Functional-Group-Directed Diastereoselective Hydrogenation of Aromatic Compounds. 1

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Diastereoselective liquid phase hydrogenation of a series of monosubstituted indane and tetralin substrates was studied on supported rhodium catalysts. Predominantly the *cis*−*cis* diastereomer, obtained by hydrogenation from the diastereoface opposite the substituent (at the stereogenic center), and the *cis*−*trans* diastereomer, obtained by hydrogenation from the diastereoface on the same side as the substituent, were formed. The diastereoselectivity between the two isomers was dependent on the steric repulsion or the electronic attraction of the substituent with the surface of the catalyst. The hydroxyl group did not exhibit a strong attraction (haptophilicity), and the *cis*−*cis* diastereomer was obtained as the major product. The amino group exhibited a very high haptophilicity, yielding primarily the *cis*−*trans* diastereomer. The diastereoselectivity obtained in the hydrogenation of all the substrates was influenced on addition of bases to the reaction mixture. In the case of alcoholic substrates, the selectivity to the *cis*−*trans* diastereomer could be substantially increased with alkaline hydroxide additives.

Introduction

Stereoselective synthesis of substituted cyclohexane compounds is of interest because the cyclohexane ring is a constituent of many naturally occurring compounds such as terpenoids, steroids, and alkaloids. These compounds can be synthesized by catalytic hydrogenation of the corresponding substituted aromatic compounds, either enantioselectively or diastereoselectively. In diastereoselective hydrogenation an auxiliary carrying chiral information is bonded temporarily to one of the substituents of the aromatic compound before its hydrogenation. Earlier investigations revealed that the diastereoselectivity obtained during hydrogenation depended strongly on the structure of the aromatic compound−auxiliary system and, to some extent, on the catalyst support.[1−4] Because these investigations were limited to only two auxiliaries, namely pyroglutamic acid and proline, the induction by these auxiliaries eluded qualitative prediction let alone quantification. The primary difficulty in rationalization of the induction is the large number of conformations that the aromatic compound−auxiliary moiety can adopt on the catalyst surface depending on the interaction of various functional groups of the moiety. In all aromatic compound−auxiliary combinations investigated so far,[1−4] the chiral center on the auxiliary was at least three covalent bonds away from the nearest substituted position on the aromatic ring, thus complicating the correlation of the configuration of the hydrogenation product with the chirality of the auxiliary.

To clarify the interaction of the individual functional groups, we have studied the hydrogenation of a series of disubstituted aromatic compounds, differing only in the functional group attached to a carbon atom near the aromatic ring. Thus a series of indane and tetralin substrates, substituted at a carbon atom in the saturated ring, were hydrogenated. The present article (part 1) elucidates the results of hydrogenation of such substrates bearing the hydroxyl, amino, and alkyl functional groups (Figure 1). Results pertaining to the hydrogenation of substrates bearing the carboxylic acid, amide, ester, and alkoxy groups will be presented in part 2. The molecules shown in Figure 1 can adopt only two conformations on the surface of the noble metal, depending on which face of the aromatic ring they adsorb. Since the chosen substrates can be considered approximately planar, the induction obtained in their hydrogenation is directed by the functional group substituent present on the saturated ring. Also, since rotation of the bonds connecting the carbon atom bearing the functional group to the aromatic ring is impossible, an unambiguous and direct correlation can be established between a functional group of a substrate and the configuration of its hydrogenation product.

It is well-known that substituents can direct the stereoselectivity in a multitude of homogeneously catalyzed reactions.[5] Directing effects have also been observed in alkene hydrogenation catalyzed particularly by homogeneous rhodium and iridium complexes.[5,6] However, since homogeneous catalysts often show a low activity in aromatic hydrogenation, studies pertaining to directing effects in these hydrogenation reactions have not been conducted. Directing effects of substituents are also known in heterogeneous hydrogenation albeit restricted primarily to cyclic olefinic substrates.[5,7,8] Heterogeneous rhodium catalysts excel in their ability to hydrogenate aromatic substrates under relatively mild reaction condi-

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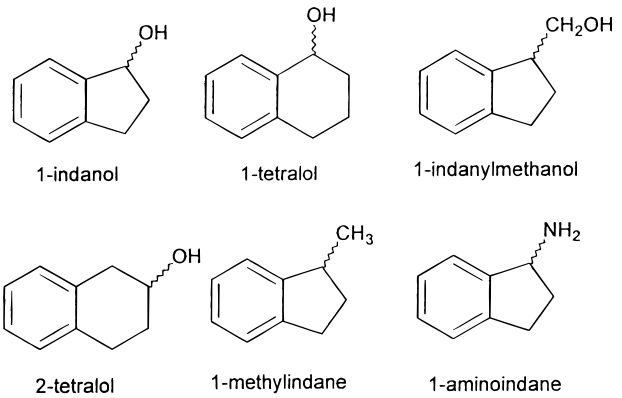

Figure 1. Aromatic substrates hydrogenated.

tions.[9,10] Therefore using these catalysts, we have shown in the present study that useful directing effects occur during hydrogenation of aromatic substrates.

