



AperTO - Archivio Istituzionale Open Access dell'Università di Torino

Chemoselective Transfer Hydrogenation of Aldehydes with HCOONH4 Catalyzed by **RuCl(CNNPh)(PP)** Pincer Complexes

This is the author's manuscript

Original Citation:

Availability:

This version is available http://hdl.handle.net/2318/1693291 since 2019-02-19T10:35:20Z

Published version:

DOI:10.1002/cctc.201600892

Terms of use:

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

Revised

ChemCatChem

Chemoselective Transfer Hydrogenation of Aldehydes with HCOONH₄ Catalyzed by RuCl(CNN^{Ph})(PP) Pincer Complexes

Salvatore Baldino,^{*[a]} Sarah Facchetti,^[b] Hans Günter Nedden,^[b] Antonio Zanotti-Gerosa,^[b] and Walter Baratta^{*[a]}

Abstract: Aldehydes are chemoselectively reduced to primary alcohols using HCOONH₄ as hydrogen donor, via transfer hydrogenation catalyzed by benzo[h]quinoline pincer complexes RuCl(CNN^{Ph})(PP) at S/C = 2000-20000. This practical reaction performed with aldehydes of commercial grade purity in a water / toluene biphasic system affords alcohols without formation of condensation or amination side products.

Keywords: aldehydes • ligands • formate • hydrogen transfer • ruthenium

The search of well-designed and productive catalysts for the selective hydrogenation^[1] and transfer hvdrogenation (TH)^[2] of aldehvdes to primary alcohols is a fundamental reaction of broad application in the industry.^[3] As matter of fact, this catalytic route promoted by transition metals, results in a lower environmental impact and an easier work-up with respect to the classical approach entailing NaBH₄, LiAlH₄, boranes and Al alkoxides as reducing agents.^[4] Among the transition metals used in catalytic homogeneous reductions, ruthenium, which is cheaper with respect to rhodium and iridium, has played a crucial role leading to a number of efficient catalysts for the aldehyde reduction using H₂ under pressure^[5] or 2-propanol.^[5e, 6] While the TH with 2-propanol is an equilibrium reaction that, on scale, requires the removal of acetone to drive the reaction to completion, the use of formic acid derivatives as hydrogen donors have the advantage of generating CO₂, which is released from the reaction solution, driving the reaction and minimizing the reversibility problems.^[7] Alkali formates HCOOM (M = Na, K) were employed in TH of aldehydes $RuCl_2(PPh_3)_3$,^[8] with $[RuCl_2(mtppms)_2]_2$ = sodium 3-(mtppms diphenylphosphinobenzenesulfonate),^[9] CpRuCl(PPh₃)(PN) (PN diphenyl-2-= pyridylphosphine),^[10] RuCl₂(PTA)₄ (PTA = 1,3,5-triaza-7-phosphaadamantane)^[11] and RuCl₂(PO)₂ (PO=(2-methoxyethyl)diphenylphosphine)^[12] catalysts at S/C \leq 1000, whereas the HCOOH-NEt₃ system has been used with [RuCl₂(benzene)]₂, but at a low S/C = 50.^[13]

Ammonium formate is a cheap and readily accessible reducing agent widely employed in organic transformations. In addition to the Leuckart-Wallach reductive amination of carbonyl compounds,^[14] the metal catalyzed version reaction has been reported by Kitamura^[15] and Talwar^[16] with Cp* Rh(III) and Ir(III) complexes, respectively, whereas Kadyrov described the asymmetric version with RuCl₂[(R)-tol-BINAP].^[17] HCOONH₄ has also been widely used in Pd/C-catalyzed conversion of carbonyl compounds into alkanes,^[18] nitro derivatives to amines^[19] and in the hydrodehalogenation of aromatic chlorides.^[20]

