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Catalytic conversion of methanol/ethanol to isobutanol – a highly selective route to an advanced biofuel

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Catalysts based on ruthenium diphosphine complexes convert methanol/ethanol mixtures to the advanced biofuel isobutanol, with extremely high selectivity (>99%) at good (>75%) conversion via a Guerbet-type mechanism.

Obtaining liquid fuels for transportation from renewable biomass sources is an important element of future energy provision.[1] (Bio)ethanol has long been used as a sustainable replacement for conventional gasoline, often in the form of a blend of the two. However, ethanol has a number of significant drawbacks compared to gasoline: it has a lower energy density (70% that of gasoline), it can be corrosive to current engine technology and fuel infrastructure, and it readily absorbs water leading to separation and dilution problems in storage tanks. Higher alcohols such as butanol are often termed advanced biofuels' since they have fuel properties that more closely resemble those of gasoline and can alleviate many of these problems associated with ethanol.[2] However, the bulk synthesis of butanol from biosustainable feedstocks remains challenged by low conversion and variable selectivity.[3] We recently reported a new family of homogeneous ruthenium-based catalysts which demonstrate excellent performance in the upgrading of ethanol to *n*-butanol, with over 94% selectivity at good conversion.[4] Key to this high selectivity was the use of small bite angle 1,1-bis(diphenylphosphino)methane (dppm) ligands, with larger bite angle diphosphines being less effective; mixed donor P-N ligands also give excellent results.[5] Other homogeneous catalysts with comparable performance have also more recently been reported.[6]

  Although *n*-butanol is a superior fuel to ethanol, the branched isomer isobutanol has even more desirable characteristics,[7] and we have been exploring catalytic routes to this fuel molecule.

    Our approach for *n*-butanol synthesis was to use 'Guerbet'

type catalysts that allow facile C-C bond formation using normally unreactive alcohols;[8] more broadly, reactions of this type are often termed 'Borrowed Hydrogen' chemistry.[9] It is not obvious how this chemistry could be adapted for the direct conversion of ethanol alone to isobutanol; however, the co-condensation of methanol (which could also be obtained via biosustainable sources) and ethanol is an attractive potential route.[10] Using these substrates, methanol and ethanol are dehydrogenated to formaldehyde and acetaldehyde, which undergo aldol coupling to yield, after re-hydrogenation, *n*-propanol. A further dehydrogenation, aldol coupling, re-hydrogenation cycle with methanol yields isobutanol (Scheme 1). Clearly, achieving high selectivity to isobutanol rather than the various other possible alcohol coupling products (for example, ethanol-ethanol to *n*-butanol) is crucial to a viable process.

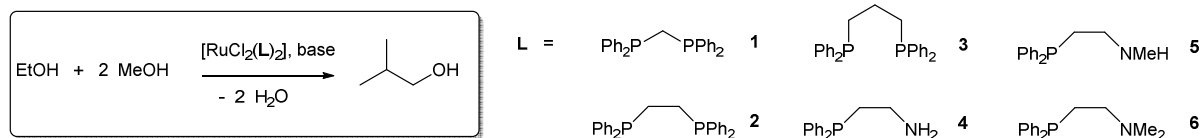Scheme 1. Proposed route for 2 MeOH + EtOH to isobutanol
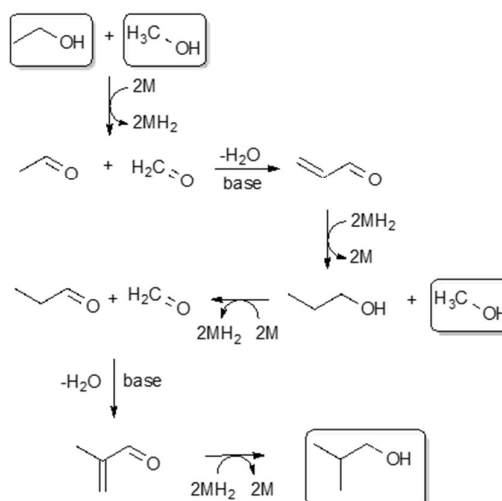
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Electronic Supplementary Information (ESI) available: Experimental details. See DOI: 10.1039/x0xx00000x

