

Article

Rh-Catalyzed Environmentally Benign Selective Hydrogenation of a Broad Variety of Functional Groups Using Al-Water as a Hydrogen Source

Guoshu Xie and Béla Török *

Department of Chemistry, University of Massachusetts Boston, 100 Morrissey Blvd, Boston, MA 02125, USA

* Correspondence: bela.torok@umb.edu

Abstract: Supported rhodium catalysts were screened to catalyze the one-step hydrogenation of a broad variety of functional groups. The results show that 5% Rh/Al₂O₃ and 5% Rh/C performed well in controlling selective hydrogenation under the desired amount of time and temperature. In this regard, partial and full hydrogenation were achieved by controlling reaction time or temperature. In addition to aliphatic C–C, C–N, C–O, and N–O multiple bonds, the applicability of this method was demonstrated by the hydrogenation of C=C double bonds of arenes, which is considered challenging. Importantly, the Al-H₂O system producing hydrogen in situ and the high, controllable selectivity make this protocol environmentally benign and highly efficient.

Keywords: hydrogenation; heterogeneous catalysis; green chemistry; Rh-Al/H₂O combination; in situ hydrogen formation; aqueous medium; heterocycles; aromatic ring

**Citation:** Xie, G.; Török, B.

Rh-Catalyzed Environmentally Benign Selective Hydrogenation of a Broad Variety of Functional Groups Using Al-Water as a Hydrogen Source. *Catalysts* **2022**, *12*, 1578. <https://doi.org/10.3390/catal12121578>

Academic Editor: Junling Lu

Received: 31 October 2022

Accepted: 1 December 2022

Published: 5 December 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Reduction is one of the most important transformations in organic chemistry [1]. Although several methods are available to achieve this goal, catalytic hydrogenation is the most applicable method in environmentally benign synthesis [2–5]. Therefore, the development of a variety of catalytic hydrogenation methods, particularly those with improved safety features, is highly desired. New developments focus on alternative hydrogen sources, since traditional hydrogenation uses hydrogen, which is an explosive gas. In addition, its production by steam reforming occurs under extreme conditions (700–1000 °C) and produces a large amount of carbon dioxide, a well-known greenhouse gas [6]. Thus, due to the severe environmental impacts of hydrogen gas production, catalytic hydrogenation is not necessarily a green process [7]. As a potential alternative hydrogen source, the use of the Al-H₂O system was investigated. The pioneering work by Tashiro and colleagues explored the use of Ni-Al alloy in catalytic hydrogenations, where the reaction of Al with dilute base solution (commonly NaOH and KOH) provided the hydrogen, and the in situ-formed Raney Ni became the hydrogenation catalysts [8–10]. More contemporary applications include the use of Ni-Al alloy in neat water, which allows for high selectivity [11]. In addition to Ni-Al alloy, the use of Al-H₂O system was extended to Pd catalysts; the mixture of a supported Pd catalyst with Al powder in aqueous medium was used, usually providing high activity and selectivity [12,13]. Recent reviews summarize the developments achieved over the past decades using the metal-Al-water hydrogenation system [14,15].

In our earlier exploration on the applicability of the Ni-Al alloy-water system, we developed highly selective reductions without the use of strong inorganic bases, which made the process environmentally more benign, including the highly selective catalytic hydrogenation of ketones and [16] aromatic heterocycles [17] or selective reductive aminations [11]. Although the Ni-based alloy and the in situ-produced catalyst have their own merits, most notably, their resistance to sulfur-containing compounds, Ni has its own limitations, e.g., the

often moderate activity and selectivity [2,14]. Therefore, we aimed to extend this catalytic system by using commercially available rhodium catalysts and Al powder that would allow us to take advantage of the higher activity of Rh. Rhodium is one of the most often used transition metals in synthetic processes and likely the most powerful hydrogenation catalyst, homogeneous and heterogeneous catalytic applications both included [4,18,19]. Rh can hydrogenate nearly all functional groups. It is a versatile metal and can also be applied as an oxidative dehydrogenation catalyst in aromatization reactions [20,21]. In addition to hydrogenation and oxidation, it is a commonly applied catalyst in the industrially important hydroformylation [22]. Most recently, titania-supported Rh-catalysts have been applied in photo-catalyzed acceptorless dehydrogenation [23] and aerobic dehydrogenation of N-heterocycles [24].

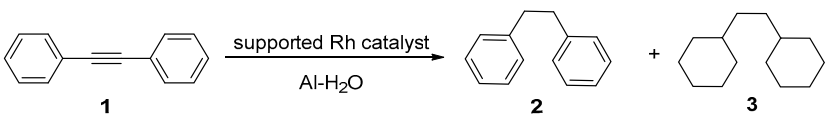
Building upon our recent efforts on the development of green synthetic methods [25–28], herein we describe the efficient and highly selective catalytic hydrogenation of a variety of functional groups using an environmentally benign supported Rh catalyst-Al-H₂O system. In comparison with protocols developed earlier by us and others, we demonstrated that the Rh-Al-H₂O system represents an effective and highly selective catalytic system for the hydrogenation of a broad range of substrates without the use of pressurized hydrogen gas. The commercial Al powder serves as a safe, inexpensive hydrogen generator in its reaction with water, an environmentally benign solvent. The major advantages of this system are that (i) the reaction occurs in water, which is an environmentally benign and inexpensive medium; (ii) no harmful by-product is generated, as Al(OH)₃ is nontoxic and recyclable; (iii) high pressure explosive hydrogen and a high pressure reaction vessel are not required; (iv) nearly all reducible functional groups can be hydrogenated; and (v) the appropriate selection of the reaction conditions (temperature/time) allows for high selectivity for the reduction of functional groups as well as aromatic rings, which was not the case with catalysts other than Rh. Therefore, this system can be considered an environmentally benign improvement compared to existing procedures.

2. Results and Discussion

By executing modifications to the original Ni-Al alloy-based system, we developed several transformations [11,14,16,17]. We also developed a better tunable system based on a Pd/C catalyst and the Al-water system for the chemoselective hydrogenation [12]. The simplicity and efficacy of the upgraded protocol are remarkable; however, the hydrogenative ability of Pd has its own limitations. Thus, it was decided to explore the applicability of more powerful hydrogenation catalysts, such as rhodium. One of the most important variables of a supported metal catalyst is the support itself [29]. The inert, acidic, basic, or special electronic (insulator, conductor, etc.) characteristics of the support materials can significantly contribute to the tailoring of the properties of the actual catalyst [30,31]. It is worth noting that the catalyst-Al/H₂O system was presonicated before the reactions. As we pointed out in a recent work on H–D exchange reactions using the Al-H₂O system for hydrogen generation, the surface of the aluminum powder is partially oxidized and covered with Al₂O₃. This causes a significant lag phase (several hours) in H₂ generation [32]. Sonication removes surface impurities and thus exposes the Al surface for the reaction with water [33]. However, it is also important that the presence of the Pd catalyst significantly improved the evolution of hydrogen during the sonication step, and using a longer than necessary presonication time may lead to the loss of H₂ in the activation process.

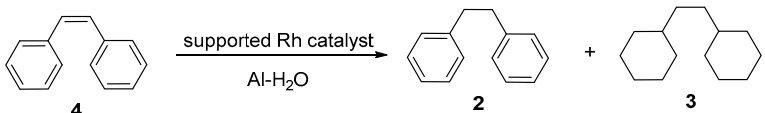
Therefore, in the preliminary experiments, we tested several commercially available supported Rh catalysts in four reactions to identify the catalyst that would be applied for the hydrogenation of a broad array of functional groups. The data are summarized in Tables 1–4 (yields were determined by GC-MS as shown in the Supplementary Material).

Table 1. Hydrogenation of 1,2-diphenylacetylene on Rh catalysts using Al-H₂O as the H₂ source ^a.

