Rhodium/Graphite-Catalyzed Hydrogenation of Carbocyclic and Heterocyclic Aromatic Compounds

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Abstract: Rhodium on graphite (Rh/Gr, $C_{24}Rh$) was prepared by reaction of anhydrous rhodium trichloride with potassium graphite (C_8K, 3 equivalents) and used as a heterogeneous catalyst for the hydrogenation of carbocyclic and heterocyclic aromatic compounds at room temperature and 1 atm of hydrogen pressure. The effect of substitution on the benzene ring was examined in a variety of derivatives, including those with alkyl, hydroxy, alkoxy, aryloxy, carboxy, amino, nitro, acyl, chloro, or functionalized alkyl groups. Reduction of carbonyl functions of aromatic aldehydes and ketones occurred with complete or partial cleavage of the benzylic C–O bond; this cleavage also occurred in the hydrogenation of benzylic alcohols and esters.

Key words: aromatic compounds, graphite, heterogeneous catalysis, hydrogenation, rhodium

Catalysis in all its forms (homogeneous catalysis, heterogeneous catalysis, biocatalysis, and organocatalysis) is playing an ever-increasing role in modern organic synthesis, as it can provide a convenient, economical, selective, and efficient method for the construction of simple or complex organic molecules. In particular, heterogeneous catalysis has two main advantages: the ease of separation of the insoluble catalyst from the organic materials merely by filtration, and the possibility of re-using the recovered catalyst without a significant loss of activity or selectivity.

Catalytic hydrogenation is a valuable tool for the synthetic organic chemist.[1] Noble metals anchored on a support that is insoluble in the reaction medium have been most frequently used as catalysts for heterogeneous hydrogenation. A variety of materials can be used as catalyst supports, e.g. metal salts, alumina, or carbon. Many metals highly dispersed on charcoal, including rhodium/charcoal, are commercially available, but the different origins of the charcoal can affect the properties of the catalyst. Switching from activated carbon to graphite has several advantages, including lower costs, easier manipulation, greater thermal conductivity, and an ordered structure (sheets). Graphite can accommodate alkali metals between the sheets. Intercalation compounds of graphite and alkali metals of known stoichiometry, e.g. C_8K or $C_{24}K$, can be prepared by melting potassium on graphite at the appropriate molar ratios at 150 °C by stirring the mixture under an inert atmosphere. In this way, the 4s electrons of the potassium are transferred to the π-system of graphite, and a compound with negatively charged graphite layers intercalated by layers of potassium cations is formed.[2]

Potassium graphite C_8K has a very high reducing power that can be exploited to reduce C=N, C=O, or activated C=C double bonds or to cleave C–S or C–CN bonds.[2] Most importantly, treatment of C_8K with metal salts, including titanium(III), titanium(IV), manganese(II), copper(II), iron(III), cobalt(II), tin(II), or zinc(II) salts in refluxing tetrahydrofuran or 1,2-dimethoxyethane gives the corresponding zero-valent metal in a highly active form.[2] An alternative approach to the preparation of highly reactive transition metals on graphite involves preliminary intercalation of metal salts in graphite followed by reduction with an organolithium reagent at a low temperature.[3] Both protocols give highly dispersed metals on the graphite surface, and almost no intercalated metal species are formed.

Dispersions of platinum,[4] palladium,[5] rhodium,[4c,6] nickel,[7] or copper[8] on graphite, prepared by reduction of the intercalated metal salts with a 1% metal loading have been commercially available for some time as Metal-Graphimet®. Reduction of metal salts by C_8K leads to metal/graphite materials with a higher metal loading, e.g. $C_{16}M$ or $C_{24}M$, that depends on the oxidation state of the metal cation. Examination by transmission electron microscopy (TEM) of samples of platinum/graphite prepared by these two protocols has shown that both materials consist of more- or less-dispersed metal on the graphite surface, and no intercalated metal is present.[9] Moreover, in the hydrogenation of 4-chloronitrobenzene, the two platinum/graphite compounds showed comparable activities that were superior to those of other supported platinum species.[4a] In our opinion, however, the procedure using C_8K is simpler and more convenient.

