

The Enantioselective Hydrogenation of Methyl Acetoacetate over Supported Nickel Catalysts

I. The Modification Procedure

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Enantioselective Ni/SiO₂ catalysts have been prepared by modification with (*R*)-(+)-tartaric acid (TA) and used in the asymmetric hydrogenation of methyl acetoacetate (MAA) to (*R*)-(–)-methyl-3-hydroxybutyrate (MHB). The effects on the overall asymmetric activity of systematically varying modification conditions, namely time, temperature, TA concentration, and pH, are discussed. The amounts of TA adsorbed have been correlated with conversion and selectivity and an optimum surface coverage of 0.2 was identified. The nature of the interaction of TA with the surface nickel metal is considered and data on the corrosive leaching and the changes in metal dispersion are presented. The consequences of adding NaBr as a subcomponent of the modification solution are examined and the results are discussed in terms of surface coverage and nonselective site poisoning. The results obtained reveal the interrelated effects of each modification variable on surface TA coverage and ultimately on enantiomeric selectivity. © 1992 Academic Press, Inc.

INTRODUCTION

The heterogeneous hydrogenation of prochiral molecules to optically active products is of particular importance if the possible enantiomers are formed in quantities deviating significantly from the equilibrium distribution. Asymmetric hydrogenation, as this process is termed, is still in a formative stage and the possible reagents used to induce catalytic enantiocontrol have not, as yet, been fully characterized. Nevertheless, it is now well established that nickel, modified by immersion in a solution of an optically active material, promotes the enantioselective hydrogenation of molecules with a prochiral center. Such a reaction is represented by the asymmetric hydrogenation of methyl acetoacetate (MAA) to methyl 3-hydroxybutyrate (MHB) over nickel modified with (*R,R*)-tartaric acid (TA). Indeed, this reaction has been widely used as a model to probe the various experimental parameters that influence enantioselectivity. Izumi (1) has reviewed the considerable literature re-

garding TA-modified Raney nickel. In contrast, apart from the work of Nitta *et al.* (2, 3) and Sachtler and co-workers (4–9), the available data on supported nickel systems are very limited.

A number of workers (6, 7, 9–12) have noted a difficulty obtaining reproducible reaction rates and optical yields. This may stem from diffusion limitations inherent in the particular reaction system. Regardless of this, there is general agreement that enantioselectivity is strongly dependent on catalyst preparation and the nature of the modification procedure employed. In a number of investigations, the effects of varying a range of modification conditions on enantioselectivity have been considered, for example, the influence of the modification time (5, 13, 14), temperature (1, 5, 7, 13, 15), pH (1, 11, 13–19), modifier concentration (4, 13), and the introduction of a comodifier (1, 4, 6, 9, 20, 21). Despite the volume of data that has issued from these reports, there is still no consensus regarding the actual source of the enantiodifferentia-

tion. A possible source of this confusion may lie in the relatively narrow range of experimental variables that have been explored in the majority of the investigations. Attempts to measure the surface coverage of the modifier have also been largely unsatisfactory (3, 4, 12, 14, 22) with the result that no direct correlation exists between the amount of adsorbed modifier and optical activity. Furthermore, while Hoek *et al.* (7, 9) have clearly shown that the modification of nickel metal with TA is a corrosive process, there have been few efforts (5, 16, 20) made to quantify the extent of nickel leaching.

It is, however, generally agreed (1, 3, 4, 20) that TA-modified catalysts exhibit two types of active site, selective and nonselective. Selective sites are associated with the TA modifier and generate an optically active product, whereas the nonselective sites are assumed to be unmodified nickel metal, which promotes racemic hydrogenation. Harada and Izumi (21) proposed that selectivity is increased by incorporating ionic species that preferentially block the nonselective sites and NaBr has been found to be the most effective additive (1, 3, 16, 20). In contrast, Bostelaar and Sachtler (6) have attributed the beneficial effects of alkali halides to a modification of the stereochemistry of the product-determining surface complex.

Optical yields in excess of 80% have been quoted for TA/NaBr-modified Raney nickel (16, 20), while Hoek *et al.* (9) have reported an enantioselectivity of 94% for a methanolic TA modification of Ni/SiO₂. The reason for such remarkable selectivities remains unknown. Indeed, the number of anomalies found in the literature has prompted us to reconsider the role of the modification process and examine systematically the most important modification parameters over a much wider experimental range than has previously been attempted before extending the study to include the possible reaction variables. We have taken the view that it is essential to pinpoint the relevant experimental effects before pro-

posing any tentative stereochemical models. In this paper we illustrate the conditions prevailing at the catalyst surface during modification and correlate these with the observed enantioselectivities under fixed reaction conditions.

EXPERIMENTAL

Catalyst Preparation and Activation

The supported catalysts were prepared by the homogeneous precipitation/deposition of nickel onto a nonporous microspheroidal Cab-O-Sil 5M silica of surface area 194 m² g⁻¹. The silica was washed with triply deionized water and dried in air for 20 h at 375–383 K before use. The precipitation was carried out in a 2 dm³ three-necked round-bottomed flask fitted with a Citenco motor-driven stirrer. A known weight of urea (Aldrich Chem. Co., 99+%) was added to a 1.5 dm³ aqueous suspension of 44 g Cab-O-Sil 5M in nickel nitrate (Aldrich, 99.999%) at 290 ± 2 K. The weights of nickel nitrate and urea were varied in order to obtain a range of nickel loadings, but the molar ratios were kept constant at Ni(NO₃)₂ · 6H₂O/H₂NCONH₂ = 0.36. The suspension was slowly heated under constant agitation (600 rpm) to 361 ± 3 K and held at this temperature for 6 h. Temperature control was maintained using an oil bath equipped with a heating element and mechanical stirring to ensure good heat transfer. The pH values prior to precipitation (as measured by a Pye Unicam Model 78 pH meter) were in the range 3.8–4.1 but were adjusted with nitric acid to pH 2.8 to prevent premature hydrolysis. It was observed in each case that the pH increased to a value of 5.3 on completion of the precipitation step. The suspension was then filtered and the filtrate washed with 4 × 400 cm³ hot deionized water and air-dried in an oven at 375–383 K for 20 h. The dried catalyst precursors were then sieved in the mesh range 150–125 μm.

Nickel loadings were determined by atomic absorption (to within ±2%) using a Perkin-Elmer 360 AA spectrophotometer. Catalyst samples, of known weight (ca.

0.2 g), were treated with 20 cm³ of a 40% HF solution (BDH, AnalaR) at room temperature for 8 h. The resultant suspension was filtered and made up to 250 cm³ with deionized water. Measurements were made in the 0–5 ppm concentration range by appropriate dilution of the sample solutions. The standards employed were prepared from a stock solution (1000 ppm) obtained from BDH Chemicals Ltd. In addition, a sample of EURONi-1 (24.7% Ni), also prepared by homogeneous precipitation and characterized by the EUROCAT group (23), was used. Thermal analyses were conducted on the prepared samples using a Pye Unicam thermobalance operating in the TG mode to measure water loss as a function of increasing temperature; water content was less than 5% for each sample.