						
Entry	Catalyst/Supplier	Time (h)	T (°C)	Conversion (%)	Yield of 2 (%)	Yield of 3 (%)
1	5% Rh/Al ₂ O ₃ (TS)	24	25	22	22	0
2	5% Rh/Al ₂ O ₃ (reduced) (AA)	24	25	83	80	3
3	5% Rh/C (AA)	24	25	0	0	0
4	1% Rh/PEI/SiO ₂ (AA)	24	25	0	0	0

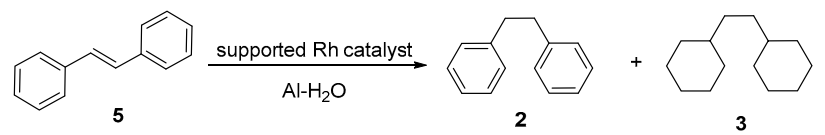
^a Reaction conditions: 0.25 mmol of substrate, 0.025 mmol (51 mg) of supported Rh catalyst, 2.5 mmol (68 mg) of Al powder in 2 mL of H₂O. One hour of presonication of the catalytic mixture (supported Rh-Al in H₂O) before adding the substrate; TS—ThermoScientific, AA—Alfa Aesar.

Table 2. Hydrogenation of *cis*-stilbene on Rh catalysts using Al-H₂O as the H₂ source ^a.

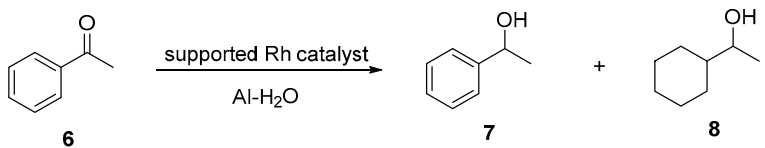
						
Entry	Catalyst	Time (h)	T (°C)	Conversion (%)	Yield of 2 (%)	Yield of 3 (%)
1	5% Rh/Al ₂ O ₃ (TS)	24	25	7	2	5
2	5% Rh/Al ₂ O ₃ (reduced) (AA)	24	25	96	23	73
3	5% Rh/Al ₂ O ₃ (AA)	24	50	12	4	8
4	5% Rh/C (AA)	24	50	100	0	100
5	1% Rh/PEI/SiO ₂ (AA)	24	50	0	0	0

^a Reaction conditions: 0.25 mmol of substrate, 0.025 mmol (51 mg) of supported Rh catalyst, 2.5 mmol (68 mg) of Al powder in 2 mL of H₂O. One hour of presonication of the catalytic mixture (supported Rh-Al in H₂O) before adding the substrate; TS—ThermoScientific, AA—Alfa Aesar.

Table 3. Hydrogenation of *trans*-stilbene on Rh catalysts using Al-H₂O as the H₂ source ^a.

						
Entry	Catalyst	Time (h)	T (°C)	Conversion (%)	Yield of 2 (%)	Yield of 3 (%)
1	5% Rh/Al ₂ O ₃ (TS)	24	25	85	73	12
2	5% Rh/Al ₂ O ₃ (reduced) (AA)	24	25	71	66	5
3	5% Rh/Al ₂ O ₃ (AA)	24	50	87	82	5
4	5% Rh/C (AA)	24	50	100	0	100
5	1% Rh/PEI/SiO ₂ (AA)	24	50	0	0	0

^a Reaction conditions: 0.25 mmol of substrate, 0.025 mmol (51 mg) of supported Rh catalyst, 2.5 mmol (68 mg) of Al powder in 2 mL of H₂O. One hour of presonication of the catalytic mixture (supported Rh-Al in H₂O) before adding the substrate; TS—ThermoScientific, AA—Alfa Aesar.

Table 4. Hydrogenation of acetophenone on Rh catalysts using Al-H₂O as the H₂ source ^a.


Entry	Catalyst	Time (h)	T (°C)	Conversion (%)	Yield of 7 (%)	Yield of 8 (%)
1	5%Rh/Al ₂ O ₃ (TS)	6	25	100	100	0
2	5%Rh/Al ₂ O ₃ (reduced)(AA)	6	25	100	100	0
3	5% Rh/C (AA)	6	25	0	0	0
4	1% Rh/PEI/SiO ₂ (AA)	6	25	0	0	0

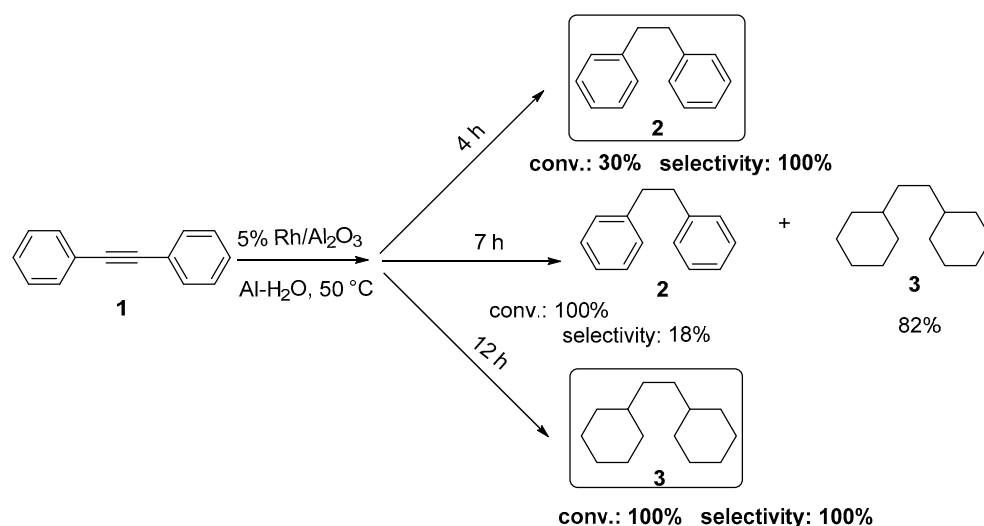
^a Reaction conditions: 0.25 mmol of substrate, 0.025 mmol (51 mg) of supported Rh catalyst, 2.5 mmol (68 mg) of Al powder in 2 mL of H₂O. One hour of presonication of the catalytic mixture (supported Rh-Al in H₂O) before adding the substrate.

Tables 1–4 describe the activity and selectivity of selected supported Rh catalysts in the hydrogenation of diphenylacetylene, *cis*-stilbene, *trans*-stilbene, and acetophenone as test reactions to evaluate the suitability of the catalysts for a broader substrate study. As a general conclusion, the 1% Rh/PEI/SiO₂ catalyst showed poor performance in all reactions and was not further investigated. It was also observed in Tables 1–3 that the reductions, depending on the catalyst applied, yielded two major products, one being the result of the C–C double or triple bond hydrogenation, and the other a perhydrogenated product when the two aromatic rings also underwent hydrogenation. A similar observation was made in the hydrogenation of the stilbene isomers. It appears that the appropriate selection of the reaction conditions would allow the preparation of two different products with high selectivity. As depicted in Table 1, alumina-supported rhodium catalysts from different sources performed effectively in the hydrogenation of diphenylacetylene, while catalysts with other supports (C, PEI/SiO₂) were not active. Comparing entry 1 with entry 2, both 5% Rh/Al₂O₃ and 5% Rh/Al₂O₃(reduced) exhibited activity and had a yield of 22% and 83%, respectively. Although the latter had a higher conversion, the former maintained 100% selectivity. This observation would warrant an optimization of reaction conditions to obtain high conversion with 100% selectivity. Table 2 shows that 5% Rh/Al₂O₃ had a poor conversion in the hydrogenation of *cis*-stilbene, even under the moderately elevated temperature of 50 °C, and the same was observed by using catalyst 5% Rh/PEI/SiO₂. As Table 3 indicates, 5% Rh/PEI/SiO₂ yielded no product, while the other three catalysts gave high to quantitative conversions. Although the hydrogenated products were obtained (Table 2, entries 1–4, Table 3, entries 1–4), the selectivity values revealed that 5% Rh/C was the best choice for the hydrogenation of *cis*-stilbene and *trans*-stilbene. Unfortunately, neither 5% Rh/C nor 5% Rh/PEI/SiO₂ was successful in hydrogenating acetophenone. In contrast, complete conversion was reached with both 5% Rh/Al₂O₃ and 5% Rh/Al₂O₃ (reduced) after 6 h at 25 °C, also giving 100% chemoselectivity.