Hydrogenation of carbocyclic and heterocyclic aromatic compounds is a straightforward route to the corresponding saturated derivatives.[10] Platinum,[11] rhodium,[12] and ruthenium[13] catalysts are most often used for this purpose. In particular, the full hydrogenation of substituted pyrroles to the corresponding pyrrolidines has been accomplished by the use of such catalysts.[14] We recently completed a stereoselective synthesis of 8-aminopyrrolizidines by a route that involved hydrogenation of fused bicyclic precursors containing the pyrrole ring.[15] For this purpose, we prepared a new heterogeneous catalyst comprising highly dispersed rhodium on graphite (Rh/Gr,

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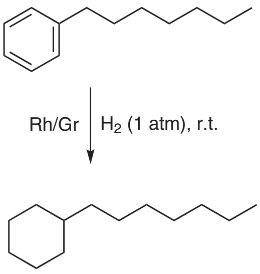
$C_{24}Rh$), and found that it had a slightly superior activity to other heterogeneous catalysts.

Rhodium on graphite (Rh/Gr, $C_{24}Rh$, 26.3% Rh by weight) was prepared by the same simple protocol used for other previously described metal/graphites, and was structurally characterized by means of TEM and powder X-ray diffraction (PXRD).

Figure 1, part A shows a representative image of $C_{24}Rh$ material. It can be seen that rhodium nanoparticles measuring about 5 nm are present as aggregates that settle on the graphite surface. These aggregates mainly form chains and sponge-like structures. Their distribution on the graphite surface, their size, and their degree of degree of branching are not homogeneous. Single nanoparticles are almost absent from the graphite surface. In the PXRD pattern [Figure 1, part B], diffraction peaks for graphite (*) and rhodium (#) are visible. The two theta positions of the former are exactly those associated with the interplanar spacings present in pure graphite, thus excluding the presence of any significant intercalation of particles in the graphite structure, in agreement with the literature data.[4a] The diffraction peaks associated with rhodium are very broad; this observation is in agreement with the nanosized nature of the particles, and also suggests that the material has a low degree of crystallinity.

Rh/Gr can be used effectively as a catalyst for the heterogeneous hydrogenation of carbocyclic or heterocyclic aromatic compounds. Heptylbenzene was chosen as a substrate to test the activity of the catalyst in the protic solvents methanol, ethanol, and isopropanol and the apolar solvent hexane (Scheme 1). All the reactions were carried out at room temperature under 1 atm of hydrogen pressure (balloon) using $C_{24}Rh$ as the catalyst (4% by weight, 1.8 mol%).

The results, graphically reported in Figure 2, show that the nature of the solvent had only a slight effect on the reaction rate, which decreased slightly in the order: MeOH > *i*-PrOH > EtOH > hexane. In these cases, complete hydrogenation was achieved after 18–24 hours. By increasing the amount of catalyst to 12% by weight (5.4 mol%), complete conversion was achieved after only six hours in MeOH (Figure 2). Moreover, we observed that the hydrogenation rate was only slightly affected by the substrate concentration, although the highest rate was observed at a 1.4 M concentration.



Scheme 1

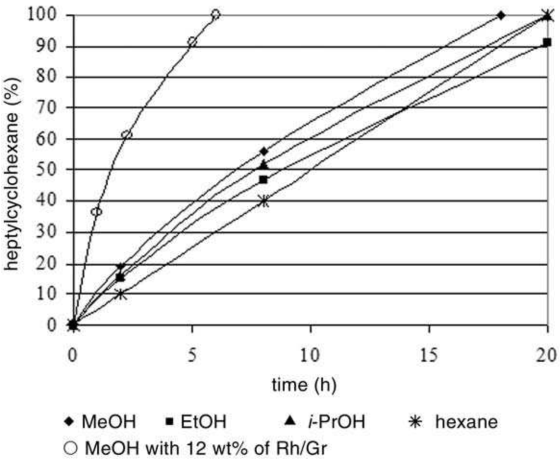


Figure 2 Hydrogenation of heptylbenzene with Rh/Gr ($C_{24}Rh$, 4 wt%) at 20 °C and 1 atm of H_2 pressure in various solvents

Having determined the optimal reaction conditions, these were used in the hydrogenation of representative carbocyclic and heterocyclic aromatic compounds. The results are listed in Table 1, in which gives the time required to achieve complete consumption of the starting compound and, in some cases, the disappearance of the partially saturated intermediates. The choice between methanol and isopropanol as the solvent was dictated by the solubility of the aromatic compound in the two solvents.

