

Mechanism of Asymmetric Hydrogenation on Modified Nickel Catalysts

Much work has been done, especially by Izumi (1) on the asymmetric hydrogenation of methylacetoacetate (MAA) and other β -diketones over modified Raney nickel as the catalyst. If the catalyst is precovered with an optically active compound (the "modifier"), the two enantiomeric forms of the reaction product, which is methyl 3-hydroxybutyrate (MHB) in the case of MAA hydrogenation, are formed in unequal quantities. Replacing the modifier by its antipode reverses the enantioselectivity of the catalytic process. Efficient modifiers are amino acids and hydroxy acids.

An experimental observation of crucial importance to any mechanism of this type of catalysis is that amino acids and hydroxy acids of identical absolute configuration, when used as modifiers, display the opposite sign of enantioselectivity. This fact clearly shows that mere consideration of the stereochemistry of the free molecules is insufficient to conclude on the causes of enantioselectivity; the structures and interactions of the adsorption complexes should also be considered. Thus far no reaction mechanism seems to have been reported, owing to total lack of reliable data on the structure of the adsorption complexes of MAA, the modifiers or any other bifunctional compounds on metal surfaces. We, therefore, have studied the adsorption complexes of amino acids, hydroxy acids and MAA on nickel using infrared spectroscopy as the analyzing tool and silica-supported nickel as the catalyst. Because of the low volatility of amino acids a special technique had to be developed to adsorb these compounds on the reduced catalyst via sublimation. The first results of these spectroscopic investiga-

tions (2-4) show that the structures of the adsorption complexes of amino acids and MAA are similar to those of the corresponding metal chelates, known in coordination chemistry (Fig. 1a and b). We assume that the plane of the chelate ring skeleton is roughly perpendicular to the surface because both the spectra and the maximum degree of coverage are inconsistent with an arrangement where the chelate ring lies flat on the surface. For this and other reasons we also assume that a Ni atom remains in its position in the metal lattice.

The structure of the adsorption complexes remains essentially unchanged when MAA and an amino acid are coadsorbed on the same surface, although there are also indications for some interaction between the coadsorbed compounds.

Hydroxy acids, unlike amino acids, form carboxylates rather than chelates (see Fig. 1c). Hence it is clear that an amino acid and a hydroxy acid of identical absolute configuration form chemisorption complexes which differ strongly in structure and reactivity. Note that the OH group of the hydroxy acid is available for the formation of a hydrogen bond with adjacent molecules, whereas the amino group of the adsorbed amino acid is bonded to the metal (see Fig. 1a and c).

Separate tests in a flow reactor proved that the Ni/SiO₂ catalyst modified by sublimation does indeed display enantioselectivity for the same MHB enantiomers as reported by Izumi for Raney nickel catalysts modified by means of a solution. The optical yield, however, is larger if modification was achieved by means of solution than by means of sublimation.

We have now succeeded in rationalizing

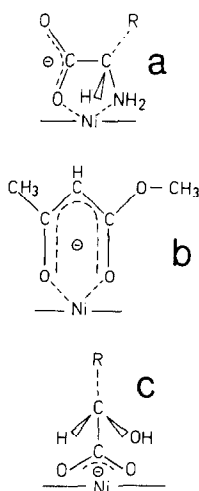


FIG. 1. Structure of the adsorption complexes on nickel of (S)- α -amino acid (a), methylacetoacetate (b) and (S)- α -hydroxy acid (c).

the cause of asymmetric catalysis with modified nickel by formulating three postulates which are related to the structure of the chemisorption complexes shown in Fig. 1 and to generally accepted chemical and stereochemical principles. Using the case of MAA hydrogenation on a catalyst modified with the α -amino acid R-CH(NH₂)COOH (where R is an alkyl group) we postulate:

1. Enantioselectivity results from adsorption on two adjacent Ni atoms of a MAA and a modifier molecule. They interfere with each other, but not with other surface atoms or adsorbed groups.

From this postulate and the known structures, sizes and shapes of the moieties involved it follows that the skeletons of the two chelates are located in planes, perpendicular to the surface and parallel to each other, the interplanar distance being equal to the Ni-Ni distance. This identification still leaves open four possible configurations of the two adsorbates. Using the projection of Fig. 1a, where the skeleton of the Ni-amino acid chelate is in the plane of the paper and the R-group below it, the MAA can either be below or above this

plane and its methoxy group can in each case point either to the right or to the left.

2. Of the four configurations consistent with postulate 1, one is energetically more favorable than each of the three others.

It is a matter of discussion which configuration has the lowest free energy. It should be noted, however, that any configuration which is distinctly preferred will lead to enantioselectivity. We believe that the preferred configuration is characterized in that:

a. MAA and -R are at opposite sides of the amino acid chelate plane to avoid the steric hindrance anticipated for configurations having these moieties on the same side of this plane.

b. The O-CH₃ group of MAA is as far as possible from the R-group of the amino acid.