The hydrated supported precursors were reduced, without a precalcination step, by heating in a 150 cm³ min⁻¹ stream of hydrogen at a fixed rate of 5 K min⁻¹ to a final temperature of 723 K, which was then maintained for 18 h. The hydrogen gas (BOC, 99.99%) was purified by passage through water and oxygen traps (activated Molecular Sieve type 5A and 1% Pd on WO₃), which were connected in series. The reduced catalysts were flushed in a purified stream of nitrogen (BOC, 99.99%) at 200 cm³ min⁻¹ and cooled to room temperature prior to modification.

Modification Procedure

On cooling to room temperature, the reduced catalyst was contacted, in a nitrogen atmosphere, with 100 cm³ aqueous solutions of TA; in certain cases 2 g NaBr was added to the modifier. The pH of the modifying solution was preadjusted to the desired value (in the range 1.5–11.8) using 1 mol dm⁻³ and 0.01 mol dm⁻³ aqueous NaOH solutions for rough and fine adjustments, respectively. The resultant solution was thoroughly purged with nitrogen to remove any entrapped air bubbles. The modification was performed in air with constant agitation (600 rpm) for up to 5 h at the desired temper-

ature (± 2 K). The tartaric acid was of AnalaR grade and the prepared solutions were found to be better than 99% pure by HPLC; the concentrations of the TA solutions used in the modifications were reproducible to within $\pm 1\%$. After modification, the catalyst was decanted and washed with distilled water (1 \times 25 cm³), methanol (2 \times 25 cm³), and butanol (2 \times 25 cm³) before being stored in the latter prior to use; the reagents used in the washing step were thoroughly degassed in helium. In accordance with the work of Smith and Musoiu (10), the total washing time was kept to within 40–50 min. The pH of the postmodifier was measured and the nickel content resulting from an acid leaching of the catalyst was determined by AA spectrophotometry as described above, correcting the calibration curve for the presence of TA.

Nickel metal dispersions, before and after modification, were determined by carbon monoxide chemisorption at 273 K, assuming a stoichiometry for nickel surface atom to adsorbed carbon monoxide of 2 : 1 (24), and by transmission electron microscopy. The carbon monoxide chemisorption measurements were made in the pulsed flow mode using 50- μ l aliquots of CO in a 40 cm³ min⁻¹ stream of purified helium and a thermal conductivity detector. After modification, the catalyst samples were heated at a rate of 1 K min⁻¹ to 623 K in a stream of purified helium (150 cm³ min⁻¹) to remove any desorbable TA, before the CO chemisorption measurements were made. The amounts of CO adsorbed on calcined (in 150 cm³ min⁻¹ stream of dry air at 723 K for 12 h) unreduced samples of the appropriate catalysts were also measured and subtracted from the corresponding amounts adsorbed by the reduced catalysts to give the total number of CO molecules adsorbed by the metal component. For electron microscopy, which was performed using a JEOL JEM-1200EX transmission microscope, samples of the reduced or modified catalysts were passivated in a 120 cm³ min⁻¹ flow of 1% O₂ in N₂ at 298 K for 1 h, before being dispersed on

standard copper grids. Particle size distributions were determined from the micrographs.

The amount of TA adsorbed on selected samples was determined by analyzing the pre- and postmodifier by HPLC (Spectra-Physics). A Spherisorb 5μ C8 packed column (Alltech Assoc., 250×4.6 mm) was used with 0.2 mol dm^{-3} phosphoric acid (Aldrich, >99%) as the mobile phase. Detection was by UV ($\lambda = 187 \text{ nm}$) in conjunction with a Pye Unicam PU4810 integrator. As nickel tartrate (NiTA) has been tentatively identified as the stereoselective active site formed by the corrosive adsorption of TA on nickel (5, 7), a correction for the presence of NiTA in the postmodifier was made by preparing a range of aqueous TA/NiTA solutions (of varying NiTA concentration), which were then used to construct a 30-point calibration curve. To enhance sensitivity and accuracy (which was within $\pm 3\%$), particularly in the case of the TA dilute modifications, the signal from the integrator was digitized and stored on disc for subsequent analysis using the WINNER LABNET routine. The amount of TA adsorbed was then calculated as the difference between the values obtained for the solutions before and after modification. Nickel tartrate was prepared according to the method of Hoek and Sachtler (7).

Catalytic Procedure

The liquid phase hydrogenation of MAA (10 cm^3), using *n*-butanol as a solvent (40 cm^3) was carried out at $343 \pm 2 \text{ K}$ in a 250-cm^3 glass vessel fitted with a condenser, a hydrogen inlet, and a thermocouple well. A $60 \text{ cm}^3 \text{ min}^{-1}$ stream of purified hydrogen

was bubbled through the suspension, which was kept under constant agitation at 500 rpm. The reactions normally reached an equilibrium conversion level after 28–35 h, at which point the catalyst was removed from the reaction mixture by filtration. The extent of hydrogenation was determined by HPLC using a Pirkle type 1A 5μ reversible column ($250 \times 4.6 \text{ mm}$) with a 10% IPA:90% hexane mixture as the mobile phase. All the HPLC grade solvents were supplied by Rathburn Chemicals, Ltd., and were thoroughly purged with helium prior to use. The overall level of hydrogenation was converted to mol% MHB using a 22-point logarithmic calibration plot; a quadratic equation was used to fit these data to better than $\pm 1\%$.

Optical yields (O.Y.) were determined from measurements of optical rotation (AA-10 Automatic Digital polarimeter) using

$$\text{O.Y.} = [\alpha]_D^T / [\alpha]_0^T = 100 \alpha / [\alpha]_0^T l c,$$

where $[\alpha]_D^T$ is the specific rotation of the product solution measured at the sodium D-line and temperature T ($293 \pm 3 \text{ K}$), $[\alpha]_0^T$ is the specific rotation of the pure enantiomer under the same conditions (-22.95° for (*R*)-(-)-MHB), α is the measured optical rotation, l is the path length (20 cm) of the cell, and c is the solute concentration. Optical rotation vs (*R*)-(-)-MHB concentration (in MAA/butanol) data were fitted to a quadratic equation to better than $\pm 2\%$, which was then used to determine the optical yield of the product. In this paper we express optical selectivity in terms of enantiomeric excess (e.e.), which is defined as

$$\text{e.e.} = 100\{[(R)\text{-}(-)\text{-MHB}] - [(S)\text{-}(+)\text{-MHB}]\} / \{[(R)\text{-}(-)\text{-MHB}] + [(S)\text{-}(+)\text{-MHB}]\}.$$

RESULTS AND DISCUSSION

We have developed a HPLC technique to measure adsorption coverages in liquid–solid systems. Using this approach, we have obtained results on TA adsorption over a wide range of modifier concentrations ($[\text{TA}] = 0.003\text{--}0.233 \text{ mol dm}^{-3}$). This tech-

nique has considerable advantages over previously reported methods (4, 14, 22). Chemical analysis determinations (22) of TA adsorption are destructive and require a considerable weight of catalyst in order to obtain detectable levels of adsorption. Auger electron spectroscopy (AES) has

proved inaccurate because of the presence of a high concentration of carbon as background (4), while the electrochemical technique applied by Fish and Ollis (14) to uptakes on nickel electrodes suffered from corrosion and passivation effects. The HPLC technique does not exhibit any of these drawbacks and yields results that are reproducible to better than $\pm 3\%$.

