ChemComm

50 2608

Accepted 6th January 2014 DOI: 10.1039/c3cc48810a www.rsc.org/chemcomm





View Article Online

using tandem catalysts[†] Cite this: Chem. Commun., 2014, Yongsheng Yang,^a Jiayi Guo,^a Huimin Ng,^a Zhiyong Chen^a and Peili Teo*^{ab} Received 19th November 2013,

Formal hydration of non-activated terminal olefins

The hydration of terminal olefins to secondary alcohols has been achieved using a Pd(II)/Ru(II) catalyst combination with high regioselectivity and yields. Both vinyl arenes and aliphatic olefins can be hydrated easily with the tandem catalyst system using a low catalyst loading of 1 mol%.

The addition of water across an olefin, commonly known as "olefin hydration", is an important process for the synthesis of alcohols in both the laboratory and industry.¹⁻³ Olefin hydration is desirable in syntheses as the precursors are abundant and it is the most atomeconomical method for alcohol production. Most hydration processes are multi-stepped in nature or acid-catalysed where strong acids are required. Functional groups that are sensitive to acids such as esters, hydroxyls and amines are not well-tolerated.⁴⁻⁶ In fact, among the various reported processes to hydrate an olefin, no process involving non-activated linear olefins has been reported.^{7,8} Non-activated olefins are abundant and commonly used in the synthesis of commodity chemicals.9 In view of the importance of hydroxyl compounds to the research lab, pharmaceutical, material and specialty chemical industry, there remains a need to develop a mild and functionalgroup tolerant catalytic system for the production of alcohols from olefins. Herein, we report a highly regioselective tandem catalyst system for the production of secondary alcohols from non-activated terminal olefins, including styrene and 1-octene. A broad range of linear olefins have been studied using our catalytic system and found to give good yields of the secondary alcohol. The net outcome of the process is a formal hydration of the C=C double bond.

In a recent report by Grubbs et al., a Pd/Ru catalyst combination was shown to be able to carry out anti-Markovnikov hydration of styrenes.^{1,10} We envisioned that a similar strategy could be employed for Markovnikov hydration, given the higher propensity for the

Table 1 Screening of TH catalysts for hydration of styrene^a

TH catalyst	3	4	5	6	Total [O]	Selectivity ^c /%
Shvo's catalyst ¹⁶	79	9	8	0	96	91
R-Mac-H ¹⁷	0	0	89	1	90	98
Funk's catalyst ¹²	0	0	84	1	85	>99
Milstein's PNN ¹³	0	0	78	1	79	>99
Milstein's PNP ¹³	0	0	81	1	82	>99
Ru-TsDPEN ^{b 14}	0	0	68	1	69	>99
Ru-TSDENEB ^{b 15}	0	0	98	1	99	>99
Ru-PNNP ^{b 15}	0	0	84	1	85	99

^a Reaction conditions: 1% PdCl₂(MeCN)₂, 1% TH catalyst, 1.5 BQ, 0.083 M, 35 °C 4 h, 85 °C, 30 h, MeOH : \overrightarrow{IPA} : H_2O6 : 3 : 1. ^b 35 °C 4 h, 60 °C 96 h, 1% MeONa added. ^c Markovnikov selectivity = $(3 + 5)/(4 + 6) \times 100\%$; yields determined by GC using tridecane as an internal standard.

ketone product to be obtained in Wacker oxidation, which is the first step of the reaction (eqn (1)). The selectivity of the tandem hydration system would be determined by the selectivity of the Wacker oxidation step in this case. We set out to screen various transfer hydrogenation (TH) catalysts that could be compatible with the Wacker oxidation catalyst, PdCl₂(MeCN)₂. Since the selectivity and yield of alcohol is dependent on the Wacker oxidation step, we first separated the oxidation and reduction steps in a single pot, by carrying out the reaction at 35 °C for 4 h, followed by stirring for another 30 h at 85 $^{\circ}$ C. Many TH catalysts require heat activation^{11–15} so by separating the oxidation and reduction steps, we may optimize the oxidation step first, in the presence of the TH catalyst. From the list of known TH catalysts screened, we found that only Shvo's catalyst is compatible with PdCl₂(MeCN)₂ to result in alcohol formation (Table 1). All other TH catalysts were unable to reduce the carbonyls formed in the oxidation step of the reaction.



