JOURNAL OF CATALYSIS 60, 184–192 (1979)

Asymmetric Hydrogenations over Modified Raney Nickel

GERARD V. SMITH AND MARIAN MUSOIU

Department of Chemistry and Biochemistry, Southern Illinois University,
Carbondale, Illinois 62901

Received November 22, 1978; revised March 19, 1979

Enantioselective Raney nickel catalyst systems are prepared by modification with asymmetric amino acids and hydroxy acids and used in the hydrogenation of prochiral ketones and prochiral C–C double bonds. A substantial increase in asymmetric induction is accomplished by paying careful attention to modification and hydrogenation variables. Important factors are (i) the contact times of modifying and washing solutions during catalyst modification, and (ii) the contact times of modified catalyst and substrate before reaction. By employing combinations of deuterated Raney nickel, deuterium gas, and deuterated modifiers it is shown that hydrogen (deuterium) in the modifying molecule is involved in the geometry determining transition state.

INTRODUCTION

Following disclosure of the enantioselective palladium-on-silk catalyst (*1*) are reports of the enantioselective Raney nickel catalyst systems (*2*) and detailed procedures for their preparation (*3*). Understanding of these modified Raney nickel systems has matured enough now that certain gross features of the surface–substrate complexes seem clear and certain mechanistic notions can be tested. All workers agree that the modifying asymmetric center (either in an α-amino acid or an α-hydroxy acid) must be in close proximity to the prochiral substrate (usually β-keto esters or β-diketones). The early proposal of a stable modifier-substrate–surface complex (*4*) has been expanded and detailed to show specific oxygen–nickel bonds (*5*). A recent refinement of this concept proposes a hydrogen bond between the hydroxyl hydrogen of a carboxyl-adsorbed α-hydroxy acid and the methoxyl oxygen of an adjacently adsorbed (chelated to Ni) methyl acetoacetate moiety (*6*). Also it has been proposed that the optical purity of the product is controlled by the interaction of substrate and modifying agent prior to the rate-determining addition of hydrogen (*7*). These modified Raney nickel catalyst systems not only present a formidable challenge to the researcher but also offer the potential of developing unique molecular probes which are capable of revealing the most sophisticated surface interactions.

We have been exploring heterogeneous asymmetric catalytic systems from both the practical and theoretical points of view. In this paper we would like to present procedures leading to improved asymmetric activity and reveal evidence leading to better mechanistic understanding.

EXPERIMENTAL

Methyl acetoacetate, ethyl acetoacetate, and methyl 2,2-dimethylacetoacetate were

0021-9517/79/140184-09$02.00/0

obtained from Matheson, Coleman and Bell Company and found to be better than 99% pure by GLC. Before use, they were filtered through a short column of basic active alumina (Ventron Corporation) to remove acidic impurities and water.

Acetoacetanilide, 4-methoxy-4-methyl-2-pentanone, and 4-hydroxy-4-methyl-2-pentanone were obtained from Matheons Coleman and Bell Company, and were used without further purification.

Methyl α-phenylcinnamate was previously prepared in this laboratory (*9*) from the corresponding acid (Aldrich Chemical Company) by the diazomethane method of esterification.

α-Acetaminocinnamic acid was obtained from Monsanto Chemical Company, and was purified by recrystallization from water. Methyl α-acetaminocinnamate was synthesized by alkylation of silver α-acetaminocinnamate (*9*).

Raney nickel No. 28 and Raney nickel chromium No. 24, as active catalysts in water, were donated by W. R. Grace & Company. Raney Catalyst Powder No. 2813 (W. R. Grace & Company), a 50% nickel aluminum alloy, was used for laboratory catalyst preparations. Active Raney nickel B 113, NiAl alloy 013, and nonpyrophoric Raney nickel B 313 were donated by Degussa Inc.

L-(+)-Tartaric acid was obtained from Aldrich Chemical Company; 99% pure (Gold Label), $[\alpha]_D^{20}$ + 12.35 (C = 20.4, H_2O).

L-(+)-Glutamic acid was obtained from Fisher Scientific Company; 99% pure, $[\alpha]_D^{20}$ + 29° (C = 1, 6 N HCl).