Preliminary studies (25) conducted in our laboratory revealed that a static atmospheric hydrogenation procedure showed considerable irreproducibility, both in terms of overall levels of hydrogenation and enantioselectivity; the scatter of results obtained for a range of modified catalysts was within $\pm 12\%$. Such a divergence in data is, we believe, due to diffusion limitations inherent in such a system that effectively reduces the concentration of hydrogen at the catalyst surface to an insufficient level. In contrast, the combination of bubbling hydrogen, at a fixed rate, through the catalyst/reactant suspension, which is kept under constant agitation, ensures that hydrogen is in constant close contact with the active surface and results, as we have observed, in enantiomeric excesses that are reproducible to better than $\pm 4\%$. In each case, modification of the catalyst with (*R*)-(+)-TA generated (*R*)-(-)-MHB as the predominant product; replacement of the modifier by its antipode yielded identical values of enantiomeric excess but with a reversal of the sign. Furthermore, modification with optically inactive meso-TA yielded a virtually racemic (e.e. $< 2\%$) product mixture.

The Effects of Modification Time

The amount of TA adsorbed as a function of time was measured and the results obtained for five representative temperatures are plotted in Fig. 1. It can be clearly observed that the extent of TA uptake is both time and temperature dependent. In contrast to the findings of Fish and Ollis (14), which showed that TA adsorption was complete after 10 min, treatment times in excess of ca. 40 min were necessary to achieve

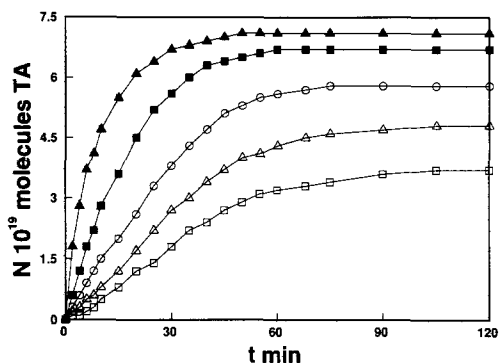


FIG. 1. The variation in the amount of TA adsorbed on a 15.2% w/w Ni/SiO₂ catalyst with t_{mod} at 273 K (\square), 298 K (\triangle), 323 K (\circ), 343 K (\blacksquare), and 373 K (\blacktriangle): $[TA]_{\text{initial}} = 3.3 \times 10^{-2} \text{ mol dm}^{-3}$; $\text{pH}_{\text{initial}} = 5.1$.

an equilibrium level of adsorption on our supported catalysts. The time necessary for maximum adsorption decreased with increasing modification temperature; e.g., at $T_{\text{mod}} = 273 \text{ K}$ uptake was complete after ca. 100 min compared to ca. 50 min at $T_{\text{mod}} = 373 \text{ K}$. In the absence of any form of agitation, a more lengthy treatment (up to 5 h) was required to attain an equivalent level of adsorption. The progress of TA adsorption was also influenced by the initial concentration of TA in the aqueous phase, as illustrated in Fig. 2. The equilibrium level of adsorption was attained in a shorter time

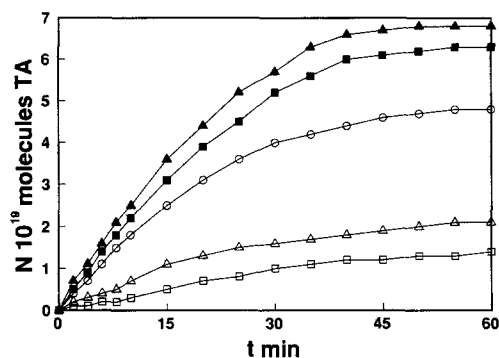


FIG. 2. The variation in the amount of TA adsorbed on an 11.9% w/w Ni/SiO₂ catalyst with t_{mod} at 343 K as a function of $[TA]_{\text{initial}}$ ($10^{-2} \text{ mol dm}^{-3}$): 0.3 (\square), 0.7 (\triangle), 3.3 (\circ), 6.7 (\blacksquare), and 13.3 (\blacktriangle); $\text{pH}_{\text{initial}} = 5.1$.

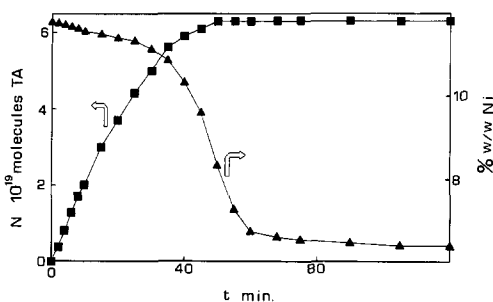


FIG. 3. The effect of t_{mod} on the amount of TA adsorbed (■) on Ni/SiO₂ (11.9% w/w Ni) and the extent of nickel leaching (▲) at 343 K: $[TA]_{\text{initial}} = 6.7 \times 10^{-2} \text{ mol dm}^{-3}$; $\text{pH}_{\text{initial}} = 5.1$.

interval when using more concentrated TA solutions. Indeed, the number of TA molecules adsorbed was greatest on treatment with the TA concentrated solutions.

As discussed elsewhere (25), TA adsorption on supported nickel catalysts is a corrosive process and is accompanied by a leaching of the active nickel metal; this effect is shown in Fig. 3. As TA is progressively adsorbed from solution, there is a corresponding increase in the concentration of nickel appearing in the modifier. This effect is more in evidence during the later stages of modification; in the initial treatment period ($t < 40 \text{ min}$), which corresponds to the bulk of the TA uptake, nickel corrosion is negligible. In accordance with the work of Sachtler and co-workers (5, 7), we can assume that TA interacts with the surface nickel to form a nickel tartrate complex (NiTA), which can either remain on the surface to form a stereoselective site or diffuse into solution. The combined effects of the inward diffusion of TA to the catalyst surface, the formation of the surface enantiocomplex, and the outward diffusion of the dissolved NiTA species, all of which vary with time, results in the appearance of nickel in the modifying solution only when TA adsorption is virtually complete.