From the TH catalyst screening results, it was observed that despite Shvo's catalyst being able to give the desired alcohol product, 3, it resulted in the poorest selectivity. Upon identifying the right

^a Department of Chemistry, National University of Singapore, 3 Science Drive 3,

^{117543,} Singapore. E-mail: peiliteo@nus.edu.sg; Tel: +65 65161377 ^b Institute of Chemical & Engineering Sciences, 1 Pesek Road, Jurong Island,

^{627833,} Singapore. Tel: +65 67998520

[†] Electronic supplementary information (ESI) available: Detailed experimental procedures, NMR data and spectra provided. See DOI: 10.1039/c3cc48810a

 Table 2
 Solvent ratios for hydration of styrene^a

Ph Ph Ph Ph Ph Ph Ph Ph Ph C CO	Ph Ph Ph CO CO	Ph	HO~ Ph	Ph H Ru CO B	Ph Ph. Ph + CO OC	Ph Ph C C C C C C
MeOH: ⁱ PrOH:H ₂ O	3/%	4/%	5/%	6/%	Total [O]/%	Selectivity ^c /%
6:3:1	39	1	11	0	51	97
4.5:4.5:1	61	3	17	0	81	96
3:6:1	74	6	10	0	90	93
3.6:5.4:1	66	3	13	0	82	96
2:2:1	30	2	16	0	48	97
$3:6:1^{b}$	80	5	6	0	91	94

^{*a*} Reaction conditions: 1% $PdCl_2(MeCN)_2$, 10% Shvo's catalyst, 1.5 BQ, 0.083 M, 35 °C 4 h, 85 °C 30 h. ^{*b*} 1% $PdCl_2(MeCN)_2$, 1% Shvo's catalyst. ^{*c*} Markovnikov selectivity = $(3 + 5)/(4 + 6) \times 100\%$.

catalyst combination, we went on to optimize the conditions required for improving the selectivity for secondary alcohols. It was found that at a high Shvo's catalyst loading of 10 mol%, a high ⁱPrOH content is required to solubilize Shvo's catalyst. When MeOH: PrOH was 2:1, the yield of 3 was only 39%. However, when MeOH: PrOH was changed to 1:2, the yield increased to 74%. This, however, was at the expense of selectivity. At high alcohol yields, the selectivity was poorer (Table 2). However, when the amount of Shvo's catalyst was decreased to 1 mol%, a 2:1 ratio of MeOH/^hPrOH was able to give 80% 1-phenylethanol from styrene. This observation stems from the relatively poor solubility of Shvo's catalyst in MeOH, and the addition of ⁱPrOH is required to solubilize the precatalyst, A. Shvo's catalyst, in the active form, is the dissociated, monomeric Ru-H species, B.¹⁶ In the heterogeneous form, most of the Shvo's catalyst remains in the non-activated A form. As such, when a large quantity of Shvo's catalyst (10 mol%) is used, much of it remains undissolved in solution, giving little B for reduction of 5 to 3. However, when the ⁱPrOH content is high for the solubilisation of A, more anti-Markovnikov product is formed, due to the attack of the bulkier alcohol on the less hindered site of the terminal olefin to form a vinyl ether that gets hydrolysed to aldehyde, 6, which gets reduced to the primary alcohol, 4.1

A series of control experiments were also carried out and it was found that both MeOH and ⁱPrOH were required to give a high product yield. In the absence of H_2O , small amounts of oxidized products were obtained, likely from trace amounts of moisture in the solvents. In the absence of BQ, the reaction did not proceed at all. In the absence of Shvo's catalyst or ⁱPrOH as the hydrogen source, no alcohols could be obtained (Table 3).

