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Enantio-differentiating Hydrogenation of 2-Alkanones over Asymmetrically Modified Nickel Catalyst and Its Application to the Preparation of Optically Pure 2-Alkanols

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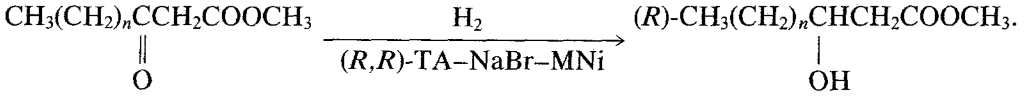
Enantio-differentiating hydrogenation of 2-alkanones over asymmetrically modified nickel catalyst was carried out with an average optical yield of about 80%. The factors affecting the optical yield of the reaction and their functions are discussed. A practical method for the optical enrichment of products of hydrogenation to optically pure 2-alkanols is also presented. © 1990 Academic Press, Inc.

INTRODUCTION

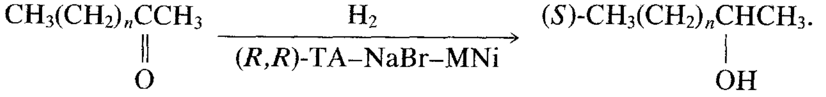
Among various enantio-differentiating hydrogenation catalysts reported in the last 20 years, an asymmetrically modified nickel catalyst (MNi) is a unique heterogeneous catalyst. Intensive studies on the improvement of MNi and the understanding of the enantio-differentiating mechanism of hydrogenation over MNi have been carried out by us (*1*), Klabunovskii *et al.* (*2*), Hoek and Sachtler (*3*), Yasumori (*4*), Orito *et al.* (*5*), Nitta and Imanaka (*6*), and Smith and co-workers (*7*).

The best asymmetrically modified nickel catalyst available to date can easily be prepared when a Raney nickel catalyst (RNi) is soaked in an aqueous solution of tartaric acid (TA) and NaBr (*8*). This catalyst (TA–NaBr–MNi) gave quantitative chemical yields and 85–88% optical yields in the hydrogenation of 3-oxoalkanoic acid esters to 3-hydroxyalkanoic acid esters:



$$\mathrm{CH_3(CH_2)}_n\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{CH_2COOCH_3} \xrightarrow[(R,R)\text{-TA–NaBr–MNi}]{\mathrm{H_2}} (R)\text{-}\mathrm{CH_3(CH_2)}_n\underset{\underset{\mathrm{OH}}{|}}{\mathrm{C}}\mathrm{HCH_2COOCH_3}. \quad (1)$$

This catalyst was also found to give around 80% optical yields in the enantio-differentiating hydrogenation of 2-alkanones to optically active 2-alkanols (*9, 10*):



$$\mathrm{CH_3(CH_2)}_n\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{CH_3} \xrightarrow[(R,R)\text{-TA–NaBr–MNi}]{\mathrm{H_2}} (S)\text{-}\mathrm{CH_3(CH_2)}_n\underset{\underset{\mathrm{OH}}{|}}{\mathrm{C}}\mathrm{HCH_3}. \quad (2)$$

As for the enantio-differentiating hydrogenation of 2-alkanone to 2-alkanol, a high optical yield (97.3%) was reported in the catalytic borane reduction of a highly branched 2-alkanone, 3,3-dimethyl-2-butanone, over optically active B-methylated oxazaborolidine (*11*). However, this was limited to a highly branched substrate and no equally satisfactory results were attained in the hydrogenation of straight-

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chain 2-alkanones to 2-alkanols. Thus, it is an outstanding result that optical yields of around 80% were attained in the hydrogenation of various kinds of straight-chain 2-alkanones to 2-alkanols over TA–NaBr–MNi. In this report, we present our efforts to determine the optimum conditions of the enantio-differentiating hydrogenation of 2-alkanones together with the effective method for the optical enrichment of the hydrogenation products to optically pure 2-alkanols.

EXPERIMENTAL

Optical rotation was measured with a Perkin Elmer 241 polarimeter. IR spectra were taken with a Jasco 810 spectrometer.

Materials. O-Benzoyl-(*R*,*R*)-tartaric acid (*12*), *O*,*O*′-dibenzoyl-(*R*,*R*)-tartaric acid (*13*), acid phthalates of 2-alkanols (*14*), and 3,5-dinitrobenzoates of 2-alkanols (*15*) were prepared by the reported methods. The other chemicals were obtained from commercial sources and used without further purification.

Raney nickel(RNi). The Ni–Al alloy (Ni/Al = 42/58, 3.8 g) was added to an alkaline solution (9 g of NaOH in 40 ml of H_2O) in small portions. The resulting suspension was held at 100°C for 1 h, after which the supernatant was removed by decantation. The catalyst was washed with twenty 50-ml portions of deionized water. The weight of the RNi thus obtained was about 1.6 g.

Acid-treated RNi(RNi-A). RNi-A was prepared by the reported method (*16*). RNi prepared from 3.8 g of the alloy by the above procedure was treated with a 1% aqueous solution of glycolic acid (200 ml) at pH 3.2, 100°C for 1 h. After removal of the solution by decantation, the catalyst was washed with twenty 50-ml portions of deionized water. Then the catalyst was treated with a 1 *M* NaOH solution (40 ml) at 100°C for 1 h to remove the adsorbed glycolic acid from the catalyst surface. The resulting catalyst was washed with twenty 50-ml portions of deionized water.

