JOC Notes

Chemoselective Hydrogenation of Substituted Nitroaromatics Using Novel Water-Soluble Iron Complex Catalysts

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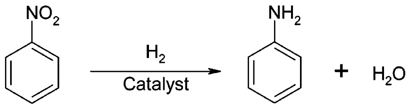
Received October 14, 2003

Abstract: Chemoselective hydrogenation of substituted nitroaromatic compounds by water-soluble iron complex catalysts with molecular hydrogen has been reported for the first time. This biphasic catalyst presents an opportunity for a solvent-free hydrogenation. This catalyst system provides a low-cost, efficient alternative to the selective but environmentally unacceptable stoichiometric reductions as well as the supported noble metal catalysts used for hydrogenation. An efficient recycling strategy has resulted in a cumulative turnover number above 6000.

Selective hydrogenation of substituted nitro aromatic compounds has been a major challenge for chemists.[1] Stoichiometric reagent-based processes are very selective toward reduction of nitro functions but generally not ecofriendly.[2] Catalytic hydrogenations using molecular hydrogen are less chemoselective than the stoichiometric methods; therefore, the catalysts have to be poisoned or tailored to achieve the desired selectivity.[3−7] In this report, a highly chemoselective catalytic hydrogenation of nitrobenzenes has been demonstrated using homogeneous iron complex catalysts. The water-soluble catalyst has also been applied to hydrogenation in a biphasic aqueous−organic system to achieve selective, robust, and recyclable catalysis.

The use of homogeneous iron complexes for the hydrogenation of nitro compounds has been reported earlier in a few cases. Iron carbonyl phosphine complexes are reportedly active for hydrogenation of nitro benzene under exclusively nonaqueous conditions.[8] Nitrobenzene has been reduced under triphasic conditions using $Fe_3(CO)_{12}$ in stoichiometric quantities, in absence of hydrogen.[9] For the reduction of nitroaromatics, the byproduct being water, a catalyst tolerant of water or, better still, applicable in a biphasic aqueous−organic solvent system would be more desirable.

TABLE 1. Hydrogenation of Nitrobenzene with Iron Compounds[a]



catalyst	solvent	time (h)	nitrobenzene conversion (%)	TOF[b] (h^{-1})
	toluene	8.33	0	0
$Fe(NO_3)_3{\cdot}9H_2O$	methanol	9.23	98.7	433
$FeSO_4{\cdot}7H_2O$	methanol	3.08	99.1	1297
$FeSO_4{\cdot}7H_2O$	water	3.08	98.5	1297
$FeSO_4{\cdot}7H_2O$	toluene	4.26	98.7	937
$Fe^{III}(acac)_3$	toluene	4.66	99.4	857
ferrocene	toluene	8.33	0	0

[a] Nitrobenzene 96 mmol, solvent 90 mL, catalyst 0.072 mmol, pH_2 400 psi, $T = 150$ °C; conversion and selectivity in all cases were found to be >98.5%. [b] Based on hydrogen consumption (mol of hydrogen consumed/mol of catalyst/h).

At the outset, the catalytic activity of the iron compounds for the hydrogenation of nitrobenzene was evaluated. Reactions were carried out with $Fe(NO_3)_3{\cdot}9H_2O$, $FeSO_4{\cdot}7H_2O$, $Fe(acac)_3$, and ferrocene in water, methanol, and toluene solvents. The results in Table 1 indicate that except for ferrocene, iron compounds efficiently catalyze nitrobenzene hydrogenation to aniline. In all the examples reported, where hydrogenation occurred, complete conversion of nitrobenzene (residual nitrobenzene less than 10 ppm) to aniline was obtained with selectivities greater than 98%. The turnover frequencies (TOF, mol of H_2 consumed/mol of iron/h) were in the range of 433−1297 h^{-1}. Under identical conditions, in the absence of iron compound, no hydrogenation was observed, thereby confirming the catalytic role of iron.