Based on these preliminary investigations, 5% Rh/Al₂O₃ (ThermoScientific, Waltham, MA, USA) and 5% Rh/C (Alfa-Aesar, Ward Hill, MA, USA) catalysts were selected for further studies with a variety of substrates. The major advantage of this catalytic system in comparison to traditional high-pressure hydrogenations is that in the current system, the catalyst works under 1 bar hydrogen pressure and that hydrogen is continuously generated in situ in the aqueous mixture resulting in milder and less hazardous conditions than those observed under high pressure conditions. The amount of aluminum added can be used to control the reactivity of the system, which is also safe and does not require an expensive high-pressure vessel. These advantages make the Rh-Al/H₂O system greener and more sustainable and broadly applicable compared to the traditional high-pressure process.

2.1. Rh-Catalyzed Hydrogenation of Aliphatic C–C Multiple Bonds

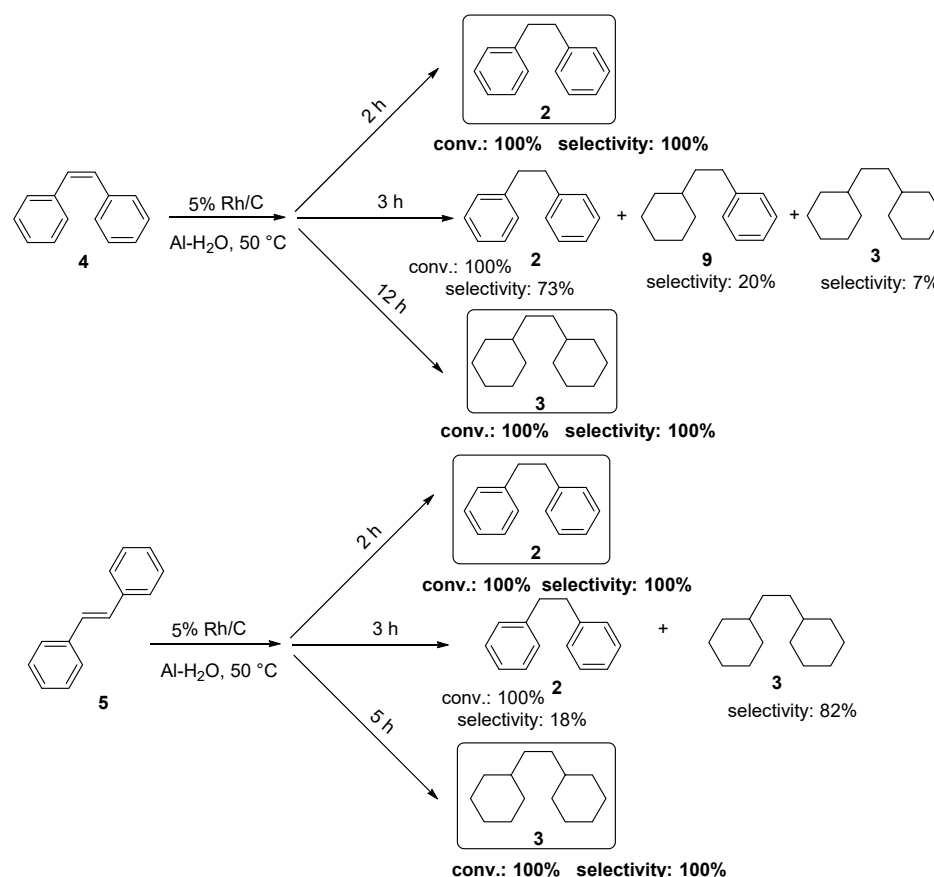
Using the selected 5% Rh/Al₂O₃ catalyst, the potential preparative applications of this catalytic system were explored. While in Tables 1–4 the goal was a simple comparison, here our goal was to identify environmentally benign conditions that controllably allow for the preparation of the products with high yields and possibly exclusive chemoselectivity. The first functional group that we explored was the reduction of aliphatic C–C multiple bonds. Therefore, the hydrogenation of diphenylacetylene, *cis*-stilbene, and *trans*-stilbene was optimized for exclusive product formations that would allow preparative isolation. It must be mentioned that although the primary goal was to achieve the C–C double and triple bond hydrogenations, the target compounds also underwent hydrogenation on their aromatic rings as the conditions changed. The data are depicted in Schemes 1 and 2. It is worth noting that the Schemes indicate the conversion of the starting material and the selectivities for each product. In most cases, the conversion was 100%, so essentially the selectivities were identical with actual yields. If the system did not reach complete conversion, the conversion should be multiplied by the selectivities (conv. × selectivity/100) to obtain the actual yield.



Scheme 1. Hydrogenation of C≡C triple bond of diphenylacetylene by the 5% Rh/Al₂O₃–Al/H₂O catalytic system.

Diphenylacetylene could be converted to 1,2-diphenylethane (2) by using 5% Rh/Al₂O₃ catalyst after 4 h at 50 °C. Although the conversion was relatively moderate at 30%, the selectivity could be maintained at 100% allowing the selective preparation of 2 after the starting material could be recycled. After 7 h, 1,2-diphenylethane (2) and 1,2-dicyclohexylethane (3) were obtained with complete conversion but split selectivity at 18% 2 and 82% 3, respectively. A gradual increase in reaction time resulted in 100% conversion, with exclusive selectivity for 1,2-dicyclohexylethane (3) at 12 h. These data show that the partial hydrogenation on the C≡C triple bond and complete hydrogenation on the aromatic rings occurred in a stepwise manner, and both products could be selectively achieved by the appropriate selection of reaction time (Scheme 1). Based on the data, however, simple kinetics alone does not explain the selectivity. While 2 that formed early in the process undergoes further hydrogenation, the second step likely has a significantly lower reaction rate. While at this early stage of the investigations these observations cannot be unambiguously explained, based on the literature [34], we propose that a limited selective poisoning effect of alkynes/alkenes may delay the hydrogenation of the aromatic rings. It is known that alkenes have strong adsorption capabilities on metal surfaces, Rh included, blocking the hydrogenation of the aromatic rings. When the C=C hydrogenation occurs, the product

alkane does not possess the high adsorption affinity anymore, thus opening the Rh centers up for the aromatic hydrogenation.



Scheme 2. Hydrogenation of *cis*- and *trans*-stilbenes by the supported 5% Rh/C-Al/H₂O catalytic system.