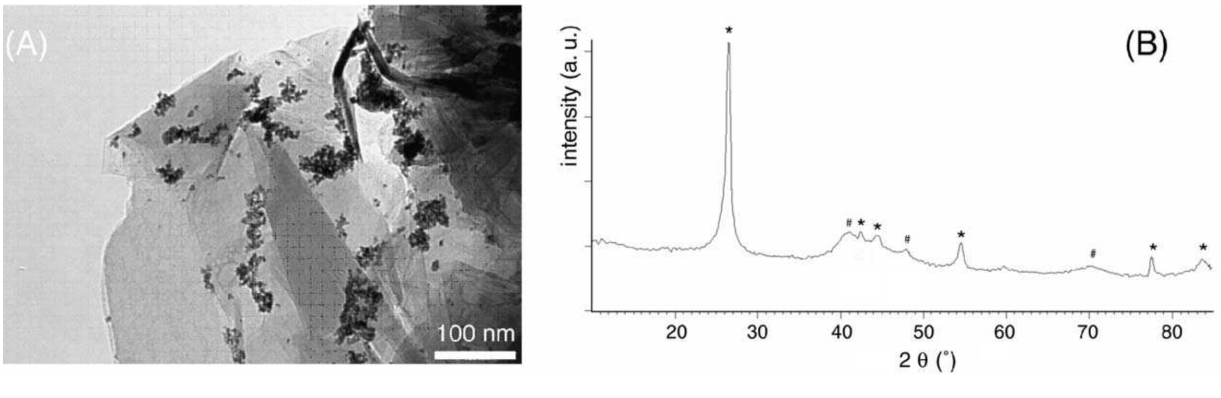


Figure 1 (A) Transmission electron photomicrograph of a fragment of the $C_{24}Rh$ catalyst. (B) PXRD pattern of the same material; the diffraction peaks of graphite and rhodium are indicated by the symbols * and #, respectively.

Benzoic acid was converted into cyclohexanecarboxylic acid in 48 hours, whereas the reduction of the carbonyl group of acetophenone could not be avoided, and 1-cyclohexylethanol was obtained in a 92% yield after 40 hours. This was accompanied by small amounts of 1-cyclohexylethanone (4%), ethylbenzene, and ethylcyclohexane, the last two compounds being formed by cleavage of the benzylic C–O bond. The same hydrocarbons were also formed in an overall yield of 14% in the hydrogenation of 1-phenylethanol, which afforded 1-cyclohexylethanol in 86% yield after 34 hours. Similarly, the reaction of ethyl *rac*-hydroxy(phenyl)acetate gave a mixture of two products: the prevalent one being formed by hydrogenation of the phenyl substituent (91%), and the byproduct (9%) being formed by concomitant hydrogenation and hydrogenolysis steps.

Table 1 Hydrogenation of Aromatic and Heteroaromatic Compounds Catalyzed by Rhodium/Graphite ($C_{24}Rh$) in 1.4 M Solutions[a]