Data on the effects of the duration of modification on the overall hydrogenation activity and enantioselectivity are presented in

TABLE 1

The Effect of t_{mod} on the Overall Levels of Hydrogenation Exhibited by Four Selected Ni/SiO₂ Catalysts of Varying Nickel Loading (% w/w): $[TA]_{\text{initial}} = 0.7 \times 10^{-2} \text{ mol dm}^{-3}$; $\text{pH}_{\text{initial}} = 5.1$; $T_{\text{mod}} = T_{\text{reaction}} = 343 \text{ K}$; $t_{\text{reaction}} = 32 \text{ h}$

$t(\text{min})$	MHB (mol%), w/w Ni			
	6.1%	11.9%	20.3%	24.7% ^a
—	78.3	71.8	75.0	75.3
2	79.6	72.6	75.6	75.6
5	80.3	73.9	76.3	76.0
10	80.7	74.4	77.2	76.8
20	81.8	75.8	78.6	78.4
30	83.0	77.5	80.3	79.5
45	83.6	78.6	81.6	80.4
60	84.0	78.9	82.3	81.3

^a 24.7% w/w Ni \equiv EURONi-I.

Table 1 and Fig. 4. In contrast to earlier reports (12, 26, 27) that suggested that the adsorbed modifier, in occluding part of the active surface, actually serves to inhibit hydrogenation, all the modified catalysts in this study exhibited an equivalent or higher activity (Table 1) than the corresponding unmodified samples. Furthermore, the equilibrium level of hydrogenation increased as the modification time (t_{mod}) was lengthened. With regard to the optical activity, at lower TA concentrations ($< 0.01 \text{ mol dm}^{-3}$) enantioselectivity increased with increasing t_{mod}

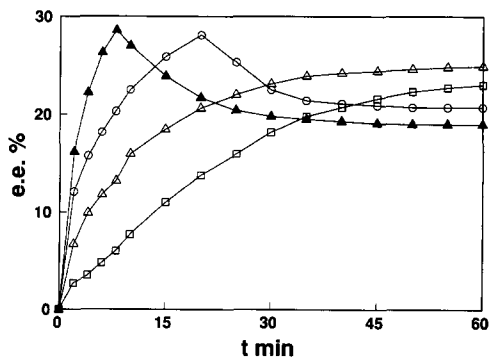


FIG. 4. The variation in enantiomeric excess (e.e.) over a 15.2% w/w Ni/SiO₂ catalyst with t_{mod} as a function of $[TA]_{\text{initial}}$ ($10^{-2} \text{ mol dm}^{-3}$): 0.3 (□), 0.7 (△), 3.3 (○), and 6.7 (▲); $\text{pH}_{\text{initial}} = 5.1$; $T_{\text{mod}} = T_{\text{reaction}} = 343 \text{ K}$.

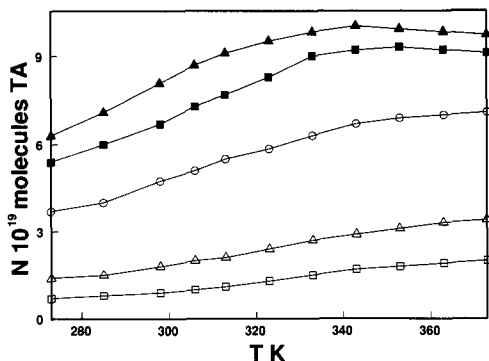


FIG. 5. The temperature dependence of TA adsorption on Ni/SiO₂ (15.2% w/w Ni) at five values of $[TA]_{\text{initial}}$ (10^{-2} mol dm⁻³): 0.3 (□), 0.7 (△), 3.3 (○), 6.7 (■), and 13.3 (▲); pH_{initial} = 5.1; t_{mod} = 2 h.

and, consequently, with increasing TA uptake. At higher concentrations, the values for e.e. passed through a maximum, the optimum enantioselectivities being attained at lower t_{mod} with increasing TA concentration (Fig. 4). While these observations differ from the earlier work of Tatsumi on modified Raney nickel (13), where extending the modification time was found to have little effect on enantioselectivity, Fu *et al.* (5) working with Ni/SiO₂ reported that longer modification times yielded higher enantioselectivities. Nevertheless, to our knowledge, t_{mod} -dependent e.e. maxima, as shown in Fig. 4, have not been reported in the literature. As the enantioselectivity passes through a maximum at a certain stage of the treatment and therefore at a particular uptake of TA, there must exist an optimum surface coverage of TA. This phenomenon was further examined by varying T_{mod} , TA concentration, and pH in a systematic manner.

The Effects of Modification Temperature

The effect of modification temperature (T_{mod}) on the extent of TA adsorption is shown in Fig. 5. Using dilute TA solutions (<0.1 mol dm⁻³), the uptake of the modifier increased on elevating the temperature from 273 to 373 K, whereas at higher concentra-

tions the profiles show a discernable maximum at around 343 K. This may be explained by the accompanying increase in nickel leaching, as illustrated in Fig. 6, at higher temperatures; a 2-h modification using a 0.13 mol dm⁻³ solution of TA at 373 K resulted in a loss of ca. 63% of the initial nickel content compared with a 25% loss at 273 K under the same conditions. Not unexpectedly, the extent of nickel dissolution therefore increases with the severity of the modification conditions. The combination of the temperature-related increase in TA adsorption with the associated progressive disappearance of the nickel metal results ultimately in a situation where a further increase in temperature reduces the concentration of the adsorbed phase. On subjecting a series of calcined samples (in a 120 cm³ min⁻¹ stream of air at 723 K) to a range of modification conditions, the residual nickel detected was always less than 10 ppm, while the adsorbed TA phase was less than 6×10^{17} molecules per gram of catalyst. This suggests that the site for TA adsorption and, therefore, stereoselective template formation, is the nickel metal and not the silica support or the unreduced nickel cations.

The relationship between T_{mod} and e.e. is strongly dependent on the initial TA concentration (see Fig. 7). Tatsumi, in his studies on modified Raney nickel (13), observed a

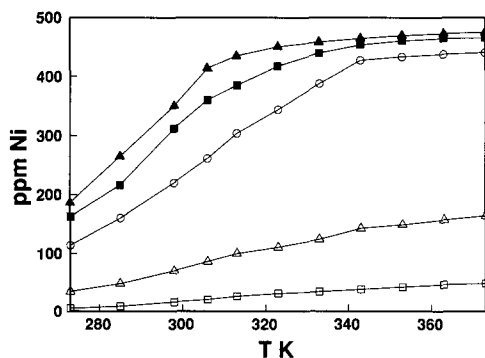


FIG. 6. The effect of T_{mod} on the extent of nickel leaching from a 15.2% w/w Ni/SiO₂ catalyst at five values of $[TA]_{\text{initial}}$ (10^{-2} mol dm⁻³): 0.3 (□), 0.7 (△), 3.3 (○), 6.7 (■), and 13.3 (▲); pH_{initial} = 5.1; t_{mod} = 2 h.