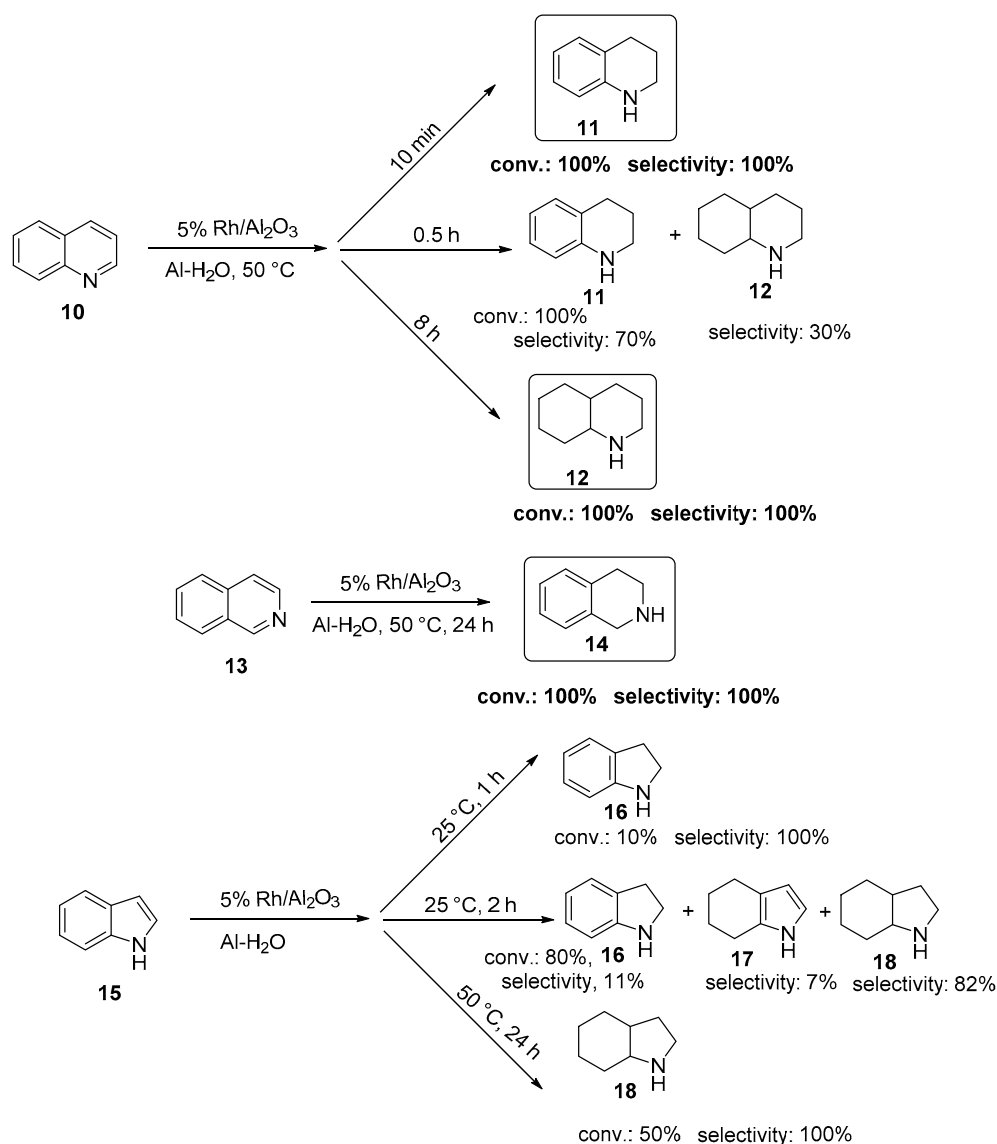
A similar step-by-step process occurred when the hydrogenation of *cis*- and *trans*-stilbenes was attempted, although in this case, the 5% Rh/C catalyst was found to exhibit the best performance. Interestingly, using *cis*-stilbene as a substrate in the presence of this catalyst, the product mixture revealed even more intermediates in the process, as three different products were found (Scheme 2).

Just as above, the reaction could be carried out to produce 1,2-diphenylethane (**2**) or 1,2-dicyclohexylethane (**3**) selectively, stopping the hydrogenation at 2 h or 12 h reaction time, respectively. However, when stopped at 3 h, a complex mixture was obtained containing **2**, **3**, and a new product, 1-cyclohexyl-2-phenylethane (**9**), which is a partially hydrogenated product, likely originating from **2** via the perhydrogenation of one phenyl ring. This provided more evidence for the above-suggested mechanism, namely, that the completely hydrogenated product **3** formed with the hydrogenation of the aliphatic C=C double bond to **2**, the intermediate of which was further hydrogenated to **9** and finally to the perhydrogenated product.

2.2. Rh-Catalyzed Hydrogenation of Aromatic Rings in Carbocyclic and Heterocyclic Compounds

In this part we focus on the hydrogenation of highly stable aromatic rings, using typical carbocyclic (naphthalene) and heterocyclic (quinoline, isoquinoline, indole) compounds that are commonly applied in synthetic processes as test substrates. 1,2,3,4-Tetrahydroquinoline derivatives are key intermediates for the synthesis of drugs [35], agrochemicals [36], and dyes [37]. We found that the hydrogenation of quinoline (**10**) was readily catalyzed by 5% Rh/Al₂O₃ yielding time-dependent products (Scheme 3). Quinoline was hydrogenated selectively in its nitrogen-containing ring in 10 min to give

1,2,3,4-tetrahydroquinoline (**11**) in a 100% yield. Similar to the above examples, applying a longer reaction time completely changed the outcome of the reaction; after 8 h, the perhydrogenated product decahydroquinoline (**12**) was obtained as the sole product, also in a quantitative yield. In order to explore more insight into the hydrogenation process, a 0.5 h reaction was tested in which both products, **11** and **12**, were obtained in a ratio of 7:3. The results illustrate that the hydrogenation only occurred in the carbocyclic ring after the nitrogen-containing ring was already fully hydrogenated. When the same reaction was carried with isoquinoline (**13**) (Scheme 3), a longer reaction time was necessary, and **13** was only converted to the partially-hydrogenated product 1,2,3,4-tetrahydroisoquinoline (**14**). Decahydroisoquinoline was not detected, indicating that both steric and electronic impacts affect the outcome of the hydrogenation.

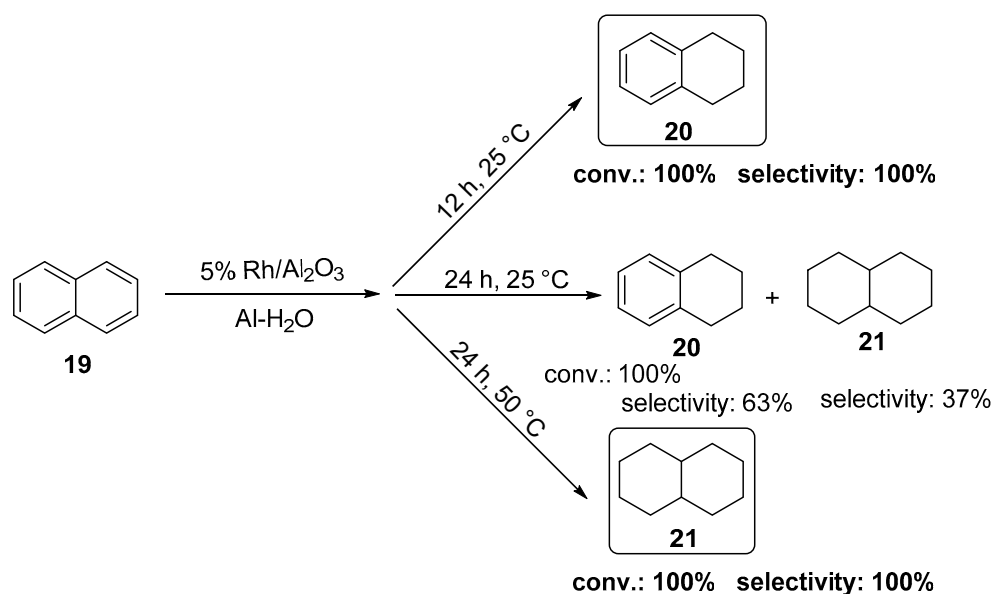


Scheme 3. Hydrogenation of heterocyclic compounds by the supported 5% Rh/C-Al/H₂O catalytic system.

Another important N-containing condensed heterocyclic compound, indole (**15**), was reduced to indoline at 25 °C with exclusive selectivity, although at low conversion. A longer time at the same temperature resulted in the formation of a product mixture favoring the formation of the perhydrogenated octahydro-1H-indole (**18**). Elevating the temperature to 50 °C resulted in the formation of **18** with 100% selectivity, but in 50% conversion. These

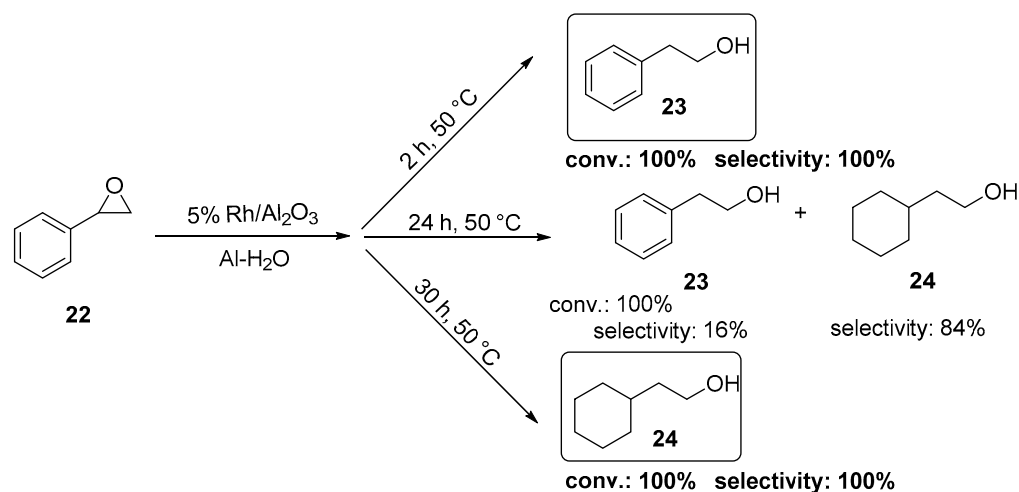
results suggest that octahydro-1H-indole (**18**) can be re-aromatized by the Rh catalyst to the starting material, indole (**15**), through an oxidative-dehydrogenation mechanism [22,23] (Scheme 3).