In addition, we investigated the hydrogenation of these relatively simple aromatic substrates to understand the intriguing effect of the addition of organic bases on stereoselectivity, reported in earlier diastereoselective aromatic hydrogenation reactions.[3,11] A complementary study investigating the influence of the addition of inorganic bases on the stereoselectivity was also conducted. The present article focuses on stereoselectivity rather than activity obtained in the hydrogenation of various aromatic substrates under different process conditions.

Results

Hydrogenation of all the substrates yielded predominantly *cis* diastereomers (usually *cis* to *trans* ratio > 10) with respect to the substituents on the six-membered ring (for example see Scheme 1 for hydrogenation of 1-indanol). Different methods were employed for identification of the relative configuration of the *cis* diastereomers (*cis*−*cis* and *cis*−*trans*), depending upon the substrate hydrogenated, and they are described in the Experimental Section. The chemoselectivity to the hydrogenated *cis* products is defined as the percentage yield of the two *cis* isomers at 100% conversion of the substrate. The selectivity between the two *cis* isomers is reported as the diastereomeric ratio (*dr*) at 100% conversion of the substrate and is defined as *dr* = [*cis*−*cis*]/[*cis*−*trans*]. For presentation of the diastereomeric ratio, the sum of the yield of the two diastereomers is normalized to 100. In the case of alcoholic substrates significant to substantial amounts of hydrogenolysis−hydrogenation byproducts (*cis* and *trans*) were obtained. The percentage yield of the hydrogenolysis−hydrogenation products is also reported for these substrates at 100% conversion of the substrates.

Small to significant amounts (up to 10%) of cyclohexene intermediates were observed (and identified by GC−MS analysis) depending on the substrate hydrogenated and the reaction conditions. In most of the substrates the hydrogenation of cyclohexene intermediate proceeded much slower than the substrate, and it caused a change

Scheme 1

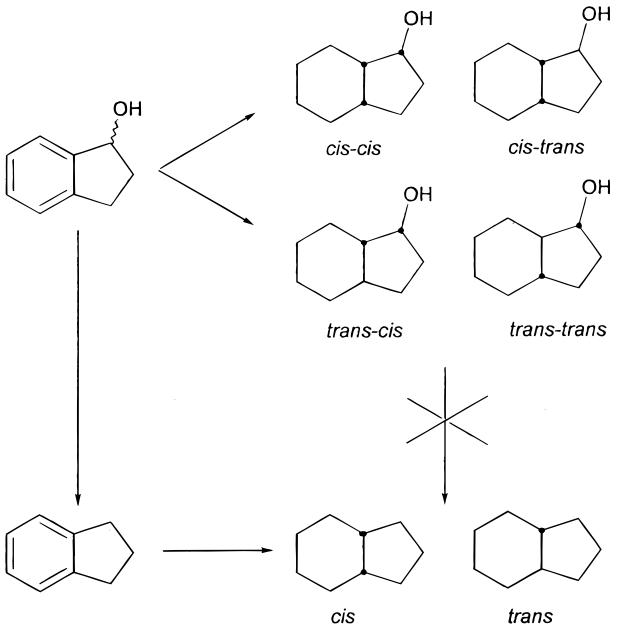

Table 1. Hydrogenation of 1-Indanol

catalyst	solvent	yield of *cis* and *trans* perhydroindane[b]	yield of *cis* perhydro-1-indanol isomers[b]	*dr*[b]
Rh/C[a]	EtOH	77	19	59:41
Rh/C[a]	hexane	42	55	47:53
Rh/Al_2O_3[a]	EtOH	10	88	65:35
Rh/Al_2O_3[c]	EtOH	6	93	67:33
Rh/Al_2O_3[a]	hexane	3	96	57:43

[a] Substrate to rhodium molar ratio = 154. [b] Determined by analyses over HP-1 and α-DEX capillary columns. [c] Substrate to rhodium molar ratio = 72.

in the diastereoselectivity, the magnitude of which depended on the substrate hydrogenated. The position of the double bond in the cyclohexene intermediates was not identified rigorously. However from steric considerations it is likely that the double bond is situated between the two junction carbon atoms.

