CHEMISTRY & SUSTAINABILITY
CHEMSUSCHEM
ENERGY & MATERIALS

Accepted Article

Title: Manganese-Catalyzed Selective Upgrading of Ethanol with Methanol into Isobutanol

Authors: Yaqian Liu, Zhihui Shao, Yujie Wang, Lijin Xu, Zhiyong Yu, and Qiang Liu

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: *ChemSusChem* 10.1002/cssc.201802689

Link to VoR: http://dx.doi.org/10.1002/cssc.201802689

A Journal of
ChemPubSoc Europe

WILEY-VCH
www.chemsuschem.org

10.1002/cssc.201802689

WILEY-VCH

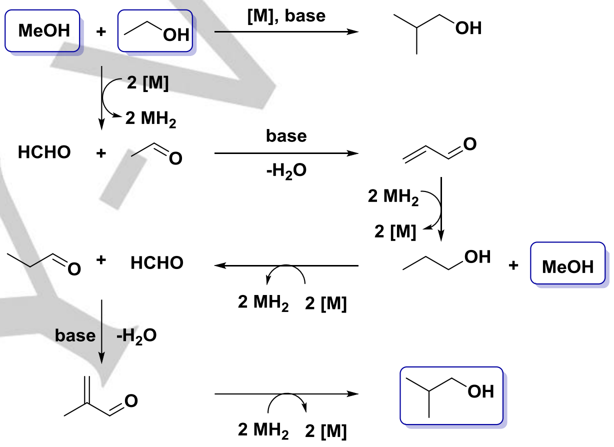
Manganese-Catalyzed Selective Upgrading of Ethanol with Methanol into Isobutanol

Yaqian Liu‡,[a,b] Zhihui Shao‡,[b] Yujie Wang,[b] Lijin Xu,*[a] Zhiyong Yu,*[a] and Qiang Liu*[b]

Abstract: Isobutanol serves as an ideal gasoline additive due to its good compatibility with current engine technology, high energy density and high octane number. Herein, we report an efficient and selective Mn-catalyzed upgrading of ethanol with methanol into isobutanol. This is the first example of deoxgenative coupling of lower alcohols to isobutanol by using a homogeneous non-noble-metal catalyst. This transformation could proceed at very low catalyst loading with high turnover number (9233) and up to 96% isobutanol selectivity was also reached.

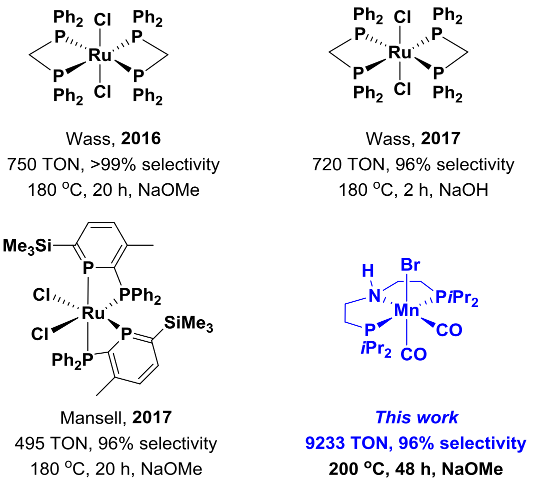
Sustainable production of liquid fuels from renewable biomass are receiving increasing industrial and scientific attention, driven by the diminishing crude oil reserves and ongoing climate change.[1] Bio-ethanol, mainly obtained by the fermentation of sugar-containing crops, is utilized currently as a blend additive with conventional gasoline in internal combustion engines.[2] However, ethanol is not an ideal alternative to gasoline due to its low energy density, water solubility and corrosivity to the engine. Higher alcohols, such as 1-butanol, can alleviate these problems caused by ethanol, because of their fuel characteristics more closer to conventional gasoline.[3] The most known approach to production of 1-butanol from bio-feedstocks, ABE fermentation process, suffers from low conversion and poor selectivity.[4] In this context, an attractive alternative method is to direct upgrading of easily available (bio)ethanol into higher alcohols. A number of homogeneous catalysts based on precious metals (Ru[5] and Ir[6]) with good performances for the upgrading of ethanol into 1-butanol have been developed. Notably, we recently reported a more sustainable version of the same transformation by using a manganese catalyst , in which high selectivity (92%) and a record turnover number (>110 000) were reached .[7]

