Highly Efficient Enantio-selective Hydrogenation of Methyl Acetoacetate over an Improved Tartaric Acid-modified Raney Nickel Catalyst

Hangning Chen, Rong Li, Huanling Wang, Liang Yin, Fushan Wang, and Jiantai Ma*
College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, P. R. China

(Received April 24, 2006; CL-060489; E-mail: majiantai@lzu.edu.cn)

Using methanol as the reaction medium (an appropriate amount of sodium bromide was directly added to it), the highly efficient enantio-selective hydrogenation of methyl acetoacetate (MAA) was achieved over a tartaric acid-modified Raney nickel catalyst. 85% ee was attained under the comparatively mild conditions (0.6 MPa, 60 °C, 1 h).

Increased attention has focused on the heterogeneous enantio-selective catalysts, because they can be separated and reused easily. One of the few heterogeneous catalytic systems identified for asymmetric hydrogenation with synthetically useful enantioselectivities is the tartaric acid-modified Raney nickel (TA-MRNi), which can hydrogenate various β-ketoesters (80–98% ee)[1–3] and 2-alkanones (72–85% ee)[4,5] with high optical yields.

In the traditional method, the TA-MRNi catalyst was prepared by soaking the Raney nickel catalyst in a hot slight acidic aqueous solution of tartaric acid and NaBr, based on the idea that the non-enantio-differentiating (n.e.d) sites could be removed at least in part by acid-corrosion and the rest could be deactivated by poisoning with the NaBr adsorbed.[6] Harada et al. demonstrated that inorganic salts in the modification solution increased the optical yield for the hydrogenation over the modified Raney nickel but retarted the hydrogenation rate.[7]

In the 1990's, Tai et al. proposed the ultrasonic-irradiation method for washing Raney nickel. The improved TA-MRNi-U catalyst showed high enantio-selectivity and hydrogenation activity in the hydrogenation of a series of β-ketoesters and 1,3-diketones. 86% ee was achieved in the hydrogenation of MAA.[2] Recently, Osawa and co-workers applied in situ modification (l-(+)-tartaric acid and NaBr were directly added to the reaction media) of fine Ni powder and reduced Ni catalysts to the enantio-selective hydrogenation of MAA.[8–10] Appling the reduced Ni, a high optical yield of 89% was attained. However, those aforementioned results were achieved under high initial hydrogen pressure (9–10 MPa) and long reaction time as those of the previous reports, which revealed the low hydrogenation activity of the TA-MRNi catalyst.

The aim of our present investigation was to enhance the enantio-selective efficiency of the TA-MRNi catalytic system and reduce the demand of reaction conditions, based on the idea of directly adding NaBr to the hydrogenation solvent as a "promoter."[11]

In the present experiment, W-4 type of Raney Ni was freshly prepared with the conventional method.[12] The obtained Raney Ni (usually 3g) was washed 5 times with 250 mL of distilled water, and then with a so-called pre-modification, 200 mL of 1 wt % aqueous solution of l-(+)-tartaric acid (Acros 99+%). This washing procedure was carried out with stirring, using a magnetic stirrer for a period of 10 min. The catalyst was again washed with 250 mL of distilled water, and introduced to a modifying solution (94 °C, 250 mL, $c_{\mathrm{TA}} = 0.2\,\mathrm{mol/L}$) and modified twice. pH of the modifying solution was adjusted to the required value using a potentiometric titration with 1 mol/L NaOH. After that, the catalyst was successively washed 5 times with 250 mL of distilled water and 100 mL of methanol. In this step, no NaBr was added into the modifying solution. Finally, the modified catalyst (0.2 g) prepared in this manner was quickly introduced into 4 mL of reaction solvent, in which an appropriate amount of NaBr was directly added, then introduced 2 mL of MAA (Acros 99+%). The hydrogenation reaction was carried out at 60 or 100 °C. A stainless steel autoclave (100 mL) with a magnetic stirrer was used for high-pressure hydrogenation reactions. The initial hydrogen pressure was 0.6–9 MPa and decreased as reaction progressed. In order to obtain 100% conversion of the substrate, all the reactions were carried out until no further consumption of hydrogen was observed.