The reaction was also attempted on the bench to probe the effect of oxygen on the hydration system. However, it was found that Shvo's catalyst is very sensitive to oxygen in our system, despite being reported that Shvo's catalyst is stable in air.^{11,16} This may be due to the acidity of our reaction system which tends to destabilize the active Ru hydride species, **B**. The reaction mixture was observed to turn deep red rapidly, from yellow, when the reaction was carried out on the bench. A low alcohol yield of 24%, with 65% ketone, was obtained in this case. The addition of CuCl₂ to the reaction as a reoxidant for the Pd(n) catalyst was also studied. However, in the presence of just 10%

 Table 3
 Control experiments for hydration of styrene^a

Experiment	3/%	4/%	5/%	6/%	Total [O]/%	Selectivity ^b /%
No Pd	0	0	0	0	0	0
No Ru	0	0	82	1	83	99
No MeOH	57	10	2	0	69	73
No ⁱ PrOH	0	0	84	0	84	100
No H_2O	12	1	5	0	18	51
No BQ	0	0	0	0	0	0

^{*a*} Reaction conditions: 1% PdCl₂(MeCN)₂, 1% Shvo's catalyst, 1.5 BQ, 0.083 M, 35 °C 4 h, 85 °C 30 h, MeOH:IPA:H₂O 6:3:1. All other conditions remain the same except for the reagent being omitted. ^{*b*} Markovnikov selectivity = $(3 + 5)/(4 + 6) \times 100\%$.

CuCl₂, the Markovnikov selectivity decreased dramatically to 52%. As a result, *p*-benzoquinone (BQ) was employed as the only reoxidant for Pd(n) in the oxidation step. The optimum quantity of BQ was found to be 1.5 equivalents. Despite the reaction being non-catalytic with respect to BQ, BQ can easily be recovered from hydroquinone *via* facile aerobic oxidation.¹⁸

$$\mathsf{R} \xrightarrow{\qquad + H_2O} \xrightarrow{1\% \operatorname{PdCl}_2(\operatorname{MeCN})_2 \qquad \qquad \mathsf{OH}}_{1.5 \ p-\mathrm{BQ}, \ 0.083 \ \mathrm{M}} \mathsf{R}^{(3)}$$

Upon developing a suitable system for hydrating styrene, we went on to combine both oxidation steps and reduction steps into one single step by carrying out the entire tandem process at 85 °C. We also probed the functional group tolerance of the catalytic system (eqn (3)). It was found that the reported tandem hydration system is tolerant to a wide variety of functional groups including esters, halides, alkyls, nitro, trifluoroalkyl and naphthyl (Table 4). In particular, p-chlorostyrene, 1f, produced 1-(4-chlorophenyl)ethanol in a high yield of 83%. Acidic substrates such as 4-vinylbenzoic acid, 1j, produced a poor yield of the corresponding alcohol, possibly due to premature degradation of active Shvo's catalyst B, in a highly acidic media. Highly electron-withdrawing substituents on phenyl rings such as nitro (1k) and bis(trifluoromethyl) (1l) tend to direct the selectivity toward anti-Markovnikov instead, to result in the formation of 2-phenylethanol. This is due to the preferential coordination of Pd(II) to the alpha carbon when the aryl group is highly electron-deficient.

