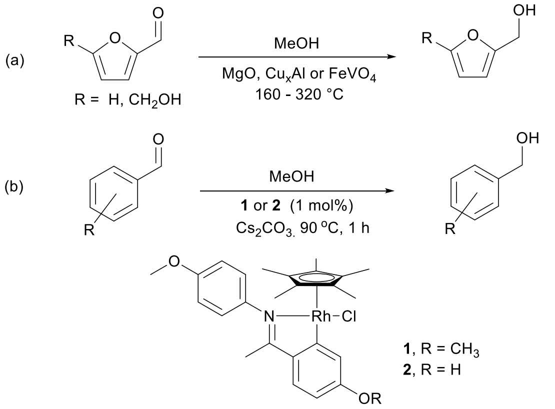
www.rsc.org/

A cyclometalated rhodium complex has been shown to perform highly selective and efficient reduction of aldehydes, deriving the hydrogen from methanol. With methanol as both the solvent and hydrogen donor under mild conditions and an open atmosphere, a wide range of aromatic aldehydes were reduced to the corresponding alcohols, without affecting other functional groups.

Reduction of carbonyl compounds is one of the most fundamental synthetic transformations in both the chemical and pharmaceutical industries.[1,2] Often, the reaction is performed using economic but highly hazardous hydrogen gas, or alternatively using stoichiometric amounts of the reducing agent $NaBH_4$.[1,3] Carbonyls such as ketones and aldehydes can also be readily reduced via transfer hydrogenation (TH), where hydrogen sources other than H_2 are used. Whilst a number of organic compounds have been used as hydrogen equivalent, isopropanol and formic acid are the most widely used for the TH of carbonyl and related functionalities.[4,5] In sharp contrast, methanol has only been sporadically explored as hydrogen source in such TH reactions.[5]

Methanol is considered one of the most important sources of energy for the future, due to its excellent hydrogen carrier ability (about 12.5 wt% hydrogen).[6,7] With a global production of ca 110 million metric tonnes a year,[8] methanol is of low cost and abundantly available. It is easy to handle and in fact has been referred to as "the safest source of hydrogen".[9] However, in comparison with iPrOH, MeOH is thermodynamically more difficult to undergo dehydrogenation to afford H_2 or metal hydride for TH.[10] In addition, its use in TH can be limited by its poisoning of catalysts through carbon monoxide generated from decarbonylation. Consequently, its use in TH reactions has been much less documented. Examples are known of the TH of C=C double bonds in α,β-unsaturated enones,[11,12] alkenes and alkynes,[13] and ketones,[14] with ruthenium, rhodium, iridium or nickel complexes as catalysts. With these catalysts, high temperatures (120-180 °C) are generally necessary to drive the TH.

Methanol has been even less explored as a hydrogen source for the TH of aldehydes. Apart from the challenges mentioned, the product of this transformation, a primary alcohol, is expected to be dehydrogenated more favourably than MeOH. Encouraging for biomass valorisation, the last a few years have witnessed methanol being explored as a hydrogen donor for the hydrogenation of furfurals with heterogeneous catalysts, albeit at relatively high temperatures (Scheme 1).[15–17] For instance, MgO was shown to catalyse the reduction of furfural at 160 °C via a Meerwein–Ponndorf–Verley pathway. However, under such conditions the yield of the TH of benzaldehyde was low.[15]



Scheme 1 TH of aldehydes using MeOH as the source of hydrogen, showing literature examples (a) and this work (b).

Herein, we report that the cyclometalated rhodium complexes shown in Scheme 1, particularly **2**, readily allow for the chemoselective TH of aromatic aldehydes under mild conditions, with MeOH as both the hydrogen donor and solvent. In recent years, we have disclosed a series of cyclometalated iridium-imino complexes, or iridacycles, which catalyse a wide

Department of Chemistry, University of Liverpool, Liverpool, L69 7ZD, UK.
E-mail: jxiao@liv.ac.uk; Fax: +44 (0)151-7943588

† Footnotes relating to the title and/or authors should appear here.

Electronic Supplementary Information (ESI) available: Experimental procedures and compound characterization data. See DOI: 10.1039/x0xx00000x

View Article Online
DOI: 10.1039/C8CC06612D

range of reactions including TH of carbonyls with formic acid as the hydrogen donor.[18–20] The promising performance of these complexes along with their air and moisture stability, combined with their facile preparation, led us to explore the efficacy of the analogous rhodacycles towards TH reactions. The rhodacycles **1** and **2** were prepared similarly to the related iridacycles (see SI for details). The structure of **2** was confirmed by X-ray diffraction (Figure 1. See SI for more details including CCDC).