Despite significant advances in upgrading of ethanol into 1-butanol mentioned above, the synthesis of its branched isomer isobutanol, as an advanced liquid fuel possessing improved octane number over 1-butanol,[8] was seldom explored.[9] The co-condensation of (bio)ethanol and widely available methanol provides an attractive route for the synthesis of isobutanol. Using this strategy, ethanol and methanol undergo sequential dehydrogenation, aldol coupling, and re-hydrogenation cycle to yield *n*-propanol, which occurs the same consecutive coupling process with methanol to produce isobutanol (Scheme 1). Clearly, it is challenging to achieve high selectivity towards isobutanol rather than various other higher alcohol products. This transformation was firstly realized via heterogeneous catalysis, in which high conversion of alcohols could be obtained but suffered from ether low selectivity, high reaction temperature or high catalysts loading.[10] With respect to homogeneous catalytic systems, to the best of our knowledge, only a handful of catalysts based on precious metals have been applied for this transformation (Figure 1).[11]



Scheme 1. Proposed route for the co-condensation of ethanol with methanol into isobutanol.

The replacement of expensive noble-metal catalysts by first-row base-metals is highly appreciated in terms of sustainability. Encouraged by the significant achievements in Mn-catalyzed alcohol dehydrogenation reactions,[12] we disclose herein the first



Firgure 1. Homogeneous metal catalysts for the upgrading of ethanol with methanol into isobutanol.

---

[a] Miss Y. Liu, Prof. Z. Yu and Prof. L. Xu
Department of Chemistry
Renmin University of China
Beijing,100872, China

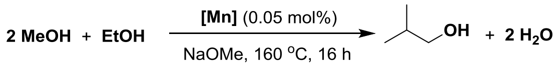
[b] Miss Y. Liu, Mr. Z. Shao, Mr. Y. Wang, Prof. Q. Liu
Center of Basic Molecular Science (CBMS), Department of Chemistry
Tsinghua University
Beijing 100084, China
E-mail: qiang_liu@mail.tsinghua.edu.cn.
‡Y. Liu and Z. Shao contributed equally to this work.

Accepted Manuscript

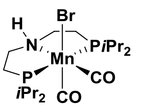
This article is protected by copyright. All rights reserved.

non-noble metal catalyzed upgrading of ethanol with methanol into isobutanol by using a well-defined manganese catalyst (Figure 1). Notably, this robust pincer Mn-catalyst achieved the highest turnover number (9233) and turnover frequency (833 h^{-1}) among all these homogeneous catalysts for the synthesis of isobutanol.

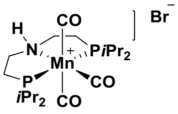
Table 1. Mn-catalyzed upgrading of ethanol with methanol to isobutanol[a]



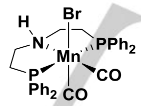
Entry	[Mn]	NaOMe (mol%)	EtOH covn. %[b]	Yield %[c]	Selectivity %[d]	TON[e]
1	**[Mn]-1**	350	36	28	80	558
2	**[Mn]-2**	350	34	26	76	514
3	**[Mn]-3**	350	37	25	68	503
4	**[Mn]-4**	350	38	26	69	521
5	**[Mn]-5**	350	trace	trace	-	trace
6	**[Mn]-6**	350	trace	trace	-	trace
7	**$Mn(CO)_5Br$**	350	0	0	-	0
8	none	350	0	0	-	0
9	**[Mn]-1**	400	35	28	79	564
10	**[Mn]-1**	300	37	26	68	521