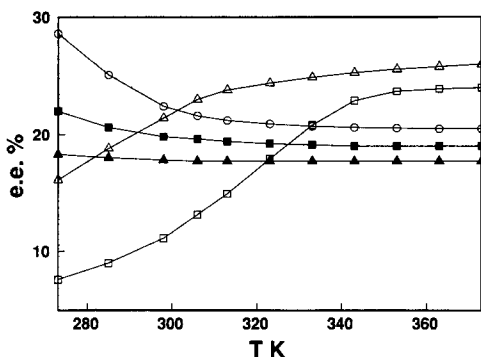


FIG. 7. The variation in enantiomeric excess over a 15.2% w/w Ni/SiO₂ catalyst with T_{mod} as a function of $[\text{TA}]_{\text{initial}}$ ($10^{-2} \text{ mol dm}^{-3}$): 0.3 (\square), 0.7 (Δ), 3.3 (\circ), 6.7 (\blacksquare), and 13.3 (\blacktriangle); $\text{pH}_{\text{initial}} = 5.1$; $t_{\text{mod}} = 2 \text{ h}$; $T_{\text{reaction}} = 343 \text{ K}$; $t_{\text{reaction}} = 32 \text{ h}$.

linear relationship between optical activity and temperature (273–373 K). In contrast, this study finds that, over the same temperature range, the values for e.e. increase at low concentrations ($[\text{TA}] < 0.01 \text{ mol dm}^{-3}$), and there is a drop in optical activity when using samples of intermediate concentration (ca. $0.01\text{--}0.1 \text{ mol dm}^{-3}$) while enantioselectivity is essentially independent of temperature for the most concentrated solutions used. Increasing T_{mod} resulted in a decrease in hydrogenation activity; taking an 11.9% w/w Ni/SiO₂ as a representative case, modification (2 h, $[\text{TA}] = 0.07 \text{ mol dm}^{-3}$) at 273 K yielded a conversion of 82.2 mol% MHB compared with 73.1% at $T_{\text{mod}} = 373 \text{ K}$. Nevertheless, modification was observed to promote hydrogenation activity over the entire temperature/concentration regime studied.

The Effects of TA Concentration

A series of representative adsorption isotherms are shown in Fig. 8. Modification at low temperatures ($< 310 \text{ K}$) is characterized by the slow attainment of an equilibrium adsorption, normally attained at $[\text{TA}]_{\text{initial}} > 0.16 \text{ mol dm}^{-3}$. As treatment at higher temperatures resulted in a higher uptake at each individual TA concentration, the equilibrium level of adsorption was established using more dilute solutions. Moreover, as in

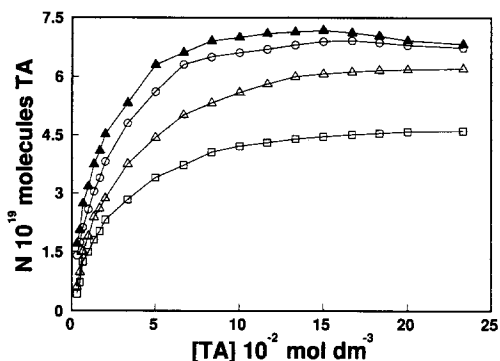


FIG. 8. TA adsorption on Ni/SiO₂ (11.9% w/w Ni) as a function of $[\text{TA}]_{\text{initial}}$ at 273 K (\square), 306 K (Δ), 343 K (\circ), and 373 K (\blacktriangle); $\text{pH}_{\text{initial}} = 5.1$; $t_{\text{mod}} = 2 \text{ h}$.

the case of the temperature dependency plots (Fig. 5), the number of adsorbed TA molecules was found to drop at higher values of $[\text{TA}]_{\text{initial}}$. This can again be attributed to a critical loss of supported nickel metal. Indeed, similar isotherms relating to nickel leaching, which mirror the equivalent adsorption isotherms, can be constructed (Fig. 9). Nickel dissolution is again promoted using more severe modification conditions and in the worse case a loss of ca. 60% of the initial metal loading was recorded.

Nickel metal dispersions expressed as $(\text{Ni}_{\text{surface}}/\text{Ni}_{\text{total}}) \times 100\%$ for a range of metal loadings, obtained from CO chemisorption

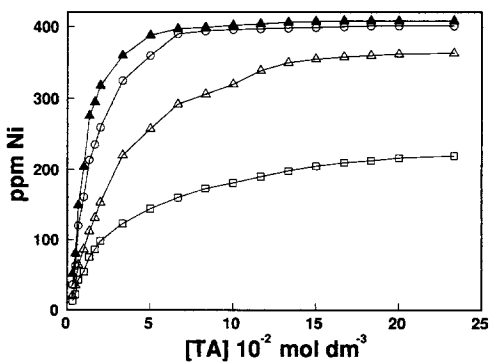


FIG. 9. Effect of $[\text{TA}]_{\text{initial}}$ on the extent of nickel leached from an 11.9% w/w Ni/SiO₂ catalyst at 273 K (\square), 306 K (Δ), 343 K (\circ), and 373 K (\blacktriangle); $\text{pH}_{\text{initial}} = 5.1$; $t_{\text{mod}} = 2 \text{ h}$.

TABLE 2

The Effect of Modification on the Extent of Nickel Leaching and Percentage Metal Dispersion for a Range of Ni/SiO₂ Catalysts of Varying Nickel Loading: [TA]_{initial} = 0.7 × 10⁻² mol dm⁻³; pH_{initial} = 5.1; T_{mod} = 343 K; t_{mod} = 1 h

% w/w Ni	Ni leached (%) ^a	D ^b	
		Before modification	After modification
1.5	51	73	39
6.1	29	54	36
11.9	19	40	33
15.2	16	33	28
20.3	14	27	25
24.7 ^c	13	24	23

^a Percentage total Ni content leached into solution.

^b Dispersion, from CO measurements.

^c EURONI-I.

measurements both before and after a selected modification procedure, are given in Table 2. The values quoted for the modified catalysts are based on the assumption that the pretreatment in flowing helium at elevated temperatures has removed all the adsorbed TA. The dispersion values obtained for the unmodified catalysts are in good agreement with values reported elsewhere (28) and are in accord with the generally accepted view (28–31) that nickel catalysts, with metal loadings up to 30% w/w, prepared by the homogeneous precipitation/deposition method exhibit a uniform dispersion of very small (<6 nm) metal particles. With the modified catalysts the corrosive action of TA adsorption clearly results in a lower metal dispersion in those catalysts with lower nickel loadings, although with nickel loadings above ca. 20% w/w, the modification had relatively little effect. The carbon monoxide chemisorption results are in good agreement with the nickel particle size distributions (Fig. 10) determined by electron microscopy for both modified and unmodified catalysts. The latter results clearly show that the modified catalysts have a much lower proportion of nickel particles in the 0- to 2-nm range, suggesting that in the TA modification treatment the smaller

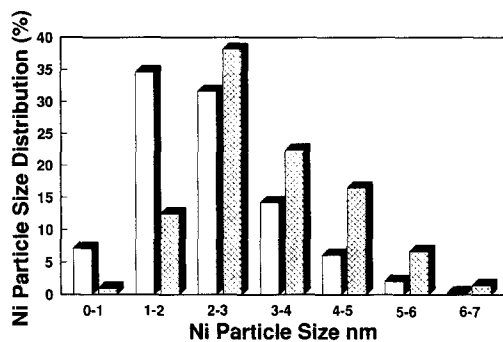


FIG. 10. Nickel particle size distributions exhibited by an 11.9% w/w Ni/SiO₂ catalyst before (open bar) and after modification (cross-hatched bar): [TA]_{initial} = 6.7 × 10⁻³ mol dm⁻³; pH_{initial} = 5.1; T_{mod} = 343 K; t_{mod} = 1 h.

nickel particles, which have the highest surface free energy (32), are preferentially leached from the sample.

