

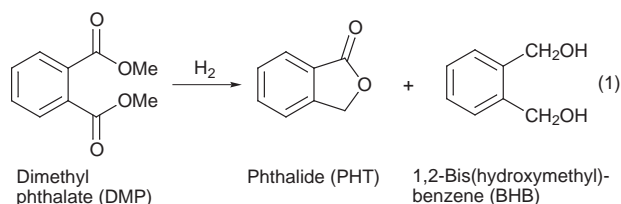
# Homogeneous ruthenium catalyzed hydrogenation of esters to alcohols†

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The homogeneous catalytic hydrogenation of aromatic and aliphatic esters to the corresponding alcohols, by a catalyst generated *in situ* from  $[\text{Ru}(\text{acac})_3]$  and  $\text{MeC}(\text{CH}_2\text{PPh}_2)_3$  in an alcoholic solvent under  $\text{H}_2$  pressure of 85 bar at 100–120 °C, is described.

The reduction of esters to the corresponding alcohols is an important reaction which is usually achieved by a stoichiometric reaction using lithium aluminium hydride,<sup>1</sup> whereas homogeneous catalytic routes have been scarcely explored.<sup>2–4</sup> For aromatic esters, the only example is concerned with the hydrogenation of dimethyl phthalate (DMP) to phthalide (PHT)



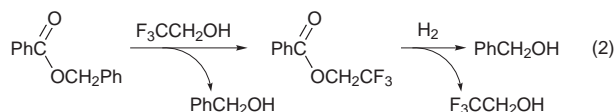
using a ruthenium hydride complex [eqn. (1)];<sup>3a</sup> PHT was obtained in a yield of 11.5% after 144 h at 180 °C under a hydrogen pressure of 130 bar.

Hydrogenation of PHT to 1,2-bis(hydroxymethyl)benzene (BHB) did not occur due to the absence of electron withdrawing substituents which enabled the conversion of DMP to PHT. Therefore, the hydrogenation of unactivated esters to the corresponding alcohols is one of the most intriguing challenges in contemporary hydrogenation catalysis. We have recently reported an important improvement using a catalyst based on  $[\text{Ru}(\text{acac})_3]$  and  $\text{MeC}(\text{CH}_2\text{PPh}_2)_3$  in methanol,<sup>4b</sup> for the homogeneous hydrogenation of dimethyl oxalate. Now, we wish to report a catalytic system which is able to catalyse the hydrogenation of unactivated aromatic and aliphatic esters with very high turnover numbers. §

From Table 1 it is evident that the hydrogenation of DMP to give mainly PHT is feasible under relatively mild conditions (entry 1) employing a system consisting of  $[\text{Ru}(\text{acac})_3]$  and  $\text{MeC}(\text{CH}_2\text{PPh}_2)_3$  in methanol. The catalytic activity (expressed as turnover number, TON) appeared to be strongly influenced by additives. Compared to entry 1, a negative effect is observed with Zn as an additive (entry 2) while positive effects are observed with  $\text{NEt}_3$  (entry 3) and  $\text{HBF}_4$  (entry 4). A further

improvement is observed when the solvent MeOH is replaced by propan-2-ol (IPA). The combination IPA– $\text{HBF}_4$  shows the highest catalytic activity and gives rise to formation of BHB in high yield (entry 5) which was not observed in any previous experiment. Comparing our system with that of Matteoli *et al.*<sup>3a</sup> (entry 6) shows that we have achieved a considerable improvement with respect to turnover numbers and turnover frequencies under relatively mild conditions.

Next, we applied our system to the hydrogenation of benzyl benzoate (BZB, an unactivated ester) which is difficult to hydrogenate to benzyl alcohol (BZO) (Table 2). In the presence of  $\text{HBF}_4$  or  $\text{NEt}_3$ , we could achieve a TON of 33 (entry 1) and 105 (entry 2), respectively at 120 °C for this conversion. Furthermore, we investigated the influence of fluorinated alcohols on the hydrogenation of benzyl benzoate. These investigations were based on the results of Grey *et al.*,<sup>2</sup> who found that an ester is more easily hydrogenated when electron withdrawing substituents are present. Therefore, we postulated that an integration of transesterification (using *e.g.* 2,2,2-trifluoroethanol) and hydrogenation would lead to a substantial increase in catalytic activity due to substrate activation [eqn. (2)].