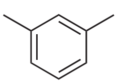
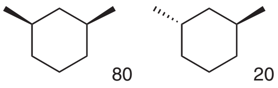
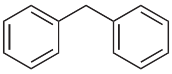
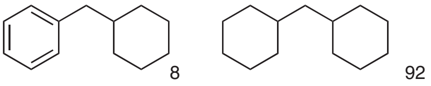
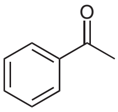
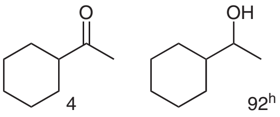
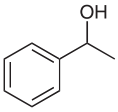
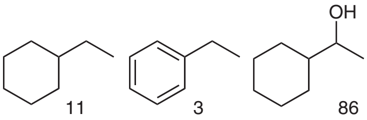
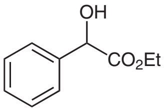
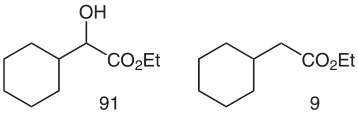
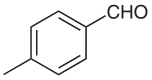
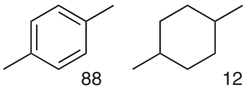
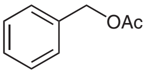
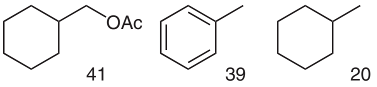
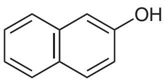
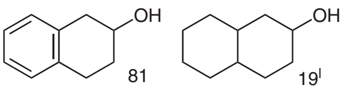
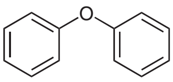
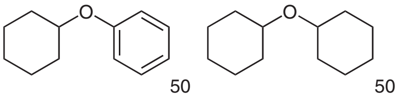
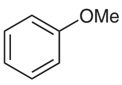
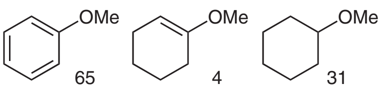
Substrate	Solvent	Rh (mol%)	Time (h)[b]	Product(s), Yield (%)[c]
toluene	–[d]	0.4	20	MeCy, quant
	*i*-PrOH	1.1	20	
	*i*-PrOH	1.7	42	
PhC≡CH	MeOH	1.0	20	EtCy, quant[e]
BzOH	MeOH	1.2	48	$CyCO_2H$, quant[f]
	MeOH	1.2	40	
	MeOH	1.2	34	
	MeOH	1.8	20	
	MeOH	1.2	24	
	MeOH	1.5	7	
methyl L-phenylglycinate hydrochloride	MeOH–37% aq HCl (9:1)	2.2	24[h]	methyl L-cyclohexylglycinate hydrochloride, quant
methyl L-phenylalaninate hydrochloride	MeOH–37% aq HCl (9:1)	2.4	32[i]	methyl L-cyclohexylalaninate hydrochloride, quant
PhOH	$MeOH–H_2O$ (95:5)[j,k]	1.0	20	CyOH, quant
	MeOH	1.5	55	
	*i*-PrOH	1.7	60	
	MeOH	1.1	48	

Table 1 Hydrogenation of Aromatic and Heteroaromatic Compounds Catalyzed by Rhodium/Graphite ($C_{24}Rh$) in 1.4 M Solutions[a] (continued)

Substrate	Solvent	Rh (mol%)	Time (h)[b]	Product(s), Yield (%)[c]
pyridine	MeOH	0.8	14	piperidine, quant
pyrrole	MeOH–AcOH (9:1)[m]	0.7	13	pyrrolidine, quant
indole	MeOH–AcOH (9:1)[m]	1.2	28	octahydro-1*H*-indole, quant
$PhNO_2$	MeOH	1.3	18	$PhNH_2$, quant

[a] The reactions were performed in on 1–2 mmol scale of substrate in 1.4 M soln at r.t. and 1 atm H_2 of pressure using Rh/Gr ($C_{24}K$, 4% loading by weight) as the catalyst.

[b] Time required for the complete consumption of the starting aromatic compound and the disappearance of partially hydrogenated derivatives, unless otherwise stated.

[c] The yields and diastereomeric ratios were determined by GC/MS analysis in the presence of an internal standard.

[d] The reaction was performed in toluene using a 1.9% loading of Rh/Gr.

[e] The formation of EtPh was observed at intermediate times (EtPh/EtCy 24:76 after 8 h).

[f] The reaction was monitored by ^1H NMR analysis.

[g] EtPh and EtCy were also formed (<4%); PhCH(Me)OH was detected at intermediate reaction times and was the major product (56%) after 20 h.

[h] Complete hydrogenation in MeOH required 36 h under the same conditions.

[i] Complete hydrogenation in MeOH required 42 h.

[j] Cyclohexanone was detected in the reaction mixture after 5 h.