For the employment of HCOONH₄ in the TH of carbonyl compounds, recently Grainger^[21] described the use of Wills' tethered Ru complexes in the reduction of ketones, while Nie^[22] observed the concomitant TH and reductive amination of acetophenone with RuCl₂(PPh₃)₃. Curiously, the TH of aldehydes with HCOONH₄ has only been described by Iyer in the reduction of 4-methoxybenzaldehyde and *trans*-cinnamaldehyde catalyzed by Ni[P(OPh)₃]₄ at 110 °C, but at a very low S/C = 30.^[23] Since the catalytically active metal-hydride species^[24] are generated in basic conditions, where aldehydes, more than ketones, may undergo several side reactions (Claisen-Tishchenko,^[25] Cannizzaro^[26] and aldol condensation reactions^[27]), the selective aldehyde reduction remains a delicate point. Recently, we described the preparation of the benzo[*h*]quinoline pincer complexes RuCl(CNN^{Ph})(PP) **1-3** which are active catalysts in the hydrogenation and TH with 2-propanol of ketones^[28] and aldehydes^[29] (Figure 1).



Figure 1. Benzo[*h*]quinoline pincer ruthenium complexes 1-3.

In the TH of aldehydes in 2-propanol the reaction was carried out at low substrate concentration (0.1 M) and under weak basic conditions to inhibit the condensation reaction with the formed acetone, a side reaction which strongly depends on the type of the aldehyde.^[29]

We report here the straightforward and chemoselective TH of aldehydes of commercialgrade purity to alcohols using ammonium formate as hydrogen donor in a water / toluene biphasic system, catalyzed by the pincer complexes **1-3** at S/C 2000-20000. Employment of HCOONH₄ with **1-3** allowed the clean reduction of aliphatic, conjugated and functionalized aromatic and heteroaromatic aldehydes, without formation of condensation and amination side products. Reaction of benzaldehyde **a** of commercial grade purity (assay 99%) in toluene (0.5 M) with 2 eq. of HCOONH₄ in water (1 M) and in the presence of complex **1** (S/C = 5000) affords selectively benzyl alcohol (76%) in 22 h at 90 °C (Table 1, entry 1), without formation of products of the



Scheme 1. TH of aldehydes with HCOONH₄ catalyzed by 1-3.

Leuckart-Wallach reductive amination (Scheme 1).

Complex **2** shows higher activity than **1** with 98 and 97% of alcohol in 9 and 15 h with S/C = 2000 and 5000, respectively (entries 2, 3). Complete conversion was also achieved at higher substrate concentration (1 M) with 2 and 4 eq. of formate (entries 4, 5). In addition, chemoselective TH of **a** to alcohol (96%) was attained with HCOONH₄ using a 2 M of substrate and at high S/C = 20000 in 48 h (entry 6). It is worth noting that performing the reaction at high aldehyde concentration is of

particular advantage for industrial applications and that the TH with 2-propanol requires lower aldehyde concentration (0.1 M) to avoid coupling reactions.^[29]

Entry	Cat.	S/C	[S] ^[a]	[DH ₂] ^[b]	$DH_2(eq.)$	Time (h)	Conv. (%) ^[c]
1	1	5000	0.5	1 ^[d]	2	16	60
						22	76
2	2	2000	0.5	1 ^[d]	2	9	98
3	2	5000	0.5	1 ^[d]	2	15	97
4	2	5000	1	1 ^[d]	2	15	85
						24	96
5	2	5000	1	1 ^[d]	4	15	97
6	2	20000	2	2 ^[d]	4	15	58
						22	89
						48	96
7	3	5000	0.5	1 ^[d]	2	16	96
8	3	10000	0.5	1 ^[d]	2	20	86
						40	96
9	none		2	2 ^[d]	4	24	11
10	2	2000	0.5	2 ^[e]	4 ^[e]	24	50
11	2	5000	4.5	6.5 ^[f]	1.5 ^[f]	24	48
12	2	2000	0.5	2 ^[g]	4 ^[g]	14	2

Table 1. TH of benzaldehyde **a** to benzyl alcohol catalyzed by **1-3** using HCOONH₄, HCOONa, and HCOOH / NEt₃ as hydrogen donors (DH₂) in water / toluene at 90 °C.

[a] Substrate concentration in toluene. [b] DH_2 concentration in water. [c] The conversion and the purity were determined by GC and NMR analyses. [d] HCOONH₄. [e] HCOOH / NEt₃ = 1 / 1. [f] Benzaldehyde was reacted in neat HCOOH / NEt₃ = 5 / 2. [g] HCOONa.