L-(−)-Malic acid was obtained from Matheson, Coleman and Bell Company; $[\alpha]_D^{20}$ + 23.5° (C = 5.6, pyridine).

L-(−)-Malic acid-d_6 was prepared by resolution of DL-malic acid (Aldrich Chemical Co.) using L-(+)-tartaric acid as the resolving agent (*10*). The resolved L-malic acid-d_6 showed $[\alpha]_D^{20}$ of +527° (0.01 g L_M and 0.025 g ammonium molybdate dissolved in 1 ml water) and its proton NMR spectrum (dissolved in heavy water) indicated light hydrogen present in the hydroxyl groups. These probably resulted from exchange with nondeuterated isopropanol and ethanol during resolution.

Methanol, absolute ethanol, and dioxane were of reagent grade (Matheson, Coleman and Bell) and were used without further purification. The solvents were mainly used as washing agents for Raney nickel preparations and also as hydrogenation media for experiments conducted in solvents.

Methanol-d_1 (Aldrich Chemical Company) and heavy water of 99.5% isotopic purity (Matheson, Coleman and Bell) were used in the preparation of deuterated asymmetric Raney nickel.

The chiral shift reagent Tris [3-(heptafluorobutyryl)-*d*-camphorato]-europium-(III) abbreviated Eu $(hfbc)_3$ or kiral-shift-E7 was obtained from Regis Chemical Company and was used without further purification for NMR determination of enantiomeric purities of hydrogenation products and reaction mixtures.

Preparation Procedures for Asymmetric Catalysts Based on Commercially Available Raney Nickel

One hundred mililiters of 2% L-(+)-tartaric acid at pH 5.0 to 5.1 was heated to 100°C in a 250-ml round bottom flask fitted with a reflux condenser. To this solution was added 0.1 to 0.15 ml of Raney nickel (W. R. Grace No. 28) and the mixture was allowed to stand for 1.5 hr. After removing the modifying solution by decantation and centrifugation the modified catalyst was washed once with 2 ml of water and twice with 2 ml of methanol. The total washing time was kept within 40 to 50 min. Finally, 0.3 to 0.45 ml of the substrate was added to the washed catalyst and the mixture was quickly transferred to the hydrogenation vessel.

To prepare the modifying solution, a somewhat more concentrated solution of tartaric acid was adjusted to pH 5 with 20% sodium hydroxide solution and then the concentration of tartaric acid was corrected to 2%. Since active Raney nickel could not be accurately measured by weight, the amount of catalyst was measured by volume in a graduated centrifuge tube after centrifugation.

Various modifying parameters such as concentration, temperature and time were varied to observe their effect on the catalyst asymmetric activity. L-Malic acid and L-glutamic acid were utilized as modifying agents in the same way as L-tartaric acid. Other catalysts, for example, Raney nickel chromium and nonpyrophoric Raney nickel, were modified by the procedure described for L-tartaric acid modified Raney nickel.

Preparation Procedure for Asymmetric Catalyst Based on Laboratory Prepared Raney Nickel

Raney nickel was prepared by a method suggested by Izumi *et al.* (*3j*). However, details on washing and handling of catalyst not given in Izumi's method were developed during the course of this work.

Five milliliters of 20% sodium hydroxide was introduced in a 10-ml round bottom flask fitted with a reflux condenser. To this solution, 0.3 mg NiAl alloy was added over a period of 2 to 3 min and the mixture was heated at 103 to 105°C for 60 min. Then, the catalyst was transferred to a 15-ml centrifuge tube, the excess alkaline solution was removed, and the Raney nickel was washed six or seven times with 5 or 10 ml portions of water. Raney nickel and water were contacted for 5 to 10 min with occasional shaking to allow time for the alkali to diffuse from the catalyst into the water. The catalyst was separated by centrifugation after each wash. The washed catalyst was allowed to stand in water overnight before modification with L-tartaric acid.

The washing procedure described above was greatly simplified in the latter part of this work. Two short washes with 2% L-tartaric acid solution or one with water and one with L-tartaric acid leads to Raney nickel of increased hydrogenation activity.