[k] The reaction in MeOH gave a 91:9 mixture of CyOH and 1,1-dimethoxycyclohexane after 20 h.

[l] Ratio *cis*/*trans* = 91:9.

[m] The product of partial hydrogenation of the pyrrole ring (indoline) was observed at intermediate reaction times; complete hydrogenation in MeOH required 26 h.

Reduction of the carbonyl group and subsequent hydrogenolysis of the benzylic alcohol was the main pathway in the hydrogenation of 4-methylbenzaldehyde in methanol, which after 24 hours gave *p*-xylene as the main product accompanied by a small amount of 1,4-dimethylcyclohexane. The reaction of benzyl acetate was not selective; after seven hours, a mixture of three compounds was produced: cyclohexyl acetate (41%), toluene (39%), and methylcyclohexane (20%). Both the starting material and the hydrocarbons were observed in the reaction mixture at intermediate reaction times.

The hydrogenation of methyl L-phenylglycinate and methyl L-phenylalaninate as their hydrochlorides in methanol was complete after 36 and 42 hours, respectively. The reaction rate increased slightly in a 9:1 mixture of methanol and 37% hydrochloric acid; for example, the hydrogenation of methyl L-phenylglycinate hydrochloride was complete in 24 hours. Conversely, no reaction occurred on the free-base forms of these esters.

Phenol was quantitatively hydrogenated to cyclohexanol in a 95:5 methanol–water mixture, whereas in methanol, the partial formation of 1,1-dimethoxycyclohexane (9%) was observed. 2-Naphthol underwent slow hydrogenation and was completely consumed after 55 hours; at this time, 1,2,3,4-tetrahydronaphthalene-2-ol was the prevalent product, although the fully hydrogenated compound was also obtained in 19% yield (dr = 91:9, GC/MS analysis).

Diphenyl ether underwent slow hydrogenation in isopropanol, and the saturation of both phenyl groups was not achieved even after 60 hours, at which time a 1:1 mixture of cyclohexyl phenyl ether and dicyclohexyl ether was obtained. Similarly, the hydrogenation of methoxybenzene was largely incomplete after 48 hours, at which time methoxycyclohexane and 1-methoxycyclohexene were formed in yields of 31% and 4%, respectively.

We then examined the reduction of aromatic azaheterocycles. Pyridine was smoothly converted into piperidine in methanol in 14 hours. On the other hand, electron-rich pyrrole required 26 hours for complete hydrogenation to pyrrolidine; however the reaction time could be shortened to 13 hours in the presence of acetic acid.

Pyrrole was smoothly hydrogenated to pyrrolidine. Similarly, indole was fully hydrogenated in 9:1 methanol–acetic acid to give its octahydro derivative in 28 hours, whereas in methanol solution, less than 5% conversion to the same product was observed. Under the former conditions, the partially hydrogenated compound, indoline, was observed at intermediate reaction times. We have previously reported that rhodium/graphite is slightly more effective than other rhodium or platinum catalysts for the hydrogenation of substituted pyrrole rings.[15] Mild experimental conditions were required to hydrogenate the pyrrole nucleus, which was highly activated by *N*- or *C*-acyl groups.[11]

Nitrobenzene was selectively converted into aniline under routine conditions, and the product resisted ring hydrogenation even after prolonged reaction times. In a separate experiment, aniline was resistant to hydrogenation, and afforded a mixture of products in low yields.

As the catalyst could be recovered from the reaction mixtures merely by filtration, we wished to check the possibility of re-using the same catalyst in a number of consecutive reactions. We therefore carried out four runs of the hydrogenation reaction of heptylbenzene, each time using the catalyst recovered from the previous run. The reactions were monitored by GC analysis at constant times for each run to determine the corresponding yields of 1-cyclohexylheptane. The reaction rate decreased only slightly after each run (Figure 3). Note that in the first two runs, the conversion of heptylbenzene into heptylcyclohexane may have been complete in less than 20 hours.