Hydrogenation of 1-indanol gave *cis* and *trans* isomers of the hydrogenation product perhydro-1-indanol and of the hydrogenolysis−hydrogenation product perhydroindane (Scheme 1). We confirmed that perhydroindane was formed directly from 1-indanol and not by hydrogenolysis of perhydro-1-indanol. The results of the hydrogenation in ethanol and hexane using the Rh/C and Rh/Al_2O_3 catalysts are presented in Table 1. With ethanol as the solvent, the Rh/C catalyst yielded predominantly perhydroindane, while the Rh/Al_2O_3 catalyst yielded predominantly perhydro-1-indanol. With hexane as the solvent, the yield of perhydroindane was lowered with both catalysts. Low *dr* values were obtained for both catalysts, and the value was lower in hexane than in ethanol. Halving the substrate to metal ratio in the case of Rh/Al_2O_3 had a negligible influence on the *dr* and the chemoselectivity.

The results obtained in the hydrogenation of 1-tetralol are reported in Table 2. The yield of the two *cis* perhydro-1-tetralol (1-decalol) isomers as well as the *dr* of the two *cis* isomers depended on the catalyst support. As for 1-indanol, severe hydrogenolysis was observed on Rh/C in ethanol. The *dr* as well as the yield of 1-decalol was higher on Rh/Al_2O_3 than Rh/C. With the Rh/Al_2O_3 and

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Table 2. Hydrogenation of 1-Tetralol

catalyst[a]	solvent	yield of *cis* and *trans* decalin[b]	yield of *cis* 1-decalol isomers[b]	*dr*[b]
Rh/C	EtOH	76	16	53:47
Rh/C	hexane	53	43	45:55
Rh/Al_2O_3	EtOH	12	81	69:31
Rh/Al_2O_3	hexane	3	91	55:45

[a] Substrate to rhodium molar ratio = 139. [b] Determined by analyses over HP-1 and α-DEX capillary columns.

Table 3. Hydrogenation of 1-Indanylmethanol

catalyst[a]	solvent	yield of *cis* and *trans* perhydro-1-methylindane[b]	yield of *cis* perhydro-1-indanylmethanol isomers[b]	*dr*[b]
Rh/C	EtOH	30	70	45:55
Rh/C	hexane	16	82	47:53
Rh/Al_2O_3	EtOH	5	92	52:48
Rh/Al_2O_3	hexane	1	97	47:53

[a] Substrate to rhodium molar ratio = 139. [b] Determined by analyses over HP-1 and α-DEX capillary columns.

Table 4. Hydrogenation of 2-Tetralol

catalyst[a]	solvent	yield of *cis* and *trans* decalin[b]	yield of *cis* 2-decalol isomers[b]	*dr*[b]
Rh/C	EtOH	25	68	63:37
Rh/Al_2O_3	EtOH	8	85	76:24
Rh/Al_2O_3	hexane	3	89	64:36
Pt/Al_2O_3	EtOH	5[c]	83[c]	65:35[c]
Pt/Al_2O_3	hexane	1	95	49:51

[a] Reaction conducted at 70 °C with Pt/Al_2O_3. Substrate to metal molar ratio = 139. [b] Determined by analyses over HP-1 and β-DEX capillary columns. [c] At 85% conversion of 2-tetralol.

Rh/C catalysts, changing the solvent from ethanol to hexane increased the yield to 1-decalol but decreased the *dr*.

Results of hydrogenation of 1-indanylmethanol on carbon- and alumina-supported rhodium catalysts in ethanol and hexane are shown in Table 3. Significant hydrogenolysis was observed on Rh/C catalyst. The value of *dr* was almost unity and changed only slightly with either the catalyst support or the solvent.

The results obtained in the hydrogenation of 2-tetralol are shown in Table 4. As in the case of hydrogenation of 1-indanylmethanol significant hydrogenolysis was observed during the hydrogenation of 2-tetralol on Rh/C catalyst. Reactions with the Pt/Al_2O_3 catalyst were conducted at 70 °C because of lower activity. As observed for 1-indanol and 1-tetralol, using hexane as the solvent instead of ethanol lowered the *dr* for Rh/Al_2O_3 as well as Pt/Al_2O_3 catalysts.