The hydrogenation of BZB to BZO in 2,2,2-trifluoroethanol (TFE) at 120 °C turned out to be very successful (Table 2) and seems to confirm our hypothesis. Compared to the experiments in propan-2-ol (entry 2) the catalytic activity in TFE has drastically increased reaching a turnover number of nearly 900 in the presence of  $\text{NEt}_3$  (entry 3). At 100 °C the catalytic activity was significantly lower, as expected (entry 4). Hydrogenation of BZB does not occur in the presence of  $\text{HBF}_4$  (entry 5). Instead, three other products are formed: 2,2,2-trifluoroethyl benzoate, benzoic acid and a polymeric material. The formation of benzoic acid (82% isolated yield, TON 1412) was unexpected and is not readily explained. Hydrogenolysis of benzyl esters using heterogeneous palladium catalysts is common<sup>5</sup> but unprecedented for ruthenium complexes. Subsequently, the hydrogenation of BZB was carried out in 1,1,1,3,3,3-hexafluoropropan-2-ol (FIPA) which gave even

**Table 1** Hydrogenation of DMP with the  $[\text{Ru}(\text{acac})_3]$ – $\text{MeC}(\text{CH}_2\text{PPh}_2)_3$  system<sup>a</sup>

Entry	DMP/mmol	$[\text{Ru}(\text{acac})_3]/\mu\text{mol}$	Additive/mmol	Conv. (%)	Yield PHT <sup>b</sup> (%)	Yield BHB <sup>b</sup> (%)	TON	TOF/h <sup>-1</sup>
1	1.16	19.1	—	31	30	1	19	1.2
2	1.00	18.3	Zn (0.82)	25	18	0	10	0.6
3	1.05	15.3	$\text{NEt}_3$ (22.70)	87	82	0	56	3.5
4	1.14	17.1	$\text{HBF}_4$ (0.82)	91	79	0	53	3.4
5	1.17	18.1	IPA <sup>c</sup> + $\text{HBF}_4$ (0.27)	100	18	78	103	5.6
6	30.9		$[\text{Ru}_4\text{H}_4(\text{CO})_8(\text{PBu}_3)_4]^d$	21	12	0	51	0.4

<sup>a</sup> Conditions: 100 °C; 85 bar  $\text{H}_2$ ; 16 h; 1.15–1.65 equiv.  $\text{MeC}(\text{CH}_2\text{PPh}_2)_3$  in MeOH (12 ml). <sup>b</sup> Yield determined by GC or NMR (entry 5). <sup>c</sup> Propan-2-ol (12 ml, instead of MeOH). <sup>d</sup> From ref. 3(a);  $T = 180$  °C;  $p(\text{H}_2) = 130$  bar, 144 h.

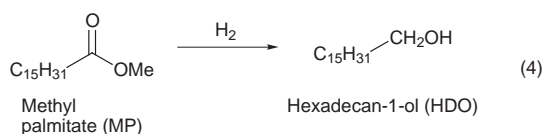
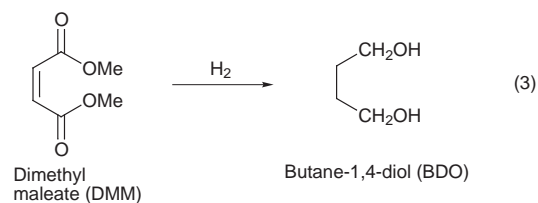
**Table 2** Hydrogenation of esters in fluorinated alcohols<sup>a</sup>

Entry	Substrate/mmol	[Ru(acac) <sub>3</sub> ]/ $\mu$ mol	Additive/mmol	Solvent	Conv. (%)	Product <sup>b</sup>	Yield <sup>c</sup> (%)	TON
1	BZB (1.3)	21.3	HBF <sub>4</sub> (0.42)	IPA	63	BZOH	56	33
2	BZB (4.2)	18.3	NEt <sub>3</sub> (0.34)	IPA	87	BZOH	82	105
3	BZB (30.5)	18.1	NEt <sub>3</sub> (2.60)	TFE	65	BZOH	53	896
4 <sup>d</sup>	BZB (17.3)	18.1	NEt <sub>3</sub> (2.46)	TFE	43	BZOH	23	219
5	BZB (29.5)	17.1	HBF <sub>4</sub> (0.47)	TFE	87	BZA	82 <sup>e</sup>	1412
6	BZB (28.4)	13.1	NEt <sub>3</sub> (2.58)	FIPA	97	BZOH	95	2071
7 <sup>f</sup>	BZB (25.9)	20.1	NEt <sub>3</sub> (2.55)	FIPA	7	BZOH	1	12
8	BZB (31.0)	10.8	NEt <sub>3</sub> (2.72)	FIPA-TFE	75	BZOH	67	1909
9	DMM (14.2)	14.1	NEt <sub>3</sub> (2.76)	FIPA	100	BDO	100	2019 <sup>g</sup>
10	MP (8.3)	13.1	NEt <sub>3</sub> (2.66)	FIPA	94	HDO	94	596

