

Catalytic coupling of 1,4-benzenedimethanol with ethanol for alcohol upgradation

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KEYWORDS: ruthenium • 1,4-benzendimethanol • dehydrogenation • Guerbet-coupling • hydrogen borrowing.

ABSTRACT: We report here a catalytic method to upgrade 1,4-benzenedimethanol to 3-(4-(hydroxymethyl)phenyl)propan-1-ol via coupling of 1,4-benzenedimethanol with ethanol using a ruthenium catalyst. Through systematic optimization of catalytic conditions, a high TON of 400,000 has been achieved. Based on previous studies and those reported herein, we suggest that the reaction proceeds via a hydrogen-borrowing mechanism in a Guerbet-style process.

INTRODUCTION

Alcohol is a valuable feedstock with applications in making a range of organic compounds such as carboxylic acids, esters, and amides.¹ Additionally, several alcohols can be sourced from renewable feedstock making them an attractive choice for the production of renewable materials. In this direction, transformation of ethanol to butanol which is also known as Guerbet Coupling

has attracted significant interest in both academia and industry due to the application of butanol and higher alcohols in advanced biofuel.²⁻⁴ A range of homogeneous catalysts has been reported^{2,5-12} for this transformation some with very high TON such as 18,209.¹³ The majority of homogeneous catalysts studied on this transformation operate via hydrogen-borrowing mechanism.¹⁴⁻¹⁶ We envisioned that this approach could be used to upgrade other alcohols such as benzylic alcohols. In particular, we were interested in 1,4-benzenedimethanol that can be produced from the hydrogenative depolymerization of polyethylene terephthalate.^{17,18} We envisioned that 1,4-benzenedimethanol could be coupled with ethanol to make higher benzylic diols that could have potential applications in polymer precursors or aviation fuel. With this motivation, we report here our investigation on the coupling of 1,4-benzenedimethanol with ethanol to make higher diols.

RESULTS AND DISCUSSION

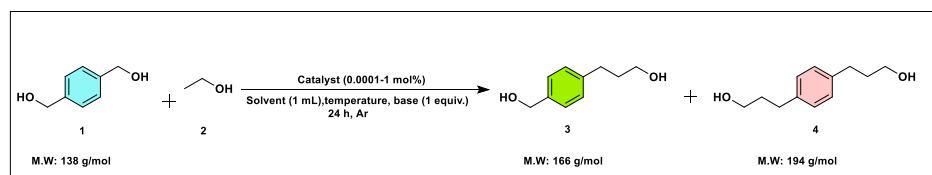
We started our investigation by studying the coupling of 1,4-benzenedimethanol (2.5 mmol) with ethanol (1 mmol) using transition-metal-based homogeneous catalysts known for the dehydrogenation of alcohols.¹⁹⁻²² The aim was to optimise reaction conditions to form the maximum yield and selectivity for 3-(4-(hydroxymethyl)phenyl)propan-1-ol (**3**) or/and 1,4-benzenedipropanol (**4**) while obtaining a high TON (e.g. >1000) of catalyst at the same time (Table 1). As such the combination of catalyst and base needs to perform a number of transformations as per the hydrogen-borrowing mechanism – (a) dehydrogenate 1,4-benzenedimethanol and ethanol to form corresponding aldehydes, (b) perform cross-aldol condensation of both the aldehydes to form alkenes with the elimination of water, and (c) hydrogenate the formed alkene intermediates to make alkylated alcohols which are the desired products. The Kinetics of the individual steps and the nature of catalysts/reaction conditions can play a huge role in achieving the desired selectivity as there are a number of side reactions that would need to be avoided such as (a)

acceptorless dehydrogenative coupling of ethanol to form ethyl acetate, (b) Guerbet coupling of ethanol to form butanol, (c) acceptorless dehydrogenative polymerisation of 1,4-benzenedimethanol to form polyester, and (d) hydrogen borrowing polymerisation of 1,4-benzendimethanol to form polyether or polyesterether. Additionally, the catalyst needs to remain tolerant to water that will be produced during the course of the reaction to achieve a high TON. Considering such demanding outputs, we performed a systematic study of catalytic conditions with the variation of precatalysts, base, solvent, temperature, and the relative concentration of 1,4-benzenedimethanol and ethanol.