To elucidate the reaction pathway intermediate, samples were withdrawn during the reaction for analysis. The formation of phenyl hydroxylamine (III), azoxybenzene(V), and azobenzene was observed. Although nitrosobenzene (II) was not detected, its formation was evident since azobenzene and azoxybenzene were formed. Azobenzene(VI) and hydrazobenzene(VII) were also formed by the hydrogenation of azoxy benzene. The major impurities observed at the end of the reaction were mainly the azo and hydrazobenzene. The probable reaction pathway as illustrated in Scheme 1 is found to be similar to that of Raney nickel-catalyzed hydrogenation.[10]

The major objective of this study was to develop an aqueous-phase catalyst so as to avoid all problems related

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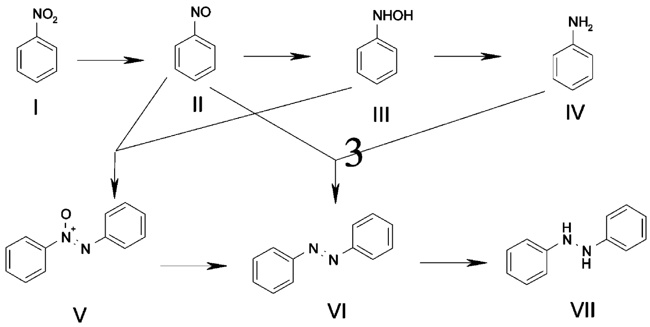
10.1021/jo035511t CCC: $27.50

TABLE 2. Hydrogenation of Nitrobenzene to Aniline in Biphasic Medium[a]

no.	catalyst	metal-to-ligand ratio	time (h)	conversion (%)	selectivity to aniline (%)
1[b]	$FeSO_4$	1:0	7.38	66.28	98.1
2	$Fe^{II}/EDTANa_2$	1:1	7.75	99.96	98.1
3	$Fe^{II}/EDTANa_2$	1:5	9.83	88.2	97.3
4[c]	$Fe^{II}/EDTANa_2$	1:5	13.3	99.9	97.4

[a] Nitrobenzene 96 mmol, toluene 50 mL, water 50 mL, catalyst $FeSO_4{\cdot}7H_2O$ 0.072 mmol, pH_2 400 psi, $T = 150$ °C. Procedure for reaction: A Parr T316 SS autoclave of 300 mL capacity was charged with the requisite amount of water. The catalyst, $FeSO_4{\cdot}7H_2O$, and the Na_2EDTA were added to the water and dissolved. A toluene solution of nitrobenzene was added to the reactor, following which the reactor was closed and flushed with nitrogen and hydrogen. The autoclave and its contents were heated to the requisite temperature, under slow stirring. On attainment of the correct temperature [150 °C], the autoclave was pressurized with hydrogen to the desired pressure [400 psig], through a constant pressure regulator, and connected to a hydrogen reservoir; the time was noted, and the stirrer was increased to 900 rpm. The consumption of gas in the reactor was measured by monitoring the pressure in the reservoir. The pressure in the reactor was held constant [at 400 psig] by a continuous feed of hydrogen from the reservoir. This ensured a constant pressure for the entire duration of the reaction. After the stoichiometric consumption of hydrogen was achieved, the reactor was cooled and discharged. A liquid sample was taken for analysis, and the mass balance of reactants and products was calculated. [b] Considerable amount (>80%) of iron leaching to organic phase was observed in the absence of a coordinating ligand. In the presence of EDTA, the Fe content of the organic phase was <5 ppm. [c] Organic phase was pure nitrobenzene 50 mL (480 mmol).

SCHEME 1. Reaction Pathway for Hydrogenation of Nitrobenzene to Aniline with Iron Catalysts



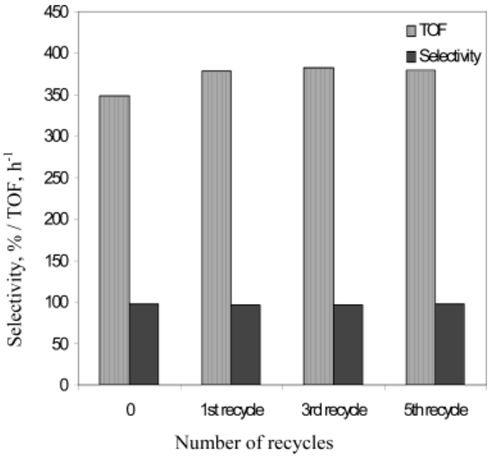


FIGURE 1. Hydrogenation of nitrobenzene to aniline in a biphasic medium. Reaction conditions: nitrobenzene 96 mmol, toluene 50 mL, water 50 mL, catalyst $FeSO_4{\cdot}7H_2O$ 0.072 mmol, Fe:$EDTANa_2$ = 1:5, pH_2 400 psi, T = 150 °C. For recycling, the excess water generated in the previous reaction was removed under vacuum at room temperature to maintain the aqueous phase volume at 50 mL.