The optical yield was determined polarimetrically by means of the optical activity measurement of the product in its concentrated state. Digital polarimeter Perkin-Elmer polarimeter-341 (U.S.A.) was used for measurements. The optical yield (ee) was then calculated in accordance with the following equation:

$$\text{e.e.} = \text{oy}\ (\%) = \frac{[\text{a}]^{20}{}_{\text{D}}\ \text{product}}{-22.95} \times 100$$

Reaction rate as well as enantio-selectivity was clearly dependent on the type of reaction medium. Kukula and Červený had tested that the reaction performed in methanol was 5 times faster than in THF, but the enantio-selectivity was significantly lower. When using methanol as the reaction medium, the highest ee of 37.3% was attained.[13] Therefore, in order to obtain a high optical yield, the aprotic semi-polar solvents were always used as the reaction medium. In contrast with previous investigations,[2,13,14] from Table 1, it could be seen that the hydrogenation activity and the enantio-selectivity were as follows, THF < BuOH < EtOH < MeOH. It showed that high reaction rate and enantio-selectivity could easily be achieved when methanol served as the reaction medium.

Modifying pH had a considerable effect on the optical yield

Table 1. Dependence of enantio-selectivity and reaction time on different types of solvent[a]

Entry	Solvent	Reaction time/h	ee/%
1	THF	3	24
2	BuOH	2	64
3	EtOH	1	71
4	MeOH	0.4	75

[a] Modifying conditions: $c_{\mathrm{TA}} = 0.2\,\mathrm{mol/L}$, pH = 4.0, $T = 94\,°\mathrm{C}$, $t = 60\,\mathrm{min}$; Reaction conditions: solvent (4 mL), MAA (2 mL), catalyst (0.2 g), NaBr (10 mg), H_2 pressure (6 MPa), 60 °C.

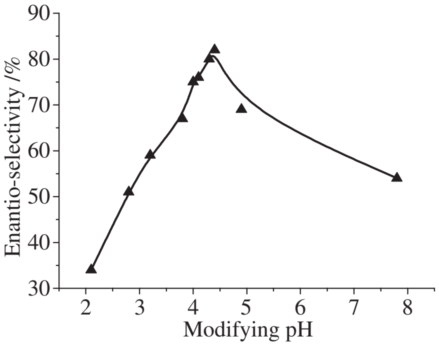

Figure 1. Dependence of the enantio-selectivity on modifying pH. Modifying conditions: $c_{\mathrm{TA}} = 0.2\,\mathrm{mol/L}$, $T = 94\,°\mathrm{C}$, $t = 60\,\mathrm{min}$; Reaction conditions: methanol (4 mL), MAA (2 mL), catalyst (0.2 g), NaBr (10 mg), H_2 pressure (6 MPa), 60 °C.

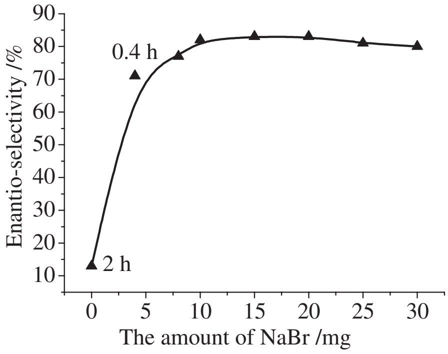

Figure 2. Dependence of enantio-selectivity on the amount of NaBr. Modifying conditions: $c_{\mathrm{TA}} = 0.2\,\mathrm{mol/L}$, $\mathrm{pH} = 4.4$, $T = 94\,°\mathrm{C}$, $t = 60\,\mathrm{min}$; Reaction conditions: methanol (4 mL), MAA (2 mL), catalyst (0.2 g), H_2 pressure (6 MPa), 60 °C.

of the reaction. As Figure 1 showed, the dependence of the optical yield on the modifying pH passed through a maximum. The optimal pH value for achieving the highest optical yields lay in the point of pH = 4.4.

The direct addition of NaBr to methanol was another important factor, which greatly enhanced the enantio-selective hydrogenation efficiency of the improved TA-MRNi catalytic system. NaBr added to the reaction medium had both of the following roles: i) Na^+ increased the optical yield and the hydrogenation rate, ii) Br^- increased the optical yield and decreased the hydrogenation rates.[9] Figure 2 showed the effect of the amount of NaBr. Without addition of NaBr, the ee value was lower than 13%, and the reaction rate was much lower. However, the addition of 4 mg of NaBr could significantly increase the enantio-selectivity and hydrogenation activity. From the data obtained, the appropriate amount of NaBr was in the range between 10 and 20 mg. These results indicated that Br^- could selectively deactivate the n.e.d sites before the hydrogenation reaction started.