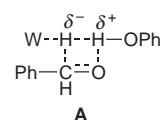
<sup>a</sup> Conditions: 120 °C; 85 bar H<sub>2</sub>; 16 h; [Ru(acac)<sub>3</sub>]; 1.15–1.65 equiv. MeC(CH<sub>2</sub>PPh<sub>2</sub>)<sub>3</sub>. <sup>b</sup> Apart from the alcohol, significant formation of transesterification product was observed: entry 3 (8%); entry 4 (16%); entry 5 not determined; entry 7 (1%); entry 8 (4%). <sup>c</sup> Yield determined by <sup>1</sup>H NMR. <sup>d</sup> T = 100 °C. <sup>e</sup> Isolated yield. <sup>f</sup> p(H<sub>2</sub>) = 0 bar. <sup>g</sup> The hydrogenation of the C=C bond is not included in the turnover number.

better results. Hydrogenation of BZB in FIPA occurs with a turnover number of >2000 (entry 6), which is an enormous step forward in the homogeneous catalytic hydrogenation of unactivated esters. This result was completely unexpected and contradicts the hypothesis of transesterification prior to hydrogenation. In principle, a primary alcohol such as TFE should give rise to transesterification more easily than a secondary alcohol like FIPA.<sup>6</sup> In view of these facts we suggest that the high catalytic activity in FIPA is due to ionic hydrogenation (*vide infra*) rather than to an integration of transesterification and hydrogenation. Compared to the experiment in FIPA, a mixture of TFE and FIPA exhibited a slightly lower activity (entry 8), which also raises objection to our initial hypothesis. Finally, we investigated the possibility of transfer hydrogenation (entry 7). The low catalytic activity in this case emphasizes that a substantial hydrogen pressure is necessary for successful catalysis. Possibly, the ruthenium catalyzed oxidative transformation of BZOH to BZB<sup>7</sup> becomes feasible in the absence of hydrogen pressure thus obstructing a successful transfer hydrogenation.

Using the optimized catalytic system for the conversion of BZB (FIPA, entry 6), we explored the scope of this system using dimethyl maleate (DMM) [eqn. (3)] and methyl palmitate (MP) [eqn. (4)] as substrates. The results show that our system is able



to catalyze the hydrogenation of these substrates to the corresponding alcohols with, compared to BZB, a high activity for DMM (entry 9) and a slightly smaller activity for MP (entry 10). Altogether we can conclude that efficient hydrogenation of unactivated aromatic and aliphatic esters is possible using [Ru(acac)<sub>3</sub>] and MeC(CH<sub>2</sub>PPh<sub>2</sub>)<sub>3</sub> in FIPA at 120 °C. Possibly, the remarkable activity in TFE and FIPA compared to IPA is related to the pK<sub>a</sub> of the alcohols and not to transesterification. Berke and Burger showed that phenol<sup>8a</sup> and FIPA<sup>8b</sup> drastically influence the rate of insertion of aldehydes into the W–H bond in tungsten nitrosyl complexes. This influence was explained by ionic hydrogenation (*via* A).



A comparable complex has been reported recently for a ruthenium hydride complex and FIPA.<sup>8c</sup> The unique features of our catalytic system are ascribed to ionic hydrogenation of the ester. Investigations pertaining to the mechanism of the hydrogenation of esters are currently in progress in our laboratory.

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## Notes and References

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§ *General procedure*: first, a solution was prepared of [Ru(acac)<sub>3</sub>], MeC(CH<sub>2</sub>PPh<sub>2</sub>)<sub>3</sub>, the appropriate ester and additive (see Tables 1 and 2) in the appropriate solvent (15 ml) under N<sub>2</sub>. Separately, a home-built stainless steel autoclave equipped with a magnetic stirring bar was flushed with dry nitrogen after which the dark red pre-catalyst solution was introduced *via* a needle. The autoclave was flushed with H<sub>2</sub> (at 50 bar), pressurized with hydrogen (85 bar at 20 °C) and heated for 16 h at the indicated temperature. The reaction products were characterized by GC–MS, the yields were determined with GC (internal standard) or <sup>1</sup>H NMR.

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