The characteristic (b) would also be in line with adsorption kinetics via the physically adsorbed enol form of MAA as the precursor of the chelate. The acidic hydrogen atom of this enol is likely to form a hydrogen bond with the nitrogen atom of the amino acid.

In the MAA-Ni chelate the carbon atom of the C-bonded methyl group is in the plane of the chelate skeleton. When the complex is hydrogenated, a hydrogen atom is attached to the β -C atom and the methyl group is pressed out of the plane. There are obviously two possibilities for the transition state as the methyl group can be pressed either below or above the chelate plane, either possibility leading to one of the two possible enantiomers of MHB.

3. The two transition states arising from the interaction of a hydrogen atom with the β -C atom of the MAA chelate have different free energies.

For obvious reasons we believe that the transition state where the said CH₃ group is bent away from the modifier molecule

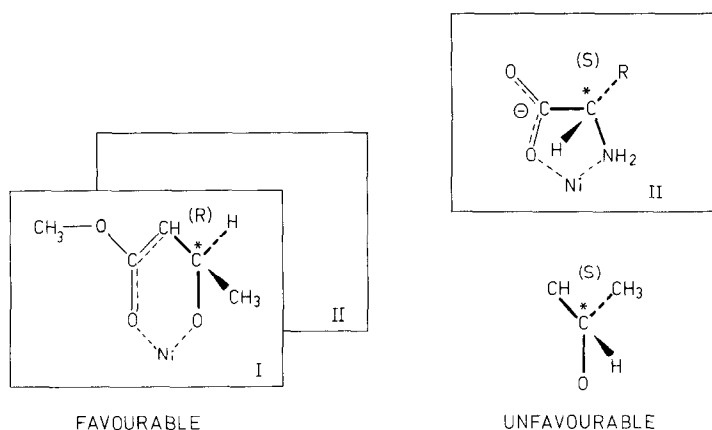


FIG. 2. Schematized transition states for (R)-(-)-MHB and (S)-(+)-MHB, α -amino acid modifier.

has the lower free energy, because severe steric hindrance would arise if the CH_3 group is pressed towards the modifier complex (see Fig. 2).

With the above three postulates the enantioselectivity is unambiguously predicted. Upon accepting our preferred configuration of the two adsorbates (Fig. 2) (R)-(-)-MHB will result if an (S)- α -amino acid is used as the modifier, its antipode if the modifier antipode is used. This prediction is in agreement with the experimental data.

For the hydroxy acids the postulates 1,

2 and 3 are equally valid. However, since the hydroxy acids form carboxylates rather than chelates the configuration resulting from postulates 1 and 2 is different from that predicted for α -amino acid modifiers. We believe that with a hydroxycarboxylate a hydrogen bond will be formed between the OH group of the hydroxy acid and the oxygen atom of the methoxy group in adsorbed MAA. Upon applying postulate 3 to this configuration the preferred formation of (S)-(+)-MHB from MAA will result provided the (S)- α -hydroxy acid is used as the modifier. This is, again, in

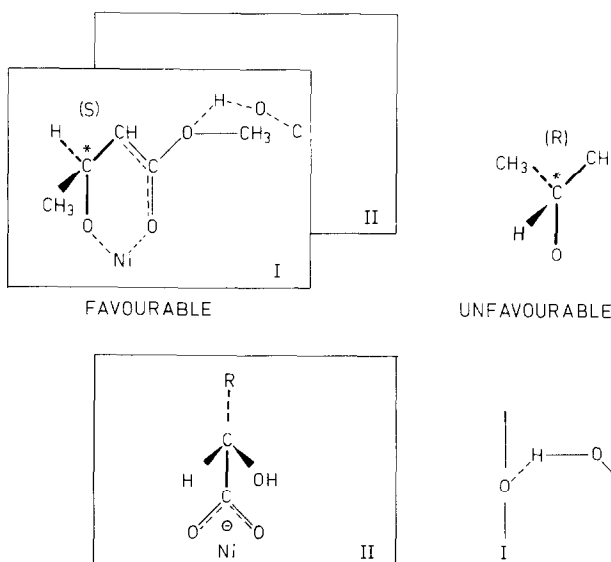


FIG. 3. Schematized transition states for (R)-(-)-MHB and (S)-(+)-MHB, α -hydroxy acid modifier.

agreement with the experimental facts (see Fig. 3).

It is further possible, but outside the scope of this note to show that a number of empirical rules on the asymmetric catalysis with modified Ni catalysts can be understood on the basis of our mechanism. These include the effect on the enantioselectivity upon changing the chemical nature and/or the size of the R-group or upon varying the pH during catalyst modification and the remarkable influence of water.

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Received August 9, 1974