The effects of varying the modifier concentration on both hydrogenation activity and selectivity are considered in Table 3 and Fig. 11. The decrease in the overall yield of MHB with increasing TA concentration must be due to the preferred removal of the smaller nickel particles, which have been shown to exhibit a high specific hydrogenation activity (3, 33). The observed increase

TABLE 3

The Effect of [TA]_{initial} on the Extent of Nickel Leaching, the Variation in Modifier pH, and the Hydrogenation Activity of an 11.9% w/w Ni/SiO₂ Catalyst: pH_{initial} = 5.1; T_{mod} = T_{reaction} = 343 K; t_{mod} = 2 h; t_{reaction} = 32 h

[TA] _{initial} ^a	Ni leached (ppm)	ΔpH ^b	MHB (Mol%)
—	5	—	71.8
0.3	36	2.7	79.4
0.7	120	2.8	78.9
1.7	236	3.2	77.3
3.3	325	3.0	76.2
5.0	360	2.0	75.0
6.7	390	1.5	73.9
8.3	394	1.7	73.3
13.3	398	1.2	72.8
20.0	401	0.9	72.4

^a Units of 10⁻² mol dm⁻³.

^b Reproducible to within ±5%.

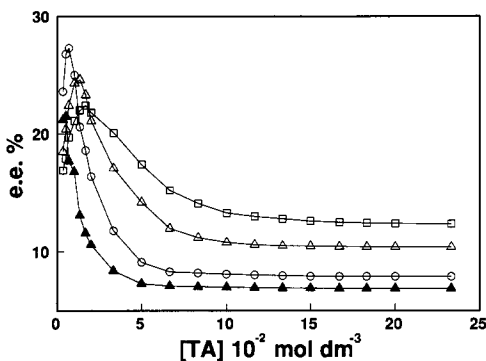


FIG. 11. The variation in enantiomeric excess over an 11.9% w/w Ni/SiO₂ catalyst with $[TA]_{\text{initial}}$ at 273 K (\square), 306 K (Δ), 343 K (\circ), and 373 K (\blacktriangle): $\text{pH}_{\text{initial}} = 5.1$; $t_{\text{mod}} = 2$ h; $T_{\text{reaction}} = 343$ K; $t_{\text{reaction}} = 32$ h.

in pH for the postmodifier, which is recorded in Table 3, has also been reported by Smith and Musoiu (10) and Wittmann *et al.* (11), but no explanation has been proffered. Addition of NiTA, NaTA, and NiNaTA to the original TA solution had no effect on the pH. Rather, the increase in pH must be due to the adsorption of TA during modification, which essentially dilutes the liquid phase; at the completion of modification, the pH value depends on $[TA]_{\text{initial}}$ and the combined effect of the degree of liquid phase TA dilution and the volume and concentration of NaOH initially added to set the pH. The data plotted in Fig. 11 clearly show that e.e. passes through a maximum at $[TA]_{\text{initial}} < \text{ca. } 0.02 \text{ mol dm}^{-3}$, the precise optimum concentration increasing as T_{mod} decreases. Tsumi (13) and Richards *et al.* (4) have found that, on increasing the TA concentration, enantioselectivity attained a maximum, but further increase in the modifier concentration was observed to have no effect on the asymmetric activity. In complete contrast, the data resulting from our study show that e.e. drops markedly at TA concentrations in excess of 0.02 mol dm^{-3} . Taking the amount of TA adsorbed under conditions of maximum e.e. and relating this to the metal content and nickel dispersion present in the modified catalyst, the surface coverage of

TA at optimum enantioselectivity can be calculated; the results for a range of temperatures are shown in Table 4. The computed fractional coverages are based on a maximum coverage of (*R*)-(+)-TA on Ni of 5.3×10^{14} molecules/cm², which has been reported in the literature by Fish and Ollis (14). It can be seen that the optimum surface coverage is highest for the least severe (low T_{mod}) treatment; however, all the tabulated values correspond to an average coverage of ca. 0.2. Indeed, the maxima in e.e. presented graphically in Figs. 4 and 7 are also associated with a $20 \pm 4\%$ coverage by TA of the available surface nickel metal atoms. Furthermore, the extent of TA adsorption at saturation represents a monolayer coverage of the available metal surface. It should be noted that even under conditions of complete surface saturation there is sufficient interaction between the substrate (i.e. the organic reactant molecule) and the adsorbed modifier to promote the selective formation of the (*R*)-(–)-MHB enantiomer.

The results presented here help establish the surface conditions prevailing during the catalytic process. We can therefore state that e.e. passes through a maximum at a fractional coverage of the surface with TA. If both TA and the reactant MAA are coadsorbed on the surface, as has been proposed by Groenewegen and Sachtler (8), the surface coverage of both components should

TABLE 4

Modification Temperature-Related Enantiomeric Excess (e.e.) Maxima and the Associated Optima in $[TA]_{\text{initial}}$ and TA Surface Coverage for an 11.9% w/w Ni/SiO₂ Catalyst: $\text{pH}_{\text{initial}} = 5.1$; $t_{\text{mod}} = 2$ h; $T_{\text{reaction}} = 343$ K; $t_{\text{reaction}} = 32$ h

T (K)	e.e. (%)	$[TA]_{\text{initial}}$ ($10^{-2} \text{ mol dm}^{-3}$)	TA surface coverage
273	22.4	1.3–2.0	0.20–0.25
285	23.0	1.3–1.7	0.20–0.24
306	24.6	1.0–1.3	0.19–0.24
323	25.9	0.7–1.0	0.18–0.23
343	27.3	0.5–0.7	0.17–0.22
373	21.5	0.3–0.5	0.17–0.20

prove critical, as our data suggest. Indeed, by positioning three-dimensional hard sphere models of TA anions on a two-dimensional scale model of the three lower index planes of nickel, Fish and Ollis (14) have shown that an average of 3–3.5 surface nickel atoms are blocked by each adsorbed TA molecule. There is strong spectroscopic evidence (8) that MAA is adsorbed on nickel as an O-bonded chelate, while TA interacts with the metal through its carboxyl group. The most favorable surface arrangement must therefore be one in which a hydrogen bond is formed between the OH group of the hydroxy acid and the methoxy oxygen atom of MAA. From our results it appears that, at a very low surface coverage of TA (< ca. 0.15), only a fraction of the adsorbed MAA can interact directly with the adsorbed modifier, with the result that racemic hydrogenation is favored. Conversely, at higher coverages, the adsorbed MAA may be “sandwiched” between two adsorbed TA molecules causing a destructive stereochemical interference, with again the preferential formation of a racemic product. Accordingly, the optimum TA modification is one in which the distance between adsorbed TA molecules is large enough to ensure that an adsorbed MAA molecule interacts with only one modifier molecule but small enough to minimize the number of bare metal sites that give rise to racemic hydrogenation. At monolayer coverages of TA, the substrate and modifier must interact by the two-site intermolecular hydrogen bondings visualized by Harada *et al.* (20) in which the MAA is in the liquid phase. Such a linkage, although promoting asymmetric hydrogenation, generates a smaller excess of (*R*)-(-)-MHB.