Complex **3** gave nearly quantitative reduction of **a** in 16 and 40 h with S/C = 5000 and 10000 (entries 7, 8). In absence of ruthenium catalyst, the reaction of **a** with 4 eq. of HCOONH₄ afforded 11% of alcohol after 24 h (entry 9), indicating that under these conditions **a** is reduced by HCOONH₄ although at much lower rate with respect to the catalytic pathway. The use of HCOOH / NEt₃ = 5 / 2 and 1 / 1 mixtures (1.5 and 4 eq. of formic acid, respectively) in the presence of **2** at S/C = 5000 and 2000, gave 48-50% of alcohol after 24 h (entries 10, 11), whereas with HCOONa the conversion was 2% in 14 h (entry 12). These results indicate that the inexpensive HCOONH₄ can be employed as practical hydrogen donor for the selective reduction of **a** catalyzed by the robust pincer complexes **1-3**. Preliminary experiments with other media different than toluene / water

system, such as methanol / water mixtures or pure methanol led to poor conversion and poor selectivity, due to the formation of aminative condensation / reduction side-products.

To broaden the scope of the aldehyde TH with HCOONH₄, aromatic, aliphatic, conjugated and heteroaromatic aldehydes were studied with complex **2**. Reduction of 4-bromobenzaldehyde **b** (2 M in toluene) with 4 eq. of HCOONH₄ afforded 97 and 98% of the corresponding alcohol in 10 and 24 h using **2** at S/C of 2000 and 10000, respectively (entries 1, 2, Table 2), whereas 75% al alcohol was obtained at S/C = 20000 (entry 3).

Table 2. TH of aldehydes (2 M in toluene) with HCOONH₄ (4 eq., 2 M in water) catalyzed by complex **2** in toluene / water 90 °C.

Entry	Aldehyde	S/C	Time (h)	Conv. (%) ^[a]
1	b	2000	10	97
2	b	10000	24	98
3	b	20000	48	75
4	c	5000	15	96
5	d	2000	6	99, 87 ^[b]
6	e	2000	3.5	99, 70 ^[b]
7	f	2000	10	98 ^[c]
8	f	2000	4	99 ^[d]
9	g	10000	20	98
10	h	10000	24	97 ^[e]
11	i	2000	10	$97^{[f]}$
12	i	5000	48	97 ^[g]
13	j	5000	20	98 ^[e] , 88 ^[b]
14	k	5000	8	95
15	1	5000	18	99 ^[e]

[a] The conversion and the purity were determined by GC and ¹H-NMR analyses. [b] Isolated yield. [c] Only the double-reduction product was detected. [d] With 1.5 eq. of HCOONH₄ a mixture of 4-(hydroxymethyl)benzaldehyde / 1,4-phenylenedimethanol in a 9 / 1 ratio was observed. [e] [HCOONH₄] = 4 M in water. [f] 91% of *trans*-cinnamol and 6% of the saturated alcohol 3phenylpropan-1-ol. [g] 85% of *trans*-cinnamol and 12% of 3-phenylpropan-1-ol. The electron-rich 4-(dimethylamino)benzaldehyde \mathbf{c} was efficiently reduced to alcohol (96%) with S/2 = 5000 in 15 h (entry 4). Conversely, the TH of the electron poor 4-nitrobenzaldehyde d and 4cyanobenzaldehyde e afforded quantitative formation of the corresponding alcohols, isolated in 87 and 70% yield at S/2 = 2000, without reduction of the NO₂ and CN functionalities or deactivation of the catalyst, i.e. by coordination at the metal center (entries 5, 6). Double TH was observed for 4formylbenzaldeyde **f** leading to quantitative formation of 1,4-phenylenedimethanol in 10 h (entry 7). Interestingly, with a lower amount of HCOONH₄ (1.5 eq.) the TH of **f** afforded the mono reduction product 4-(hydroxymethyl)benzaldehyde / 1,4-phenylenedimethanol in a 9 / 1 molar ratio, respectively (entry 8). Also the heteroaromatic 2-formylfuran g and 2-formylthiophene h were selectively reduced to alcohols 98 and 97% at S/2 = 10000 in 20 and 24 h, respectively (entries 9, 10). Unsaturated *trans*-cinnamaldehyde i gave almost complete conversion (97%) to *trans*-cinnamol (91%) and 3-phenylpropan-1-ol (6%) at S/2 = 2000 in 10 h, whereas at lower loading (S/2 = 5000), formation of 85% of trans-cinnamol and 12% of the saturated alcohol was observed in 48 h, indicating that higher selectivity is achieved at higher catalyst loading and in shorter reaction time (entries 11, 12). On the other hand, $trans-\alpha$ -methylcinnamaldehyde **j** was chemoselectively transformed into *trans*- α -methylcinnamol, and isolated in 88% yield at S/2 = 5000 in 20 h, with no reduction of the C=C double bond (entry 13). In addition, the aliphatic aldehydes hexanal k and *rac*-citronellal I were reduced to 1-hexanol and *rac*-citronellol 95 and 99%, with 2 at S/C = 5000(entries 14, 15). By contrast, with 2 (S/C = 2000) the TH of vanillin and pyrrole-2-carboxaldehyde, displaying relatively acidic hydrogens, failed, leading to the unreacted starting material. It is worth noting that cis-RuCl₂(ampy)(dppf) (S/C = 2000), which is a complex related to **3** and efficiently catalyzes the TH of aldehydes with 2-propanol,^[29] has been proven to be significantly less active in the TH of benzaldehyde (18 % conv., 15 h) with HCOONH₄ (4 eq.). All spectral data were in the agreement with the literature, as all the obtained compounds are known.