From 40 to 60 ml of 2% L-tartaric acid solution adjusted to pH 5.1 to 5.2 was heated to 100°C in a 100-ml flask fitted with a reflux condenser. To this solution was added the Raney nickel resulting from 0.3 g of NiAl alloy. After 20 min, the catalyst was recovered by decantation and centrifugation. Next, the catalyst was washed once with 2 ml of water and twice with 2 ml of methanol. Finally, substrate or solvent was added and the mixture was transferred to a hydrogenation flask.

Preparation Procedures for Asymmetric Catalysts Based on Deuterated Raney Nickel

Deuterated Raney nickel was prepared by leaching NiAl alloy with sodium hydroxide-d following a procedure suggested for light hydrogen Raney nickel (*14*). Sodium hydroxide-d solution was prepared by adding freshly cut sodium metal to heavy water in a dry inert atmosphere.

To 3.5 ml of 20% sodium hydroxide-d solution was added 0.2 g of NiAl alloy. The resulting mixture was heated on an oil bath at 80°C for 50 min. Next, the catalyst was separated by decantation and centrifugation. The removed catalyst (Deuterated Raney nickel) was washed six times with 1.5 ml heavy water.

Deuterated Raney nickel was also modified with L-malic acid-d_6 by the same method.

Hydrogenation procedures. Hydrogenation experiments were conducted in a one atmosphere hydrogenation apparatus previously described (*11*). Following preparation, the catalyst was quickly mixed with substrate and transferred to a hydrogenation vessel.

The vessel was attached to the hydrogenation apparatus and immediately immersed in a dry ice–acetone mixture. The system was evacuated and filled with hydrogen three or four times. The reaction vessel was then brought to a constant temperature (25–60°C) by circulating water through the reactor jacket. After about 5 min the reaction was started by agitating the reaction vessel with a vortex mixer.

After separation from Raney nickel by centrifugation the reaction mixture still contained colloidal nickel and dissolved nickel complexes. These impurities were removed by a one stage vacuum distillation.

Analytical procedures. The hydrogenation mixtures, free from nonvolatile impurities, were analyzed by gas liquid chromatography (GLC) (Wilkens Instrument Co. Aerograph A-700).

Preparative GLC separations of the individual components in reaction mixtures were accomplished by injecting 50- to 150-μl samples and trapping the individual components in collection tubes immersed in dry ice–acetone.

A $\frac{3}{8}$ OD by 10-ft column packed with 20% Carbowax M on Chromasorb W was used for both analytical and preparative work. This type of column allows good separations of the β-ketoesters and their hydrogenation products at temperatures of 85 to 100°C. At temperatures over 120°C, decomposition of the β-ketoesters occurs.

The vacuum-distilled hydrogenation mixtures and the GLC separated hydrogenation products were analyzed for optical rotation with a Bendix-NPL Automatic Polarimeter. All measurements were made at room temperature (about 25°C) in a one piece glass cell of 0.995-mm path length.

A mercury green filter (λ5461 Å) was used in the early experiments. This filter was replaced with a sodium line filter (λ5893 Å) so that optical rotations could be readily compared with reference values generally given for the sodium D line.

All NMR determinations were made on a Varian A 56/60 instrument using chiral shift reagent E-7 (Regis Chemical Co.). A molar ratio of reagent-to-substrate of 1:1 is needed for this analysis. To obtain this ratio requires a relatively high concentration of chiral shift reagent E-7 (MW 1193) and a rather low concentration of substrate (MW 118). This low concentration results in rather weak signals and makes integration difficult.

The absolute rotations at the green line of mercury were calculated from the optical purity determined by NMR and the observed optical rotation measured at the mercury line. The rotation for methyl 3-hydroxybutyrate was found to be $[\alpha]_{\mathrm{Hg}}^{25} = 24°$ and this value was used in the calculation of its product optical purities. The absolute rotation for ethyl hydroxybutyrate of $[\alpha]_{\mathrm{D}}^{25} = 25°$ (*13*) was used for the calculation of its product optical purities. A different value, $[\alpha]_{\mathrm{D}}^{25} = 16.4°$, was used by Izumi (*3f*) in reporting the results on ethyl acetoacetate hydrogenation.