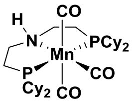
[Mn]-1



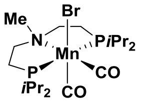
[Mn]-2



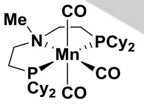
[Mn]-3



[Mn]-4



[Mn]-5



[Mn]-6

[a] Reaction conditions: 1 mL (17.13 mmol) ethanol, 10.4 mL (256.95 mmol) methanol, **[Mn]** (0.00857 mmol, 0.05 mol%), and NaOMe (51.39-68.52 mmol, 300-400 mol%) at 160 °C for 16 h under Ar in 25 mL autoclave. [b] Total conversion of ethanol to all alcohol products. [c] Yield was determined by GC. [d] Selectivity was determined by mmol of isobutanol per mmol of higher alcohol products. [e] TON based on mmol of EtOH converted to isobutanol per mmol of **[Mn]** catalysts.

We initially evaluated the reactivity of different Mn-pincer catalysts in this transformation by reacting 1 mL of ethanol, 10.4 mL of methanol, 0.05 mol% Mn catalysts, and 350 mol% NaOMe (mol% based on ethanol substrate) at 160 °C for 16 h (Table 1). It is worth mentioning that the TON, conversion, yield, and selectivity of these Mn-catalyzed upgrading reactions of ethanol with methanol were calculated in the same manner as previous reports for comparison (see SI for more detail). All the manganese catalysts shown in Table 1 were prepared as reported in our previous work.[7, 13] Isolated dicarbonyl ^{iPr}PNP-Mn(I)complex **[Mn]-1** and tricarbonyl ^{iPr}PNP-Mn(I) complex **[Mn]-2** gave similar results due to the conversion of the tricarbonyl complex **[Mn]-2** to dicarbonyl species **[Mn]-1** at high temperature (table1, entries 1 and 2).[7] ^{Ph}PNP-Mn(I) complex **[Mn]-3** and ^{Cy}PNP-Mn(I) complex **[Mn]-4** displayed comparable ethanol conversion but lower selectivity of isobutanol than **[Mn]-1** (entries 1, 3 and 4). There was no reaction in the absence of Mn-catalysts or employing commercially available $Mn(CO)_5Br$ as the catalyst, indicating the importance of the Mn-catalysts and the supporting pincer ligands (entries 7 and 8). Besides, the *N*-methylated complexes **[Mn]-5** and **[Mn]-6** showed much lower reactivity, revealing the essential role of the "N-H moiety" for the hydrogen transfer process (entries 5 and 6). Further increase or decrease of base loading could neither improve ethanol conversion nor yield and selectivity of isobutanol for this transformation (entry 9 and 10). In these Mn-catalyzed reactions for the synthesis of isobutanol, the selectivity was significantly influenced with bases (Table S1). *n*-Propanol along with C5, C6 aliphatic alcohols and C8, C9, C10 aromatic alcohols were also detected in the liquid fraction as side products when using other strong bases, such as NaOEt, NaO^{t}Bu or NaOH (Table S1, entries 2, 3 and 4). The proposed reaction pathways for the generation of these higher alcohols were discussed in detail in the supporting information (Scheme S1). Using weaker base, Na_2CO_3, could not promote this transformation (Table S1, entry 5). Acceptorless alcohol dehydrogenative coupling (ADC) products, such as ethyl acetate and methyl formate, were not detected in any of these reactions. HCOONa and NaOAc could be formed in the solid-phase verified by NMR analysis, indicating a process of Mn-catalyzed dehydrogenative coupling of alcohols with hydroxides into carboxylates was involved.[14]

