Stereoselective Reduction of 4-*tert*-Butylcyclohexanone to *cis*-4-*tert*-Butylcyclohexanol catalysed by Zeolite BEA

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Zeolite BEA is found to be the first stereoselective and regenerable heterogeneous catalyst for the Meerwein–Ponndorf–Verley reduction of 4-*tert*-butylcyclohexanone to *cis*-4-*tert*-butylcyclohexanol.

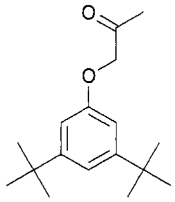
The Meerwein–Ponndorf–Verley (MPV) reduction of aldehydes and ketones is a highly selective reaction that can be performed under mild conditions, without affecting other reducible functional groups. The hydrogen donors are easily oxidizable secondary alcohols and the reductions are usually catalysed by metal alkoxides such as $Al(OPr^i)_3$. The catalytic activity of metal alkoxides is related to their Lewis acidic character in combination with ligand exchangeability. A major advantage of heterogeneous over homogeneous catalysts is that they can easily be separated from the liquid reaction mixture. However, only a few examples of heterogeneously catalysed MPV reductions have been reported.[1]

The stereoselective reduction of 4-*tert*-butylcyclohexanone to *cis*-4-*tert*-butylcyclohexanol is a commercially interesting conversion. The *cis*-alcohol is in use on a substantial scale as an intermediate in the fragrance industry. However, the homogeneous MPV reduction of 4-*tert*-butylcyclohexanone catalysed by $Al(OPr^i)_3$ invariably yields the thermodynamically more stable *trans*-isomer.[2] Similar results were obtained with the heterogeneous catalysts γ-alumina[3] and X-type zeolites.[4]

In this paper we report on the first stereoselective reduction of 4-*tert*-butylcyclohexanone to *cis*-4-*tert*-butylcyclohexanol with secondary alcohols (propan-2-ol, butan-2-ol and pentan-2-ol) employing zeolite beta (BEA) as heterogeneous catalyst. This high-silica zeolite has a three-dimensional pore system containing 12-membered ring apertures (7.4 × 6.5 Å).

Zeolite BEA was synthesised following the patent of Wadlinger and Kerr.[5] After calcination at 540 °C, the zeolite (1 g in 50 ml) was ion-exchanged with 1 mol l^{-1} NH_4NO_3 at room temperature for 24 h. The H-form was obtained by calcination at 500 °C. The Na-form was made by three subsequent ion-exchanges (1 g in 50 ml) with 1 mol l^{-1} $NaNO_3$ at room temperature for 24 h. Zeolite MCM-41 was synthesised according to a literature method.[6] The Na-form was obtained as described elsewhere.[7] Zeolite USY and a silica-alumina catalyst (HA-HPV) were kindly donated by AKZO-Nobel Chemicals Amsterdam.

Some catalytic results obtained with various heterogeneous catalysts are presented in Table 1. The catalysts, except for Na-Y which proved inactive, yielded 4-*tert*-butylcyclohexanol with >95% selectivity. However, only zeolite BEA was found to be selective towards the *cis*-alcohol. That the reaction took place in the micropores of BEA and not on the outer surface was confirmed by the following test reaction. A probe molecule, 1-(3,5-di-*tert*-butylphenoxy)propan-2-one **1**, which is too bulky to enter the micropores of BEA, did not undergo reduction over zeolite H-BEA, though it was converted to the corresponding alcohol over both silica–alumina and the mesoporous MCM-41. It is therefore proposed that steric constraints imposed by the zeolite structure play a role in the observed selectivity.



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Re-use of the H-BEA catalyst was found to be possible without loss of activity or selectivity. The catalyst was separated from the reaction mixture by filtration and reactivated at 500 °C. After three cycles no significant loss in X-ray powder diffraction (XRD) crystallinity was observed. The Si/Al ratios also remained constant, indicating that no aluminium was leached during reaction.