RESULTS

Preliminary experiments were conducted to optimize procedures for preparation of enantioselective catalysts. Products from these experiments exhibited large variations in optical purities even though they were conducted under similar conditions. For example optical purities of 39 to 48% were obtained from hydrogenations performed in the one atmosphere apparatus and optical purities of 32 to 39% were obtained from hydrogenations in a Paar Instrument Co. apparatus (15 psig). Moreover, extents of reduction did not correlate well with optical purities. Additionally, catalysts modified at 80°C led to relatively higher optical purities (46–53% at 40–48% reduction) compared to catalysts modified at room temperature. Also, lower product optical purities (20%) were obtained with a catalyst prepared from Raney nickel chromium. Finally, Raney nickel was modified with L-glutamic acid, but only 6% optical purity resulted at 50% reduction.

A large number of experiments were carried out with methyl acetoacetate under a wide variety of modification and hydrogenation conditions. Under identical conditions, when the modifier is L-tartaric acid, the commercial Raney nickels always produce products with lower optical purities than the fresh, laboratory prepared catalysts produce. In contrast, when the modifier is L-malic acid, the reverse is true. Typical examples of each of these catalyst systems are shown in Tables 1, 2, and 3. Under identical conditions rotations are usually reproducible to within 3%.

Table 1 shows some results for the W. R. Grace Active Raney nickel No. 28 (#28). For comparison, the other commercial catalysts gave lower optical purities in the decreasing order of Degussa Raney-nickel, W. R. Grace Raney nickel chromium No. 24, and Degussa nonpyrophoric Raney nickel. This order is the reverse of their hydrogenation activities.

Table 2 shows some results over the laboratory prepared catalyst (#2813) which was made from W. R. Grace No. 2813 Ni/Al alloy. One of these experiments (267) was conducted under an atmosphere of nitrogen, and one catalyst preparation (303) was washed extensively before modification. Both treatments lower optical purities.

Table 3 shows some results for both the active Raney nickel (#28) and the laboratory prepared (#2813) modified with L-malic acid (L-M) and L-malic acid-d_6 (L-M-d_6). The purpose of modifications with L-M-d_6 in combination with deuterated Raney nickel and deuterium gas was to search for an isotope effect in the geometry determining step. Evidences for such an isotope effect are found in experiment 204 for catalyst #28 and experiments 212 and 213 for catalyst #2813.

Over the #28 catalyst methyl 2,2-dimethylacetoacetate yields a product of 30% optical purity compared to 38.0% for methyl acetoacetate under nearly identical conditions.

TABLE 1

Product Optical Purities for Some Methyl Acetoacetate Hydrogenations (Asymmetric Catalyst Based on W. R. Grace No. 28 Active Raney Nickel)

Expt number	Modifying variables		Hydrogenation variables		Temp (°C)	Conv (%)	Optical activity[a]	
	Vol (ml)	Time (hr)	Temp (°C)	Solv			$[\alpha]_\lambda^{25}$	OP (%)
194	25	2.5	25	—	25	60.4	−6.9	28.9
195	25	2.5	90	—	25	59.4	−8.9	37.2
230	100	20	25	Diox	30	100.0	−8.8	36.7
236	100	19	25	—	30	100.0	−9.1	38.0
237	100	21	25	MeOH	30	100.0	−7.7	36.8
254	100	1.5	100	—	30	100.0	−9.0	43.1
255	100	1.5	100	—	50	97.0	−12.8	61.2
256	200	1.5	100	—	60	100.0	−12.2	58.4
257	200	1.5	100	—	40	97.7	−11.7	56.0
261[b]	250	1.5	100	—	50	100.0	−11.5	54.8
262	250	1.5	100	—	50	100.0	−12.3	58.6

[a] Absolute rotation for methyl 3-hydroxybutyrate was taken as $[\alpha]_{Hg}^{25}$ 24° as determined by NMR method for Expts 194–236 and as $[\alpha]_D^{25}$ 20.9 (*15*) for others.

[b] Raney nickel was pretreated with about 0.3 ml of 30% hydrogen peroxide.