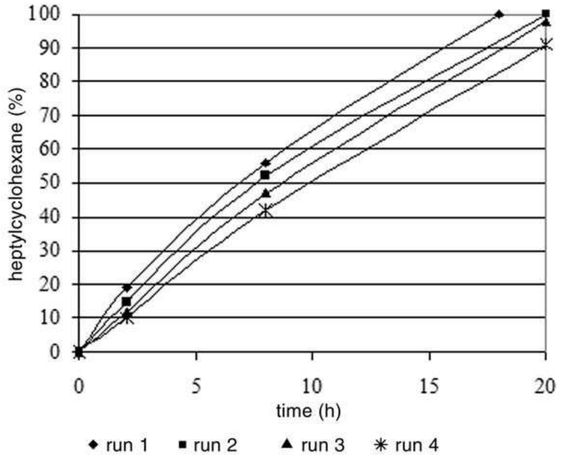


Figure 3 Progress in the formation of heptylcyclohexane in four consecutive hydrogenation reactions of heptylbenzene (1.4 M in MeOH, r.t., 1 atm H_2) using the catalyst Rh/Gr ($C_{24}K$, 4% by weight) recovered each time from the previous run

Finally, the lack of reactivity of the following aromatic compounds is worthy of note: naphthalene, 2-naphthaldehyde, chlorobenzene, 2-phenylpropanal, methyl benzoate, and 2-methylpyrazine. At the moment, we cannot offer a plausible explanation for all the observed failures.

A more thorough comparative investigation of the behavior of rhodium/graphite and 5% rhodium/alumina in hydrogenation reactions was carried out, taking heptylbenzene and methoxybenzene as the substrates. In all cases, the hydrogenation reactions were conducted under the same typical experimental conditions using the identical loading of the catalyst (1.8 mol%), and the progress of the reactions with time was monitored (Figure 4). With heptylbenzene and 5% rhodium/alumina, the reaction rate was very high at the beginning of the reaction, but decreased continuously with time so that the formation of heptylcyclohexane was incomplete (74% yield) after 18 hours. On the other hand, in the same reaction with rhodium/graphite, the rate was lower but remained almost constant with time and complete conversion of the substrate to the product was observed after 18 hours. Note that the reaction with rhodium/graphite was complete after 10 hours at 30 atm.

A similar trend was observed in the hydrogenation reactions of methoxybenzene, a less reactive substrate. A satisfactory reaction rate was observed with rhodium/graphite at 30 atm of hydrogen pressure, and an even more satisfactory rate was observed at 100 atm. In the latter case, complete hydrogenation was achieved after 26 hours with either C_8K or rhodium/alumina, although the reaction rate was higher with the latter catalyst. Hence, similar forcing conditions should be used to hydrogenate less reactive aromatic compounds.

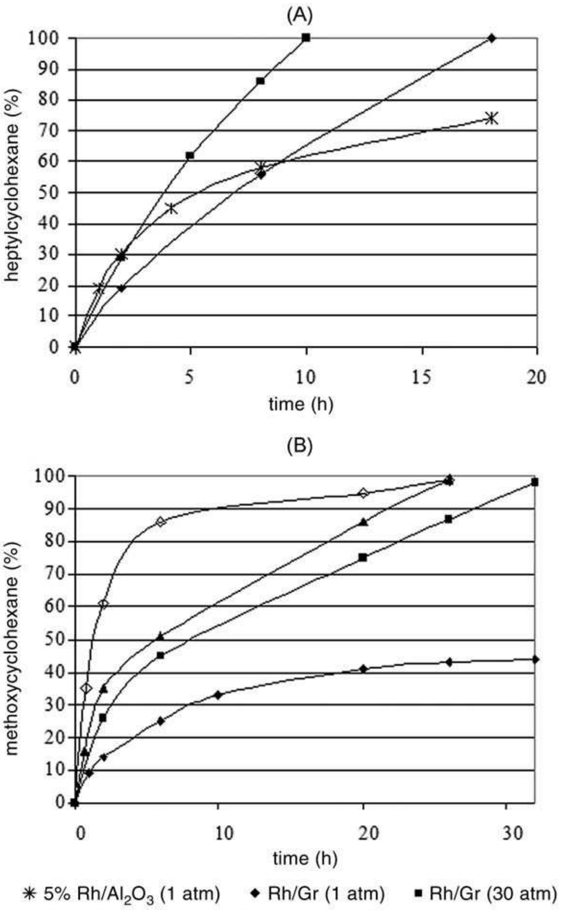


Figure 4 Progress in the formation of heptylcyclohexane from heptylbenzene (A) and of methoxycyclohexane from methoxybenzene (B) in hydrogenation reactions performed in MeOH using 1.8 mol% of catalyst