The activity of H-BEA was found to increase with activation temperature (Fig. 1). Activation at up to 700 °C was found to be possible without significant loss in XRD-crystallinity, while the high selectivity was also maintained. Essentially complete conversion of the ketone to 4-*tert*-butylcyclohexanol (*cis* : *trans* 95 : 5) was obtained within 1 h over the 700 °C-activated BEA. These results suggest that the activity of BEA in the MPV reduction is related to Lewis acid sites, which is consistent with the lower activity of sodium- exchanged BEA. Recently, it was found by FTIR and ^{27}Al MAS-NMR studies that some of the aluminium atoms in H-BEA, formed by high-temperature treatment of NH_4-BEA, can be transformed from tetrahedral to octahedral coordination by exposure to oxygen ligands such as water or pentane-2,4-dione. This transformation was found to be totally reversible since the tetrahedral coordination of the Al atoms was found to be restored by exchange with Na-, K- or

Table 1 MPV reduction of 4-*tert*-butylcyclohexanone over various heterogeneous catalysts[a]

Catalyst	Si/Al	T_{act}/°C[b]	Conv. (%)[c]	*cis* : *trans*[d]
H-BEA	16	500	38	95 : 5
Na-BEA	16	430	10	98 : 2
Na-Y	2.5	430	0	—
USY	2.5	500	22	9 : 91
Na-MCM-41	15	430	10	16 : 84
HA-HPV	2	500	19	9 : 91

[a] Reaction conditions: 5 mmol 4-*tert*-butylcyclohexanone, 50 ml propan-2-ol, 1.0 g catalyst, under reflux and stirring. [b] Heating rate 1 °C min^{-1}, 6 h at the final activation temperature. [c] Conversion after 6 h. [d] Selectivities to 4-*tert*-butylcyclohexanol >95% in all cases.

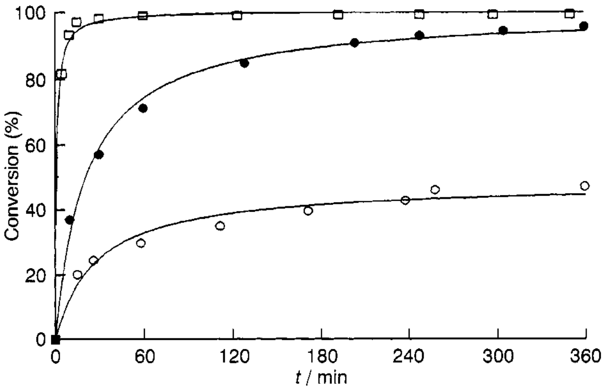

Fig. 1 Effect of the activation temperature on the activity of H-BEA; (○) 500 °C, (●) 600 °C, (□) 700 °C. Reaction conditions as given in Table 1.

NH_4-salts.[8–10] These observations indicate that octahedral aluminium can still be associated with the framework. In the present work also, the formation of octahedrally coordinated aluminium following activation of our catalyst and exposure to water vapour was observed by ^{27}Al MAS-NMR. It is generally accepted that MPV reactions proceed *via* a complex in which both the carbonyl compound and the reducing alcohol are coordinated to the Al ion.[1] It is therefore proposed that octahedrally coordinated lattice aluminium is the active site in MPV reactions in H-BEA.

MPV reductions are considered to proceed *via* a six-membered transition state.[1] It is seen in Fig. 2 that the transition states leading to the *cis*- and *trans*-alcohols differ substantially in size. That for the *cis*-isomer is more or less linear in form while the formation of the trans-alcohol requires a much bulkier transition state. Although the latter might still fit in the intersections of BEA it is questionable whether there is an Al site available at the required position. More coordination possibilities are available for the *cis*-transition state, which is small enough to be accommodated within the straight channels of BEA. In the proposed mechanism for the formation of the *cis*-isomer the R-group at the 4-position of the cyclohexane ring is not expected to play a role and this was indeed found; 4-methylcyclohexanone was also found to be reduced to the corresponding *cis*-alcohol with 98% selectivity.

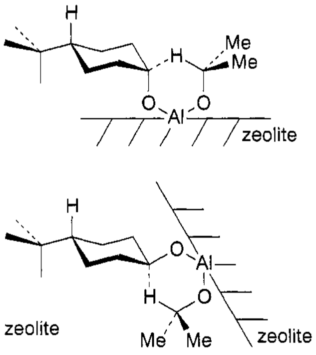

Fig. 2 Transition states for the formation of cis-4-*tert*-butylcyclohexanol (top) and *trans*-4-*tert*-butylcyclohexanol (bottom).

In conclusion, H-BEA is a regenerable, stereoselective catalyst for the MPV reduction of 4-*tert*-butylcyclohexanone to *cis*-4-*tert*-butylcyclohexanol. The active sites are proposed to be Lewis-acid Al atoms in the zeolite framework. The observed selectivity to the thermodynamically less stable *cis*-alcohol is suggested to result from transition-state selectivity. The extension of this work to other ketones is continuing.

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