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Table 1: Catalytic results

Run[a]	Catalyst	Base	EtOH conversion (%)[b]	Selectivity (%)[c]		
				isobutanol	n-propanol	n-butanol
1	**1**	NaOMe	66.4	98.1	1.8	0.1
2	**2**	NaOMe	3.3	95.4	4.6	-
3	**3**	NaOMe	4.7	59.2	40.8	-
4	**4**	NaOMe	41.6	92.3	7.3	0.4
5[d]	**4**	NaOMe	56.3	89.7	9.9	0.4
6[d]	**5**	NaOMe	48.6	95.5	4.2	0.3
7[d]	**6**	NaOMe	31.1	93.2	6.5	0.3
8	**1**	NaO^{t}Bu	55.2	98.0	1.9	0.1
9	**1**	NaOH	73.8	95.6	4.4	0.1
10	**1**	KOH	60.8	94.9	4.9	0.2
11[e]	**1**	NaOMe	69.6	97.5	2.5	-
12[f]	**1**	NaOMe	49.9	93.6	6.2	0.2
13[g]	**1**	NaOMe	12.0	90.2	8.9	0.8
14[h]	**1**	NaOMe	11.2	81.2	18.6	0.3
15[i]	**1**	NaOMe	67.1	96.0	3.9	0.1
16[j]	**1**	NaOMe	75.2	99.8	0.1	0.1
17[k]	**1**	NaOH	73.0	97.1	2.9	0.1

[a] Conditions: 1 mL (17.13 mmol) ethanol, 10 mL (247.13 mmol) methanol, 0.1 mol% [Ru], 200 mol% base (mol% based on ethanol substrate), 180 °C, 2h. [b] Conversion of ethanol based on total amounts of liquid products obtained as determined by GC. [c] Total selectivity to products in the liquid fraction determined by GC. [d] 20h. [e] 150 mol% base. [f] 100 mol% base. [g] 50 mol% base. [h] 120 °C, 20h. [i] 150 °C, 20h. [j] 180 °C, 20h. [k] 0.62 mL water added (200 mol% based on ethanol substrate).

Initially, we screened a variety of the ruthenium systems[11] that have shown promise in ethanol homocoupling based on bis chelate diphosphine and mixed donor P-N ligand complexes.

Reaction conditions are similar to those used before, with NaOMe base, 180 °C and a 2 hour run time; in line with previous studies for isobutanol synthesis a higher concentration of base was typically used.[10c] An excess of methanol (molar methanol:ethanol 14.4:1)[‡] was chosen to minimise possible ethanol homocoupling. Results are given in Table 1.

It is clear that complexes based on small bite angle 1,1-bis(diphenylphosphino)methane ligands are again the most successful (compare run 1 with 2 and 3). Only extremely low activity and poor selectivity is observed for wider bite angle diphosphines. Selectivity is remarkably high for the best systems, up to 99.8% in the case of run 16, even at high conversion. In ethanol to n-butanol coupling, selectivity generally tails off at high conversion for batch reactions, since the increasing concentration of n-butanol facilitates further coupling reactions with this product.[4-6] In the case of isobutanol, further Guerbet catalysis is disfavoured due to the difficulty in dehydrogenation to isobutanal.[10c] The main product observed other than isobutanol, is a small amount

(1.8% in run 1) of propanol – the intermediate in isobutanol production. The P-N ligand systems that we recently reported to also be highly efficient and water tolerant catalysts for ethanol to n-butanol catalysis are reasonably successful here (run 4) and with a longer reaction time (20 h) good conversion at similar selectivity can be achieved (run 5). Some loss in activity is observed as the amine group is methylated (runs 6 and 7) but moderate activity is still observed with the fully methylated ligand **6**, seemingly ruling out an outer-sphere type mechanism.

Catalyst **1** works well with a variety of bases (runs 8-10), in particular even hydroxide bases give excellent results (runs 9 and 10). Reducing base concentration is to the detriment of performance (runs 11-13), as has been observed in other systems.[10] Activity also drops dramatically below 120 °C (run 14), typical for many borrowed hydrogen catalysts. However good activity and selectivity is restored at 150 °C when the reaction time is increased to 20 h (run 15).

Experiments were conducted to investigate whether the catalyst system could be recycled (see ESI for data and more details). Removal of all volatiles post reaction and adding fresh substrate (ethanol/methanol) gave a 40% drop in activity compared to a virgin run. However, addition of fresh substrate and fresh base at the end of a run allows the catalyst to be

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recycled three times and still produce isobutanol in good yield. These results suggest that base deactivation may be a deciding factor. Deactivation may also occur due to the formation of water as the reaction proceeds. However, when water was added at the start of a run (0.62 mL, 2 molar equivalents with respect to ethanol) the catalyst was remarkably robust, the same results within error being obtained compared to an absence of initial water (compare runs 9 and 17).

The proposed Guerbet mechanism is supported by the observation of the intermediate propanol as a minor product in reactions. This is further corroborated by a labelling study in which $^{13}CH_3OH$ is used under standard conditions with unlabelled ethanol. The ^{13}C label is observed by NMR spectroscopy to be exclusively in the methyl positions of the isobutanol product, as expected from the proposed series of aldol condensations (see ESI).

In conclusion, we report an extremely selective and productive homogeneous ruthenium catalyst for the production of the advanced biofuel molecule isobutanol from methanol-ethanol mixtures. Complexes supported by small bite angle disphosphines give the best performance, with preliminary mechanistic studies supportive of a Guerbet-type mechanism.

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