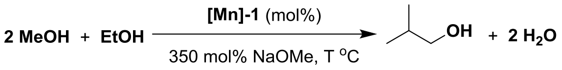
We then examined different reaction parameters to improve the efficiency of this transformation (Table 2 and Table S3). The choice of bases is of great importance for this Guerbet reaction process. NaOMe was found to be the optimal base likely because its protonation product MeOH could be used as the excessive component for this transformation (Table S1, entry 1). It is envisioned that the ratio of ethanol and methanol would play a key role for the selectivity of isobutanol.[10d] Specifically, increase of the amount ethanol from 1 mL to 1.25 mL in combination with 10.4 mL of methanol gave lower yield, conversion and TON for isobutanol production (table 2, entries 1 and 2). An increase of methanol amount to 15 mL resulted in lower selectivity of isobutanol as well (entry 3), in which *n*-propanol was obtained with 37% selectivity (for more details, see Table S3). Higher TON and selectivity were observed by increasing reaction temperature (entries 1, 4, 5 and 6), which could be resulted from more efficient dehydrogenation of *n*-propanol and methanol at high temperature. Notably, increasing reaction time to 48 h could be beneficial to the conversion, yield as well as selectivity (entry 7).To our delight, up to 40% yield and 96% selectivity could be acquired under 0.1 mol% catalysts loading in 48 hours (entry 9). In order to boost the efficiency of the catalyst, we further investigated the performance of this Mn-catalytic system at lower catalyst loading. Notably, an obvious improvement of TON was realized as the decrease of catalyst loadings without any loss of the selectivity (entries 10 and 11). A synergetic increase of the amount of ethanol and methanol along with the use of 0.031 mol% of **[Mn]-1** resulted in a remarkable TON of 9233 after 48 hours (entry 13). Moreover, the

Accepted Manuscript

This article is protected by copyright. All rights reserved.

TOF of catalyst **[Mn]-1** in this reaction could reach up to 833 h^{-1} for the first 7 hours (entry 12). However, the selectivity for isobutanol was decreased to 75% along with 25% *n*-propanol selectivity.

Table 2. Optimization of the reaction conditions.[a]



Entry	[Mn]-1	T (°C)	time (h)	EtOH conv. (%)	Yield (%)	Selectivity (%)	TON
1	0.05	160	16	36	28	80	558
2[b]	0.04	160	16	26	20	78	495
3[c]	0.05	160	16	27	16	58	318
4	0.05	140	16	20	7	33	133
5	0.05	180	16	28	25	87	502
6	0.05	200	16	33	27	83	548
7	0.05	180	48	33	29	88	576
8	0.1	180	16	40	36	92	360
9	0.1	180	48	42	40	96	397
10	0.025	180	16	27	24	88	950
11	0.0125	180	16	26	23	89	1873
12[d]	0.003125	200	7	24	18	75	5828
13[d]	0.003125	200	48	32	29	91	9233

[a]Reaction conditions: 1 mL (17.13 mmol) ethanol, 10.4 mL (256.95 mmol) methanol, 0.05 mol% **[Mn]-1**, and 350 mol% NaOMe at given temperature and reaction time under Ar in 25 mL autoclave. Conversion, yield, selectivity and TON were determined in the same way as in Table 1. [b]1.25 mL (21.41 mmol) ethanol, 280 mol% NaOMe. [c]15 mL MeOH. [d]In 60 mL autoclave, using 4 mL ethanol, 41.6 mL methanol.

In summary, we have developed an effective and sustainable synthesis of advanced biofuel isobutanol via upgrading of (bio)ethanol with methanol. This transformation was realized by using a well-defined pincer PNP Mn-catalyst, reaching a remarkable turnover number (9233) and turnover frequency (833 h^{-1}).

Acknowledgements

We are grateful for the financial supports from National Program for the National Natural Science Foundation of China (91845107, 21822106) and the 111 project.

Keywords: Methanol • Ethanol • Isobutanol • Manganese • Guerbet reaction

[1] a) M. Poliakoff, J. M. Fitzpatrick, T. R. Farren, P. T. Anastas, *Science* **2002**, *297*, 807-810; b) D. R. Dodds, R. A. Gross, *Science* **2007**, *318*, 1250-1251; c) D. M. Alonso, J. Q. Bond, J. A. Dumesic, *Green Chem.* **2010**, *12*, 1493-1513; d) C. O. Tuck, E. Pérez, I. T. Horváth, R. A. Sheldon, M. Poliakoff, *Science* **2012**, *337*, 695-699.

[2] J. Goldemberg, *Science* **2007**, *315*, 808-810.