The Effects of Modifier pH

Of the possible experimental variables, modifier pH has been the subject of the majority of investigations to date. These studies have only dealt with a limited number of experimental conditions and contained no reference to any nickel leaching effects. The

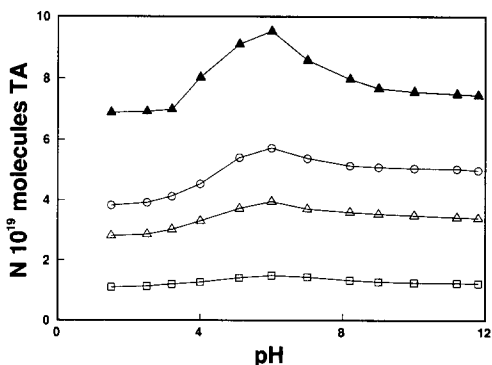


FIG. 12. The pH dependence of TA adsorption on a 15.2% w/w Ni/SiO₂ catalyst at $t_{\text{mod}} = 2$ h: $T_{\text{mod}} = 273$ K, $[\text{TA}]_{\text{initial}} = 6.7 \times 10^{-3} \text{ mol dm}^{-3}$ (□); $T_{\text{mod}} = 273$ K, $[\text{TA}]_{\text{initial}} = 3.3 \times 10^{-2} \text{ mol dm}^{-3}$ (△); $t_{\text{mod}} = 273$ K, $[\text{TA}]_{\text{initial}} = 6.7 \times 10^{-2} \text{ mol dm}^{-3}$ (○); $T_{\text{mod}} = 373$ K, $[\text{TA}]_{\text{initial}} = 6.7 \times 10^{-2} \text{ mol dm}^{-3}$ (▲).

effect of pH on the uptake of TA molecules is given in Fig. 12. It can be observed that under acidic conditions, the number of TA molecules adsorbed increases in the pH range 1.5–6, whereas in basic media there is a noticeable drop in TA uptake. This effect is particularly marked for modifications at elevated temperatures. Under basic conditions, the TA reagent is predominantly in the form of its alkali salt (13), which must not interact with the surface nickel metal to the same extent. Consequently, there is very little change in pH throughout the course of the modifications in basic media (Table 5). These observations differ from previous reports (on Raney nickel) in which TA adsorption decreased steadily with increasing pH in both acidic and basic media (13, 22). While modification under neutral or basic conditions results in a smaller uptake of modifier, the extent of nickel corrosion is considerably lower, as shown in Fig. 13. The data plotted in Fig. 13 encompass a maximum and a minimum loss of nickel content of ca. 50 and 1%, respectively. The combination of TA adsorption and the dissolution of nickel results in an increase in surface coverage in the pH range 5.1–11.2 and a decrease in the range pH 5.1–1.5 (Table 5).

TABLE 5

The Effect of the Initial Modifier pH and the Accompanying Change in pH on the TA Surface Coverage and Hydrogenation Activity of a 15.2% w/w Ni/SiO₂ Catalyst: [TA]_{initial} = 3.3 × 10⁻² mol dm⁻³; T_{mod} = T_{reaction} = 343 K; t_{mod} = 2 h; t_{reaction} = 32 h

pH _{initial}	ΔpH ^a	MHB (mol%)	TA surface coverage
—	—	74.6	—
1.5	1.9	74.8	0.83
3.2	1.8	75.0	0.86
5.1	1.5	76.0	0.93
6.0	0.8	77.7	0.84
7.0	0.4	79.8	0.69
8.2	0.2	82.1	0.47
9.0	0.3	84.4	0.40
10.0	0.1	85.8	0.37
11.2	0	86.4	0.37

^a Reproducible to within ±5%.

The dependence of enantioselectivity on modifier pH is rather complex (Fig. 14). Two broad maxima arise in the acidic and basic pH regimes, depending on the nature of the modification conditions. In previous studies on modified Raney nickel, e.e. maxima have been variously reported at pH 3 (11, 16), pH 10 (19), and over the range 5–9 (13, 14, 22). In our study, modification at low temperatures (<300 K) and low concentrations

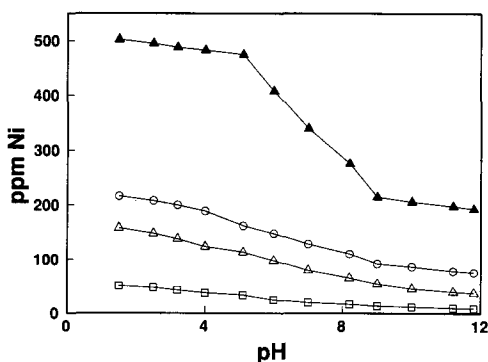


FIG. 13. The effect of the initial pH on the extent of nickel leached from a 15.2% w/w Ni/SiO₂ catalyst at t_{mod} = 2 h: T_{mod} = 273 K, [TA]_{initial} = 6.7 × 10⁻³ mol dm⁻³ (□); T_{mod} = 273 K, [TA]_{initial} = 3.3 × 10⁻² mol dm⁻³ (Δ); T_{mod} = 273 K, [TA]_{initial} = 6.7 × 10⁻² mol dm⁻³ (○); T_{mod} = 373 K, [TA]_{initial} = 6.7 × 10⁻² mol dm⁻³ (▲).

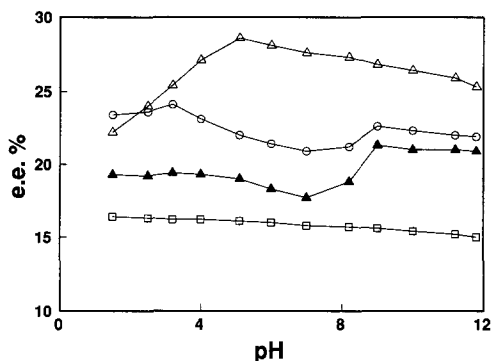


FIG. 14. The variation in enantiomeric excess over a 15.2% w/w Ni/SiO₂ catalyst (T_{reaction} = 343 K, t_{reaction} = 32 h) with initial pH at t_{mod} = 2 h: T_{mod} = 273 K, [TA]_{initial} = 6.7 × 10⁻³ mol dm⁻³ (□); T_{mod} = 273 K, [TA]_{initial} = 3.3 × 10⁻² mol dm⁻³ (Δ); T_{mod} = 273 K, [TA]_{initial} = 6.7 × 10⁻² mol dm⁻³ (○); T_{mod} = 373 K, [TA]_{initial} = 6.7 × 10⁻² mol dm⁻³ (▲).