As illustrated in Scheme 4, the hydrogenation of naphthalene (**19**), similar to the above examples, is a consecutive reaction, yielding tetralin (**20**) as the partially-hydrogenated product at 25 °C, at 12 h, and the perhydrogenated decalin (**21**) at 50 °C, after 24 h reaction. The stepwise process times between 12 and 24 h result in the formation of a tetralin (**20**)–decalin (**21**) mixture at 25 °C at 24 h.



Scheme 4. Hydrogenation of naphthalene by the supported 5% Rh/Al₂O₃-Al/H₂O catalyst system.

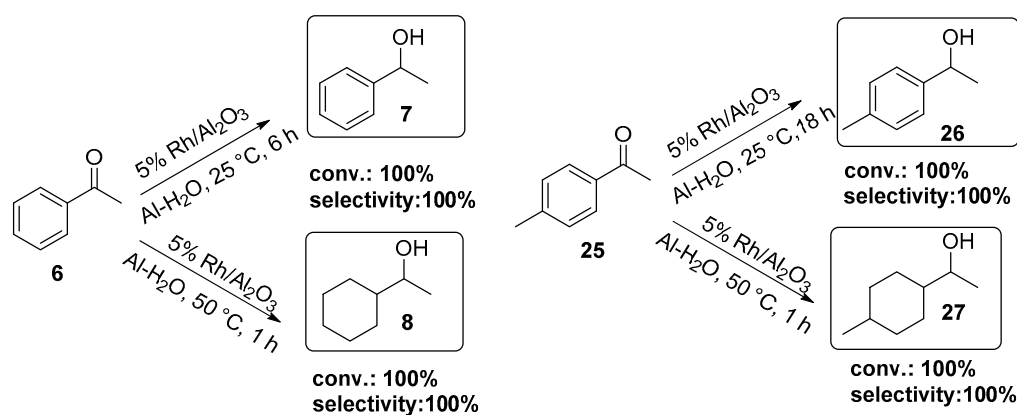
Epoxide, or oxiranes, although not aromatic heterocycles, are important intermediates and building blocks in synthetic chemistry, and many are commercially available as a large-scale product. One of them, styrene oxide (**22**), was subjected to hydrogenolysis/hydrogenation by the 5% Rh/Al₂O₃-Al/H₂O system (Scheme 5). Similar to the above reactions, this process led to 2-phenylethanol (**23**) at 50 °C, at 2 h reaction time. This product could be converted to 2-cyclohexylethanol (**24**) as the sole product after 30 h. Both 2-phenylethanol (**23**) and 2-cyclohexylethanol (**24**) could be obtained at 24 h due to the stepwise nature of the reaction.



Scheme 5. Consecutive hydrogenolysis/hydrogenation of styrene oxide by the supported 5% Rh/Al₂O₃-Al/H₂O catalyst system.

2.3. Rh-Catalyzed Hydrogenation of Carbonyl Compounds

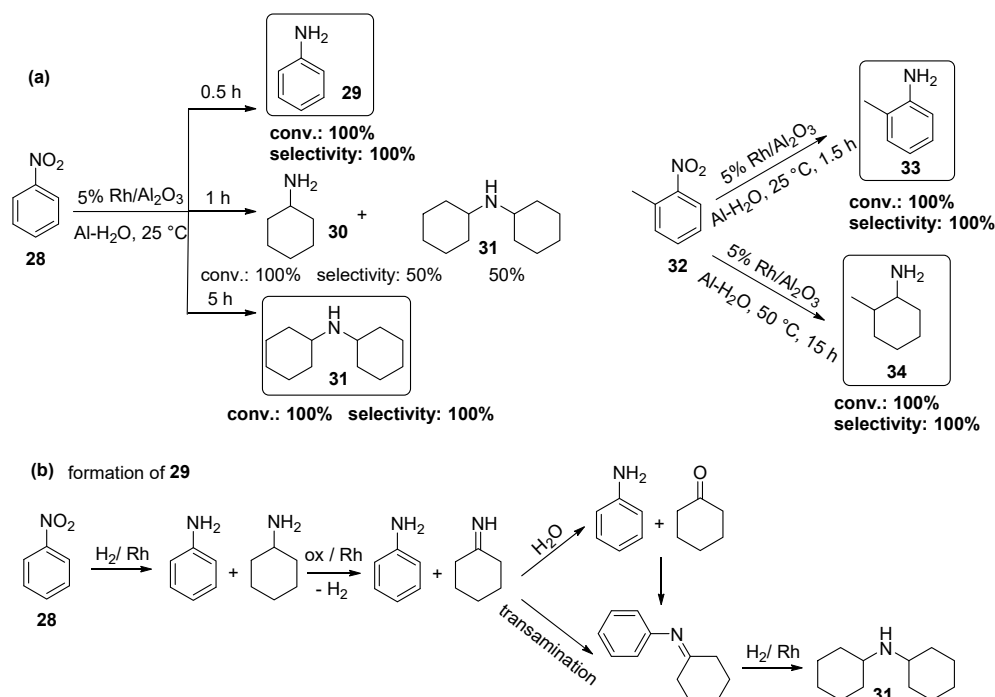
The hydrogenation of carbonyl compounds is one of the most commonly used methods in synthetic chemistry [2]. The optimization of the hydrogenation of acetophenone (**6**) (Scheme 6) indicates that it can be selectively reduced to methylbenzylalcohol (**7**) at 25 °C in a quantitative yield. Further hydrogenation of the aromatic ring proceeded at an elevated temperature of 50 °C, giving 1-cyclohexylethanol (**8**) with 100% yield. In the presence of 5% Rh/Al₂O₃ catalyst, 4-methylacetophenone (**25**) was also reduced to 1-(*p*-tolyl)ethanol (**26**) with 100% selectivity at 25 °C as well. After a moderate increase in temperature, 1-(4-methylcyclohexyl)ethanol (**27**) was obtained as the sole product. These results revealed that the reaction pathway of hydrogenation of aromatic ketones involved hydrogenation of the C=O group to give C–OH, and then the product underwent further hydrogenation on its aromatic ring. An important aspect can be noted, namely, that aromatic ketones were hydrogenated preferentially via reduction of the C=O group, and then the hydrogenation of the aromatic ring occurred.



Scheme 6. Hydrogenation of acetophenones by the supported 5% Rh/Al₂O₃-Al/H₂O catalyst system.