TABLE 2

Product Optical Purities for Some Methyl Acetoacetate Hydrogenations (Asymmetric Catalyst Based on Laboratory Prepared Raney Nickel from W. R. Grace No. 2813 Ni/Al Alloy)

Expt number	Modifying variables[a]			Hydrogenation variables[b]			Optical activity	
	Vol (ml)	Time (hr)	pH start–end	Subst cat ratio	Rate[c] (ml/hr)	Conv (%)	$[\alpha]_D^{25}$	OP[d] (%)
265	40	1.5	5.05–7.1	4:1	42.0	85.8	−13.7	65.6
267[e]	50	1.5	5.05–6.7	1.2:1	—	5.8	−0.4	40
268	40	1.5	5.05–7.0	8:1	42.0	74.1	−14.0	67.0
269	50	1.5	5.05–6.8	2.5:1	52.6	82.1	−13.7	65.6
270	50	1.5	5.05–6.6	1.2:1	49.0	85.0	−12.5	60.0
273	40	1.5	5.05–6.4	4:1	42.2	41.8	−14.7	70.1
276	50	0.5	5.05–6.3	8:1	72.0	40.0	−13.5	64.6
278	50	0.5	5.05–6.2	12:1	74.0	40.0	−13.2	63.2
284	20	0.5	5.05–6.8	4:1	46.0	40.0	−14.5	69.4
299	40	1.5	5.0–6.05	4:1	32.0	40.0	−14.3	68.4
300	60	1.5	5.0–6.1	4:1	28.0	40.0	−15.0	71.3
301	40	1.5	5.1–6.7	4:1	48.0	40.0	−13.5	64.6
303[f]	60	1.5	5.1–6.0	3:1	12.7	40.0	−12.6	60.0
304	120	1.5	5.0–5.6	4:1	26.0	40.0	−14.8	70.8
306	60	0.5	5.0–5.8	4:1	54.7	41.7	13.2	63.2
315[g]	60	0.5	4.9–5.6	3.3:1	47.4	40.0	−13.5	64.6
316[g]	60	0.5	5.1–6.0	3.3:1	121.0[h]	40.0	−5.0	23.9
317[g]	60	0.5	5.1–5.9	3.3:1	38.0[i]	40.0	−13.0	62.2

[a] Raney nickel modified with 2% L-T at 100°C.

[b] Reactions conducted at 50°C, except Expts 265–275 at 60°C.

[c] Initial rate refers to volume of hydrogen absorbed in the initial hour.

[d] Optical purity was calculated using $[\alpha]_D^{25} = -20.9°$ (*15*) for absolute rotation of methyl 3-hydroxybutyrate.

[e] Reaction was conducted under nitrogen atmosphere.

[f] Raney nickel washed 25 times with water before being modified.

[g] Raney nickel washed with either L-tartaric acid solution or first water and then L-tartaric acid solution.

[h] Substrate injected in reaction vessel under reaction conditions after stirring was started.

[i] Substrate injected in reaction vessel under reaction conditions and allowed to stand for 10 min before stirring was started.

Over both the #28 and #2813 catalysts modified with L-tartaric acid a series of hydrogenations of ethyl acetoacetate were conducted. In methanol and ethanol solvents optical purities of 13 to 28% were obtained. However, in the absence of solvent, optical purities of 42.0 and 44.0% were obtained under conditions which yielded 58.6 and 65.1%, respectively, for methyl acetoacetate. Optical rotations at the mercury green line (calculated from percentage reductions and optical rotations of reaction mixtures) for products from the hydrogenation of other compounds are as follows: methylethylketone over L-tartaric acid modified Raney nickel (L-T) at 55.0% reduction (red.), +0.36°, at 22.4% red., +0.44° (at 31.4% red., +0.68° at sodium D line); 4-methyl-4-methoxy-2-pentanone over L-T at 50.3% red., −0.92 ± 0.08°; 4-methyl-4-hydroxy-2-pentanone over L-T at 82.5% red., −1.58°, at 51.3% red., −1.56; α-acetoaminocinnamic acid over L-T in MeOH at 68.3% red., +1.76°, at 97.5% red. (neutralized with triethylamine prior to reduction), +1.2°; methyl α-acetaminocinnamic acid in MeOH over L-T at 98.2% red., +0.62°, over D-phenylalanine-modified Raney nickel at 94.6% red., +1.28°, over L-glutamic acid modified Raney nickel at 82.6% red., +1.0°; methyl α-phenylcinnamate over L-T in dioxane at 76.5% red., 0°.