(<0.01 mol dm⁻³) revealed no pH dependence with regard to the overall enantioselectivity. The acidic maxima correspond to the attainment of the optimum surface coverage (0.2). By way of contrast, the maxima recorded under basic conditions are associated with a higher surface coverage, normally greater than ca. 0.4. This suggests the existence of a different mode of adsorption at higher pH values, which, under certain conditions (high T_{mod} and [TA]_{initial}), results in the laydown of a more efficient optically active template. Contacting the catalysts with neutral and basic TA solutions enhanced the overall levels of hydrogenation (Table 5), due to the less corrosive nature of the treatment in which a larger proportion of the active small nickel particles remains on the surface.

As an addendum to our pH studies, we also applied the technique devised by Wittmann *et al.* (11) for modifying Raney nickel to our supported nickel systems. In their study, they reported a marked improvement in enantioselectivity on maintaining the pH constant throughout the duration of the modification procedure. Applying identical experimental conditions ([TA]_{initial} = 0.2 mol dm⁻³, t_{mod} = 0.5 h, T_{mod} = 293 K, pH 4) to

a range of catalysts of varying nickel loading and keeping pH constant, we observed no significant difference in the resultant e.e. values compared with the same treatment in which the pH was not controlled. Under the stated conditions, surface coverage for each loading exceeded ca. 0.4, which is in the region of e.e. (modifier) concentration independence. From the standpoint of the model we have proposed, the inclusion of additional TA to the depleted solution should have no effect on e.e. at these levels of surface coverage, as was indeed the case. As a consequence of keeping the pH constant, there was a slight increase in both the number of TA molecules adsorbed and the concentration of nickel appearing in solution (<3% in each case). The divergence in behavior exhibited by our Ni/SiO₂ catalysts and the Raney nickel samples studied by Wittmann *et al.* (11) really serves to highlight the underlying basic differences in the modification process for supported and unsupported systems.

The Effects of NaBr Addition

The use of NaBr as a comodifier has been well documented (1). Previous work has shown that NaBr addition enhances the selectivity of both Raney nickel (1, 16, 20) and Ni/SiO₂ (3, 4, 6, 7, 9). This effect has been interpreted in terms of a poisoning of the nonselective sites (1). As can be seen from Table 6, addition of NaBr to the modification solution results in a decrease in adsorbed TA, an effect that has previously been reported for the case of Raney nickel (10). In addition, the inclusion of NaBr also lowers the concentration of nickel in the postmodifier. The latter observation may support the contention of Bostelaar and Sachtler (6) that NaBr interaction with the adsorbed NiTA complex lowers the solubility of the adsorbed species resulting in an increased stability of the surface complexed nickel. Our data (Table 6) reveal that NaBr does indeed promote selective hydrogenation to (*R*)-(-)-MHB but not to the extent reported for Raney nickel (1, 16, 20). The

greater enhancement observed for the Raney nickel system may be rationalized in terms of the additional poisoning of any residual aluminum that has been shown to be detrimental to the asymmetric process (1, 16, 25). Our e.e. data are in keeping with the selectivity increases observed by Bostelaar and Sachtler for modified Ni/SiO₂ (6).

All the promoted catalysts displayed a decreased hydrogenation activity, which suggests a preferential blocking of the nonselective sites. However, this effect is not very pronounced and, as with the TA-treated catalysts, the NaBr/TA-treated samples all exhibited activities equivalent or higher than those of the corresponding unmodified samples. It is nevertheless significant that the improved selectivities correspond to a change in the TA surface coverage toward our optimum value of 0.2 due to the combined effects of a decreased TA uptake and lower nickel leaching. At very low TA concentrations corresponding to low surface coverages (<0.1), NaBr addition has no effect on enantioselectivity. While our studies do not exclude the possibility of NaBr modifying the stereochemistry of the product determining surface complex (6), our data suggest that such an effect would not be as pronounced as any TA coverage considerations.

CONCLUSIONS

The data reported in this paper illustrate the complex nature of the TA modification process. TA adsorption takes place on the available surface nickel metal and increases with the duration, temperature, and concentration of the modifier. A maximum in TA uptake at high [TA]_{initial}, which is dependent on the starting pH, was observed; the initial pH may also govern the mode of adsorption. Treatment with TA is corrosive and the amount of nickel leached from the catalyst surface has been shown to depend on t_{mod} , T_{mod} , [TA]_{initial}, and pH. In general terms, nickel dissolution can be said to increase with increasing severity of modification and losses of up to 60% of the initial nickel load-

TABLE 6

The Effect of NaBr Addition (2 g NaBr/100 cm³ TA) on TA Adsorption, Nickel Leaching, and the Activity and Selectivity of an 11.9% w/w Ni/SiO₂ Catalyst: pH_{initial} = 5.1; T_{mod} = T_{reaction} = 343 K; t_{mod} = 2 h; t_{reaction} = 32 h

[TA] _{initial} (10 ⁻² mol dm ⁻³)	NaBr added	TA adsorbed ^a	Ni leached (ppm)	MHB (mol%)	e.e. (%)
—	—	—	5	71.8	1.1
0.3	Yes	1.2	32	75.0	24.4
	No	1.4	36	79.4	23.6
0.7	Yes	1.8	106	74.2	32.0
	No	2.1	120	78.9	27.3
3.3	Yes	4.4	296	73.5	14.1
	No	4.8	325	76.2	11.8
6.7	Yes	5.9	352	72.1	11.4
	No	6.3	390	73.9	8.3
13.3	Yes	6.3	356	72.0	11.4
	No	6.8	398	72.8	8.0

^a Units of 10¹⁹ TA molecules.

ing have been observed. The removal of the supported nickel metal phase results in a lowering of the metal dispersion, most notably in the case of the nickel-dilute samples. Nickel metal dissolution reaches a limiting situation where the increased uptake of TA is outweighed by the increased loss of surface metal. Maximum levels of TA adsorption correspond to a monolayer surface coverage. While enantioselectivity is induced on treating the reduced catalysts with TA, the overall level of hydrogenation is also enhanced. We have identified a TA coverage of 0.2 as providing the conditions for optimum enantioselectivity and have outlined the various experimental conditions under which this level of adsorption is attained. The promoting effect of NaBr addition results from the combined effects of a poisoning of the nonselective sites and a beneficial regulation of the TA surface coverage.

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