A comparison of the effectiveness and selectivity of our new catalyst with the outcomes of previously described hydrogenation reactions of arenes using other heterogeneous rhodium catalyst showed some analogies, but also a few discrepancies. For example, the hydrogenation rate of typical aromatic compounds catalyzed by silica-supported rhodium hydride (500 psi H_2, 22 °C) decreased in the order: benzene > anisole > naphthalene> aniline.[16] In hydrogenation reactions catalyzed by rhodium powder prepared by reduction of a rhodium complex by hydrogen in dichloromethane, the presence of any substituent on the benzene ring decreased the reaction rate with respect to benzene, and benzoic acid was not hydrogenated at all; moreover, hydrogenolysis of the hydroxy group of phenol as well as those of benzylic alcohols occurred along with the hydrogenation of the aromatic ring.[17]

Catalytic reductions of phenylglycine and phenylalanine derivatives were previously performed with 5% rhodium/charcoal or rhodium/alumina to give excellent yields of the corresponding cyclohexyl derivatives under typical conditions of aqueous phosphoric, hydrochloric, or sulfuric acid, 60 °C, 50 psi hydrogen, and 24 hours reaction time.[18] Similarly, aromatic-ring hydrogenations of (*R*)-3-phenyllactic acid and (*R*)-3-phenylalanine were accomplished by using either 5% or 10% rhodium/charcoal in protic solvents at 4–15 bar hydrogen pressure.[19] 10% Rhodium/charcoal was more active than analogous palladium, iridium, platinum, or ruthenium catalysts in the hydrogenation of arenes in water at 80 °C and 3–5 atm of hydrogen pressure,[20] as well as in the hydrogenation of 1-phenylethanol[13b] or benzoic acid[21] in supercritical carbon dioxide at 50 °C and 3–10 mPa of hydrogen pressure.

Rhodium nanoparticles stabilized or supported on polymeric matrices,[22] zeolites,[23]or nanofibers,[24] and homogeneous rhodium catalysts[25] often display excellent performances in hydrogenation reactions of arenes; these performances, especially those of the homogeneous catalysts, are far superior to those of more common heterogeneous rhodium catalysts.

In conclusion, we have described the easy preparation of a new heterogeneous catalyst, rhodium/graphite. In this catalyst, rhodium nanoparticles are assembled in sponge-like clusters on the graphite surface, and no intercalation appears to be present. This catalyst was highly effective in the hydrogenation of carbocyclic and heterocyclic aromatic rings under mild conditions of room temperature and atmospheric pressure. Unsaturated functionalities, such as alkyne, alkene, nitro, formyl, and acetyl groups directly linked to the benzene ring were concomitantly reduced. On the other hand, ester, chloro, and amino substituents inhibited the hydrogenation of the benzene ring. Moreover, benzylic C–O bonds underwent partial or complete hydrogenolysis. However, a number of functionalities were tolerated, allowing the selective hydrogenation of carboxylic acids, phenols, and aryl ethers. Optically active phenyl-substituted α-amino acids could be easily hydrogenated without loss of optical activity. More forcing conditions could be used for the hydrogenation of more resistant substrates, such as diphenylmethane or aryl ethers.

Among the advantages of the new catalyst are its two-step preparation, the ready availability of the starting reagents, and the possibility of recovering and reusing the catalyst. Although the precursor C_8K is pyrophoric, it is immediately transformed into rhodium/graphite, which has been safely stored for months under air without loss of activity. Therefore, despite the mildness of experimental conditions and excellent selectivity and stereospecificity offered by other heterogeneous and homogeneous rhodium catalysts, extended applications of rhodium/graphite in organic synthesis are expected.