As regards the mechanism, it is likely that the pincer complex $RuCl(CNN^{Ph})(PP)$ in the presence of HCOONH₄ leads to the formate complex $Ru(O_2CH)(CNN^{Ph})(PP)$, with formation of the hydride $RuH(CNN^{Ph})(PP)^{[30]}$ by elimination of CO₂. The subsequent reaction with the RCHO substrate gives the alkoxide $Ru(OCH_2R)(CNN^{Ph})(PP)$ which is protonated by HCOONH₄, affording the alcohol product, ammonia and the formate complex, closing the cycle, as inferred from TCD-gas analysis, showing that CO₂ and NH₃ are evolved during the reaction. Since HCOONH₄ displays better performances with respect to HCOONa and the HCOOH / NEt₃ system, it is reasonable that the elimination of NH₃ during the catalysis has positive effects, shifting the reaction toward the alcohol product, preventing a significant increase of the OH⁻ concentration, thus disfavoring the base catalyzed aldehyde side reactions. As a matter of fact, control experiments carried out during

the catalytic reduction of benzaldehyde and *rac*-citronellal showed that the pH values of the aqueous phase were in the range 7.5-8.5.

In conclusion, simple and functionalized aldehydes have been chemoselectively reduced to primary alcohols using HCOONH₄ as hydrogen donor with the benzo[*h*]quinoline pincer complexes RuCl(CNN^{Ph})(PP) at S/C up to 20000. This straightforward reaction carried out with aldehydes of commercial grade purity at high substrate concentration (2 M) in a water / toluene biphasic system gives alcohols without formation of condensation or amination side products. These reaction conditions are experimentally simple and provide significant options for industrial applications with respect to the use of 2-propanol as reducing agent. Further studies on ruthenium catalyzed transfer hydrogenation reactions are underway.

Acknowledgments

We thank Dr. P. Martinuzzi (Università di Udine) for NMR assistance.

- [a] Dr. S. Baldino, Prof. W. Baratta
 Dipartimento DI4A
 Università di Udine, Via Cotonificio 108, 33100 Udine (Italy)
 Fax: +39-0432-558803
- [b] Dr. S. Facchetti, Dr. A. Zanotti-Gerosa, Dr. H. G. Nedden Johnson Matthey Fine Chemicals Division
 28 Cambridge Science Park, Milton Road Cambridge, CB4 0FP, United Kingdom

E-mails: salvatore.baldino@uniud.it, walter.baratta@uniud.it

References and notes

- [1] a) *The Handbook of Homogeneous Hydrogenation*, *Vols. 1-3* (Eds. J. G. de Vries, C. J. Elsevier) Wiley-VCH, Weinheim, **2007**; b) *Transition Metals for Organic Synthesis*, 2nd ed. (Eds. M. Beller, C. Bolm) Wiley-VCH, Weinheim, **2004**, p. 29.
- [2] a) D. Wang, D. Astruc, *Chem. Rev.* 2015, *115*, 6621; b) W. Baratta, P. Rigo, *Eur. J. Inorg. Chem.* 2008, 4041; c) J. S. M. Samec, J. E. Bäckvall, P. G. Andersson, P. Brandt, *Chem. Soc. Rev.*, 2006, 35, 237.
- [3] J. Magano, J. R. Dunetz, Org. Process Res. Dev. 2012, 16, 1156.