DISCUSSION

Catalyst Preparation Variables

It is clear from both the literature (*3*) and this work that a variety of factors (*12*) influence the reproducibility and asymmetric activity of these modified catalyst systems. For example, for L-tartaric acid modification, a pH of 5.0 and modifying temperature of 100°C lead to optical purities of 71.3%, Expt 300. A slight pH change results in a drop in optical purity. A modifying solution volume of less than 40 ml gives results which are lower and less reproducible, and lower modifying times gives lower optical purities. These results are similar to previous reports (*3e*) and suggest that L-tartaric acid complexation with nickel proceeds rapidly at 100°C and is almost complete in 0.5 hr. A maximum asymmetry appears to be reached after 1.5 hr.

A number of factors suggest a complicated relationship between asymmetric induction, gaseous hydrogen, and surface hydrogen. Aged and hydrogen peroxide-treated Raney nickel result in lower asymmetric yields. Lowest optical yields were reported for the most active, W-6, and highest for the less active W-1 and W-2 type Raney nickels (*16*). Increased prereaction contact time of methyl acetoacetate with modified Raney nickel decreases hydrogenation activity but increases asymmetric activity (Expts 316 and 317, Table 2). Similar decrease of hydrogenation activity (*17*) and increase in asymmetric activity (*18*, *20*) upon pretreatment with unsaturated compounds and poisons are known.

TABLE 3

Product Optical Purities for Methyl Acetoacetate Hydrogenation (L-Malic Acid Modified Raney Nickel)

Expt number	Hydrogenation variables			Optical activity	
	Ra–Ni[a] (g)	Subst (ml)	Conv (%)	$[\alpha]_D^{25}$	OP[b] (%)
197	0.341	0.6	5.5	+4.16	17.3
202	0.179	0.3	60.0	+3.96	16.5
204	0.170[c]	0.4	51.9	+3.76	15.7
205	0.170	0.4	49.4	+4.08	17.0
210	0.2	0.4	51.0	+3.14	13.1
212	0.2[d,e]	0.4	50.7	+2.16	9.0
213	0.2[d,e]	0.4	51.1	+2.2	9.2
214	0.2[e,f]	0.4	55.0	+3.15	13.1
215	0.2	0.4	52.9	+3.00	12.5
216	0.2	0.4	54.3	+3.00	12.5

[a] Active Raney nickel (W. R. Grace No. 28) used in Expts 197 through 205 and laboratory prepared Raney nickel (W. R. Grace No. 2813 Ni/Al alloy) in Expts 207 through 216.

[b] Optical purity was calculated using the absolute rotation of methyl 3-hydroxybutyrate $[\alpha]_{Hg}^{25} = 24°$ as determined by NMR method.

[c] Light hydrogen Raney nickel modified with L-malic-d_6 acid.

[d] Deuterated Raney nickel modified with L-malic-d_6 acid.

[e] Deuterium gas.

[f] Deuterated Raney nickel modified with light L-malic acid.

Hydrogenation Variables

In contrast to most previous studies (*3j*, *16*), relatively low temperatures and pressures were used in this work. We found an optimum temperature of 50°C (Expts 254–257, Table 1) in agreement with a recent report (*7*). Additionally, we found that gaseous H_2 is necessary for high optical purities. In Expt 267 (Table 2) an N_2 atmosphere replaced H_2. Thus, only adsorbed, surface hydrogen was available for the resulting hydrogenation. Since the hydrogenation stopped at 5.8%, we assume the supply of adsorbed hydrogen was low and the low optical purity was due to the deficiency of surface hydrogen. Also, we found that substrate-to-catalyst ratios are critical. Below a ratio of 2.5:1 optical purities are low, but above that ratio no significant change occurs. In contrast, we found no significant solvent effects, a fact which contradicts an early report (*19*).

Because of the report that optical purity correlates with conversion (percentage reduction) (*16*) we examined this variable carefully. At low substrate-to-catalyst ratios optical purity is not significantly affected by increase in conversion. High ratios were used in previous work (*3b*, *16*, *17*).