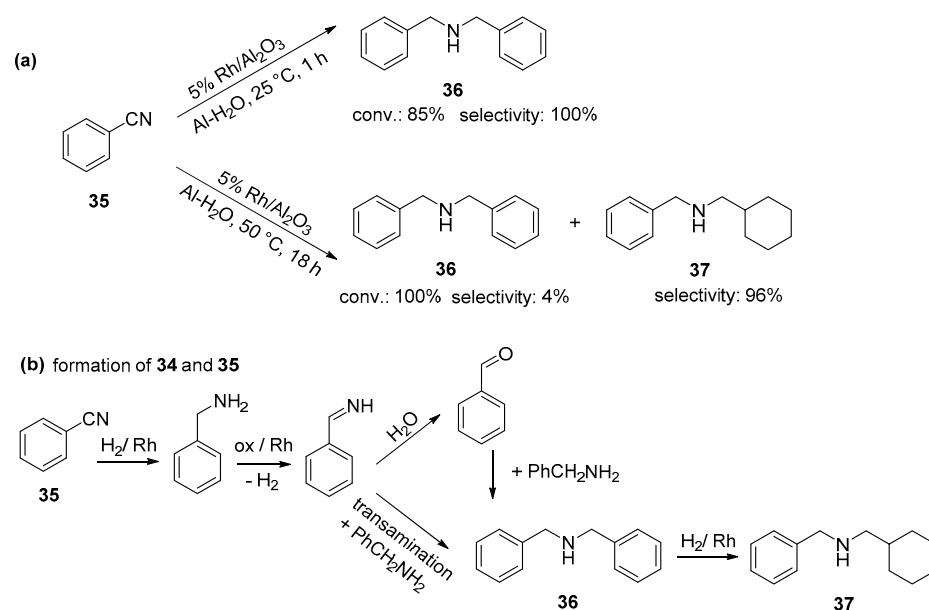
2.4. Rh-Catalyzed Hydrogenation of Nitriles and Nitro-Compounds

As the Rh-Al/H₂O system appears to work efficiently in C–C and C–O multiple bond hydrogenations, it was decided to further explore the hydrogenation of C–N multiple bond using nitriles as substrates [38], as well as the reduction of N–O bonds in nitro compounds [39,40]. As test reaction substrates, nitrobenzene (**28**), 2-nitrotoluene (**32**), and benzonitrile (**35**) were selected. As shown in Scheme 7, nitrobenzene was successfully reduced to aniline (**29**) within 0.5 h. When the reaction time was increased to 1 h, 100% conversion was obtained with 50% selectivity of cyclohexane amine (**30**) and 50% selectivity of an unexpected product, dicyclohexylamine (**31**). With a continuous increase of reaction time to 5 h, dicyclohexylamine (**31**) was obtained with 100% selectivity. The formation of **31** can be explained by the oxidative dehydrogenation (Scheme 7) that Rh catalysts are also known for and that was also observed in the hydrogenation of indole in this study (Scheme 3). The reaction mechanism (Scheme 7b) involves the dehydrogenative oxidation of the cyclohexylamine intermediate to an imine, which is not stable under aqueous conditions, and hydrolyzed to cyclohexanone, which reacted with the remaining aniline to form a stable imine that finally underwent C=N double bond hydrogenation. An alternative pathway could be the simple transamination of the cyclohexylimine with aniline and the final hydrogenation of the same imine. A detailed mechanistic study of this reaction can be found in our earlier works [41,42]. In the reaction of 2-nitrotoluene (**32**) at 1.5 h at 25 °C, 2-methylaniline (**33**) was obtained with 100% selectivity. A slight heating to 50 °C resulted in the formation of 2-methylcyclohexylamine (**34**) as the sole product.



Scheme 7. Hydrogenation of nitrobenzenes (a) by the supported 5%Rh/Al₂O₃-Al/H₂O catalyst system and the proposed reaction mechanism (b) for the formation of dicyclohexylamine (31).

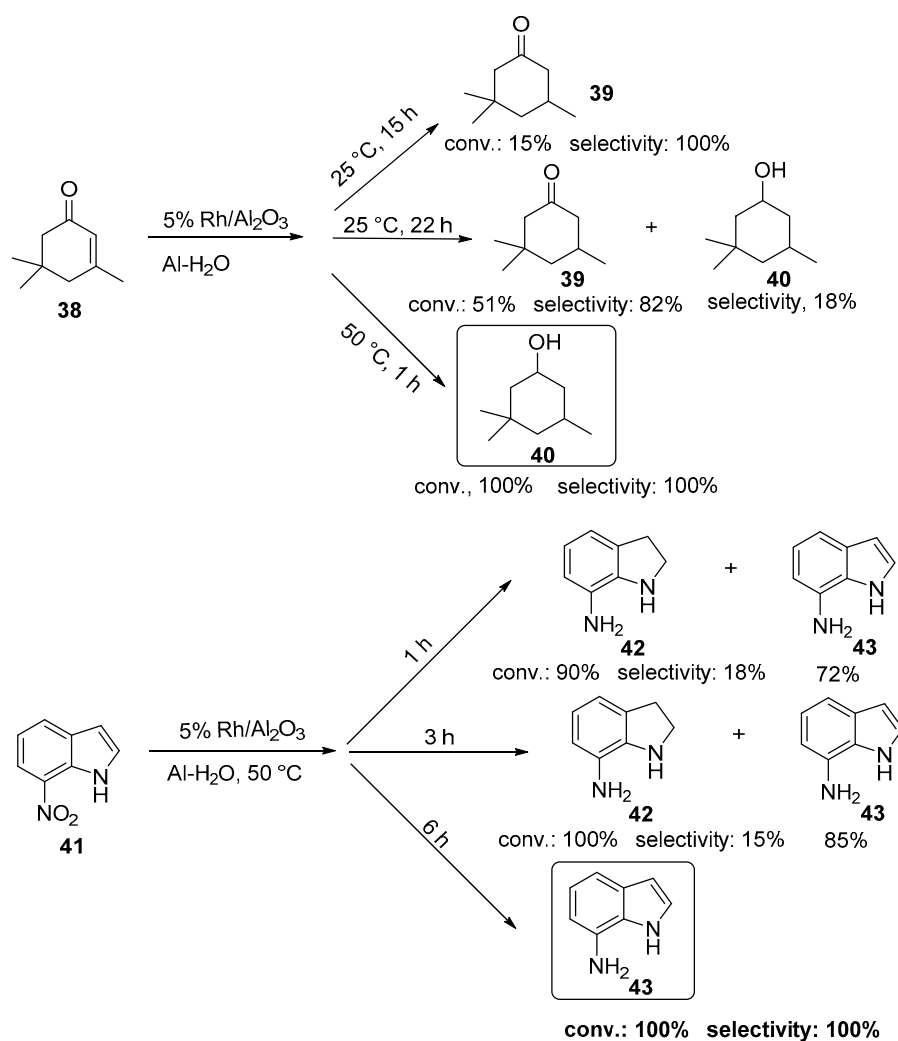
In the hydrogenation of benzonitrile (Scheme 8) at 25 °C, only the formation of dibenzylamine (36) was observed with exclusive selectivity. Increasing the temperature to 50 °C resulted in the hydrogenation of one aromatic ring yielding N-benzyl-cyclohexylamine (37) as a major product with a 96% yield. The formation of dibenzylamine can be explained by the same dehydrogenative oxidation mechanism [41,42] catalyzed by the Rh catalyst and the subsequent hydrolysis of the imine to benzaldehyde and the formation of benzylidene-benzylamine, and intermediate to 36 (not shown), which underwent final hydrogenation in the last step (Scheme 8b).



Scheme 8. Hydrogenation of benzonitrile (a) by the supported 5%Rh/Al₂O₃-Al/H₂O catalyst system and the proposed reaction mechanism (b) for the formation of dibenzylamine (36) and benzyl-cyclohexylamine (37).

2.5. Rh-Catalyzed Hydrogenation of Compounds with Multiple Functional Groups

As shown above, the hydrogenation of individual functional groups is often a challenge; the real difficulty is when two or more hydrogenation sensitive groups are present in a substrate. Thus, it was explored how supported Rh catalysts perform in substrates which have multiple functional groups. Thus, an α,β -unsaturated carbonyl compound, isophorone (**38**) [43,44], was examined using 5% Rh/ Al_2O_3 catalyst at 50 °C. Isophorone can be hydrogenated to the corresponding saturated ketone (**39**) at 25 °C after 15 h with 100% selectivity at low conversion values (Scheme 9). After allowing a longer reaction time (22 h), the conversion increased; however, the product of the complete hydrogenation, the saturated alcohol (**40**), also appeared in the product mixture. At 50 °C, isophorone underwent complete hydrogenation to the corresponding saturated alcohol (**40**) with 100% selectivity. Additionally, hydrogenation of 7-nitroindole (**41**) was carried out at 50 °C. It was observed that the nitro group was reduced to amine readily, while indole was converted to indoline (**42**), also giving 7-aminoindole (**43**) at 3 h. After 6 h, only 7-aminoindole (**43**) was obtained because the indoline product rearomatized via oxidative aromatization to indole to retain its aromatic nature in the presence of Rh. If the reaction was carried out at 25 °C, the same aromatic aminoindole (**43**) was obtained with 100% yield and 100% selectivity in a 24 h long reaction.