1-Methylindane was prepared in ethanol by hydrogenolysis of 3-methyl-1-oxoindane and was contaminated with the water formed during its preparation. The separation of 1-methylindane from ethanol and water was difficult because of its low boiling point and azeotrope formation with ethanol. Hence, its solution in the ethanol/water mixture was directly used in the hydrogenation experiments. Table 5 reports the results obtained at different process conditions and on the Rh/C catalyst and at one condition on the Rh/Al_2O_3 catalyst. The difference in the performance of Rh/C and Rh/Al_2O_3 is negligible. The yield of the *cis* isomers and the *dr* were almost unaffected by a change in hydrogen pressure and the substrate to rhodium molar ratio.

The hydrogenation of 1-aminoindane proceeded very slowly at room temperature and hence was conducted at

Table 5. Hydrogenation of 1-Methylindane

catalyst	solvent	yield of *cis* perhydro-1-methylindane isomers[b]	*dr*[b]
Rh/Al_2O_3[a]	EtOH	92	64:36
Rh/C[a]	EtOH	93	63:37
Rh/C[c]	EtOH	92	62:38
Rh/C[a,d]	EtOH	92	64:36

[a] Substrate to rhodium molar ratio = 156. [b] Determined by analyses over HP-1 and α-DEX capillary columns. [c] Substrate to metal molar ratio = 312. [d] H_2 pressure = 15 bar.

Table 6. Hydrogenation of 1-Aminoindane

catalyst	solvent	yield of *cis* perhydro-1-aminoindane isomers[b]	*dr*[b]
Rh/C[a]	EtOH	100	2:98
Rh/Al_2O_3[a]	EtOH	100	1.5:98.5
Rh/Al_2O_3[c]	EtOH	90	32:68

[a] Reaction conducted at 70 °C with substrate to rhodium molar ratio = 77. [b] Determined by analyses over RTX-200 capillary column after derivatization of product with MBTFA. [c] Hydrogenation of 1-aminoindane, hydrochloride salt at room temperature with substrate to rhodium molar ratio = 122.

Table 7. Hydrogenation in Ethanol with Triethylamine Additive

substrate	catalyst[a]	substrate to rhodium molar ratio	yield of *cis* isomers	*dr*
1-indanol	Rh/C	154	97	50:50
1-methylindane	Rh/C	156	86	56:44
1-methylindane	Rh/Al_2O_3	156	90	59:41

[a] Triethylamine to rhodium molar ratio = 10.

70 °C and with approximately half the normal substrate to rhodium molar ratio (~77). Irrespective of the catalyst support, a very low *dr* (i.e., high selectivity to the *cis*−*trans* diastereomer of perhydro-1-aminoindane) was obtained (Table 6). A small amount of 1-aminoindane was converted to 1-aminoindane hydrochloride in a diethyl ether solution by bubbling dry hydrogen chloride gas. After isolation of the salt, 0.5 g of it was hydrogenated at the standard temperature and pressure on the Rh/Al_2O_3 catalyst in ethanol. The yield of the *cis*−*trans* isomer decreased, and the *dr* increased to 32:68. The relative configuration of the other diastereomer formed was not identified rigorously but in analogy with the results of hydrogenation of all other substrates was assumed to be *cis*−*cis*.

Addition of amines has been used before to influence the diastereoselectivity in aromatic hydrogenation reactions.[3,11] We studied the effect of the addition of triethylamine to reaction mixtures of the different substrates before their hydrogenation in ethanol. The results of the experiments are reported in Table 7. Addition of amine resulted in a substantial decrease in the activity of the rhodium catalysts for all the substrates. Very little activity was detected for hydrogenation of 1-tetralol and 1-indanylmethanol. The hydrogenolysis activity of Rh/C catalyst in the hydrogenation of 1-indanol was almost completely suppressed, thus increasing the yield of the *cis* perhydro-1-indanol isomers. The value of *dr* decreased on addition of amine for both 1-indanol and 1-methylindane.

Addition of an aqueous solution (0.3 mL of 0.5 N) of inorganic bases to the reaction mixture with ethanol and Rh/C resulted in a decrease in the activity of the catalyst by an order of magnitude. The activity decreased with

Table 8. Hydrogenation on Rh/C in Ethanol with Inorganic Base Additives

substrate	substrate to rhodium molar ratio	base[a]	time (days)	conversion	yield of *cis* isomers[b]	*dr*[b]
1-indanol	154	LiOH	1	100	96	41:59
1-indanol	154	NaOH	1	91	95	19:81
1-indanol	154	Na_2CO_3	1	92	96	31:69
1-indanol	154	KOH	4	81	89	15:85
1-tetralol	139	NaOH	3	100	84	28:72
1-methylindane	156	NaOH			88	53:47