Hydrogenation of other Ketones and α,β-Unsaturated Compounds

The highest optical purities were obtained with methyl acetoacetate and ethyl acetoacetate. All other substrates gave lower optical purities. In contrast to the theory that β-ketoesters give high optical yields because they form fairly stable enol complexes with nickel (*3h*, *19*, *20*), we obtained a reasonable optical purity from methyl 2,2-dimethylacetoacetate.

Mechanistic Considerations

Recently, from infrared studies of adsorbed modifiers on supported nickel, proposals of the modifier-surface–substrate interactions have been made (*6*). Hydroxy acids are believed to adsorb through their carboxyl group, amino acids through both their carboxyl and amino groups (chelated), and β-ketoesters as the enolate anion through both of their carboxyl oxygens (chelated). Hydrogen bonding between the free hydroxyl of the adsorbed hydroxy acid and the methoxyl oxygen of an adjacently adsorbed substrate is postulated.

Because we had suspected similar interactions (*21*, *22*) we searched for deuterium isotope effects in asymmetric inductions (*23*). Initially, over a poorly standardized L-glutamic acid-d_1 modified Raney nickel, we observed slightly greater (an increase of 13%) optical rotations for methyl 3-hydroxybutyrate than for the catalyst modified with light L-glutamic acid (*23*). Then, as the catalyst aged, this difference gradually decreased.

Now, during this study we have used perdeutero L-malic acid (L-M-d_6) to modify the Raney nickel. Experiments 212 and 213 in Table 3 demonstrate the isotope effect which results in decreased optical purity. Although the exact nature of the effect is not clear, we believe these preliminary results show that intermolecular forces involving a H in L-M play a role in the geometry determining step. Had only steric interactions determined asymmetric induction, no isotope effect would have been observed. Further, it seems that if the proposed (*6*) hydroxyl hydrogen were more than casually involved, its expected exchange during experiment 214 would have been reflected by a lower optical purity of the product.

ACKNOWLEDGMENT

Dr. Marian Musoiu (*24*) gratefully acknowledges support for his Ph.D. dissertation (*25*) work from the Southern Illinois University Office of Research and Development.

REFERENCES

1. Akabari, S., Izumi, Y., Fujii, Y., and Sakurai, S., *Nature (London)* **178**, 325 (1956).

2. Isoda, T., Ichikawa, A., and Shimamato, T., *J. Sci. Res. Inst.* (*Ricken hokoku*) **34**, 143 (1958); *Chem Abst.* **54**, 287f (1960).

3. (a) Izumi, Y., Fukawa, H., Komatsu, S., and Akabori, S., *Bull. Chem. Soc. Japan* **35**, 1703 (1962); (b) Izumi, Y., Imaida, M., Fukawa, H., and Akabori, S., *Bull. Chem. Soc. Japan* **36**, 21, 55 (1963); (c) Izumi, Y., Tatsumi, S., Imaida, M., Fukuda, Y., and Akabori, S., *Bull. Chem. Soc. Japan* **37**, 846 (1964); **38**, 1206 (1965); **39**, 361 (1966); (d) Izumi, Y., Tatsumi, S., and Imaida, M., *Bull. Chem. Soc. Japan* **39**, 1087 (1966); (e) Tatsumi, S., *Bull. Chem. Soc. Japan* **41**, 408 (1968); (f) Izumi, Y., Imaida, M., Haroda, T., Tanabe, T., Yajina, S., and Ninomiya, T., *Bull. Chem. Soc. Japan* **42**, 241 (1969); (g) Izumi, Y., and Ninomiya, T., *Bull. Chem. Soc. Japan* **43**, 579 (1970); (h) Tanabe, T., Ninomiya, T., and Izumi, Y., *Bull. Chem. Soc. Japan* **43**, 2276 (1970); (i) Izumi, Y., and Ohkubo, K., *Bull. Chem. Soc. Japan* **44**, 1330 (1971); (j) Izumi, Y., *Angew. Chem. Int. Ed. Engl.* **10**, 871 (1971); (k) Izumi, Y., Akabori, S., Fukawa, H., Tatsumi, S., Imaida, M., Fukurda, T., and Komatu, S., "Proceedings of the Third International Congress on Catalysis," Amsterdam, 1964, p. 1364. North-Holland, Amsterdam, 1965; (l) Ajinomoto Co., Inc., Fr. 1, 348, 326, Jan. 3, 1964; Japan Appl. Mar. 30, 31, 1962 (*Chem. Abst.* **60**, 10554b, 1964); (m) Fish, M. J., and Ollis, D. F., *Catal. Rev. Sci. Eng.* **18**, 259 (1978).