Scheme 9. Hydrogenation of compounds with multiple hydrogenation-sensitive functional groups, isophorone (**38**) and 7-nitroindole (**41**), by the supported 5%Rh/ Al_2O_3 -Al/ H_2O catalyst system.

3. Materials and Methods

General information. All substrates were purchased from Sigma Aldrich (Burlington, MA, USA) and used without further purification. The reactions were carried out in de-ionized water. The supported rhodium catalysts were from ThermoFisher Scientific (Waltham, MA, USA) and Alfa-Aeasar (Ward Hill, MA, USA). The catalysts used were all commercial samples containing Rh particles. The general particle sizes of the catalysts were 27 microns (Rh/C) and 70 microns (Rh/Al₂O₃) based on the reference from the producers. The aluminum powder was also obtained from Alfa-Aeasar (99.5% purity, 11 067, Lot#: K05Z034, 325 mesh, particle size 7–15(M)). The ¹H NMR spectra were recorded on a 400 MHz Agilent MR400DD2 spectrometer (Agilent: Santa Clara, CA, USA) at 399.96 MHz. The products were also characterized by gas chromatography–mass spectrometry (GC-MS, Agilent: Santa Clara, CA, USA) with an Agilent 6850 gas chromatograph–5973 mass spectrometer system (70 eV electron impact ionization) using a 30 m long DB-5 type column (J&W Scientific, Folsom, CA, USA). All products were known compounds, and their spectra were in agreement with earlier sources.

Procedure. Supported rhodium catalysts (0.025 mmol, 51 mg, 0.1 equiv.) and Al powder (2.5 mmol, 68 mg, 10 equiv.) were mixed in 2 mL of H₂O in a capped vial and sonicated for 1 h (Branson 1510 sonicator). The substrate (0.25 mmol, 1 equiv.) was added to the mixture in a round-bottom flask and stirred for the desired amount of time and temperature. After the reaction was complete, the product was extracted by CH₂Cl₂. After extraction, the organic phase was dried and the solvent was removed and the yield was determined by an Agilent 6850 gas chromatograph–5973 mass spectrometer system as described above.

4. Conclusions

In conclusion, the highly efficient catalytic hydrogenation of a broad variety of functional groups was accomplished by applying commercially available supported Rh catalysts without using explosive hydrogen gas. The Al–H₂O system that in situ produces hydrogen is considered environmentally benign and easily accessible. This protocol successfully achieved high and mostly complete conversions and controllable chemoselectivity via the effects of reaction time and temperature. An important feature that distinguishes the Rh catalyst from others used in conjunction with the Al/H₂O system is the high selectivity in the reduction of compounds with C–heteroatom bonds. While Pd or Ni both initiate deamination and deoxygenation, Rh appears to be selective in its tolerance for those functionalities and thus allows for the preparation of several valuable products. In nearly all examples, it was also observed that first the hydrogenation sensitive functional group always underwent saturation, and the hydrogenation of the aromatic ring only occurred after that; likely due to the high stability of the aromatic ring systems, their hydrogenation is significantly slower than that of the common functional groups. Rh, being a powerful catalytic material, was able to achieve even perhydrogenation at moderate temperatures that cannot be accomplished with other common catalysts.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/catal12121578/s1>, Mass Spectra of the products.

Author Contributions: Conceptualization, B.T.; methodology, G.X.; validation, G.X. and B.T.; formal analysis, G.X. and B.T.; investigation, G.X.; data curation, G.X.; writing—original draft preparation, G.X. and B.T.; writing—review and editing, G.X. and B.T.; supervision, B.T.; project administration, B.T. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: Data is contained within the above article and the supplementary material. No other data has been generated. Samples of the compounds are not available from the authors. Synthetic details are in the experimental section.

Acknowledgments: Support of our work by the University of Massachusetts Boston is gratefully acknowledged.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Smith, M.B.; March, J. *March's Advanced Organic Chemistry*, 6th ed.; Wiley: Hoboken, NJ, USA, 2007.
2. Török, B.; Schäfer, C.; Kokel, A. *Hydrogenation in Heterogeneous Catalysis in Sustainable Synthesis*; Elsevier: Amsterdam, The Netherlands; Cambridge, MA, USA; Oxford, UK, 2021; Chapter 3.1; pp. 85–156.
3. Nishimura, S. *Handbook of Heterogeneous Catalytic Hydrogenation for Organic Synthesis*; Wiley: New York, NY, USA, 2001.
4. Blaser, H.-U.; Malan, C.; Pugin, B.; Spindler, F.; Steiner, H.; Studer, M. Selective hydrogenation for fine chemicals: Recent trends and new developments. *Adv. Synth. Catal.* **2003**, *345*, 103–151. [[CrossRef](#)]
5. Kulkarni, A.; Török, B. Heterogeneous catalytic hydrogenations as an environmentally benign tool for organic synthesis. *Curr. Org. Synth.* **2011**, *8*, 187–207. [[CrossRef](#)]
6. Press, R.J.; Santhanam, K.S.V.; Miri, M.J.; Bailey, A.V.; Takacs, G.A. *Introduction to Hydrogen Technology*; Wiley: Hoboken, NJ, USA, 2009; Chapter 4.1; pp. 195–210.
7. Török, B.; Dransfield, T. *Green Chemistry: An Inclusive Approach*; Elsevier: Amsterdam, The Netherlands; Cambridge, MA, USA; Oxford, UK, 2017.
8. Tsukinoki, T.; Kanda, T.; Liu, G.; Tsuzuki, H.; Tashiro, M. Organic reaction in water. Part 3: A facile method for reduction of aromatic rings using a raney Ni–Al alloy in dilute aqueous alkaline solution under mild conditions. *Tetrahedron Lett.* **2000**, *41*, 5865–5868. [[CrossRef](#)]
9. Ishimoto, K.; Mitoma, Y.; Nagashima, A.; Tashiro, H.; Prakash, G.K.S.; Olah, G.A.; Tashiro, M. Reduction of carbonyl groups to the corresponding methylenes with Ni–Al alloy in water. *Chem. Commun.* **2003**, 514–515. [[CrossRef](#)]
10. Liu, G.; Zhao, H.; Zhu, J.; He, H.; Yang, H.; Thiemann, T.; Tashiro, H.; Tashiro, M. New method for the reduction of benzophenones with Raney Ni–Al alloy in water. *Synth. Commun.* **2008**, *38*, 1651–1661. [[CrossRef](#)]
11. Schäfer, C.; Nisanci, B.; Bere, M.P.; Dastan, A.; Török, B. Heterogeneous Catalytic Reductive Amination of Carbonyl Compounds with Ni–Al Alloy in Water as Solvent and Hydrogen Source. *Synthesis* **2016**, *48*, 3127–3133.
12. Schäfer, C.; Ellstrom, C.J.; Cho, H.; Török, B. Pd/C–Al–Water Facilitated Selective Reduction of a Broad Variety of Functional Groups. *Green Chem.* **2017**, *19*, 1230–1234. [[CrossRef](#)]
13. Rayhan, U.; Kowser, Z.; Redshaw, C.; Yamato, T. Reduction of diphenylacetylene using Al powder in the presence of noble metal catalysts in water. *Tetrahedron* **2016**, *72*, 6943–6947. [[CrossRef](#)]
14. Cho, H.; Schäfer, C.; Török, B. Hydrogenations and Deuterium Labeling with Aluminum-based Metal Alloys under Aqueous Conditions. *Curr. Org. Synth.* **2016**, *13*, 255–277. [[CrossRef](#)]
15. Rayhan, U.; Kowser, Z.; Islam, M.N.; Yamato, T. A Review on the Recent Advances in the Reductions of Carbon–Carbon/Oxygen Multiple Bonds Including Aromatic Rings Using Raney Ni–Al Alloy or Al Powder in the Presence of Noble Metal Catalysts in Water. *Top. Catal.* **2018**, *61*, 560–574. [[CrossRef](#)]
16. Tomin, A.; Lazarev, A.; Bere, M.P.; Redjeb, H.; Török, B. Selective reduction of ketones using water as a hydrogen source under high hydrostatic pressure. *Org. Biomol. Chem.* **2012**, *10*, 7321–7326. [[CrossRef](#)] [[PubMed](#)]
17. Cho, H.; Török, F.; Török, B. Selective reduction of condensed N-heterocycles using water as a solvent and a hydrogen source. *Org. Biomol. Chem.* **2013**, *11*, 1209–1215. [[CrossRef](#)] [[PubMed](#)]
18. Ilamanova, M.; Mastuyugin, M.; Schäfer, C.; Kokel, A.; Török, B. Heterogeneous Metal Catalysis for the Environmentally Benign Synthesis of Medicinally Important Scaffolds, Intermediates and Building Blocks. *Curr. Org. Chem.* **2021**, *25*, 2304–2330. [[CrossRef](#)]
19. Rylander, P.N. *Catalytic Hydrogenation over Platinum Metals*; Academic Press: New York, NY, USA; London, UK, 1967.
20. Kulkarni, A.; Török, B. Heterogeneous catalytic hydrogenation of unprotected indoles in water: A green solution to a long-standing challenge. *Org. Lett.* **2011**, *13*, 5124–5127. [[CrossRef](#)] [[PubMed](#)]
21. Pálinkó, I. Heterogeneous Catalysis: A Fundamental Pillar of Sustainable Synthesis. In *Green Chemistry: An inclusive Approach*; Török, B., Dransfield, T., Eds.; Elsevier: Oxford, UK; Cambridge, MA, USA, 2018; Chapter 12; pp. 416–447.
22. Franke, R.; Selent, D.; Börner, A. Applied Hydroformylation. *Chem. Rev.* **2012**, *112*, 5675–5732. [[CrossRef](#)] [[PubMed](#)]
23. Balayeva, N.O.; Mamiyev, Z.; Dillert, R.; Zheng, N.; Bahnemann, D.W. Rh/TiO₂-Photocatalyzed Acceptorless Dehydrogenation of N-Heterocycles upon Visible-Light Illumination. *ACS Catal.* **2020**, *10*, 5542–5553. [[CrossRef](#)]
24. Balayeva, N.O.; Zheng, N.; Dillert, R.; Bahnemann, D.W. Visible-Light-Mediated Photocatalytic Aerobic Dehydrogenation of N-heterocycles by Surface-Grafted TiO₂ and 4-amino-TEMPO. *ACS Catal.* **2019**, *9*, 10694–10704. [[CrossRef](#)]
25. Kokel, A.; Schäfer, C.; Török, B. Application of microwave-assisted heterogeneous catalysis in sustainable synthesis design. *Green Chem.* **2017**, *19*, 3729–3751. [[CrossRef](#)]
26. Pandey, G.; Török, B. K-10 montmorillonite-catalyzed solid phase diazotizations: Environmentally benign coupling of diazonium salts with aromatic hydrocarbons to biaryls. *Green Chem.* **2017**, *19*, 5390–5395. [[CrossRef](#)]
27. Mishra, M.; Twardy, D.; Ellstrom, C.; Wheeler, K.A.; Dembinski, R.; Török, B. Catalyst-free ambient temperature synthesis of isoquinoline-fused benzimidazoles from 2-alkynylbenzaldehydes via alkyne hydroamination. *Green Chem.* **2019**, *21*, 99–108. [[CrossRef](#)]