Pure nickel catalyst (PNi). The fine nickel powder with a mean particle diameter of 20 nm, manufactured by Vacuum Metallurgical Company Ltd. (Chiba, Japan) (1.6 g), was treated with a hydrogen stream (8 liters/h) at 200°C for 0.5 h.

Modifying solution. Three kinds of modifying solution were used in this study: (1) An optically active compound (13 mmol) was dissolved in deionized water (200 ml); the pH was adjusted to a specified value with 1 *M* NaOH solution. (2) An optically active compound (13 mmol) and NaBr (the amount stated in the text) were dissolved in deionized water (200 ml); the pH was adjusted to a specified value with 1 *M* NaOH solution. (3) Tartaric acid (the amount stated in the text) was dissolved in deionized water (200 ml).

Modification. The catalyst was soaked in the modifying solution for 1 h at the temperature stated in the text. After removal of the solution by decantation, the modified catalyst was washed successively with a 20-ml portion of deionized water, two 100-ml portions of methanol, and two 30-ml portions of tetrahydrofuran.

Hydrogenation of 2-alkanone. Two kinds of reaction mixture were subjected to the hydrogenation over MNi in this work: (1) a mixture of 2-alkanone (10 ml), pivalic acid (the amount stated in the text), and tetrahydrofuran (20 ml); and (2) a mixture of 2-octanone (7.4 ml) and the previously stated amounts of pivalic acid, sodium pivalate, and tetrahydrofuran in the text. Hydrogenation was carried out in a 100-ml autoclave under an initial hydrogen pressure of 90–100 kg/cm^2 at 60 or 100°C until no further consumption of hydrogen was observed. After removal of the catalyst by decantation and removal of tetrahydrofuran by evaporation, the hydrogenation product was dissolved in 100 ml of ether and washed with a saturated aqueous solution of K_2CO_3. The ether solution was then dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. As for 2-hexanol, 2-heptanol, 2-octanol, 2-decanol, or 2-tridecanol, simple distillation was carried out to remove the solvent. The chemical purity of each distillate was more than 98% (GLC analyses: 5% Tween 80 on Shimalite W at 110–130°C; 2% OV-17 on Chromosorb W at 100–220°C). In the case of 2-butanol, simple distillation gave 2-butanol contaminated with the solvent. Some parts of the distilled 2-butanol were further purified by preparative GLC (20% PEG 20M on Chromosorb W at 100°C) for the analyses of chemical and optical purity.

Determination of optical yield. The optical yield of the reaction was evaluated based on the optical purity of the product. The optical purity was determined by polarimetry:

$$\text{Optical yield (\%)} = \frac{[\alpha]_D^{20} \text{ of hydrogenation product}}{[\alpha]_D^{20} \text{ of pure enantiomer}} \times 100.$$

The specific optical rotations $[\alpha]_D^{20}$ of optically pure 2-butanol, 2-hexanol, 2-heptanol, 2-octanol, 2-decanol, 2-tridecanol, 3-methyl-2-butanol, 3,3-dimethyl-2-butanol, and 3-octanol are +13.87 (neat) (*17*), +11.57 (neat) (*17*), +10.32 (neat) (*17*), +9.76 (neat) (*17*), +8.68 (neat) (*17*), +8.74 (c 5, benzene) (*18*), +4.85 (neat) (*19*), +7.71 (neat) (*20*), and +8.22 (neat) (*18*), respectively. The specific rotation of optically pure 4-octanol has been reported to be very small ($[\alpha]_D^{20}$ +0.74 (neat)) (*21*). Thus, the enantiometer excess (%) of the hydrogenation product of 4-octanone was determined by an NMR method according to the procedure of Yamaguchi *et al.* (*22*), as a substitute for the optical yield.

Optically pure 2-alkanols. The outline of the optical enrichment is shown at the top of Table 4. The hydrogenation products were subjected to esterification with either phthalic anhydride (*23*) or 3,5-dinitrobenzoyl chloride (*24*). The crude acid phthalate or 3,5-dinitrobenzoate of 2-alkanol was dissolved in boiling solvent and crystallized at room temperature to enrich its optical purity. This procedure was repeated (three to four times) until the optically pure ester of 2-alkanol was obtained. The optically pure crystals were further recovered effectively from the combined mother liquors of the above process when the concentrated mother liquors were seeded with optically pure crystals previously obtained. The optically pure ester thus obtained was dissolved in a minimum amount of methanol and treated with KOH at room temperature for 1 day. After removal of the insoluble material by filtration, the filtrate was concentrated *in vacuo*. Ether was added to the residue, and then the ether solution was washed with water. After being dried over anhydrous Na_2SO_4, the ether solution was subjected to fractional distillation *in vacuo* to give optically pure 2-alkanol. The overall yields from 2-alkanone to optically pure 2-alkanol are listed in Table 4.

RESULTS AND DISCUSSION

The preparation of MNi and the enantio-differentiating hydrogenation with this catalyst are simple chemical processes. However, the variables affecting the optical yield are considerable in number. In the course of studies of the enantio-differentiating hydrogenation of 3-oxoalkanoic acid esters, we have found that, although the optical yield of the reaction is governed by both the variables of catalyst preparation and the variables of hydrogenation, each variable can be optimized independently. The approach based on this experience was effectively applied to the present work.

Variables of the catalyst preparation. MNi can be prepared when activated nickel powder (base catalyst) is immersed in an aqueous solution of an optically active material (modifying solution). Thus, variables to be optimized are the source of base catalyst and components of the modifying solution.

The results of the hydrogenation of 2-octanone over MNi prepared under different conditions are listed in Table 1 together with reported data for the hydrogenation of methyl acetoacetate (MAA) as references.