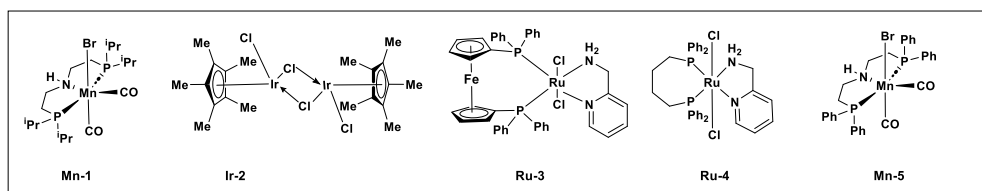
Initial reactions were conducted using 1 mol% precatalyst (**Mn-1**, **Ir-2**, **Ru-3**, **Ru-4**, **Mn-5**), NaOEt (1 mmol) at 135 °C for 24 h in a sealed 10 mL Young's flask in *t*-AmOH solvent. These reaction conditions were inspired by previous work conducted on the Guerbet coupling (ethanol to butanol) using such catalysts.^{2,19} Higher concentration of 1,4-benzenedimethanol relative to ethanol was used to avoid self-coupling of ethanol to butanol. Interestingly, complex **Mn-1** led to the formation of 3-(4-(hydroxymethyl)phenyl)propan-1-ol (**3**) in 66% yield (relative to ethanol), and the formation of butanol was not observed by the GC-MS presumably due to the high relative concentration of 1,4-benzendimethanol (Table 1, entry 1). The formation of 1,4-benzenedipropanol (**4**) was observed in only 1% yield. The remaining 1,4-benzenedimethanol were either unreacted or led to the formation of a polymer (see ESI). A similar result was obtained using the iridium complex **Ir-2** under identical condition which has also been reported for the coupling of benzyl alcohol with ethanol in the past (entry 2). Remarkably, ruthenium complexes **Ru-3**, and **Ru-4** led to the formation of 3-(4-(hydroxymethyl)phenyl)propan-1-ol (**3**) in 91%, and 86% yields, respectively (entries 3, 4). A lower yield (30%) was obtained in the case of manganese MACHO pincer complex **Mn-5** (entry 5). Considering the high performance of complexes **Ru-3**

and **Ru-4**, we chose them for further optimization. Performing the catalysis using complex **Ru-3** but in the presence of different bases (NaOH and KO^tBu) instead of NaOEt led to lower yields of 3-(4-(hydroxymethyl)phenyl)propan-1-ol (**3**) (entries 6, 7). Based on these we chose complex **Ru-3** and NaOEt to be the best catalytic combination. Performing the catalysis using complex **Ru-3** and NaOEt in 1,4-dioxane, Toluene and THF instead of *t*-AmOH lowered the yield of 3-(4-(hydroxymethyl)phenyl)propan-1-ol (**3**) (entries 8, 19 and 20). Interestingly, a high yield (88%) was also obtained when the reaction was performed without using any solvent (entry 9). Increasing or decreasing the temperature from 135°C also lowered the yields (entries 10, 11). Based on these experiments, our best catalytic conditions are complex **Ru-3** or **Ru-4**, NaOEt (1 equivalent relative to EtOH), *t*-AmOH, 135 °C and 24 h. Having established these, we wanted to see how far we can push the TON of precatalysts **Ru-3** and **Ru-4**. Remarkably, using 0.01 mol% catalytic loading of complex **3** led to the formation of 3-(4-(hydroxymethyl)phenyl)propan-1-ol (**3**) in 81% yield making the TON 8100 (entry 12). A similar TON (7500) was obtained when complex **Ru-4** was used keeping the remaining conditions the same (entry 13). Remarkably, we managed to push the TON further up and achieved 40% and 37% yields using 0.0001 mol% loading of complexes **Ru-3** and **Ru-4** making the TON 0.4 million and 0.37 million, respectively (entry 14 and 15). Performing the reaction without using any transition-metal complex but in the presence of NaOEt also led to the formation of 3-(4-(hydroxymethyl)phenyl)propan-1-ol (**3**) in 15% yield suggesting that some background transformation can occur just in the presence of base. The ability of such base to perform oxidation of alcohol or reduction of carbonyl compounds has been observed in the past. Interestingly, performing the reaction just in the presence of complex **Ru-3** without using any base did not lead to any conversion of the starting material. This is likely because base is needed for the generation of active species via deprotonation of N-H proton.

Table 1. Table of optimisation for the coupling of 1,4-benzendimethanol with ethanol.^[a]



Entry	Catalyst	Catalyst amount (mol%)	Base	Solvent	Temperature (°C)	3 (% of yield) ^[b]	TON	4 (% of yield) ^[b]
1	Mn-1	1	NaOEt	t-AmOH	135	66	66	1
2	Ir-2	1	NaOEt	t-AmOH	135	69	69	5
3	Ru-3	1	NaOEt	t-AmOH	135	91	91	2
4	Ru-4	1	NaOEt	t-AmOH	135	86	86	14
5 ^{c,g}	Mn-5	1	NaOEt	t-AmOH	135	30	30	0
6	Ru-3	1	NaOH	t-AmOH	135	32	32	0
7	Ru-3	1	KO ^t Bu	t-AmOH	135	69	69	0
8	Ru-3	1	NaOEt	1,4-dioxane	135	41	41	1
9	Ru-3	1	NaOEt	Neat	135	88	88	0
10	Ru-3	1	NaOEt	t-AmOH	150	70	70	0
11	Ru-3	1	NaOEt	t-AmOH	100	15	15	0
12 ^d	Ru-3	0.01	NaOEt	t-AmOH	135	81	8100	3
13 ^d	Ru-4	0.01	NaOEt	t-AmOH	135	75	7500	1
14 ^d	Ru-4	0.0001	NaOEt	t-AmOH	135	37	370000	0
15 ^d	Ru-3	0.0001	NaOEt	t-AmOH	135	40	400000	0
16	No catalyst	-	NaOEt	t-AmOH	135	15	15	0
17 ^{c,g}	Ru-3	1	No base	t-AmOH	135	0	0	0
18 ^e	Ru-3	1	NaOEt	t-AmOH	135	48	48	32
19	Ru-3	1	NaOEt	Toluene	135	47	47	0
20	Ru-3	1	NaOEt	THF	135	46	46	3



