

Base-Catalysed Hydrogenation of Sulphur-Containing Aldehydes

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Abstract: The present work reports the first selective catalytic hydrogenation of bifunctional compounds containing a carbonyl and sulphur moieties, using hydrogen transfer from alcohols and a basic catalyst. The reaction was performed in batch at 371 K at atmospheric pressure with 3-mercaptopropionaldehyde, thiophene-2-carboxaldehyde, 5-bromothiophene-2-carboxaldehyde and 4-methylthiobenzaldehyde. The only product of reaction was the alcohol, formed with yields > 80%, except with 3-mercaptopropionaldehyde which did not give the alcohol but

rather afforded unidentified heavy products. 5-Bromothiophenemethanol was obtained with 100% yield in 3 h. The reaction obeys a mechanism of competitive adsorption of the reactants, and the reaction rates are higher than those reported for supported rhodium catalysts.

Keywords: basic catalysis; 5-bromothiophene-2-carboxaldehyde; hydrogen transfer; hydrotalcites; selective hydrogenation of aldehydes; thiophenecarboxaldehyde

Introduction

The preparation of alcohols by reduction of the carbon-oxygen double bond of aldehydes and ketones is one of the most fundamental and useful transformations in organic chemistry. Catalytic methods have been reported and are considered in terms of ease, efficiency, and commercial viability, as the most attractive procedures for reduction. Carbonyl reduction can be performed at relatively high pressures, using hydrogen and metals such as Pt/C, Raney Ni, and Pd/C.^[1] However carbonyl compounds containing sulphur moieties cannot be reduced using supported metal catalysts, as the metal itself gets poisoned by the sulphur; almost no conversion is observed. Recently, an immobilised cationic rhodium(I) catalyst bearing the diphosphine 1,1'-bis(diisopropylphosphino)ferrocene as ligand has been proposed.^[2,3] In spite of the good stability of the complex, some leaching of Rh was observed in the first runs, and these Rh(DiPPf)/Al₂O₃ catalysts are extremely expensive.

We reported earlier that the Meerwein-Ponndorf-Verley (MVP) reduction of 4-*tert*-butylcyclohexanone and unsaturated aldehydes to the corresponding unsaturated alcohol could be catalysed in the liquid phase at 353 K by the mixed oxides derived from hydrotalcites and 2-propanol as hydrogen donor.^[4] The acid and basic catalysis for the MVP reduction were compared using MgAl mixed oxides and BEA zeolites:^[5] basic catalysis gave selectively the alcohol whereas acid catalysis yielded the ether by consecutive reaction with the

solvent, therefore basic catalysis is preferable for the synthesis of alcohols. This reaction has now been extended to the hydrogenation of benzaldehyde,^[6] citral,^[7,8] aryl alkyl ketones,^[9] and propiophenone.^[10] The reduction of carbonyl compounds based on thiophene permits one to synthesise the corresponding thiophenemethanols which are intermediates for the synthesis of some herbicides^[11] and pharmaceutical compounds.^[12,13] This prompted us to investigate an extension of the base-catalysed hydrogen transfer to substrates containing sulphur moieties.

Results and Discussion

The experiments were performed in 2-propanol at 355 K with 3-mercaptopropionaldehyde, thiophene-2-carboxaldehyde (Equation 1, X = H), 5-bromothiophene-2-carboxaldehyde (Equation 1, X = Br) and 4-methylthiobenzaldehyde (Equation 2). The only products of the reactions are the alcohol (products **2** and **4**), and fairly high yields (> 80%) were reached at this temperature, except with 3-mercaptopropionaldehyde which gave not the alcohol but unidentified heavy products. From their GC-MS these products could correspond to a partial decomposition of a dimer. The simpler path to dimerisation is here aldolisation which is known to proceed rapidly and with a favourable thermodynamic equilibrium below room temperature.^[14] This suggests that this hydrogenation cannot probably be extended to