- [4] a) J. Seyden-Penne, Reductions by the Alumino- and Borohydrides in Organic Synthesis, VCH, New York, 1991; b) J. S. Cha, Org. Process Res. Dev. 2006, 10, 1032.
- [5] a) X. Tan, G. Wang, Z. Zhu, C. Ren, J. Zhou, H. Lv, X. Zhang, L. W. Chung, L. Zhang, X. Zhang, Org. Lett. 2016, 18, 1518; b) L. Bonomo, L. Kermorvan, P. Dupau, ChemCatChem. 2015, 7, 907; c) T. Miyada, E. H. Kwan, M. Yamashita, Organometallics 2014, 33, 6760; d) P. Dupau, L. Bonomo, L. Kermorvan, Angew. Chem. Int. Ed. 2013, 125, 11557; e) E. Putignano, G. Bossi, P. Rigo, W. Baratta, Organometallics 2012, 31, 1133; f) K. E. Jolley, A. Zanotti-Gerosa, F. Hancock, A. Dyke, D. M. Grainger, J. A. Medlock, H. G. Nedden, J. J. M. Le Paih, S. J. Roseblade, A. Seger, V. Sivakumar, I. Prokes, D. J. Morris, M. Wills, Adv. Synth. Catal. 2012, 354, 2545.
- [6] a) N. Kharat, A. Bakhoda, B. T. Jahromi, *Inorg. Chem. Commun.* 2011, *14*, 1161; b) B. Deb, P. P. Sarmah, D. K. Dutta, *Eur. J. Inorg. Chem.* 2010, 1710; c) M. Zhao, Z. Yu, S. Yan, Y. Li, *Tetrahedron Lett.* 2009, *50*, 4624; d) B. Deb, B. J. Borah, B. J. Sarmah, B. Das, D. K. Dutta, *Inorg. Chem. Commun.* 2009, *12*, 868; e) W. Baratta, K. Siega, P. Rigo, *Adv. Synth. Catal.* 2007, *349*, 1633.
- [7] X. Zhou, X. Wub, B. Yang, J. Xiao, J. Mol. Catal A: Chem. 2012, 357, 133.
- [8] R. Bar, L. K. Bar, Y. Sasson, J. Blum, J. Mol. Catal. 1985, 33, 161.
- [9] I. Szatmári, G. Papp, F. Joó, Á. Kathó, Catal. Today 2015, 247, 14.
- [10] P. Kumar, A. K. Singh, S. Sharma, D. S. Pandey, J. Organomet. Chem. 2009, 694, 3643.
- [11] D. J. Darensbourg, F. Joo, M. Kannisto, A. Katho, J. H. Reibenspies, *Organometallics* 1992, 11, 1990.
- [12] S. Sabata, J. Vcelak, J. Hetflejs, Collect. Czech. Chem. Commun. 1995, 60, 127.
- [13] H. Cheng, R. Liu, J. Hao, Q. Wang, Y. Yu, S. Cai, F. Zhao, *Appl. Organomet. Chem.* 2010, 24, 763.
- [14] a) R. Leuckart, Ber. Dtsch. Chem. Ges. 1885, 18, 2341; b) O. Wallach, Ber. Dtsch. Chem. Ges. 1891, 24, 3992; c) M. L. Moore, Org. React. 1949, 5, 301; d) H. W. Gibson, Chem. Rev. 1969, 69, 673.
- [15] M. Kitamura, D. Lee, S. Hayashi, S. Tanaka, M. Yoshimura, J. Org. Chem. 2002, 67, 8685.
- [16] D. Talwar, N. P. Salguero, C. M. Robertson, J. Xiao, Chem. Eur. J. 2014, 20, 245.
- [17] R. Kadyrov, T. H. Riermeier, Angew. Chemie Int. Ed. 2003, 42, 5472.
- [18] S. Ram, L. D. Spicer, Tetrahedron Lett. 1988, 29, 3741.