^[a]General reaction conditions: **(1)** 1,4-Benzenedimethanol (2.5 mmol), base (1 mmol), metal-complex (1 mol%) and **(2)** Ethanol (1 mmol), 1 mL solvent were placed into 10 mL ampule with J-Young's valve under an argon atmosphere and heated at 135 °C for 24 h; the mol% of the metal-complex depends on the amount of ethanol; ^[b]The yields are determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. ^[c] GC-MS yields have been considered. ^[d] The reactions were done in a 150 mL pressure vessel by increasing the starting material amount by 20 equivalent. ^[e] 1.5 mmol of 1,4-benzenedimethanol was taken. ^[g] The Ester product was formed as a major product, as confirmed by GC-MS data.

Having optimized the reaction conditions for the coupling of 1,4-benzendimethanol and ethanol to form 3-(4-(hydroxymethyl)phenyl)propan-1-ol (**3**), we conducted some mechanistic studies. Analysis of the gas from the headspace of the Young's flask after the reaction conducted as per entry 3 confirmed the presence of H₂. No other gases e.g. CO or CO₂ were detected. Although in an ideal hydrogen-borrowing no H₂ should be evolved, we suspect the formation of H₂ is likely due to the dehydrogenation of remaining 1,4-benzendimethanol as it is used in excess in the reaction conditions. Based on these studies and previous reports, we suggest that the process undergoes a hydrogen-borrowing transformation (Figure 1). The first step is likely to be the dehydrogenation of 1,4-benzendimethanol, and ethanol to form 4-(hydroxymethyl)benzaldehyde, and acetaldehyde, respectively. This is followed by cross-aldol condensation between both the aldehydes to form an alkene intermediate that can subsequently be hydrogenated to form 3-(4-(hydroxymethyl)phenyl)propan-1-ol.

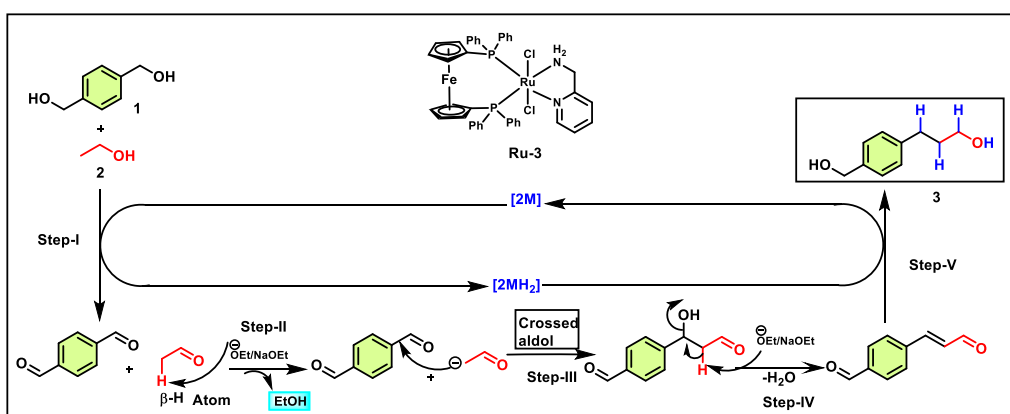


Figure 1. Proposed pathway for the coupling of 1,4-benzendimethanol with ethanol to form 3-(4-(hydroxymethyl)phenyl)propan-1-ol.

CONCLUSION

In conclusion, we report here a highly active catalyst for the coupling of 1,4-benzodimethanol with ethanol to form 3-(4-(hydroxymethyl)phenyl)propan-1-ol. A TON up to 0.4 million has been achieved using a ruthenium complex **Ru-3**. Based on our mechanistic studies and previous report, we suggest that the transformation occurs via hydrogen-borrowing pathway as described in Figure 1.

ASSOCIATED CONTENT

Supporting Information

The following data are available in the ESI.

Experimental details, characterization data, TGA, DSC curves, PXRD and NMR spectra

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Conflict of Interest

The authors declare no conflict of interest.

ACKNOWLEDGMENT

This research is funded by EPSRC (selected by ERC, EP/Y005449/1).

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