[a] Alkali metal to rhodium molar ratio = 6. [b] At 81% conversion of 1-indanol in experiment with KOH additive and at 100% conversion of substrates in all other experiments.

increasing concentration of the base and with increasing size of the cation. The results are shown in Table 8. A drastic suppression of hydrogenolysis activity was observed on addition of inorganic bases, as observed with triethylamine. In the case of 1-indanol and 1-tetralol, the *cis*−*trans* diastereomer was the major product. The *dr* depended on the base added and increased with the size of cation in the case of alkaline hydroxide additives. On increasing the amount of NaOH solution from 0.3 mL to 1 mL in the hydrogenation of 1-indanol, the *dr* decreased further from 19:81 to 12:88 and was accompanied by a further decrease in the activity.

Discussion

The aromatic substrates undergoing hydrogenation can adsorb in two ways on the catalyst surface depending on the interaction of the functional group present on the neighboring saturated ring. The interaction of a functional group with the catalyst surface depends on steric and electronic factors. When the electronic interaction dominates, hydrogenation of the aromatic ring takes place from the side of the substituent leading to the *cis*−*trans* diastereomer. Contrarily, when the steric repulsion dominates, hydrogenation occurs from the side opposite the substituent, leading to the *cis*−*cis* diastereomer. Similar studies correlating various functional groups with their ability to influence the adsorption of olefinic substrates in hydrogenation reactions on noble metal catalysts have been conducted by Thompson et al.[12−14] and more recently by MaGee et al.[15] In their studies, Thompson and co-workers found that some functional groups had a strong affinity (also termed as haptophilicity) for the catalyst, resulting in hydrogenation products with a configuration opposite of that expected when considering only steric repulsion of the functional group. While their study was conducted on the hydrogenation of olefinic substrates over platinum- and palladium-based catalysts, our study was conducted on the hydrogenation of aromatic substrates over rhodium-based catalysts.

In the hydrogenation of the aromatic substrates, cyclohexene intermediates were often observed. The formed cyclohexene intermediates hydrogenated further only after the complete conversion of substrate or when the substrate concentration was very low. The diastereoselectivity obtained in their hydrogenation was different from that obtained in the direct hydrogenation of the parent aromatic substrate. A rigorous examination of the diastereoselectivity−functional group relationship in the aromatic substrates should include a separate investigation of a similar relationship in the corresponding cyclohexene intermediates. Since the latter investigation was not done, we are unable to separate the directing effect of the functional group in the aromatic compound from that in the corresponding cyclohexene intermediates. However, the influence on the final diastereoselectivity is relatively small since only a small percentage of the aromatic compound desorbs as the cyclohexene intermediate after its partial hydrogenation. For example, in the hydrogenation of 1-tetralol in hexane over the Rh/Al_2O_3 catalyst, the *dr* changed from 56:44 at 12% conversion to 55:45 at 100% conversion.

Results shown in Table 1 indicate that the haptophilicity of the hydroxyl group to the rhodium catalyst, if at all present, is definitely not high, since the *cis*−*cis* instead of the *cis*−*trans* isomer is obtained in excess with Rh/C and Rh/Al_2O_3 catalysts. The Rh/C catalyst showed considerably more hydrogenolysis selectivity than the Rh/Al_2O_3 catalyst. Labeling experiments indicated that hydrogenolysis on Rh/C occurs by elimination of the protonated hydroxyl group followed by hydrogenation by spillover hydrogen on the mildly acidic carbon support.[16] Hydrogenation was also investigated in hexane because the ethanol hydroxyl groups could compete with and/or solvate the 1-indanol hydroxyl groups, thus masking its haptophilicity. The selectivity to perhydroindane is lower in hexane than in ethanol, because of lower stability of the intermediate in the hydrogenolysis reaction. In hexane the selectivity to the *cis*−*cis* isomer is reduced, indicating that the hydroxyl group in 1-indanol probably interacts mildly with the catalyst surface. Results of hydrogenation of 1-tetralol are qualitatively similar to those obtained with 1-indanol (Table 2). The influence of the nature of the catalyst support on the diastereoselectivity could be due to the difference in the magnitude of interaction of the hydroxyl group of the substrate with the catalyst support and/or a contribution of hydrogenation with spillover hydrogen in some supports. Since the adsorption of an aromatic ring is much stronger than that of a double bond, on rhodium,[17] the difference in energy between the two adsorbed structures leading to the two different *cis* diastereomers is probably smaller than that for the highly hindered olefinic substrates investigated by Thompson and co-workers. This can explain why the interaction of the hydroxyl group with the rhodium catalyst is much weaker than that in their investigation. We were unable to study hydrogenation of the benzylic aromatic substrates with platinum or palladium catalysts, because of even more hydrogenolysis than with rhodium.

