Highly Efficient Enantio-differentiating Hydrogenation over an Ultrasonicated Raney Nickel Catalyst Modified with Tartaric Acid

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A tartaric acid–NaBr-modified Raney nickel catalyst prepared from ultrasonicated Raney nickel showed excellent enantio-differentiating and hydrogenating activity in the hydrogenation of a series of 3-oxoalkanoate and 1,3-diketones.

An asymmetrically modified Raney nickel catalyst which can easily be prepared by soaking Raney nickel catalyst (RNi) in an aqueous solution of tartaric acid (TA), is a unique heterogeneous catalyst for the enantio-differentiating hydrogenation of prochiral ketones to the corresponding chiral alcohols. Our long-term investigations on this catalyst have revealed that the hydrogenation-active sites of MRNi consist of enantio-differentiating (e.d.) sites which give optically active products by the aid of adsorbed tartaric acid and non-enantio-differentiating (n.e.d.) sites which give racemic products, and that the pure crystalline nickel domains function as the e.d. sites and the disordered nickel domains containing residual aluminum compounds work as the n.e.d. sites.[1] Thus the elimination of n.e.d. sites from the catalyst is a crucial but hard task for the preparation of a catalyst with excellent enantio-differentiating ability. The RNi catalyst modified with a slightly acidic (pH 3 to 3.5) hot aqueous solution of tartaric acid and NaBr (TA–NaBr–MRNi) has hitherto been developed, based on the idea that the n.e.d. sites are expected to be chemically sensitive, so that they can be removed at least in part by acid-corrosion and the rest can be deactivated by poisoning with the NaBr adsorbed.[2]

Although the TA–NaBr–MRNi catalyst prepared as above shows fairly good enantio-differentiating ability, the hydrogenation rate and durability are not satisfactory especially in the reaction of 1,3-diketones such as pentane-2,4-dione **1** and 2,6-dimethylheptane-3,5-dione **2**.[3]

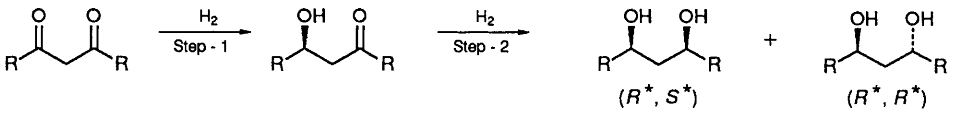
Our present study is based on a simple idea that the treatment of the RNi catalyst by ultrasound prior to the modification could smash off the n.e.d. sites selectively from the catalyst's surface, since the n.e.d. sites comprising the disordered nickel domain are expected to be more fragile than the crystalline e.d. sites. This treatment is also expected to increase finely pulverized pure nickel domains in the resulting catalyst enhancing the hydrogenating activity of the catalyst.

A freshly prepared conventional Raney nickel (W-1 type) suspended in water was subjected to ultrasonication (48 kHz, 600 W) for 5 min and the turbid supernatant solution was removed by decantation from paramagnetic nickel powders fixed with a magnet. The same treatment was repeated until the supernatant solution became transparent; 2 to 3 repetitions were required. The resulting catalyst (RNi–U) was then modified with an aqueous solution of tartaric acid and NaBr according to the method reported.[2]

As expected, the TA–NaBr–MRNi–U thus obtained showed a much faster rate of hydrogenation rate and excellent enantio-differentiating ability in the hydrogenation of **1** and **2** to pentane-2,4-diol **3** and 2,6-dimethylheptane-3,5-diol **4**, respectively; see Table 1. The hydrogenating activity of TA–NaBr–MRNi–U, evaluated by the time required for the completion of reaction, was 5 to 10 times higher than that of the conventional TA–NaBr–MRNi. The increment of catalytic activity is synthetically significant, especially in the case of **2** for which a much longer period was required to complete hydrogenation. The higher content of the (*R**,*R**)-isomer of high enantiomeric excess (e.e.) in the reaction mixture substantially increased the isolated yield of the optically pure (*R**,*R**)-isomer after two successive recrystallizations. Thus, the present procedure enables abundant supply of optically pure 1,3-diols of C_2 symmetry, which have been utilized as efficient chiral auxiliaries.[3]