4. Klabunovskii, E. I., and Petrov, Y. I., *Dokl. Acad. Nauk SSSR* **173**, 1125 (1967).

5. (a) Klabunovskii, E. I., Neupokoev, V. I., and Petrov, Yu. I., *Isv. Akad. Nauk SSSR Ser. Khim.* 2681 (1970); (b) Klabunovskii, E. I., and Levitina, E. S., *Russ. Chem. Rev.* **39**, 1025 (1970); (c) Klabunovskii, E. I., Neupokoev, V. I., and Petrov, Yu. I., *Isv. Akad. Nauk SSSR Ser. Khim.* 1954 (1971); (d) Klabunovskii, E. I., Sokolova, N. P., Vedenyapin, A. A., and Talanov, Yu. M., *Isv. Akad. Nauk SSSR Ser. Khim.* 1964 (1971); (e) Klabunovskii, E. I., Sokolova, N. P., Vedenyapin, A. A., Talanov, Yu. M., Zubareve, N. D., Polyakova, V. P., and Gorian, N. V., *Isv. Akad. Nauk SSSR Ser. Khim.* 2306 (1972).

6. Groenewegen, J. A., and Sachtler, W. M. H., *J. Catal.* **38**, 501 (1975).

7. Ozaki, H., Tai, A., and Izumi, Y., *Chem. Lett.* 935 (1974).

8. Delich, J., M.S. thesis, Southern Illinois University, Carbondale, Illinois, 1971.

9. Allen, C. F. H., and Wilson, C. V., "Organic Synthesis," Vol. 3, p. 578. John Wiley, New York, 1955.

10. Arsenijevic, V. C., *Compt. Rend.* **1958**, 245, 317.

11. Siegel, S., and Smith, G. V., *J. Amer. Chem. Soc.* **82**, 6082 (1960).

12. Izumi, Y., Harada, T., Tanabe, T., and Okuda, K., *Bull. Chem. Soc. Japan* **44**, 1418 (1971).

13. Levene, P. A., and Marker, R. E., *J. Biol. Chem.* **102**, 297 (1933).

14. Padgett, R. E., Jr., and Beamer, R. L., *J. Pharm. Sci.* **53**, 589 (1964).

15. Lavene, P. A., and Haller, H. L., *J. Biol. Chem.* **65**, 51 (1962).

16. Gross, L. H., and Rys, P., *J. Org. Chem.* **39**, 2429 (1974).

17. Hubbell, D. O., and Rys, P., *Chimia* **24**, 442 (1970).

18. Ninomiya, T., *Bull. Chem. Soc. Japan* **45**, 2555 (1972).

19. Petrov, Yu. I., Klabunovskii, E. I., and Balandin, A. A., *Kinet. Katal.* **8**, 814 (1967).

20. Yasumori, I., Inove, Y., and Okabe, K., "Proceedings of the International Symposium on the Relations between Heterogeneous and Homogeneous Catalytic Phenomenon, 1974, pp. 41–52. Elsevier, Amsterdam, 1975.

21. Smith, G. V., Boyd, W. A., and Hinckley, C. C., *J. Amer. Chem. Soc.* **93**, 6319 (1971).

22. Hinckley, C. C., Boyd W. A., and Smith, G. V., *Tetrahed. Lett.* 879 (1972).

23. Boyd, W. A., Ph.D. dissertation, Southern Illinois University, Carbondale, Illinois, 1972.

24. Present address: Research Institute for Oil, Refineries and Petrochemistry, Ploiesti, Romania.

25. Musoiu, M., Ph.D. dissertation, Southern Illinois University, Carbondale, Illinois, 1975.