TABLE 1

Effects of Variables of Catalyst Preparation on the Optical Yield of the Hydrogenation of 2-Octanone[a] and MAA[b]

No.	Ni catalyst (base catalyst)	Modifying solution				Optical yield (%)/configuration of hydrogenation product	
		Modifying reagent	NaBr/modifying reagent (g/g)	pH	Temperature (°C)	2-Octanol	Methyl 3-hydroxybutyrate
1	PNi	(*R*,*R*)-Tartaric acid	0	5.0	0	45/(*S*)	51/(*R*)
2	RNi	(*R*,*R*)-Tartaric acid	0	3.2	100	38/(*S*)[c]	39/(*R*)[d]
3	RNi	(*R*,*R*)-Tartaric acid	0.5	3.2	100	55/(*S*)[c]	57/(*R*)[d]
4	RNi	(*R*,*R*)-Tartaric acid	2.0	3.2	100	60/(*S*)[c]	75/(*R*)[d]
5	RNi	(*R*,*R*)-Tartaric acid	6.0	3.2	100	61/(*S*)[c]	79/(*R*)[d]
6	RNi	(*R*,*R*)-Tartaric acid	8.0	3.2	100	—	83/(*R*)[d]
7	RNi	(*S*)-Malic acid	0	3.2	100	10/(*R*)	23/(*S*)
8	RNi	(*S*)-Malic acid	2.2	3.2	100	20/(*R*)	61/(*S*)[e]
9	RNi	*O*-Benzoyl-(*R*,*R*)-tartaric acid	0	3.2	100	3/(*S*)	—
10	RNi	*O*-Benzoyl-(*R*,*R*)-tartaric acid	4.7	3.2	100	—	65/(*R*)[e]
11	RNi	*O*,*O*′-Dibenzoyl-(*R*,*R*)-tartaric acid	0	3.2	100	2/(*S*)	—
12	RNi	*O*,*O*′-Dibenzoyl-(*R*,*R*)-tartaric acid	3.3	3.2	100	—	8/(*R*)[e]
13	RNi-A	(*S*)-Glutamic acid	0	5.0	0	1/(*S*)	18/(*R*)[f]
14	RNi-A	(*S*)-Leucine	0	6.0	0	0.3/(*S*)	—

[a] Reaction mixture: MNi (1.6 g), 2-octanone (10 ml), pivalic acid (15.7 g), and tetrahydrofuran (20 ml). Reaction conditions: 100°C, initial H_2 pressure 95 kg/cm^2.

[b] Reaction mixture: MNi (0.8 g), MAA (11.5 ml), acetic acid (0.2 ml), and methyl propionate (23 ml).

[c] Reference (*27*).

[d] Modifying pH, 3.0; Ref. (*16*)

[e] Reference (*9*).

[f] Reference (*16*).

Of the commercially available optically active α-hydroxy or α-amino acids, the best modifying reagent was tartaric acid (TA). The order of the efficiency of representative modifying reagents was TA > malic acid > glutamic acid > leucine (Table 1, entries 2, 7, 13, and 14). When one or two hydroxy groups of TA were esterified, the efficiency of the resulting material was extremely low (Table 1, entries 9–12). These results were the same as those found in the hydrogenation of MAA, indicating that the enantio-differentiation of two types of substrate (2-alkanones and 3-oxoalkanoic acid esters) required the same structural features of the modifying reagent adsorbed on the catalyst surface.

The investigation of the working conditions of the MNi in the hydrogenation of MAA suggested the presence of two types of hydrogenating active sites on MNi: an enantio-differentiating site where an optically active product is produced by the aid of modifying reagent and a non-enantio-differentiating site where a racemic product is produced (*25*, *26*). The former site is the surface consisting of relatively large, pure nickel crystallites, while the latter is composed mostly of the surface with amorphous or small nickel crystallites partially contaminated with aluminum or other elements. Thus, the enantio-differentiating ability of MNi is expected to be a function of the ratio of the two reaction sites as well as of the efficiency of modifying reagent on the enantio-differentiating site. The function of NaBr in the modifying solution has also been suggested to be the deactivation of non-enantio-differentiating site by partial poisoning (*25*). On modification with TA, the use of pure nickel powder activated in a flow of hydrogen (PNi) gave a better MNi than the use of the RNi (Table 1, entries 1 and 2). Addition of NaBr to the modifying solution resulted in a great increase in the enantio-differentiating ability of the resulting catalyst. The enhancement of enantio-differentiating ability was dramatic in the case of RNi. These tendencies were quite similar to those found in the hydrogenation of MAA (Table 1, entries 2–6), indicating that the enantio-differentiating hydrogenation of 2-octanone and MAA took place at the same kind of site on the catalyst surface.

The conclusions drawn from the present results are that the enantio-differentiating hydrogenations of 2-alkanones and 3-oxoalkanoic acid esters on the MNi are carried out at the same site (enantio-differentiating site) with the same mode of adsorbed modifying reagent, and, eventually, the best MNi for the hydrogenation of 3-oxoalkanoic acid esters (TA–NaBr–MRNi) is also the best one for the hydrogenation of 2-alkanones.