The new catalyst was also highly effective for the hydrogen-

Table 1 Comparison of (*R*,*R*)-TA–NaBr–MRNi and (*R*,*R*)-TA–NaBr–MRNi–U in the enantio-differentiating hydrogenation of 1,3-diketones

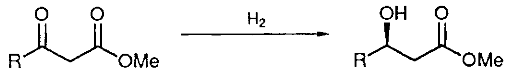


I II III (meso) IV

Substrate R	Catalyst	Reaction[a] conditions T/°C	t/h	Product ratio[b] I:II:III:IV	E.e. of[c] IV (%)	Isolated yield[d] of optically pure IV (%)	Configuration
Me	MRNi	100	24	0:20:10:70	90	21	(2*R*,4*R*)
	MRNi	100	36	0:0:13:87	86	41	(2*R*,4*R*)
	MRNi–U	100	4	0:7:7:86	91	60	(2*R*,4*R*)
$(Me)_2CH$	MRNi	100	192	1:17:16:66	85	32	(3*S*,5*S*)
		110	48	[e]			
	MRNi–U	100	60	0:6:22:72	90	59	(3*S*,5*S*)
		110	12	0:0:19:81	89	62	(3*S*,5*S*)

[a] *Reaction conditions:* substrate (100 g); tetrahydrofuran THF (100 cm^3); catalyst (19 g); initial H_2 pressure 100 KPa. [b] Determined by gravimetry after separation of each component by MPLC. [c] Determined by polarimetry, $[\alpha]_D^{20}$ −54.7° (*c* 10, EtOH) for (2*R*,4*R*)-**3** and $[\alpha]_D^{20}$ −64.5° (*c* 1.0, MeOH) for (3*S*,5*S*)-**4**. [d] Two successive recrystallizations of the reaction products from diethyl ether gave optically pure **IV**. [e] Dehydration of **II** took place under these conditions.

Table 2 Comparison of (*R,R*)-TA–NaBr–MRNi and (*R,R*)-TA–NaBr–MRNi–U in the enantio-differentiating hydrogenation of methyl 3-oxoalkanoates



No	Substrate (R)	Catalyst	Reaction time/h	E.e. of Product (%)
1	Me	MRNi–U[a]	2.5	86[c]
2		MRNi	5.0	80
3		MRNi–U[b]	18	81
4	n-C_7H_{15}	MRNi–U[a]	36	89[d]
5		MRNi	144	83
6	n-C_9H_{19}	MRNi–U[a]	48	91[d]
7		MRNi	192	86
8	n-$C_{11}H_{23}$	MRNi–U[a]	48	94[d]
9		MRNi	192	86

[a] *Reaction conditions*: substrate (10 g); catalyst (1.9 g): methyl propionate (20 cm^3); initial pressure of H_2 100 KPa; temperature 100 °C. [b] *Reaction conditions*: substrate (10 Kg); catalyst (190 g); methyl propionate (100 dm^3); initial pressure of H_2 100 KPa; temperature. 100 °C. [c] Determined by polarimetry, $[\alpha]_D^{20} = -22.4°$ (neat) for (*R*)-methyl 3-hydroxybutanoate. [d] Determined by NMR spectroscopy with a chiral shift reagent.

ation of a series of 3-oxoalkanoic acid esters. Representative results are listed in Table 2. The reaction period was shortened by a factor of 2 to 4 and the optical yield increased up to 86 to 94% e.e. The catalyst proved to be useful for a large scale hydrogenation carried out at much lower catalyst : substrate ratio (Table 2, entry 3). By the combination of this hydrogenation process and the facile and effective optical enrichment process developed by us,[4] it becomes possible to obtain large amounts of optically pure 3-hydroxyalkanoic acids which have been employed as chiral synthetic blocks of various natural products.[5]

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