Optical rotations were measured on a digital polarimeter (Perkin Elmer 343) in a 1-dm cell, and $[\alpha]_D^{25}$ values are given in degrees $cm^3 g^{-1}$. MS spectra were recorded at an ionizing voltage of 70 eV on an Agilent Technologies 5975 spectrometer with GLC injection. Analytical gas chromatography (GC) was performed on an HP6890 (HP-5 column, 30 m, ID 0.25 mm) instrument equipped with a flame-ionization detector and a split-mode capillary-injection system. Rhodium chloride hydrate (99.98% purity) was purchased from Aldrich and dried by heating at 50 °C under reduced pressure for 3 h before use. Graphite (< 500 ppm) was obtained from Roth. All the products are known compounds; their spectra matched those reported in the corresponding references.

Rhodium/Graphite ($C_{24}Rh$)

Graphite powder (0.690 g) was poured into a three-necked flask equipped with a condenser, a dropping funnel, an argon inlet, and a magnetic stirrer bar, and the contents of the flask were heated under argon at 150 °C for 10 min. Freshly cut potassium (0.280 g, 7.19 mmol) was slowly added to the graphite at 150 °C with stirring. After all the potassium pieces had melted and bronze-colored C_8K powder was formed, the flask was allowed to cool to r.t. and the C_8K was covered with anhyd THF (15 mL) without stirring. A suspension of anhyd $RhCl_3$ (0.50 g, 2.40 mmol) in THF (50 mL) was slowly added with stirring. The mixture was then refluxed for 3 h, cooled to 0 °C, and H_2O (10 mL) was slowly added. The mixture was stirred for 30 min and then filtered. The solid was washed successively with H_2O, MeOH, and Et_2O (30 mL each), then dried at r.t. under vacuum for 6 h to give $C_{24}Rh$ as a dark grey powder; yield: 0.901 g (96%).

Structural Characterization of Rhodium/Graphite ($C_{24}Rh$)

PXRD patterns were collected using a PanAnalytical X'Pert Pro equipped with X'Celerator detector powder diffractometer using Cu Kα radiation (λ = 1.5418 Å) generated at 40 kV and 40 mA. The instrument was configured with a 1/4° divergence and 1/4° antiscattering slits. A standard quartz sample holder 1-mm deep, 20-mm high, and 15-mm wide was used. The diffraction patterns were collected within the 2Θ range from 10° to 85° with a step size (Δ 2Θ) of 0.02° and a counting time of 10 s.

TEM observations were carried out by using a Philips CM 100 instrument (80 kV). The powdered samples were dispersed in H_2O and then few droplets of the slurry were deposited on porous carbon foils supported on conventional copper microgrids. The images were recorded by using a charge-coupled device digital camera.

Methyl L-Cyclohexylglycinate Hydrochloride; Typical Procedure for Hydrogenation

Rh/Gr ($C_{24}Rh$, 0.010 g, 4% by weight) was added to a soln of methyl L-phenylglycinate hydrochloride (0.250 g, 1.2 mmol) in anhyd MeOH (1.2 mL) containing 37% aq HCl (0.1 mL), and the mixture was magnetically stirred under H_2 (1 atm, balloon). The progress of the reaction was monitored by GC/MS, after treatment of the sample with 2 M aq NaOH and extraction with EtOAc. The starting material disappeared within 24 h. The solid was filtered off through a pad of Celite, and the organic phase was concentrated at reduced pressure to give methyl L-cyclohexylglycinate hydrochloride as a white powder; yield: 0.241 g (97%, 1.16 mmol).

The free amine was obtained by treatment with base: $[\alpha]_D^{25}$ +32.8 (*c* 0.5, MeOH) [Lit.[26] +33.4 (*c* 0.52, MeOH)].

Methyl L-Cyclohexylalaninate hydrochloride was similarly obtained from methyl L-phenylalaninate hydrochloride (0.250 g, 1.16 mmol); yield: 0.246 g (96%); free base $[\alpha]_D^{25}$ +24.3 (*c* 1.0, MeOH) [Lit.[27] +23.4 (*c* 1.0, MeOH)].

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