Reaction variables. A series of comparative studies of the hydrogenation of MAA and 2-octanone indicate that the optical yields of the two reactions are dependent on such reaction variables as solvent, additives in the reaction system, and temperature, in different manners. The hydrogenation of MAA over (*R*,*R*)-TA–NaBr–MRNi under optimum conditions (11.5 ml of substrate dissolved in 23 ml of methyl propionate and 0.2 ml of acetic acid was subjected to hydrogenation over 0.8 g of TA–NaBr–MRNi at 100°C) gave methyl (*R*)-3-hydroxybutyrate in 83% optical yield, while the hydrogenation of 2-octanone under the same conditions gave (*S*)-2-octanol in only 9% optical yield. By omission of acetic acid from the system, the optical yield remained almost unchanged in the case of MAA but became negligible in the case of 2-octanone. The results of these early experiments provided a clue to the improvement of the optical yield of the hydrogenation of 2-alkanone. The intensive search for additives to the reaction system revealed that addition of a carboxylic acid, especially one highly branched at the α position such as pivalic acid, and its sodium salt to the reaction system was essential to improvement of the optical yield of the hydrogenation of 2-alkanone (*27*, *28*). Since pivalic acid and sodium pivalate are solids, the use of appreciable amounts of the solvent was required to carry out the hydrogenation smoothly. Thus, the amounts of pivalic acid and sodium pivalate in the reaction system, as well as the amount of solvent employed, were considered the important reaction variables to be optimized.

The optical yields of the hydrogenation of 2-octanone in the presence of representative solvents are listed in Table 2. Either the use of methanol, a good solvent for sodium pivalate, or the use of hexane, a poor solvent for sodium pivalate, resulted in a poor optical yield. Methyl propionate, the best solvent for the hydrogenation of MAA, could not be utilized, because it was transesterified with the hydrogenation product *in situ* in giving 2-methylheptyl propionate. Among various solvents employed, tetrahydrofuran, which is a moderate solvent for sodium pivalate, was found to be the best for the hydrogention of 2-alkanone.

Figure 1 shows the relationship between the optical yield and the amount of sodium pivalate in the reaction system. As a base catalyst, PNi freed of sodium ions was employed. The optical yield was negligible in the absence of sodium salt. The value increased steeply with the addition of sodium pivalate, and then reached the optimum value. When RNi was employed as

TABLE 2

Effect of Solvent on Optical Yield of the Hydrogenation of 2-Octanone[a]

Solvent	Optical yield (%)
Tetrahydrofuran	66
Hexane	50
Methanol	2
Methyl proprionate	—

[a] Catalyst: RNi (1.6 g) modified with an aqueous solution of TA (2 g) and NaBr (12 g) at pH 3.2, 100°C. Reaction mixture: 2-oxtanone (10 ml), pivalic acid (15.7 g), and solvent (20 ml).

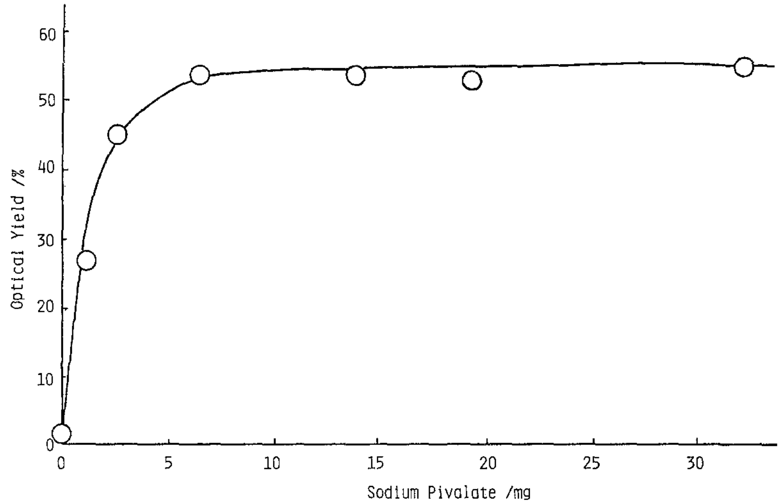


FIG. 1. Relationship between optical yield and amount of sodium pivalate in the reaction system with PNi as base catalyst. Catalyst: PNi (1.6 g) modified with TA (16 mg) in H_2O (200 ml) at 0°C. Reaction mixture: pivalic acid (19.5 g), tetrahydrofuran (16 ml), and 2-octanone (7.4 ml). Reaction conditions: 100°C, initial H_2 pressure of 95 kg/cm^2.

the base catalyst, a similar result was obtained (Fig. 2). From these data, the presence of an appropriate but not too excessive an amount of sodium pivalate in the reaction system was found to be an unavoidable factor in obtaining a good optical yield.

Figure 3 shows the relationship between the optical yield and the amount of pivalic acid added to the reaction system. Plots 1 and 2 depict the results of experiments carried out in the presence of different amounts of sodium pivalate. As shown in the figure, the optical yield increased with

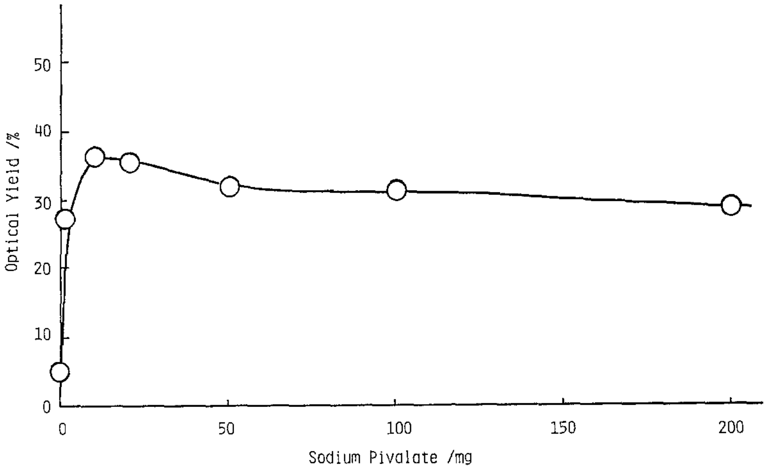


FIG. 2. Relationship between optical yield and amount of sodium pivalate in the reaction system with RNi as base catalyst. Catalyst: RNi (1.6 g) modified with TA (2 g) in H_2O (200 ml) at 100°C. Reaction mixture: pivalic acid (15.7 g), tetrahydrofuran (20 ml), and 2-octanone (10 ml). Reaction conditions: 60°C, initial H_2 pressure of 95 kg/cm^2.