In 1-indanol and 1-tetralol the hydroxyl group is attached to a carbon at the α position with respect to the aromatic ring. The effect on the selectivities on shifting the location of the hydroxyl group to the *β* carbon was studied by hydrogenating 1-indanylmethanol and 2-tetralol (Tables 3 and 4). The values of *dr* as well as the variation of the *dr* with catalyst support and solvent are considerably different in 1-indanylmethanol and 2-te-

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tralol. In the case of 1-indanylmethanol the haptophilic effect is stronger than in 1-indanol or 1-tetralol since the value of *dr* is almost unity and it does not vary with catalyst support or the solvent. In contrast, the results of hydrogenation of 2-tetralol indicate the presence of a mild haptophilic effect, the magnitude of which changes with the solvent, as in the cases of 1-indanol and 1-tetralol. The difference in the diastereoselectivities of hydrogenation of 2-tetralol and 1-indanylmethanol is probably due to the orientation of the hydroxyl group when these molecules adsorb on the catalyst surface. Hydrogenation of 2-tetralol was conducted on Pt/Al_2O_3 catalyst to compare the haptophilicity of the hydroxyl group to platinum with that to rhodium. Although a quantitative comparison between platinum and rhodium catalysts is not possible because the hydrogenation reactions were conducted at different temperatures, a similar trend is observed on changing the solvent from ethanol to hexane with platinum as with rhodium.

1-Methylindane can interact only sterically with the surface of the catalyst, and hence both the Rh/C and the Rh/Al_2O_3 catalysts give the same results (Table 5). Since each substrate molecule bears the chiral element necessary for stereoselective hydrogenation, we do not expect a big effect on diastereoselectivity of the substrate to rhodium ratio and hydrogen pressure, as observed in hydrogenation of 1-methylindane. This is confirmed also in the case of 1-indanol where a change in the substrate to catalyst ratio by a factor of 2 resulted in hardly any change in the *dr*. The purely steric interaction of the methyl group is unable to prevent the adsorption of the aromatic substrate from the methyl-group side, and only a small preference to the *cis*−*cis* isomer is observed. The reason for the low selectivity must be the small size of the methyl group. The magnitude of the steric hindrance of the hydroxyl group in 1-indanol is comparable to that of the methyl group in 1-methylindane in ethanol.

It is a well-known that amines adsorb strongly on noble metal catalysts.[9,10] In some of the diastereoselective hydrogenation reactions reported earlier, amine additives were used. These additives decreased the rate of reaction by strongly adsorbing on the metal and modified the selectivity. Thus, as expected, strong adsorption of 1-aminoindane during reaction resulted in a very low hydrogenation activity at room temperature, and hence the reactions had to be conducted at 70 °C. The amino group showed a strong haptophilic effect, giving an almost quantitative yield of the *cis*−*trans* isomer. The effect is seen irrespective of whether Rh/C or Rh/Al_2O_3 is used as the catalyst because the substrate interacts primarily with the rhodium metal during hydrogenation. On neutralizing the basicity of the amino group by converting 1-aminoindane to its hydrochloric acid salt before hydrogenation, the selectivity to the *cis*−*trans* isomer was drastically reduced, clearly demonstrating the haptophilicity of the amino group.

Addition of triethylamine reduces the activity of the catalyst due to strong adsorption. The *dr* decreases on addition of amine in the hydrogenation of 1-indanol over Rh/C and somewhat surprisingly also in the hydrogenation of 1-methylindane. The decrease in diastereoselectivity of 1-methylindane indicates that the amine modifies the stereoselectivity not only by an electronic mechanism but also by a steric mechanism.

The influence of inorganic base additives on stereoselectivity in the hydrogenation of substituted phenolic aromatic compounds on rhodium catalysts has been reported before.[18] The results in Table 8 show that the addition of inorganic bases induces a substantial change in diastereoselectivity of the benzylic aromatic substrates investigated. The addition of alkali hydroxides in the hydrogenation of benzylic alcohols not only reduced the value of the *dr* below unity but even produced the *cis*−*trans* diastereomer with a moderately high selectivity. This could be due to the interaction of the hydroxyl group of the substrate with the alkali metal cations on the surface of the catalyst. The activity decreases with an increase in the size of cation, probably because a bigger cation blocks more surface rhodium atoms than a smaller cation. The higher *dr* obtained for Na_2CO_3 than NaOH is probably due to a lower extent of dissociation in the ethanol/water mixture. Addition of NaOH in the hydrogenation of 1-methylindane also reduced the *dr*. Reduction of the *dr* in the hydrogenation of 1-methylindane by organic as well as inorganic bases indicates that the decrease is primarily a result of steric constraints imposed on its adsorption on the surface of the catalyst by the adsorbed bases. It is not clear if the addition of the inorganic bases also causes an electronic modification of the rhodium atoms at the surface.