[3] a) P. Durre, *Biotechnol. J.* **2007**, *2*, 1525-1534; b) S. Atsumi, A. F. Cann, M. R. Connor, C. R. Shen, K. M. Smith, M. P. Brynildsen, K. J. Chou, T. Hanai, J. C. Liao, *Metab Eng* **2008**, *10*, 305-311; c) B. G. Harvey, H. A. Meylemans, *J. Chem. Technol. Biotechnol.* **2011**, *86*, 2-9.

[4] C. Jin, M. Yao, H. Liu, C.-f. F. Lee, J. Ji, *Renew. Sust. Energy Rev.* **2011**, *15*, 4080-4106.

[5] a) G. R. Dowson, M. F. Haddow, J. Lee, R. L. Wingad, D. F. Wass, *Angew. Chem. Int. Ed.* **2013**, *52*, 9005-9008; b) R. L. Wingad, P. J. Gates, S. T. G. Street, D. F. Wass, *ACS Catal.* **2015**, *5*, 5822-5826; c) K. N. Tseng, S. Lin, J. W. Kampf, N. K. Szymczak, *Chem. Commun.* **2016**, *52*, 2901-2904; d) Y. Xie, Y. Ben-David, L. J. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2016**, *138*, 9077-9080.

[6] a) K. Koda, T. Matsu-ura, Y. Obora, Y. Ishii, *Chem. Lett.* **2009**, *38*, 838-839; b) S. Chakraborty, P. E. Piszel, C. E. Hayes, R. T. Baker, W. D. Jones, *J. Am. Chem. Soc.* **2015**, *137*, 14264-14267.

[7] S. Fu, Z. Shao, Y. Wang, Q. Liu, *J. Am. Chem. Soc.* **2017**, *139*, 11941-11948.

[8] A. M. Brownstein, in *Renewable Moto Fuels: The Past, the Present and the Uncertain Future, Vol. 5*, Butterworth-Heinemann, Oxford, **2014**, p. 47.

[9] H. Aitchison, R. L. Wingad, D. F. Wass, *ACS Catal.* **2016**, *6*, 7125-7132.

[10] a) W. Ueda, T. Kuwabara, T. Ohshida, Y. Morikawa, *J. Chem. Soc., Chem. Commun.* **1990**, 1558-1559; b) C. Carlini, M. Di Girolamo, A. Macinai, M. Marchionna, M. Noviello, A. M. Raspolli Galletti, G. Sbrana, *J. Mol.Catal. A: Chem.* **2003**, *200*, 137-146; c) E. S. Olson, R. K. Sharma, T. R. Aulich, *Appl. Biochem. Biotechnol.* **2004**, *115*, 913-932; d) Q. Liu, G. Xu, X. Wang, X. Mu, *Green Chem.* **2016**, *18*, 2811-2818; e) Q. Liu, G. Xu, Z. Wang, X. Liu, X. Wang, L. Dong, X. Mu, H. Liu, *ChemSusChem* **2017**, *10*, 4748-4755.

[11] a) R. L. Wingad, E. J. Bergstrom, M. Everett, K. J. Pellow, D. F. Wass, *Chem. Commun.* **2016**, *52*, 5202-5204; b) R. J. Newland, M. F. Wyatt, R. L. Wingad, S. M. Mansell, *Dalton Trans.* **2017**, *46*, 6172-6176; c) K. J. Pellow, R. L. Wingad, D. F. Wass, *Catal. Sci. Technol.* **2017**, *7*, 5128-5134.