28. Schäfer, C.; Cho, H.; Vlocskó, R.B.; Xie, G.; Török, B. Recent Advances in the Green Synthesis of Heterocycles: From Building Blocks to Biologically Active Compounds. *Curr. Org. Synth.* **2022**, *19*, 426–462. [[CrossRef](#)] [[PubMed](#)]
29. Coq, B.; Figueras, F. Structure–activity relationships in catalysis by metals: Some aspects of particle size, bimetallic and supports effects. *Coord. Chem. Rev.* **1998**, *178–180*, 1753–1783. [[CrossRef](#)]
30. Corma, A. Preparation and catalytic properties of new mesoporous materials. *Top. Catal.* **1997**, *4*, 249–260. [[CrossRef](#)]
31. Davis, R.J. New perspectives on basic zeolites as catalysts and catalyst supports. *J. Catal.* **2003**, *216*, 396–405. [[CrossRef](#)]
32. Kokel, A.; Kadish, D.; Török, B. Preparation of Deuterium Labeled Compounds by Pd/C-Al-D₂O Facilitated Selective H-D Exchange Reactions. *Molecules* **2022**, *27*, 614. [[CrossRef](#)] [[PubMed](#)]
33. Török, B.; Balázsik, K.; Felföldi, K.; Bartók, M. Asymmetric Reactions in Sonochemistry. *Ultrasonics Sonochem.* **2001**, *8*, 191–200. [[CrossRef](#)]
34. Pálincó, I.; Notheisz, F.; Bartók, M. A Competitive Reaction which is Able to Make Fine Distinctions Between Reacting Surfaces. *Stud. Surf. Sci. Catal.* **1989**, *48*, 729–737.
35. Ferranti, A.; Garuti, L.; Giovanninetti, G.; Gaggi, R.; Roncada, P.; Nardi, P. Preparation and analgesic activity of tetrahydroquinolines and tetrahydroisoquinolines. *Farmaco Sci.* **1987**, *42*, 237–249.
36. Kurahashi, Y.; Shiokawa, K.; Goto, T.; Kagabu, S.; Kamochi, A.; Moriya, K.; Hayakawa, H. Eur. Patent 173208. *Chem. Abstr.* **1986**, *105*, 78937s.
37. Nizamov, S.; Sednev, M.V.; Bossi, M.L.; Hebisch, E.; Frauendorf, H.; Lehnart, S.E.; Belov, V.N.; Hell, S.W. “Reduced” Coumarin Dyes with an O-Phosphorylated 2,2-Dimethyl-4-(hydroxymethyl)-1,2,3,4-tetrahydroquinoline Fragment: Synthesis, Spectra, and STED Microscopy. *Chem. Eur. J.* **2016**, *22*, 11631. [[CrossRef](#)]
38. Lévay, K.; Hegedűs, L. Recent Achievements in the Hydrogenation of Nitriles Catalyzed by Transitional Metals. *Curr. Org. Chem.* **2019**, *23*, 1881–1900. [[CrossRef](#)]
39. Tafesh, A.M.; Weiguny, J. A Review of the Selective Catalytic Reduction of Aromatic Nitro Compounds into Aromatic Amines, Isocyanates, Carbamates, and Ureas Using CO. *Chem. Rev.* **1996**, *96*, 2035–2052. [[CrossRef](#)] [[PubMed](#)]
40. Song, J.; Huang, Z.-F.; Pan, L.; Li, K.; Zhang, X.; Wang, L.; Zou, J.-J. Review on selective hydrogenation of nitroarene by catalytic, photocatalytic and electrocatalytic reactions. *Appl. Catal. B Environ.* **2018**, *227*, 386–408. [[CrossRef](#)]
41. Landge, S.M.; Atanassova, V.; Thimmaiah, M.; Török, B. Microwave-assisted oxidative coupling of amines to imines on solid acid catalysts. *Tetrahedron Lett.* **2007**, *48*, 5161–5164. [[CrossRef](#)]
42. Atanassova, V.; Ganno, K.; Kulkarni, A.; Landge, S.M.; Curtis, S.; Foster, M.; Török, B. Mechanistic study on the oxidative coupling of amines to imines on K-10 montmorillonite. *Appl. Clay Sci.* **2011**, *53*, 220–226. [[CrossRef](#)]
43. Mhadgut, S.C.; Török, M.; Esquibel, J.; Török, B. Highly asymmetric heterogeneous catalytic hydrogenation of isophorone on proline modified base-supported palladium catalysts. *J. Catal.* **2006**, *238*, 441–448. [[CrossRef](#)]
44. Mhadgut, S.C.; Török, M.; Dasgupta, S.; Török, B. Nature of Proline-induced Enantiodifferentiation in Asymmetric Pd Catalyzed Hydrogenations: Is the Catalyst Really Indifferent? *Catal. Lett.* **2008**, *123*, 156–163. [[CrossRef](#)]