Conclusions

The aromatic substrates investigated give very different stereoselectivities depending on the functional group substituent. The hydroxyl group in most of the alcoholic substrates has a mild haptophilic effect, which becomes evident on conducting the reaction in hexane. The *dr* obtained in the hydrogenation of these substrates depends on the exact location and orientation of the hydroxyl group and is influenced by the nature of the catalyst support. Aromatic substrates with a hydroxyl group at the β position are also significantly hydrogenolyzed on Rh/C catalyst in ethanol. The methyl group in 1-methylindane, because of its relatively small steric repulsion, leads to only a small preference for the *cis*−*cis* isomer. Since it interacts exclusively sterically with the catalyst surface, the diastereoselectivity is independent of the catalyst support. The amino group in 1-aminoindane interacts very strongly (high haptophilicity) with the catalyst, and the *cis*−*trans* isomer is obtained almost exclusively. The haptophilicity of the amino group is diminished considerably on converting it to its salt. The addition of organic and inorganic bases results in a reduction of the diastereoselectivity to the *cis*−*cis* diastereomer in the case of 1-methylindane, primarily by constraining its adsorption on the surface of the catalyst. In the case of benzylic alcohols, the magnitude of the *dr* decreases to a value significantly below unity, on addition of inorganic bases because of the interaction of the hydroxyl group with the alkali metal cations. From a synthetic point of view, the high haptophilicity of the amino group and the ability of the inorganic base additives to influence the selectivity in the hydrogenation of benzylic alcohols should be of interest.

Experimental Section

Hydrogenation Experiments. Hydrogenation reactions were conducted under efficient mass-transport conditions in a 60 mL stainless steel autoclave equipped with a gas-inducing

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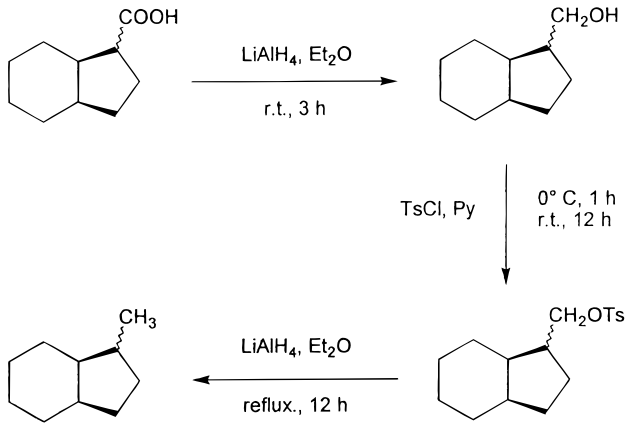
impeller at a stirring speed of 1100 rpm. In a typical experiment, a solution of 0.5 g of substrate in 15 mL of ethanol or hexane (and basic additive, if any) was added to 50 mg of catalyst in the autoclave. Pt/Al_2O_3, Rh/Al_2O_3 (Fluka), and Rh/C (Aldrich) catalysts (metal loading 5 wt %) were used as supplied. The autoclave was closed, flushed three times successively with nitrogen and hydrogen, and then pressurized to 50 bar with hydrogen. Hydrogenation of 1-aminoindane on the rhodium catalysts and that of 2-tetralol on the platinum catalyst were conducted at 70 °C. All other reactions were conducted at room temperature. Samples could be taken with a sample tube during the reaction to detect the completion of the reaction (typically less than 12 h, in experiments without base addition), but no kinetic measurements were done. Analysis of samples for determination of conversion and selectivity was done using a GC equipped with a FID detector and various capillary columns depending on the substrate hydrogenated. Although the diastereomeric products in most cases could be separated on a nonchiral HP-1 column, chiral columns were also used for GC analyses. In the case of 1-aminoindane, the reaction samples were dried free of ethanol, derivatized with *N*-methyl-bis(trifluoroacetamide) (MBTFA) overnight at room temperature and then injected in a RTX-200 capillary column after redissolving the sample in dichloromethane.