[12] a) S. Elangovan, J. Neumann, J.-B. Sortais, K. Junge, C. Darcel, M. Beller, *Nat. Commun.* **2016**, *7*, 12641; b) M. Mastalir, M. Glatz, E. Pittenauer, G. Allmaier, K. Kirchner, *J. Am. Chem. Soc.* **2016**, *138*, 15543-15546; c) A. Mukherjee, A. Nerush, G. Leitus, L. J. W. Shimon, Y. Ben David, N. A. Espinosa Jalapa, D. Milstein, *J. Am. Chem. Soc.* **2016**, *138*, 4298-4301; d) M. Peña‐López, P. Piehl, S. Elangovan, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2016**, *55*, 14967-14971; e) M. Andérez-Fernández, L. K. Vogt, S. Fischer, W. Zhou, H. Jiao, M. Garbe, S. Elangovan, K. Junge, H. Junge, R. Ludwig, M. Beller, *Angew. Chem. Int. Ed.* **2017**, *56*, 559-562; f) A. Bruneau-Voisine, D. Wang, V. Dorcet, T. Roisnel, C. Darcel, J.-B. Sortais, *J. Catal.* **2017**, *347*, 57-62; g) A. Bruneau-Voisine, D. Wang, V. Dorcet, T. Roisnel, C. Darcel, J.-B. Sortais, *Org. Lett.* **2017**, *19*, 3656-3659; h) F. Kallmeier, B. Dudziec, T. Irrgang, R. Kempe, *Angew. Chem. Int. Ed.* **2017**, *56*, 7261-7265; i) M. Mastalir, E. Pittenauer, G. Allmaier, K. Kirchner, *J. Am. Chem. Soc.* **2017**, *139*, 8812-8815; j) D. H. Nguyen, Y. Morin, L. Zhang, X. Trivelli, F. Capet, S. Paul, S. Desset, F. Dumeignil, R. M. Gauvin, *ChemCatChem* **2017**, *9*, 2652-2660; k) D. H. Nguyen, X. Trivelli, F. Capet, J.-F. Paul, F. Dumeignil, R. M. Gauvin, *ACS Catal.* **2017**, *7*, 2022-2032; l) U. K. Das, Y. Ben-David, Y. Diskin-Posner, D. Milstein, *Angew. Chem. Int. Ed.* **2018**, *57*, 2179-2182; m) U. K. Das, S. Chakraborty, Y. Diskin-Posner, D. Milstein, *Angew. Chem. Int. Ed.* **2018**, *57*, 13444-13448; n) F. Kallmeier, R. Kempe, *Angew. Chem. Int. Ed.* **2018**, *57*, 46-60; o) N. Gorgas, K. Kirchner, *Acc. Chem. Res.* **2018**, *51*, 1558-1569; p) G. Zhang, T. Irrgang, T. Dietel, F. Kallmeier, R. Kempe, *Angew. Chem. Int. Ed.* **2018**, *57*, 9131-9135.

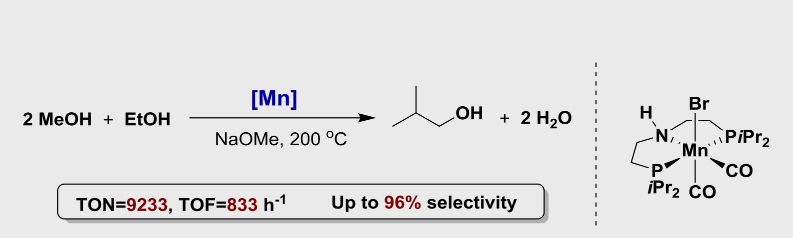
[13] Y. Wang, Z. Shao, K. Zhang, Q. Liu, *Angew. Chem. Int. Ed.* **2018**, *57*, 15143-15147.

[14] Z. Shao, Y. Wang, Y. Liu, Q. Wang, X. Fu, Q. Liu, *Org. Chem. Front.* **2018**, *5*, 1248-1256.

Accepted Manuscript

This article is protected by copyright. All rights reserved.

COMMUNICATION



Yaqian Liu, Zhihui Shao, Yujie Wang, Lijin Xu, Zhiyong Yu*, Qiang Liu**

Page No. – Page No.

Manganese-Catalyzed Selective Upgrading of Ethanol with Methanol into Isobutanol

Isobutanol is currently an desired gasoline alternative because of its compatibility with modern engine technology, high energy density and octane number. In this work, we disclosed here the first homogeneous non-noble metal catalyst for a sustainable production of isobutanol by upgrading of (bio)ethanol and widely availble methanol. This transformation could proceed at an very low catalyst loading with remarkable turnover number (9233) and up to 96% isobutanol selectivity was also reached.

WILEY-VCH

Accepted Manuscript

This article is protected by copyright. All rights reserved.