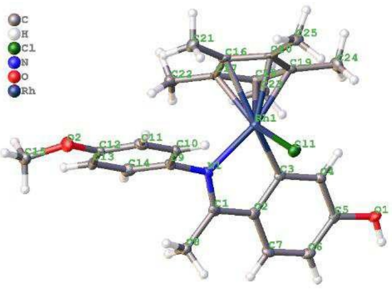
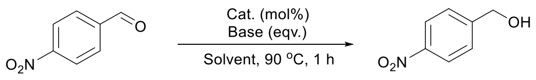


Figure 1 Single crystal X-ray structure of the rhodium complex **2**. Selected bond distances (Å): Rh1-C3 2.019(4); Rh1-N1 2.102(3); Rh1-Cl1 2.416(10); average Rh1-Cp* 2.199(9). Selected bond angles (°): Cl1-Rh1-N1 89.66(9); Cl1-Rh1-C3 87.02(5); N1-Rh1-C3 78.71(15).

We initially explored the possibility of catalysing the TH of 4-nitrobenzaldehyde using MeOH with rhodacycle **1** (Table 1). As can be seen, the TH of 4-nitrobenzaldehyde proceeded only insignificantly in refluxing MeOH (Entry 1). However, upon addition of a base, a significantly higher conversion to the corresponding benzyl alcohol was observed, with Cs_2CO_3 being most effective (Entries 2-7). Thus, using catalyst **1** in refluxing MeOH, the aldehyde was reduced in 60% conversion in the presence of 1 equivalent of Cs_2CO_3 in 1 h reaction time (Entry 7).

Table 1. Optimising reaction conditions for the TH of aldehydes



Entry[a]	Catalyst	Cat. (mol%)	Solvent	Base (Eqv.)	Conversion (%)[b]
1	**1**	1	MeOH	-	6
2	**1**	1	MeOH	$NaHCO_3$ (1)	40
3	**1**	1	MeOH	Na_2CO_3 (1)	42
4	**1**	1	MeOH	NaOAc (1)	43
5	**1**	1	MeOH	NaOH (1)	46
6	**1**	1	MeOH	K_2CO_3 (1)	50
7	**1**	1	MeOH	Cs_2CO_3 (1)	60
8	**2**	1	MeOH	Cs_2CO_3 (1)	100
9	**2**	1	MeOH	Cs_2CO_3 (0.5)	100
10	**2**	1	MeOH	Cs_2CO_3 (0.2)	83
11	**2**	0.5	MeOH	Cs_2CO_3 (0.5)	70
12	**2**	1	EtOH	Cs_2CO_3 (0.5)	20

[a] Reaction conditions: aldehyde (0.25 mmol), catalyst and base in solvent (1.5 mL), stirred at 90 °C, 1 h. [b] Determined by ^1H NMR.

The hydroxy-functionalised rhodacycle **2** is more efficient. Under these same reaction conditions, a full conversion of the aldehyde was observed, with no need for an inert gas atmosphere (Entry 8). Reducing the amount of base to 0.5 equivalent showed no visible effect under the conditions used. However, further lowering adversely affected the TH (Entry 10), and a similar observation was made when the catalyst loading was reduced (Entry 11).[21] Surprisingly, the catalyst appears to be more effective towards transferring hydrogen from MeOH to the aldehyde than from the thermodynamically more favourable EtOH (Entry 12).[22] The lower hydrogen donating ability of EtOH is surprising and the reason is not immediately clear. However, introduction of the EtOH dehydrogenation product acetaldehyde (14 μL, one equivalent) inhibited considerably the TH in MeOH (50% instead of 100% conversion in 1 h), indicating MeCHO may exert some poisoning effect on **2**.

Using catalyst **2** under the optimised conditions (Entry 9, Table 1), a wide variety of aromatic aldehydes were reduced with MeOH to the corresponding benzyl alcohols in high yields in the open air (Table 2). As can be seen, the substituent on the aryl ring, be it electron donating or withdrawing, appears to have an insignificant effect on the yields during the 1 h reaction. Of practical significance is that various substituents, including nitro, halides and acetyls, were tolerated, and the yield of the product does not vary considerably with the position of substitution, e.g. *para* vs *ortho* (Entries 1 & 3; 13 & 15; 17 & 19). Heterocyclic aldehydes, both electron rich and poor, are also viable substrates (Entries 4, 5, 8, 9, 34 & 35). Similarly, aliphatic aldehydes (Entries 36 & 37) and unsaturated aldehydes (Entries 38, 39 & 40) were reduced with high yields. Notably, the C=C bonds in the latter were reduced as well, and the platform molecule hydroxymethylfurfural was readily reduced with methanol under such mild conditions.