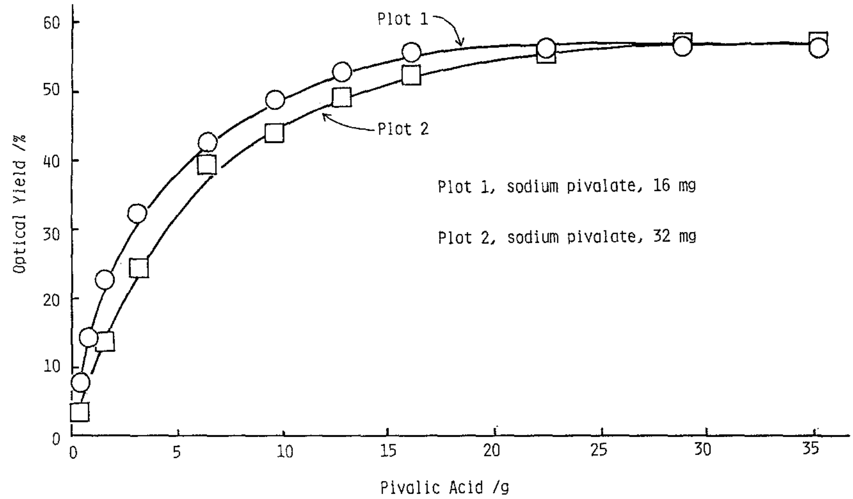


FIG. 3. Relationship between optical yield and amount of pivalic acid in the reaction system. Catalyst: PNi (1.6 g) modified with TA (16 mg) in H_2O (200 ml) at 0°C. Reaction mixture: Plot 1—sodium pivalate (16 mg), tetrahydrofuran (16 ml), and 2-octanone (7.4 ml); Plot 2—sodium pivalate (32 mg), tetrahydrofuran (16 ml), and 2-octanone (7.4 ml). Reaction conditions: 100°C, initial H_2 pressure of 95 kg/cm^2.

an increase in the amount of added pivalic acid. When the amount of pivalic acid added was less than 20 g, the optical yields were affected by the amount of sodium pivalate already in the system as well as the amount of pivalic acid added. An optical yield of about 60% was attained by the addition of more than 30 g of pivalic acid in the presence of both 16 and 32 mg of sodium pivalate.

The amount of tetrahydrofuran in the system also affected the optical yield as shown in Fig. 4. In the range of 1–20 g of added pivalic acid, the greater the amount of tetrahydrofuran already in the system, the greater the amount of pivalic acid was required to attain the same optical yield.

All the results mentioned above may be rationalized by the assumption that the sodium pivalate in the system was partitioned between the catalyst surface and the liquid phase, and the optical yield of reaction was optimum when the amount of sodium ions on the catalyst was controlled to a certain level under the equilibrium. Thus, one function of pivalic acid in the system may be to reduce the amount of adsorbed sodium ions on the catalyst by increasing the solubility of sodium pivalate in the liquid phase. The presence of tetrahydrofuran in the system would counteract the function of pivalic acid, because tetrahydrofuran is not as good a solvent for sodium pivalate as is pivalic acid. These considerations are also compatible with the results of solvent effects shown in Table 2.

The effective chiral adsorption species for the enantio-differentiation of MAA on the tartaric acid modified nickel catalyst (TA–MNi) has been proved to be monosodium and/or disodium tartrate (*29, 30*). When it is taken into account that the pK_{a1} of TA is lower than the pK_a of pivalic acid, one of the functions of pivalic acid/sodium pivalate is expected to be regulator, to keep TA as monosodium salt under the working conditions of the catalyst, and the preferable chiral species on the catalyst for the enantio-differentiation of 2-alkanone is monosodium tartrate.

From a practical point of view, the present work indicates that the hydrogenation of 2-octanone over sodium-free TA–MNi requires the presence of sodium pivalate,

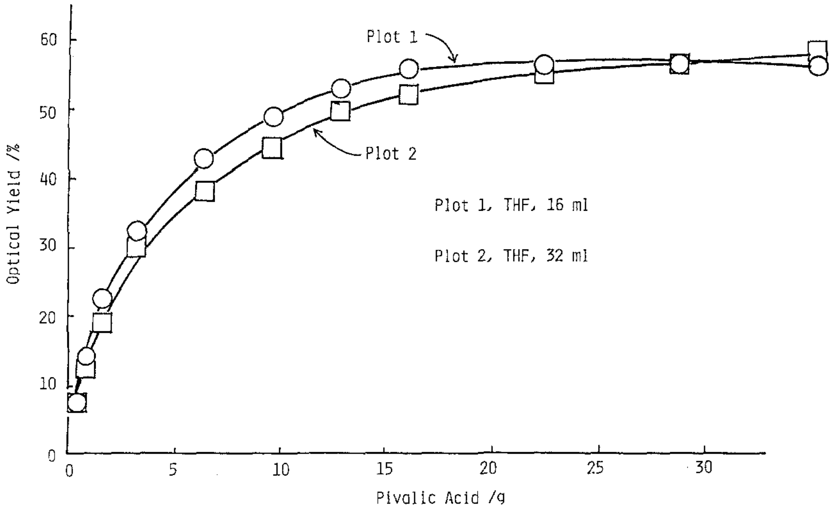


FIG. 4. Relationship between optical yield and amount of tetrahydrofuran in the reaction system. Catalyst: PNi (1.6 g) modified with TA (16 mg) in H_2O (200 ml) at 0°C. Reaction mixture: Plot 1—tetrahydrofuran (16 ml), sodium pivalate (16 mg), and 2-octanone (7.4 ml); plot 2—tetrahydrofuran (32 ml), sodium pivalate (16 mg), and 2-octanone (7.4 ml). Reaction conditions: 100°C, initial H_2 pressure of 95 kg/cm^2.