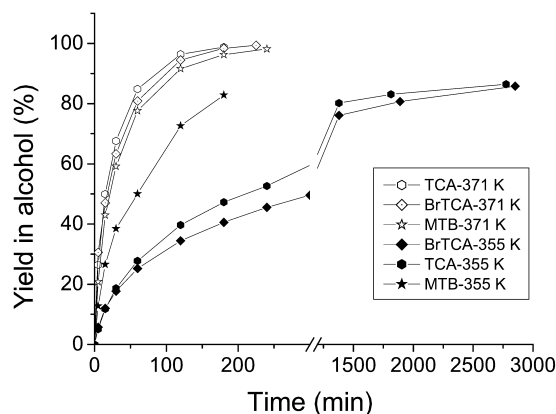
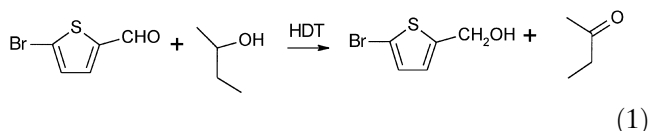
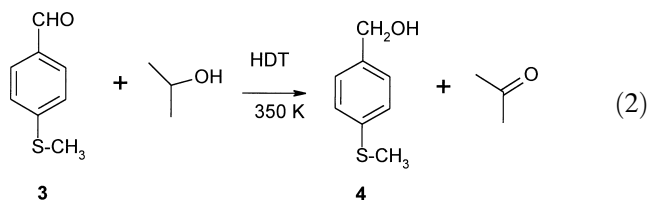


Figure 1. Yields of alcohol as a function of time for thiophene-2-carboxaldehyde (TCA), 5-bromothiophene-2-carboxaldehyde (BrTCA) and 4-methylthiobenzaldehyde (MTB) for the reactions with 2-propanol at 355 K and with 2-butanol at 371 K.

enolisable aldehydes, and indeed the best results were obtained with non-aldolisable substrates. The results of this reaction with 2-propanol at 355 K are reported in Figure 1.



Equation 1. Hydrogenation of thiophene-2-carboxaldehyde [1a, X = H] and 5-bromothiophene-2-carboxaldehyde [1b, X = Br] with 2-propanol.



Equation 2. Hydrogenation of 4-methylthiobenzaldehyde with 2-propanol.

Since the reaction time was long using 2-propanol, the reaction was also studied at 371 K using 2-butanol as hydrogen donor and solvent. In this case the time required to reach the final conversion of thiophenecarboxaldehyde decreases from 41 h to 2 h, without loss of selectivity (Figure 1). At 355 K the initial reaction rate with 2-butanol is twice that observed with 2-propanol, thus the better yield in 2-butanol results from the sum of two factors: a higher reaction temperature and better hydrogen donor. The rate of hydrogenation of thiophene-carboxaldehyde (0.1 M) to thiophenemethanol was measured at several temperatures in 2-butanol. The

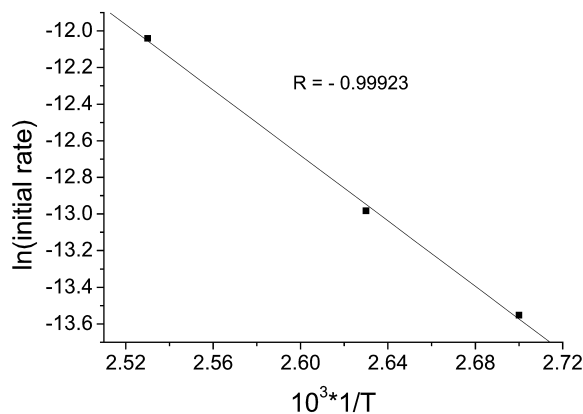


Figure 2. Arrhenius plot of the initial rates of hydrogenation of thiophene-2-carboxaldehyde by reaction with 2-butanol.

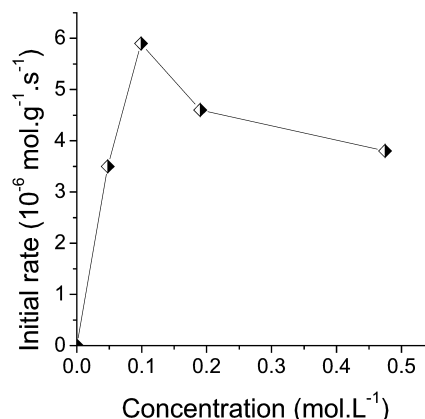


Figure 3. Influence of the concentration of thiophene-2-carboxaldehyde on the initial rate of reaction with 2-butanol at 371 K.

plot of the initial rate at low conversion against reciprocal temperature (Figure 2) gives an activation energy of 74 kJ/mol.

It is interesting to compare the activities reached by this process to those reported for immobilised homogeneous Rh(DiPFc)/Al₂O₃ catalysts. This is reported in Table 1 for the three substrates, in which basic catalysis compares favourably with hydrogenation over supported Rh. In particular, bromobenzaldehyde, which is debrominated on Pd/C and shows a low reactivity on immobilised homogeneous Rh catalysts, is quantitatively hydrogenated over the mixed oxide, therefore HDT is the first catalytic system to reach a good selectivity in this difficult hydrogenation.