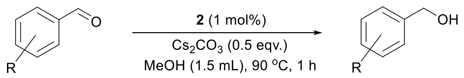
To demonstrate the application potential of this catalysed TH, the model reaction shown in Table 1 was scaled up, using 1 g of 4-nitrobenzaldehyde. The substrate was reduced efficiently to give the corresponding alcohol in 87% isolated yield.

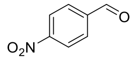
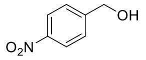
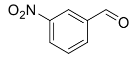
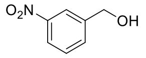
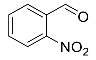
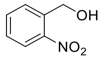
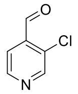
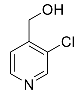
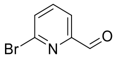
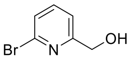
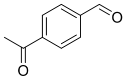
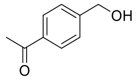
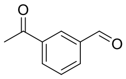
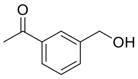
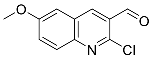
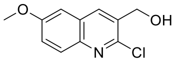
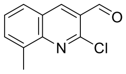
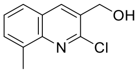
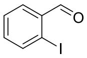
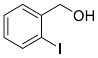
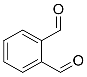
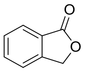
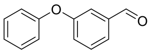
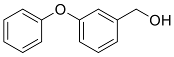
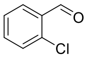
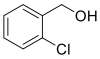
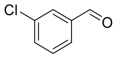
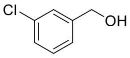
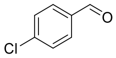
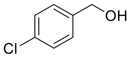
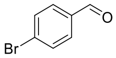
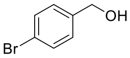
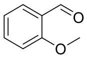
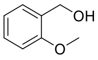
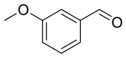
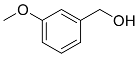
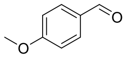
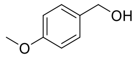
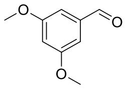
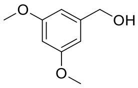
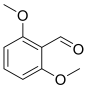
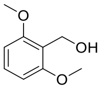
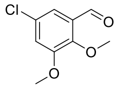
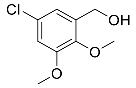
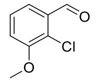
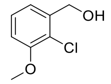
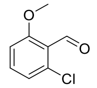
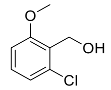
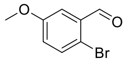
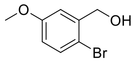
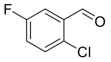
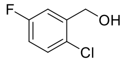
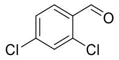
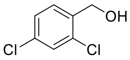
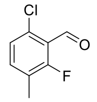
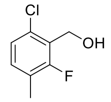
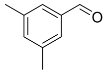
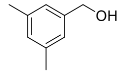
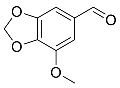
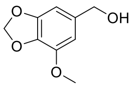
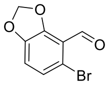
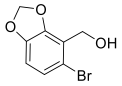
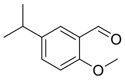
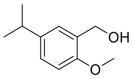
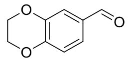
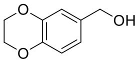
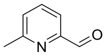
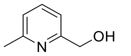
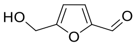
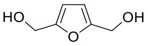
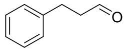
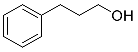
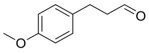
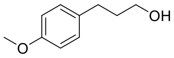
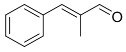
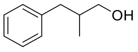
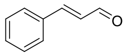
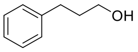
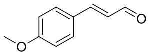
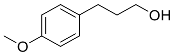
On the basis of our previous study of iridacycle-catalysed TH with formic acid and related literature,[23,24] a proposed catalytic cycle for the TH of aldehydes with MeOH is shown in Scheme 2. In the presence of the base, methanol substitution of the chloride in **2** leads to the formation of the methoxide complex **A**,[25] from which β-hydrogen elimination takes place presumably via the transition state shown, affording the Rh-H species **B** while releasing formaldehyde as a co-product. Hydride transfer from **B** to the aldehyde substrate leads to the alkoxide **C**, a reaction similar to the reverse reaction of methanol dehydrogenation, i.e. **B** plus formaldehyde to give **A**. Judging from the distance of chloride to the hydroxyl oxygen (Cl1…O1: 5.71 Å) in complex **2** (Figure 1), it is unlikely that the hydroxyl group in the ligand could participate in the transition state of hydride formation or transfer via hydrogen bonding, although it may become possible if MeOH is involved.[26]