As Table 2 showed, the ee was unaffected by the initial H_2 pressure between 0.6 and 6 MPa, while the reaction time was obviously dependent on the pressure. It also showed that the enantio-selectivity and hydrogenation rate were prominently affected by the reaction temperatue. In addition, it could be seen that the enantio-selectivity and the hydrogenation activity had not been significantly improved by employing the ultrasonic-irradiated Raney nickel. In our research, the high enantio-selectivity of 85% was achieved in the hydrogenation of MAA under the much less demanding conditions (0.6 MPa, 60 °C, 1 h), which strongly suggested the highly enantio-selective hydrogenation efficiency of the improved TA-MRNi/methanol, NaBr catalytic system.

Table 2. Enantio-selective hydrogenation of MAA under different reaction conditions[a]

Entry	Catalyst	T/°C	H_2/MPa	t_{React}/h	ee/%
1	TA-MRNi-U[b]	60	6	0.4	81
2	TA-MRNi	60	9	0.3	77
3	TA-MRNi	60	6	0.4	83
4	TA-MRNi	60	2	0.8	84
5	TA-MRNi	60	0.6	1	85
6	TA-MRNi	100	6	0.3	75
7	TA-MRNi	100	2	0.6	75
8	TA-NaBr-MRNi[c]	100	9–10	5	80
9	TA-MRNi-U[d]	100	9–10	2.5	86

[a] Modifying conditions: $c_{\mathrm{TA}} = 0.2\,\mathrm{mol/L}$, $\mathrm{pH} = 4.4$, $T = 94\,°\mathrm{C}$, $t = 60\,\mathrm{min}$; Reaction conditions: MAA (2 mL), methanol (4 mL), catalyst (0.2 g), NaBr (15 mg). [b] The ultrasonic-irradiated Raney nickel was used. [c] Ref. 14, modifying condition: $c_{\mathrm{TA}} = 1\,\mathrm{wt}\,\%$, $c_{\mathrm{NaBr}} = 10\,\mathrm{wt}\,\%$, $\mathrm{pH} = 3.2$; Reaction solvent: methyl propionate. [d] Ref. 2, the modifying conditions and reaction solvent were the same as Ref. 14, except that the ultrasonic-irradiated Raney nickel was used.

References

1 A. Tai, T. Harada, Y. Hiraki, S. Murakami, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1414.
2 A. Tai, T. Kikukawa, T. Sugimura, Y. Inoue, T. Osawa, S. Fujii, *J. Chem. Soc., Chem. Commun.* **1991**, 795.
3 S. Nakagawa, T. Sugimura, A. Tai, *Chem. Lett.* **1997**, 859.
4 T. Osawa, T. Harada, A. Tai, *J. Catal.* **1990**, *121*, 7.
5 T. Osawa, T. Harada, O. Takayasu, *Top. Catal.* **2000**, *13*, 155.
6 T. Harada, Y. Izumi, *Chem. Lett.* **1978**, 1195.
7 T. Harada, A. Tai, M. Yamamoto, H. Ozaki, Y. Izumi, *Stud. Surf. Sci. Catal.* **1981**, *7*, 364.
8 T. Osawa, A. Ozawa, T. Harada, O. Takayasu, *J. Mol. Catal. A: Chem.* **2000**, *154*, 271.
9 T. Osawa, Y. Hayashi, A. Ozawa, T. Harada, O. Takayasu, *J. Mol. Catal. A: Chem.* **2001**, *169*, 289.
10 T. Osawa, S. Sakai, T. Harada, O. Takayasu, *Chem. Lett.* **2001**, 392.
11 L. J. Bostelaar, W. M. H. Sachtler, *J. Mol. Catal.* **1984**, *27*, 377.
12 A. A. Pavlic, H. Adkins, *J. Am. Chem. Soc.* **1946**, *68*, 1471.
13 P. Kukula, L. Červený, *J. Mol. Catal. A: Chem.* **2002**, *185*, 195.
14 A. Tai, T. Kikukawa, T. Sugimura, Y. Inoue, S. Abe, T. Osawa, T. Harada, *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2473.