pivalic acid, and tetrahydrofuran in the reaction system to attain the optimum optical yield. In the case of conventional TA–NaBr–MRNi, which contains sodium ions (ca. 0.6 mg/g catalyst) (*28*), no further addition of sodium pivalate is required; i.e., addition of 5 to 50 mg of sodium pivalate in the system results in no further increase in optical yield. Therefore, the optimum optical yield is attained as long as the amount of pivalic acid and tetrahydrofuran added are optimized.

The effect of reaction temperature on the optical yield of hydrogenation of 2-octanone was significant, in contrast to the fact that the optical yield of hydrogenation of MAA remained almost unchanged in the range of 60 to 120°C, as shown in Fig. 5. As has been reported, the difference in the temperature effect in the hydrogenations of MAA and 2-octanone was explainable by our stereochemical model shown in Fig. 6 (*9*). That is, the enantio-differentiation of MAA is carried out by the formation of dual hydrogen bonds with TA, and dissociation of this interaction is expected to show higher thermal resistance, while that of 2-octanone is done by a single hydrogen bond and steric hindrance, and the degree of dissociation of this single hydrogen bond

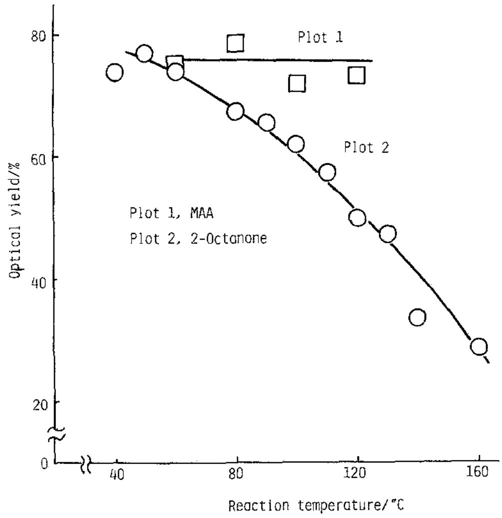


FIG. 5. Relationship between optical yield and reaction temperature. Catalyst: RNi (1.6 g) modified with TA (2 g) and NaBr (12 g) in H_2O (200 ml) pH 3.2, 100°C. Reaction mixture: Plot 1—MAA (10 ml) and tetrahydrofuran (20 ml); plot 2—2-octanone (10 ml), pivalic acid (15.7 g), and tetrahydrofuran (20 ml).

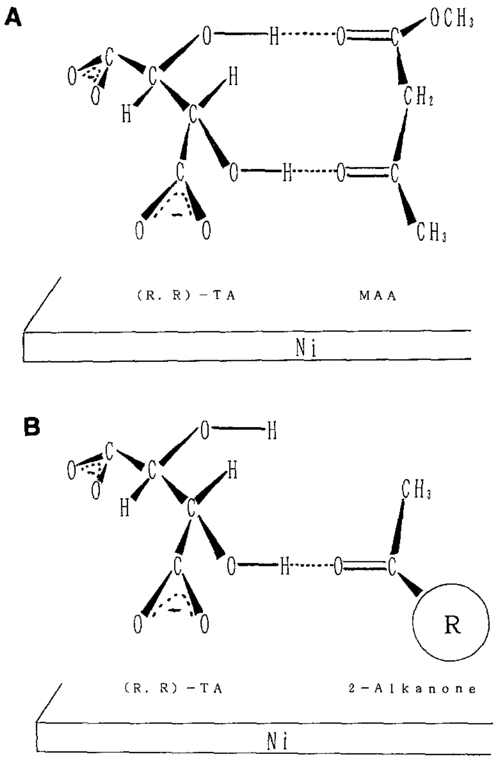


FIG. 6. Schematic representations of the interactions between (*R*,*R*)-TA and MAA (A) and between (*R*,*R*)-TA and 2-alkanone (B).

would increase with an increase in reaction temperature.

The highest optical yield, 80%, was attained in the hydrogenation of 2-octanone over TA-NaBr-MRNi when the reaction was conducted at 60°C under the optimum reaction variables mentioned above. On application of a reaction temperature lower than 60°C, the rate became too sluggish to complete the reaction. The results of the hydrogenation of various 2-alkanones carried out under optimum conditions for 2-octanone are summarized in Table 3. Except for 2-butanone, a series of 2-alkanones gave 2-alkanols in optical yields of 70–80%.