Preparation of 1-Indanylmethanol and 1-Methylindane. Racemic 1-indanol, 1-tetralol, 1-aminoindane (all Fluka), and 2-tetralol (Acros) were used as obtained. Racemic 1-indanylmethanol was prepared in two steps from racemic 3-oxoindan-1-carboxylic acid (Aldrich). In the first step the keto group was hydrogenolyzed over 10 wt % Pd/C catalyst (Fluka). In the second step the carboxylic acid group was hydrogenated to the hydroxymethylene group using $LiAlH_4$. The product of synthesis was identified as 1-indanylmethanol by comparison of its NMR data with that reported in the literature.[19] Hydrogenolysis of racemic 3-methyl-1-oxoindanone (Aldrich) over Pd/C catalyst in ethanol under 3 bar hydrogen yielded racemic 1-methylindane quantitatively. It was identified by comparison of MS data with that reported in the literature.[20] The catalyst was filtered off, and the solution of racemic 1-methylindane in ethanol was used in its hydrogenation. The purity of all substrates exceeded 97% as determined by GC analysis.

Identification of *cis*−*cis* and *cis*−*trans* Product Isomers. Isomers of perhydro-1-indanol were identified by comparison of a ^{13}C NMR spectrum of the product mixture with their spectra reported in the literature.[21] Isomers of perhydro-1-tetralol were identified by comparison of a ^1H NMR spectrum of the product mixture to their spectra reported in the literature.[22] The *cis*−*cis* perhydro-2-tetralol (2-decalol) isomer was identified by comparison of a ^{13}C NMR spectrum of the product mixture to the spectrum reported in the literature. The identification of the other isomeric product was difficult, however, because of conflicting ^{13}C NMR data in the literature for the *cis*−*trans* isomer.[23,24] The product mixture was therefore oxidized to 2-decalone using chromic acid as reported by Brown and Garg.[25] ^{13}C NMR of the 2-decalone product showed only one C═O group, indicating that the hydrogenation product consisted of *cis*−*cis* and *cis*−*trans* isomers. The *cis* configuration of 2-decalone was also confirmed by comparison of its ^{13}C NMR spectrum to that reported in the literature.[26]

Scheme 2



Identification of the absolute configuration of the perhydro-1-methylindane product posed considerable difficulty because no separate spectral data of the isomers were available in the literature. Therefore a reference mixture of *cis*−*cis* and *cis*−*trans* diastereomers was synthesized starting from perhydroindan-1-carboxylic acid (*cis*−*cis* to *cis*−*trans* ratio of 3:1) using the route reported by Brewster and Buta.[27] The mixture of perhydroindan-1-carboxylic acid was obtained by hydrogenation of indan-1-carboxylic acid on Rh/C catalyst.[28] Comparison of the gas chromatograms of the reaction product obtained using a α-DEX capillary column and that of the synthesized reference sample enabled identification of the relative configuration. As shown in Scheme 2, the synthesis of the reference sample involved reduction of the mixture of *cis*−*cis* and *cis*−*trans* diastereomers of perhydroindan-1-carboxylic acid to the corresponding perhydro-1-indanylmethanol isomers using $LiAlH_4$. The isomeric mixture of alcohols was converted into their tosyl derivatives. These tosyl derivatives were then reduced using $LiAlH_4$ to give a mixture of *cis*−*cis* and *cis*−*trans* perhydro-1-methylindane in approximately the same ratio as the diastereomeric mixture of the starting acid. The intermediate mixture of perhydro-1-indanylmethanol isomers was used as a reference for identification of the product isomers obtained in the hydrogenation of 1-indanylmethanol.

The relative configuration of the product perhydro-1-aminoindane was identified by converting it to the *N*-benzoyl derivative, by treatment of the isolated product with benzoyl chloride in a dilute NaOH solution. A two-dimensional ^1H NOE NMR spectrum of the resulting amide enabled us to determine that the proton at the carbon atom bearing the amide group was *trans* to the protons attached to both junction carbon atoms. Further proof of the structure was obtained by X-ray crystallography (see Supporting Information) on a monoclinic crystal of the *N*-benzoyl derivative, obtained by crystallization from a diisopropyl ether/hexane solvent mixture.

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Supporting Information Available: NMR and MS data of *cis*−*cis* and *cis*−*trans* isomers of perhydro-1-indanylmethanol, perhydro-1-methylindane, and perhydro-1-aminoindane and NMR, MS, and crystal structure data of the *N*-benzoyl derivative of *cis*−*trans* perhydro-1-aminoindane. This material is available free of charge via the Internet at http://pubs.acs.org.

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