To gain support for the suggested mechanistic pathway, dimedone (5,5-dimethyl-1,3-cyclohexanedione) was treated with MeOH under the same optimised conditions, but without an aldehyde substrate. The formation of the expected condensation product confirms formaldehyde being produced during the TH (Eq. 1; also see SI).[27,28]

View Article Online
DOI: 10.1039/C8CC06612D

Table 2. Transfer hydrogenation of aldehydes under optimised conditions

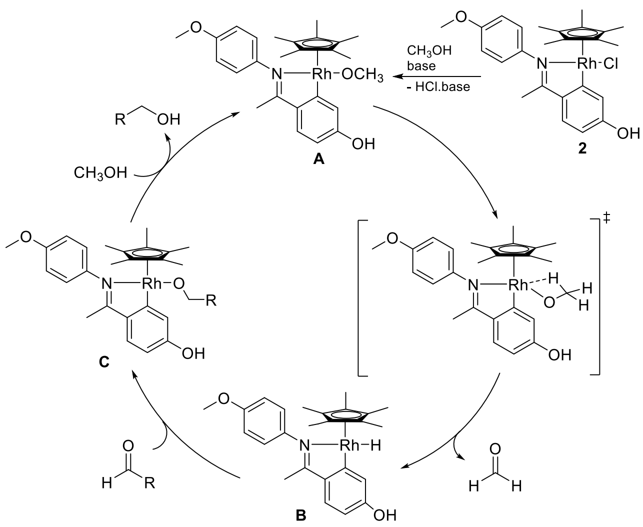


Entry[a]	Substrate	Product	Yield[b] %
1			90
2			85
3			91
4			85
5			82
6			83
7			88
8			81
9			87
10			85
11			73
12			76
13			87
14			89
15			79
16			66
17			82
18			83
19			71
20			85
21			78
22			82
23			84
24			74
25			63
26			80
27			88
28			73
29			66
30			74
31			73
32			79
33			70
34			61
35			82
36			79
37			82
38			83
39			89
40			85

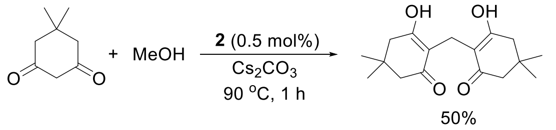
[a] Reaction conditions: aldehyde (0.25 mmol), catalyst **2** (0.0025 mmol), Cs_2CO_3 (0.125 mmol) and MeOH (1.5 mL), stirred at 90 °C, 1 h. [b] Yield of isolated product.

To demonstrate that methanol was the primary and only source of hydrogen during the TH, the reaction was repeated with deuterated methanol (CD_3OD). As shown by ^1H NMR (see SI), the benzyl alcohol contained 90% deuterium (relative to full mono-deuteration) at the benzylic position, showing that methanol acts as the hydrogen donor, as illustrated in Eq. 2.

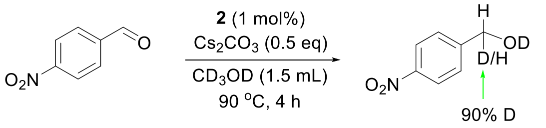
View Article Online
DOI: 10.1039/C8CC06612D



Scheme 2 Proposed catalytic cycle for the transfer hydrogenation of aldehydes.



(1)



(2)

In conclusion, we have developed, to the best of our knowledge, the first examples of high-yielding TH of various aldehydes using methanol as both the hydrogen source and solvent under moderate conditions, necessitating no inert atmosphere or special equipment. The rhodium catalyst showed high chemoselectivity towards the reduction of aldehydes in the presence of different functional groups, allowing further transformations to be performed.

We thank The Higher Committee for Education Development in Iraq for financial support.

Conflicts of interest

There are no conflicts of interest to declare.