$$\mathsf{R} \xrightarrow{\qquad + H_2O} \xrightarrow{1\% \operatorname{PdCl}_2(\operatorname{MeCN})_2 \qquad \qquad \mathsf{OH}}_{\begin{array}{c} \frac{1\% \operatorname{Shvo's catalyst}}{1.5 \ p-\mathrm{BQ}, \ 0.083 \ \mathrm{M}} \\ \operatorname{MeOH:iPrOH:H_2O} 6:3:1 \\ 85 \ ^{\circ}\mathrm{C} \ (48 \ \mathrm{h}, \ \mathrm{R} = \operatorname{alkyl}) \end{array}} \mathsf{R} \xrightarrow{\qquad } \mathsf{OH} \xrightarrow{\qquad } \mathsf{Shvo's catalyst} \xrightarrow{\qquad } \mathsf{R} \xrightarrow{\qquad } \mathsf{R} \xrightarrow{\qquad } \mathsf{Shvo's catalyst} \xrightarrow{\qquad } \mathsf{R} \xrightarrow{\qquad } \mathsf{R$$

Aliphatic olefins such as 1-octene (2a) and 4-phenyl-1-butene (2f) were also hydrated using the tandem hydration system developed (eqn (4)). With 1-octene, a much higher Markovnikov selectivity of >99% could be obtained, with 2-octanol obtained in a yield of 71% using 1 mol% catalyst. Isolation of the alcohol was difficult, resulting in high loss of the product after purification. Gram-scale synthesis of 2-dodecanol was also attempted and 69% isolated yield could be obtained (1.29 g 2-dodecanol from 0.01 mol 1-dodecene). The system is also tolerant to functional groups on the olefin chain such as ester, hydroxyl and carboxylic acid, despite the mildly acidic reaction medium (Table 5). Esters in particular, such as ethyl-6-heptenoate

 Table 4
 Hydration of vinyl arenes

Entry	Substrate	Yield of $3^a/\%$
1	la	$\frac{66}{74^b}$
2	lb	68
3	le	54
4	1d	59
5	le	58
6	Cl	83
7	MeO 1g	49
8	MeO ₂ C 1h	56
9	F ₃ C 1i	55
10	HO ₂ C 1j	33
11	O ₂ N 1k	33 (3k) 51 (4k)
12	F ₃ C 11 CF ₃	24 (3l) 56 (4l)
13	1m	72
² Isolated yield, 0	.6 mmol reaction. ^b GC yield.	

(2d) and 8-nonenyl acetate (2e), gave excellent isolated product yields of 85% and 82%, respectively, with >99% selectivity for the secondary alcohol. Unsaturated alcohols such as 3-buten-1-ol (2i) and 5-hexen-1-ol (2j) could be hydrated easily to give 1,3-butanediol and 1,5-pentanediol, respectively, in modest yields of up to 58% using just 1 mol% catalyst. 1,3-Butanediol is an important industrial solvent and monomer for synthesis of polyurethane and polyester.^{19,20} Using chlorohexene, on the other hand, resulted in little alcohol being formed, with a significant amount of the product being unreduced ketone (40%). The ketone functionality on the

		View Article Online
		communication
Table 5	Hydration of linear olefins ^a	
Entry	Substrate	Yield of $3^a/\%$
1	$\begin{pmatrix} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$	59 $(71)^b$
2	$\langle \cdot \rangle_9$ 2b	63 (69) ^c
3	CO ₂ H 2c	59^d
4	\bigcirc CO ₂ Et 2d	85
5	6 OAc 2e	82
6	2f°	64
7	∑ 2g	42
8	4 3 Cl $2h$	9 (3hh) ^{<i>f</i>} 40 (4hh)
9	OH 2i	52
10	(-) ₃ ОН 2ј	58
11	2k	34 ^g
12	21	_
	$\sim \sim \sim 2m$	

13

^{*a*} Isolated yield, 0.6 mmol reaction. ^{*b*} GC yield. ^{*c*} 0.01 mol reaction, isolated yield. ^{*d*} Isolated as lactone, NMR yield. ^{*e*} 2 mol% PdCl₂(MeCN)₂, 1 mol% Shvo's catalyst. f NMR yield. g 2-(2-Hydroxypropyl)cyclohexanol obtained.

olefin is not tolerated where the ketone gets reduced to alcohol in the transfer hydrogenation step to result in a diol (2k). Internal olefins could not be oxidized in our system as can be seen from substrates 2l and 2m.