The influence of the concentration of substrate was investigated in the case of 2-thiophenecarboxaldehyde at 371 K. The results reported in Figure 3 show a maximum of the rate at a concentration of about 0.1 mol L⁻¹. The usual mechanism accepted for MVP hydrogenation involves the coordination of the aldehyde to a surface alkoxide.^[15] The competition for adsorption between the two substrates (aldehyde and

Table 1. Comparison of the results^[a] of hydrogen transfer hydrogenations using 2-butanol at its boiling point and hydrogenation on Rh and Pd catalysts from ref.^[2]

Substrate	Catalyst	Alcohol Yield [%]	Reaction Time [h]
1a Thiophenecarboxaldehyde	Rh(DiPFc)/Al ₂ O ₃	100	18
	10% Pd/C	8	18
	HDT	100	3
1b 5-Bromothiophene-2-carboxaldehyde	Rh(DiPFc)/Al ₂ O ₃	37.2	18
	10% Pd/C	0	18
	HDT	100	3
2 4-Methylthiobenzaldehyde	Rh(DiPFc)/Al ₂ O ₃	100	18
	Pd/C	5	18
	HDT	100	3

^[a] Reaction conditions: for the immobilised complex: 293 K, 100 psi H₂; molar ratio substrate/Rh = 300 – 350, concentration: 0.1 M, solvent 10 mL of 2-PrOH/H₂O (1/1 v/v); for Pd/C: 293 K, 14 psi H₂, concentration 0.1 M, 10 mg of 10% Pd w/w for reaction 1 (X = H) and 2.5 mg for reaction 1 (X = Br), solvent 10 mL of 2-PrOH/H₂O (1/1 v/v); for hydrotalcites standard conditions: 371 K, atmospheric pressure, concentration 0.1 M, 0.1 g of catalyst corresponding to 1.2 wt % of the reaction mixture, solvent 10 mL of 2-PrOH.

alcohol) leads to the maximum in the rate observed here. A lower but still acceptable rate is, however, observed in more concentrated solutions. Since MgAl mixed oxides contain about 0.4 meq/g of active sites,^[16] at the optimal concentration, the catalyst converts 25 mol per active site in 2 h, therefore the reaction is truly catalytic. On the same reaction, the supported Rh catalyst converts 320 mol per mol Rh in 16 h, therefore the activities per active site are of the same magnitude.

Conclusion

We have shown for the first time that the mixed oxides obtained by calcination of MgAl hydrotalcites can be successfully used to selectively reduce carbonyl compounds to alcohols in the presence of sulphur moieties. The selectivity is also excellent, with retention of Br, with 5-bromothiophenecarboxaldehyde. The process uses an inexpensive catalyst, operates at atmospheric pressure and low temperature. The hydrotalcite can be regenerated several times by calcination provided it contains no chlorine at the surface.^[17] These catalysts are suitable for aldolisation^[18] and hydrogen transfer hydrogenation^[4] and can be reused several times after calcination at 723 K in air.

Experimental Section

General Remarks

An MgAl hydrotalcite [HDT]^[19] with a ratio Mg/Al = 2 was prepared according to experimental procedures described in detail earlier, and activated by calcination in air at 723 K. The physico-chemical characterisation of this solid has been also reported previously.^[16] The catalytic test was carried out in a 3-

necked glass reactor using 2-propanol or 2-butanol as hydrogen donors at their boiling points. The pre-treated catalyst (0.15 g of original solid, reduced to about 0.1 g after activation) was carefully transferred to the reactor swept by a small flow of nitrogen and containing the alcohol (10 mL, Aldrich) at the reaction temperature without exposure to air. Afterwards the substrate (1 mmol, purity 99% from Aldrich) was introduced. The amount of catalyst in the reaction mixture is therefore about 1.2 wt %. Periodically withdrawn samples were analysed on a Shimadzu GC 14B gas chromatograph using a Supercowax capillary column (30 m, 0.5 mm ID and 0.3 µm film thickness). The products were identified by GC-MS analysis and calibrations were done using authentic samples of the corresponding alcohols.

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- [19] Hydrotalcite is used on an industrial scale as an anion exchanger and PVC stabiliser, and is therefore commercially available from several manufacturers.
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