- [19] a) S. Ram, R. E. Ehrenkaufer, *Tetrahedron Lett.* 1988, 29, 5733; b) A. Saha, B. Ranu, J. Org. Chem. 2008, 73, 6867.
- [20] R. Nakao, H. Rhee, Y. Uozumi, Org. Lett. 2005, 7, 163.
- [21] D. M. Grainger, A. Zanotti-Gerosa, K. P. Cole, D, Mitchell, S. A. May, P. M. Pollock, J. R. Calvin, *ChemCatChem.* 2013, *5*, 1205.
- [22] H. Nie, H. Zhou, X. Li, Y. Li, J. Wang, Chin. J. Org. Chem. 2013, 33, 2412.
- [23] S. Iyer, A. K. Sattar, Synth. Commun. 1998, 28, 1721.
- [24] a) S. E. Clapham, A. Hadzovic, R. H. Morris, *Coord. Chem. Rev.* 2004, 248, 2201; b)
 P. Espinet, A. C. Albéniz, *Fundamentals of Molecular Catalysis, Current Methods in Inorganic Chemistry, Vol. 3* (Eds. H. Kurosawa, A. Yamamoto) Elsevier, Amsterdam, 2003, Chap. 6, p. 328.
- [25] a) A. M. P. Koskinen, A. O. Kataja, Org. React. 2015, Chap. 2, p. 105; b) T. Werner, J. Koch, Eur. J. Org. Chem. 2010, 6904; c) K. Ekoue-Kovi, C. Wolf, Chem. Eur. J. 2008, 14, 6302.
- [26] T. A. Geissman, Org. React. 1944, 2, 94.
- [27] M. B. Smith, J. March, *Advanced Organic Chemistry 5th ed.*; New York, Wiley Interscience, **2001**, p. 1218.
- [28] a) S. Facchetti, V. Jurcik, S. Baldino, S. Giboulot, H. G. Nedden, A. Zanotti-Gerosa, A. Blackaby, R. Bryan, A. Boogaard, D. B. McLaren, E. Moya, S. Reynolds, K. S. Sandham, P. Martinuzzi, W. Baratta, *Organometallics* 2016, *35*, 277; b) W. Baratta, M. Ballico, S. Baldino, G. Chelucci, E. Herdtweck, K. Siega, S. Magnolia, P. Rigo, *Chem. Eur. J* 2008, *14*, 9148; c) G. Chelucci, S. Baldino, W. Baratta, *Coord. Chem. Rev.* 2015, *300*, 29.
- [29] S. Baldino, S. Facchetti, A. Zanotti-Gerosa, H. G. Nedden, W. Baratta, *ChemCatChem*. 2016, *8*, 2279.
- [30] a) W. Baratta, S. Baldino, M. J. Calhorda, P. J. Costa, G. Esposito, E. Herdtweck, S. Magnolia, C. Mealli, A. Messaoudi, S. A. Mason, L. F. Veiros, *Chem. Eur. J.* 2014, 20, 13603. b) W. Baratta, M. Ballico, A. Del Zotto, E. Herdtweck, S. Magnolia, R. Peloso, K. Siega, M. Toniutti, E. Zangrando, P. Rigo, *Organometallics* 2009, 28, 4421.

Graphical abstract

Chemoselective Transfer Hydrogenation of Aldehydes with HCOONH₄ Catalyzed by RuCl(CNN^{Ph})(PP) Pincer Complexes

Salvatore Baldino,^{*[a]} Sarah Facchetti,^[b] Hans G. Nedden,^[b] Antonio Zanotti-Gerosa,^[b] and Walter Baratta^{*[a]}

Ammonium formate efficiently reduces commercial-grade aldehydes to alcohols, via transfer hydrogenation, catalyzed by benzo[h]quinoline pincer ruthenium complexes without formation of condensation or amination side products.



S/C up to 20000