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Heterogeneous catalytic hydrogenation of olefinic substrates by *poly*-NAP

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Abstract

With our previously described *poly*-NAP, various olefinic substrates were reduced with selectivities comparable to those obtained by BINAP. For substrates which contained a methyl ester, the selectivities were higher than those observed for their carboxylic acid analogues. © 2000 Elsevier Science Ltd. All rights reserved.

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One of the first examples of successful enantioselective catalysis was described as the hydrogenation of prochiral acetamidoacrylic acid derivatives. By the introduction of diphosphine ligands such as DIOP,[1] CHIRAPHOS,[2] BINAP[3] and DUPHOS[4] enantioselectivities of up to 99.8% were obtained in the rhodium- or ruthenium-catalyzed reactions. Besides these acetamidoacrylic acid derivatives, a wide variety of other functionalized olefins, such as itaconates[5] or enol esters,[6] have been successfully reduced.

To extend the utility of these (already) useful catalysts we decided to heterogenize BINAP in order to obtain a catalyst which could combine both the advantages of homogeneous catalysis (high enantioselectivities and TONs) and heterogeneous catalysis (easy work-up procedures and reusability). As recently described,[7] our philosophy of heterogenization was to polymerize a methylamine functionalized BINAP with a diisocyanate (Scheme 1) to yield *poly*-NAP. This is in contrast with recently published work of Bayston et al.[8] in which a functionalized BINAP was anchored to an already existing polymer. Simultaneous to our work, however, Chan et al. published the synthesis of chiral polyester-supported BINAP ligands,[9] also containing a chiral diol in the main chain. These chelating polymers were tested in the Ru-catalyzed hydrogenation of 2-arylacrylic acids to the reduced products in high yields and enantioselectivities. These activities and enantioselectivities, arising from a double-induction, proved to be maintained during several runs.

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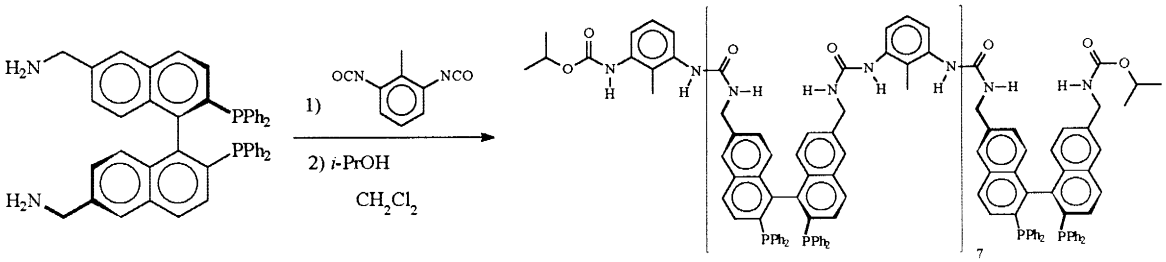
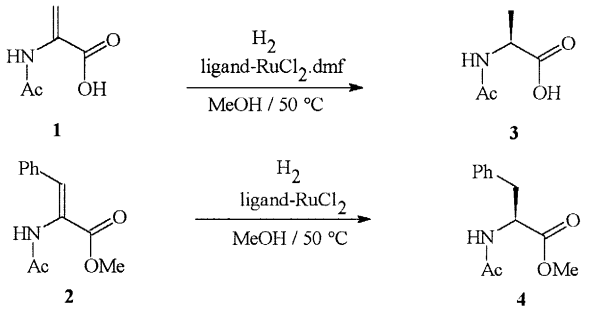


Scheme 1. Synthesis of polymerized BINAP

It was shown that with *poly*-NAP, various β-keto-esters could be hydrogenated with excellent enantioselectivities and low catalyst/substrate ratios. Furthermore, the catalyst could easily be reused by simple filtration without loss of either selectivity or activity. In this article, we wish to present the extension of this heterogeneous catalyst, *poly*-NAP, towards the hydrogenation of olefinic substrates. The catalyst was prepared by modification of the procedure described by Noyori et al., which gives the $RuCl_2 \cdot$dmf complex[10] and the procedure described by Takaya et al., which yields the $RuCl_2$ complex.[11] Both catalysts were brown solids and used without purification for the hydrogenation.

Since the degree of enantioselection is highly affected by the hydrogen pressure, by the substrate concentration, the temperature and the solvent,[12] we decided to perform the same reaction with BINAP, parallel to our catalytic tests, in order to get a real comparison between the homogeneous and heterogeneous hydrogenation systems. The results for the reduction of α-acetamido acrylic acid **1** and methyl-α-acetamido cinnamate **2**, yielding the products **3** and **4**, respectively, are summarized in Table 1.