We have presented here a tandem hydration system that is able to hydrate a broad range of olefins, including substituted styrenes and aliphatic olefins, with varying functional groups attached. As the catalyst used is achiral, we do not expect enantioselectivity in the secondary alcohols obtained. Nevertheless, the simplicity of the method makes it an attractive process for obtaining secondary alcohols from olefins. Current known asymmetric ketone reduction catalysts operate in multisteps to produce secondary alcohols from olefins. Efforts in our group are directed towards turning the asymmetric olefin hydration process into a single step system, based on the existing system. Catalyst modification to ensure enantioselectivity in the products is currently underway.

The authors would like to thank National University of Singapore for a generous start-up grant (R143-000-523-133) and Agency of Science, Technology and Research (A*STAR) for research funding (R143-000-535-305). The authors are grateful to Dr Timothy Funk for his generous contribution of the Fe catalyst.

Notes and references

- 1 G. Dong, P. Teo, Z. K. Wickens and R. H. Grubbs, *Science*, 2011, 333, 1609–1612.
- 2 J. Haggin, Chem. Eng. News, 1993, 22, 23.
- 3 S.-F. Zhu, C. Chen, Y. Cai and Q.-L. Zhou, Angew. Chem., Int. Ed., 2008, 47, 932–934.
- 4 K. Weissermel and A. H.-J. Guo, *Industrial Organic Chemistry*, Wiley-VCH, New York, 1979.
- 5 P. Wiseman, *An introduction to industrial organic chemistry*, Applied science, London, 1979.
- 6 S. Isayama, Bull. Chem. Soc. Jpn., 1990, 63, 1305-1310.
- 7 L. Hintermann, Top. Organomet. Chem., 2010, 31, 123.
- 8 I. Schnapperelle, W. Hummel and H. Groger, *Chem.-Eur. J.*, 2012, **18**, 1073–1076.

- 9 S. Mizuta, S. Verhoog, K. M. Engle, T. Khotavivattana, M. O'Duill, K. Wheelhouse, G. Rassias, M. Médebielle and V. Gouverneur, J. Am. Chem. Soc., 2013, 135, 2505–2508.
- 10 P. Teo, Z. K. Wickens, G. Dong and R. H. Grubbs, *Org. Lett.*, 2012, 14, 3237–3239.
- 11 Y. Shvo and D. Czarkie, J. Organomet. Chem., 1986, 315, C25-C28.
- 12 S. A. Moyer and T. W. Funk, Tetrahedron Lett., 2010, 51, 5430-5433.
- 13 C. Gunanathan and D. Milstein, Acc. Chem. Res., 2011, 44, 588-602.
- 14 S. Hashiguchi, A. Fujii, J. Takehara, T. Ikariya and R. Noyori, J. Am.
- *Chem. Soc.*, 1995, **117**, 7562–7563. 15 R. Noyori and S. Hashiguchi, *Acc. Chem. Res.*, 1997, **30**, 97–102.
- 16 B. L. Conley, M. K. Penningtono-Boggio, E. Boz and T. J. Williams, *Chem. Rev.*, 2010, **110**, 2294–2312.
- 17 S. G. Ouellet, J. B. Tuttle and D. W. C. MacMillan, J. Am. Chem. Soc., 2005, 127, 32.
- 18 S. Kim, D. Kim and J. Parka, Adv. Synth. Catal., 2009, 351, 2573-2578.
- 19 Y. Wang, F. Wang, Q. Song, Q. Xin, S. Xu and J. Xu, *J. Am. Chem. Soc.*, 2013, **135**, 1506–1515.
- 20 N. Itoh, M. Nakamura, K. Inoue and Y. Makino, *Appl. Microbiol. Biotechnol.*, 2007, 75, 1249–1256.