Optical enrichment of reaction product. Although the optical yields of 70–80% are significant in the enantio-differentiating hydrogenation of 2-alkanones, the present method is not satisfactory for the practical preparation of optically pure 2-alkanols. To utilize this convenient method for the production of optically pure 2-alkanols, the development of a simple method for the optical enrichment of the reaction products was required. Along this line, the hydrogenation products were converted to crystal-

TABLE 3

Hydrogenation of Alkanone over (*R*,*R*)-TA-NaBr-MRNi[a]

No.	Substrate	Optical yield (%)		Configuration of product
		Reaction at 100°C	Reaction at 60°C	
1	2-Butanone	49[b]	63[c]	*S*
2	2-Hexanone	66[b]	80[c]	*S*
3	2-Heptanone	66[b]	71[c]	*S*
4	2-Octanone	66[b]	80[c]	*S*
5	2-Decanone	58[b]	76[c]	*S*
6	2-Tridecanone	65[b]	75[c]	*S*
7	3-Methyl-2-butanone	63[b]	—	*S*
8	3,3-Dimethy-2-butanone	74[b]	—	*S*
9	3-Octanone	14	—	*S*
10	4-Octanone	6	—	*S*

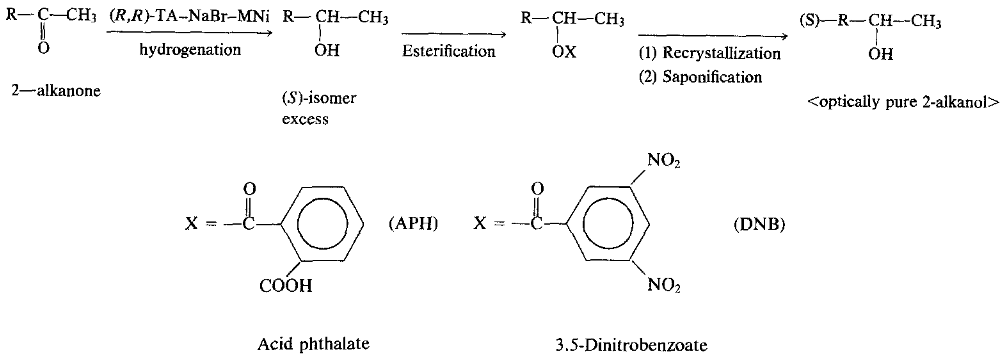
[a] By the use of (*S*,*S*)-TA-NaBr-MNi, (*R*)-2-alkanols can be obtained. Catalyst: RNi (1.6 g) modified with an aqueous solution of TA (2 g) and NaBr (12 g) at pH 3.2, 100°C. For Nos. 7 and 8, a tenfold amount of TA-NaBr-MRNi was employed. Reaction mixture: 2-octanone (10 ml), pivalic acid (15.7 g), and tetrahydrofuran (20 ml).

[b] Reference (*27*).

[c] Reference (*10*).

TABLE 4

Preparation of Optically Pure 2-Alkanols from Hydrogenation Products



No.	Hydrogenation product	*R*—	Optical purity (%)	Crystalline derivative, X	Solvent for recrystallization	Optically pure crystals, $[\alpha]_D^{20}$	Optically pure (*S*)-2-alkanol	
							$[\alpha]_D^{20}$	Yield (%)[a]
1	2-Hexanol	$CH_3(CH_2)_3$-	80	DNB	MeOH	+35.8 (c 5.1, $CHCl_3$)	+12.1 (neat)	23
2	2-Heptanol	$CH_3(CH_2)_4$-	71	APH	Hexane	+48.7 (c 2.7, EtOH)	+10.5 (neat)	21
3[b]	2-Octanol	$CH_3(CH_2)_5$-	77	APH	CH_3CN	+47.0 (c 6.0 EtOH)	+9.8 (neat)	37
4	2-Decanol	$CH_3(CH_2)_7$-	76	DNB	EtOH	+32.6 (c 4.6, $CHCl_3$)	+8.7 (neat)	28
5	2-Tridecanol	$CH_3(CH_2)_{10}$-	75	DNB	EtOH	+29.0 (c 5.1, $CHCl_3$)	+8.9 (c 5, C_6H_6)	56

[a] Overall chemical yield from 2-alkanone to (*S*)-2-alkanol.
[b] Reference (*10*).

line esters with phthalic or 3,5-dinitrobenzoic acid, and the resulting esters were subjected to the optical enrichment by recrystallization.

As shown in Table 4, 2-heptanol and 2-octanol were optically purified as their acid phthalates (APH), and 2-hexanol, 2-decanol, and 2-tridecanol were purified as their 3,5-dinitrobenzoates (DNBs). The mixed melting point determintion of optically pure and racemic crystals and the comparison of the IR spectra of these crystals indicated that there existed two different types of enrichment (Table 5). That is, the optical enrichment of APH ester of 2-heptanol and DNB esters of 2-decanol and 2-tridecanol was carried out by the separation of optically pure and racemic

TABLE 5

Classification of Racemic Crystals of the 3,5-Dinitrobenzoate or Acid Phthalate of 2-Alkanol

No.	Alkanol	Crystalline derivative	Melting point (°C)			IR spectra of optically pure and racemic crystals	Classification of racemic crystals
			Optically pure crystals	Racemic crystals	Mixture (1/1) of optically pure and racemic crystals		
1	2-Hexanol	DNB	67.5	37.5–38.0	37.5–62.0	Slightly different	?
2	2-Heptanol	APH	73.5	66.5	63.0–64.0	Different	Racemic compound
3	2-Octanol	APH	70.5	52.5–53.0	56.0–64.0	Same	Conglomerate
4	2-Decanol	DNB	55.5	52.5	47.0–48.0	Different	Racemic compound
5	2-Tridecanol	DNB	58.5	60.0	53.0–54.0	Different	Racemic compound

crystals, while that of the APH ester of 2-octanol was conducted by direct resolution because the crystals produced were conglomerate. As for the DNB ester of 2-hexanol, classification of the racemic crystals was obscure.

