

ENANTIOSELECTIVE CATALYSIS. 54¹. HYDROGENATION OF METHYL ACETOACETATE
USING NICKEL POWDER MODIFIED WITH NaBr/(R,R)-TARTARIC ACID

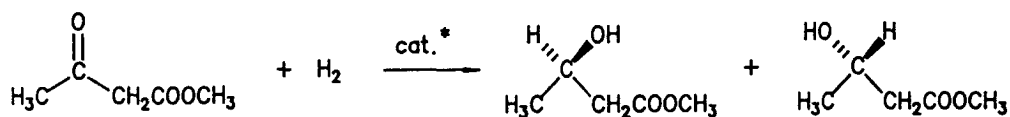
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Abstract. Commercial Ni powders, activated with H₂ and modified with NaBr/(R,R)-(+)-tartaric acid are heterogeneous catalysts for the enantioselective hydrogenation of methyl acetoacetate (MAA) to give (R)-(-)-methyl 3-hydroxybutanoate (MHB) in up to 76.9 % ee.

Raney nickel modified with optically active compounds was one of the earliest heterogeneous catalysts for the enantioselective hydrogenation of organic substrates.² The success of the system modified with tartaric acid stimulated continuous research.^{3,4} In 1978 it was found that NaBr was an important co-modifier.^{3,5,6} The NaBr/tartaric acid modified Raney nickel catalyst gave about 90 % ee in the hydrogenation of methyl/ethyl acetoacetate to methyl/ethyl 3-hydroxybutanoate (Scheme 1). Embedding the catalyst in silicone rubber^{7,8} or adding amines such as pyridine or 1-methylpropylamine⁹ makes it keep its original performance after repeated use.



Scheme 1

We found that commercial nickel powders, much easier to handle than Raney nickel, are suitable precursors for highly enantioselective catalysts. Treatment of the nickel powder with H₂ prior to the NaBr/tartaric acid modification in most cases proved to be beneficial for hydrogenation activity and optical induction.¹⁰

400 mg of Ni powder were activated in the glass insert of an autoclave by treatment with 35 bar H₂ at room temperature for several hours. In N₂ atmosphere, the activated catalyst

was added to the solution of (R,R)-(+)-tartaric acid (1 g) and NaBr (10 g) in water (100 ml), brought to pH 5 with 2 N NaOH. The mixture was stirred for 1 h at 90 °C. After cooling, the supernatant solution was decanted, the catalyst was washed with 10 ml of water, two times with 10 ml of methanol, and with 10 ml of methyl propanoate and used in wet form. The modified catalyst and 10 ml of methyl acetoacetate (MAA) were transferred to a 100 ml autoclave. 1-2 drops of glacial acetic acid were added. The autoclave was pressurized with

Table 1. Hydrogenation of MAA with 45 bar H₂ at 100 °C for 17 h catalysed by commercial Ni powders, activated with H₂ and modified with NaBr/tartaric acid (modification p_H = 5)

entry	Ni powder	chemical yield (%)	degree of hydrogenation (%)	optical yield (%)	number of experiments
1	Aldrich, 99.99 % Ni	73 - 75	68 - 100	1.2 - 2.8	3
2	Fluka, puriss.	70 - 72	33 - 39	63.3 - 69.1	3
3	Ventron A, 99.999 %	71 - 78	100	66.3 - 75.3	23
4	Ventron A, 99.999 % ^{a,b}	70 - 78	41 - 75	67.0 - 76.9	7
5	Ventron B, 99.999 %	71 - 75	40 - 60	32.0 - 34.5	3
6	Ventron C, 99.999 %	65 - 70	15 - 26	19.2 - 38.6	3
7	Heraeus, 25-51	70 - 75	100	39.8 - 49.0	5
8	Heraeus, 25-61	71 - 76	100	57.0 - 66.2	7
9	Heraeus, 873263	73 - 79	95 - 100	53.1 - 63.2	14
10	Heraeus, 873263 ^c	69 - 75	97 - 100	51.2 - 56.6	4

^a The catalyst was coated with silicone rubber by removing the toluene from a solution of a phenyl methyl substituted silicone in toluene.

^b Modification p_H = 6.

^c The catalyst was not activated with H₂.

45 bar H₂ and heated to 100 °C. During the reaction, the pressure dropped to 15-20 bar. The catalyst was separated by filtration and the product (R)-(-)-methyl 3-hydroxybutanoate (MHB) was distilled at 48-56 °C/0.1 Torr and weighed to determine the chemical yield. If no solvent was used, about 10 % of the product remained in the filter.¹⁰ Another factor which lowered the chemical yield was the transesterification of MHB with itself or with MAA, giving products with molecular ions at m/z 202 and 204 in the EI-mass spectrum,^{6,10} which do not distill with MHB. This transesterification came into play at hydrogenation temperatures above 100 °C.

The degree of hydrogenation was determined ^1H nmr spectroscopically in CDCl_3 by integrating the peak areas of the methyl singlet ($\delta = 2.48$ ppm) of MAA and the methyl doublet

Table 2. Repeated use of commercial Ni powders, activated with H_2 and modified with NaBr/tartaric acid, in the hydrogenation of MAA with 45 bar H_2 at 100 °C for 17-20 h (modification pH = 5)

catalyst	number of repeated uses	chemical yield (%)	degree of hydrogenation (%)	optical yield (%)
Ni powder	1	68	100	72.1
Ventron	2	71	100	74.4
99.999 % Ni	3	65	100	71.3
	4	67	100	65.5
	5	70	87	66.7
Ni powder	1	65	100	43.7
Heraeus	2	71	100	41.4
25-51	3	67	100	39.0
Ni powder	1	68	100	59.4
Heraeus	2	72	100	62.2
25-61	3	63	100	63.6
Ni powder	1	66	100	60.4
Heraeus	2	69	100	62.8
873263	3	67	85	59.2

($\delta = 1.23$ ppm) of MHB. The optical yield was determined polarimetrically (neat, Na_D line)¹¹ or with $\text{Eu}(\text{hfc})_3$ in a 1.1 molar excess in CDCl_3 .¹⁰ If unreacted MAA was present, a correction was made assuming that MAA had no effect on the optical rotation of MHB.¹⁰

Table 1 shows that commercial Ni powders, activated with H_2 and modified with NaBr/tartaric acid, exhibit varying catalytic activity. There are good hydrogenation catalysts with poor enantioselectivity (entry 1), poor hydrogenation catalysts with middle to good enantioselectivities (entries 4-6, 2) and excellent hydrogenation catalysts with middle to

high enantioselectivities (entries 7-10, 3). According to Table 2 these catalysts can be used several times without a decrease in hydrogenation activity and enantioselectivity. The Ni powders from Ventron, designated A, B, C, had been ordered under the same catalogue number but obviously were different specimen, type A being by far the best. This demonstrates that it is probably the size and the structure of the surface which differentiate the Ni powders and determine the properties of the catalyst. This is corroborated by the



Fig. 1: Scanning electron micrographs (Hitachi S-570) of the commercial specimen Ventron A (left) and Ventron C (right)

scanning electron micrographes of specimen Ventron A, a very good catalyst, and Ventron C, a poor catalyst (Fig. 1).¹⁰ Thus, the correlation of hydrogenation activity and enantioselectivity with surface properties of the catalyst will have to guide further investigations.

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