References

1 R. A. W. Johnstone, A. H. Wilby and I. D. Entwistle, *Chem. Rev.*, 1985, **85**, 129–170.

2 J. Magano and J. R. Dunetz, *Org. Process Res. Dev.*, 2012, **16**, 1156–1184.

3 N. M. Yoon, *Pure Appl. Chem.*, 1996, **68**, 843–848.

4 (a) G. Zassinovich, G. Mestroni and S. Gladiali, *Chem. Rev.*, 1992, **92**, 1051–1069. (b) T. Ikariya and A. J. Blacker, *Acc. Chem. Res.*, 2007, **40**, 1300–1308. (c) T. C. Johnson, W. G. Totty and M. Wills, *Org. Lett.*, 2012, **14**, 5230–5233. (d) R. J. Wakeham, J. A. Morris and J. M. J. Williams, *ChemCatChem*, 2015, **7**, 4039–4041. (e) R. Wang, Y. Tang, M. Xu, C. Meng and F. Li, *J. Org. Chem.*, 2018, **83**, 2274–2281. (f) J. Song, Z. Xue, C. Xie, H. Wu, S. Liu, L. Zhang and B. Han, *ChemCatChem*, 2018, **10**, 725–730.

5 D. Wang and D. Astruc, *Chem. Rev.*, 2015, **115**, 6621–6686.

6 C. E. Taylor, B. H. Howard and C. R. Myers, *Ind. Eng. Chem. Res.*, 2007, **46**, 8906–8909.

7 Y. Shen, Y. Zhan, S. Li, F. Ning, Y. Du, Y. Huang, T. He and X. Zhou, *Chem. Sci.*, 2017, **8**, 7498–7504.

8 The Methanol Industry|Methanol Institute, http://www.methanol.org/the-methanol-industry/, (accessed July 2018).

9 E. Śmigiera, J. Kijeński, O. Osawaru, A. Zgudka and A. R. Migdał, *Chemik*, 2013, **67**, 502–513.

10 R. H. Crabtree, *Chem. Rev.*, 2017, **117**, 9228–9246.

11 T. A. Smith and P. M. Maitlis, *J. Organomet. Chem.*, 1985, **289**, 385–395.

12 N. Castellanos-Blanco, M. Flores-Alamo and J. J. García, *Organometallics*, 2012, **31**, 680–686.

13 K. Tani, A. Iseki and T. Yamagata, *Chem. Commun.*, 1999, **0**, 1821–1822.

14 J. Campos, L. S. Sharninghausen, M. G. Manas and R. H. Crabtree, *Inorg. Chem.*, 2015, **54**, 5079–5084.

15 T. Pasini, A. Lolli, S. Albonetti, F. Cavani and M. Mella, *J. Catal.*, 2014, **317**, 206–219.

16 J. Zhang and J. Chen, *ACS Sustain. Chem. Eng.*, 2017, **5**, 5982–5993.

17 L. Grazia, D. Bonincontro, A. Lolli, T. Tabanelli, C. Lucarelli, S. Albonetti and F. Cavani, *Green Chem.*, 2017, **19**, 4412–4422.

18 C. Wang and J. Xiao, *Chem. Commun.*, 2017, **53**, 3399–3411.

19 Y.-M. He and Q.-H. Fan, *ChemCatChem*, 2015, **7**, 398–400.

20 D. Talwar, X. Wu, O. Saidi, N. P. Salguero and J. Xiao, *Chem. Eur. J.*, 2014, **20**, 12835–12842.

21 Full conversion was also achieved when using K_2CO_3 as the base. However, the reduction with Cs_2CO_3 was slightly faster, e.g. 93% conversion with the latter vs 85% with the former in 0.5 h under otherwise the same conditions as in Table 1 (Entry 9).

22 G. E. Dobereiner and R. H. Crabtree, *Chem. Rev.*, 2010, **110**, 681–703.

23 H.-Y. T. Chen, C. Wang, X. Wu, X. Jiang, C. R. A. Catlow and J. Xiao, *Chem. Eur. J.*, 2015, **21**, 16564–16577.

24 R. H. Perry, K. R. Brownell, K. Chingin, T. J. Cahill, R. M. Waymouth and R. N. Zare, *Proc. Natl. Acad. Sci.*, 2012, **109**, 2246–2250.

25 J. Cheng, M. Zhu, C. Wang, J. Li, X. Jiang, Y. Wei, W. Tang, D. Xue and J. Xiao, *Chem. Sci.*, 2016, **7**, 4428–4434.

26 G. Zhou, A. H. Aboo, C. M. Robertson, R. Liu, Z. Li, K. Luzyanin, N. G. Berry, W. Chen and J. Xiao, *ACS Catal.*, 2018, **8**, 8020–8026.

27 M. de S. Ferreira and J. D. Figueroa-Villar, *J. Braz. Chem. Soc.*, 2014, **25**, 935–946.

28 Under the catalytic conditions (Entry 9, Table 1) but in the presence of one equivalent of dimedone, the conversion of 4-nitrobenzaldehyde was reduced to 80%. The condensation product (Eq 1) was again formed, albeit in *ca* 20% yield, indicating the formation of HCHO during the catalysis.