Regardless of the difference in types of enrichment, optically pure crystals were obtained by three or four successive recrystallizations in all cases. The yields of optically pure 2-alkanols based on 2-alkanones (including hydrogenation, esterification, recrystallizations, and saponification) were 21–56%. Thus, the combination of enantio-differentiating hydrogenation of 2-alkanones and optical enrichment of the hydrogenation products by the recrystallization of crystalline derivatives provided a practical procedure for the preparation of optically pure 2-alkanols, so long as the optical yield of the hydrogenation was around 80%.

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REFERENCES

1. Tai, A., Watanabe, H., and Harada, T., *Bull. Chem. Soc. Japan* **52,** 1468 (1979); Tai, A., Harada, T., Tsukioka, K., Osawa, T., and Sugimura, T., *in* "Proceedings, 9th International Congress on Catalysis, Calgary, 1988," p. 1082 and references therein.
2. Klabunovskii, E. I., Vedenyapin, A. A., Karpeiskaya, E. I., and Pavlov, V. A., *in* "Proceedings, 7th International Congress on Catalysis, Tokyo, 1980" (T. Seiyama and K. Tanaka, Eds.), p. 390, Elsevier, Amsterdam, 1981; Zubareva, N. D., and Klabunovskii, E. I., *Izv. Akad. Nauk SSSR Ser. Khim.,* 1172 (1988) [*Chem. Abstr.* **110,** 38604c (1989)].
3. Hoek, A., and Sachtler, W. M. H., *J. Catal.* **58,** 276 (1979); Fu, L., Kung, H. H., and Sachtler, W. M. H., *J. Mol. Catal.* **42,** 29 (1987) and references therein.
4. Yasumori, I., *Pure Appl. Chem.* **50,** 971 (1978); Inoue, Y., Okabe, K., and Yasumori, I., *Bull. Chem. Soc. Japan* **54,** 613 (1981) and references therein.
5. Orito, Y., Niwa, S., and Imai, S., *Yuki Gosei Kagaku KyokaiShi* **35,** 753 (1977) and references therein.
6. Nitta, Y., and Imanaka, T., *Bull. Chem. Soc. Japan* **61,** 295 (1988) and references therein.
7. Bartok, M., Wittmann, Gy., Condos, Gy., and Smith, G. V., *J. Org. Chem.* **52,** 1139 (1987).
8. Harada, T., Yamamoto, M., Onaka, S., Imaida, M., Ozaki, H., Tai, A., and Izumi, Y., *Bull. Chem. Soc. Japan* **54,** 2323 (1981).
9. Tai, A., Harada, T., Hiraki, Y., and Murakami, S., *Bull. Chem. Soc. Japan* **56,** 1414 (1983).
10. Osawa, T., *Chem. Lett.,* 1609 (1986).
11. Corey, E. J., Bakshi, R. K., Shibata, S., Chen, C.-P., and Singh, V. K., *J. Amer. Chem. Soc.* **109,** 7925 (1987).
12. Langenbeck, W., and Herbst, O., *Chem. Ber.* **86,** 1526 (1953).
13. Butler, C. L., and Cretcher, L. H., *J. Amer. Chem. Soc.* **55,** 2605 (1933).
14. Levene, P. A., and Mikeska, L. A., *J. Biol. Chem.* **75,** 585 (1927).
15. Malone, G. B., and Reid, E. E., *J. Amer. Chem. Soc.* **51,** 3424 (1929).
16. Harada, T., Yamamoto, M., Onaka, S., Imaida, M., Ozaki, H., Tai, A., and Izumi, Y., *Bull. Chem. Soc. Japan* **54,** 2323 (1981).
17. Pickard, R. H., and Kenyon, J., *J. Chem. Soc.* **99,** 45 (1911).
18. Pickard, R. H., and Kenyon, J., *J. Chem. Soc.* **103,** 1923 (1913).
19. Pickard, R. H., and Kenyon, J., *J. Chem. Soc.* **101,** 620 (1912).
20. Pickard, R. H., and Kenyon, J., *J. Chem. Soc.* **105,** 1115 (1914).
21. Levene, P. A., and Marker, R. E., *J. Biol. Chem.* **91,** 405 (1931).
22. Yamaguchi, S., Yasuhara, F., and Kabuto, K., *Tetrahedron* **32,** 1363 (1976).
23. Reid, E. E., *J. Amer. Chem. Soc.* **39,** 1250 (1917).
24. Bryant, W. M. D., *J. Amer. Chem. Soc.* **54,** 3758 (1932).
25. Harada, T., Tai, A., Yamamoto, M., Ozaki, H., and Izumi, Y., *in* "Proceedings, 7th International Congress on Catalysis, Tokyo, 1980" (T. Seiyama and K. Tanaka, Eds.), p. 364. Elsevier, Amsterdam, 1981.
26. Nitta, Y., Imanaka, T., and Teranishi, S., *J. Catal.* **80,** 31 (1983) and references therein.
27. Osawa, T., and Harada, T., *Bull. Chem. Soc. Japan* **57,** 1518 (1984).
28. Osawa, T., and Harada, T., *Bull. Chem. Soc. Japan* **60,** 1277 (1987).
29. Tai, A., and Harada, T., "Tailored Metal Catalysts" (Y. Iwasawa, Ed.), p. 265. Reidel, Dordrecht, 1986.
30. Inoue, Y., Okabe, K., and Yasumori, I., *Bull. Chem. Soc. Japan* **54,** 613 (1981).