Table 1
Hydrogenation of substrates **1** and **2**



entry	substrate	catalyst	substrate/ catalyst	pressure (bar)	conversion (%)	e.e. (%) (conf.)
1	**1**	*poly*-NAP-$RuCl_2$.dmf	100	10	100	70[a,b] (*S*)
2	**1**	BINAP-$RuCl_2$.dmf	100	10	100	78[a,b] (*S*)
3	**2**	*poly*-NAP-$RuCl_2$	100	40	100	72[c] (*S*)
4	**2**	BINAP-$RuCl_2$	100	40	100	74[c] (*S*)

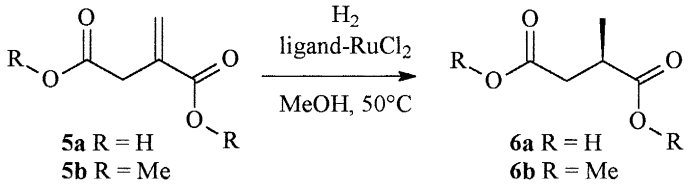
[a]e.e. was determined after conversion to its methyl ester. [b]determined by GC (β-Dex 225). [c]determined by HPLC (Chiracel OD).

As shown in Table 1, the results for *poly*-NAP and BINAP are comparable for substrate **2**. Substrate **1** was reduced with our polymeric catalyst with a slightly lower enantioselectivity as compared to BINAP. The advantage of this heterogeneous catalyst is the easier work-up procedure (a filtration allows the

obtention of the reduced products). Most importantly, the residue could be reused without loss of activity or enantioselectivity as was observed for substrate **1**.

Encouraged by these results we decided to test other substrates with unsaturated double bonds. The hydrogenation of substrates **5a** and **5b** at 50°C are summarized in Table 2.

Table 2
Hydrogenation of itaconic acid and dimethyl itaconate



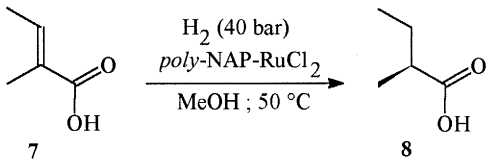
entry	substrate	catalyst	substrate/ catalyst	pressure (bar)	conversion (%)	e.e. (%) [b] (conf.)
1	**5a**	*poly*-NAP-$RuCl_2$.dmf	100	40	100	71[a] (*S*)
2	**5a**	BINAP-$RuCl_2$.dmf	100	40	100	88[a](*S*)
3	**5b**	*poly*-NAP-$RuCl_2$.dmf	100	40	100	94 (*S*)
4	**5b**	BINAP-$RuCl_2$.dmf	100	40	100	94 (*S*)

[a]e.e. was determined after conversion to its methyl ester. [b]determined by chiral GC analysis (β-Dex 225).

Comparable results were obtained for both *poly*-NAP and BINAP for substrate **5b**. In the case of the itaconic acid, bearing a hydroxy instead of a methoxy group, the enantioselectivity was slightly reduced (entries 1 and 2). The same effect was observed for the dehydro-amino acids, where the acid also conducted to a small decrease of enantioselectivity, whereas the ester gave comparable results for both *poly*-NAP and BINAP.

Surprisingly, tiglic acid **7** was hydrogenated with the *poly*-NAP–$RuCl_2$ complex to give product **8**, with the same enantioselectivity as obtained for the corresponding BINAP complex (see Table 3).

Table 3
Hydrogenation of tiglic acid



7 8

entry	substrate	catalyst	substrate/ catalyst	pressure (bar)	conversion (%)	e.e. (%) (conf.)
1	7	*poly*-NAP-$RuCl_2$	1000	40	100	82[a] (*S*)
2	7	BINAP-$RuCl_2$	1000	40	100	89[a](*S*)

[a]e.e. was determined after conversion to its methyl ester by chiral GC analysis (β-Dex 225).

In conclusion, we can say that dehydro-amino acids, itaconic acid and tiglic acid were quantitatively reduced with enantioselectivities similar to those obtained by the BINAP in the ruthenium-catalyzed hydrogenation. The methyl esters of these substrates gave enantioselectivities which were comparable to

those obtained by the BINAP reduction. After filtration, the catalyst can be reused without loss of either activity or enantioselectivity.

This method offers a heterogeneous alternative for BINAP-catalyzed hydrogenations of olefinic substrates.

1. Experimental

$RuCl_2$ catalyst: 5 mg (0.0058 mmol) of (*S*)-*poly*-NAP was stirred with 1.3 mg (0.0027 mmol) of a 8:1 mixture of EtOH:benzene for 1 h at 50°C. The solvent was removed under reduced pressure to give a brown solid.

$RuCl_2 \cdot$dmf catalyst: 5 mg (0.0058 mmol) of (*S*)-*poly*-NAP was stirred with 1.3 mg (0.0027 mmol) of $[RuCl_2(benzene)]_2$ in 1 mL DMF at 100°C for 1 h. The solvent was removed under reduced pressure to yield a brown solid.

Typical procedure: To the prepared catalyst were added the substrate and 2 mL of MeOH. The resulting suspension was stirred overnight at 50°C under 40 bars of hydrogen pressure. After centrifugation of the suspension, the liquid phase was recovered by syringe. The free carboxylic acids were converted to their methyl esters by addition of $SOCl_2$ and further stirring for 2 h. The esters were analyzed either by GC or HPLC to determine both conversion and enantiomeric excess (GC: Supelco β-dex™ 225, 30 m. HPLC: J. T. Baker, Chiracel OD, heptane:isopropanol 9:1, 1 mL/min).

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