to product separation and catalyst recovery.[11] We therefore investigated iron ethylenediaminetetraaceticacid disodium salt ($Fe^{II}/EDTANa_2$) as a catalyst for the hydrogenation of nitro-aromatics in a two-phase system. In this reaction, $Fe^{II}/EDTANa_2$ complex remains exclusively in the aqueous phase, while the solvent, substrate nitrobenzene, and products form an immiscible organic phase. With this catalyst, a TOF of 136 h^{-1} and a turnover number (TON, mol of product formed per mol of catalyst) of 1333 for nitrobenzene were achieved with complete conversion of nitrobenzene and a selectivity to aniline greater than 98% (Table 2). The activity of the Fe(II) system in the presence of $EDTANa_2$ is reduced due to coordination, which can restrict the access of nitrobenzene, and also due to the fact that the catalyst is retained in the aqueous phase. In the absence of the ligand, the catalyst is predominantly in the organic phase where the reaction takes place with no constraints on solubility phenomena.

To examine the stability and recyclability of the catalyst, the aqueous phase was successively recycled five times with fresh organic phase to obtain a cumulative TON of 6665 without loss of either the hydrogenation activity or the selectivity to aniline (see Figure 1). In the absence of $EDTANa_2$, the $FeSO_4$ catalyst hydrogenated nitrobenzene in a toluene−water biphasic system (TOF 120 h^{-1}). However, at the end of the reaction the catalyst was found to be in the organic phase. Hence, the presence of a strongly coordinating hydrophilic ligand such as $EDTANa_2$ is essential to retain iron catalyst in the aqueous phase.

To establish the generality of the catalyst system, we further investigated hydrogenation of numerous substituted nitrobenzenes in the absence of organic solvents. In all cases, almost complete conversion of the nitro compound could be obtained with a high selectivity to the corresponding amine (Table 3). The $Fe^{II}/EDTANa_2$ catalyst system was assessed for its chemoselectivity in the hydrogenation of the nitro group in preference to other reducible functional groups.

As seen from Table 3, hydrogenation of 4-nitroacetophenone, 4-nitrophenyl acetonitrile, and 4-nitrobenzoic acid gave the corresponding amino derivatives without affecting the other reducible groups. Even the hydrogenation of chloronitrobenzenes showed high selectivity for chloroanilines without any dehalogenation of chloronitrobenzenes, which is normally observed with heterogeneous catalysts.[1] The reduced selectivity to

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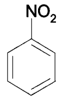
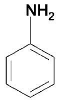
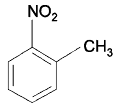
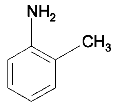
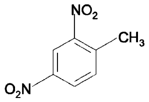
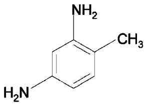
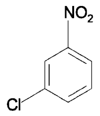
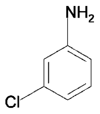
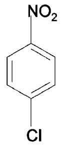
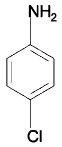
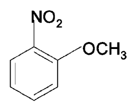
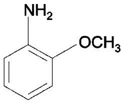
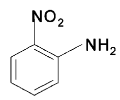
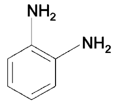
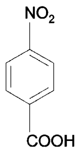
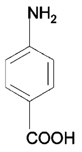
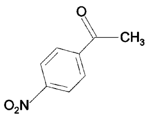
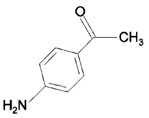
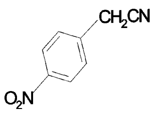
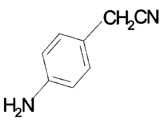
TABLE 3. Hydrogenation of Substituted Aromatics in Biphasic Medium[a]

No	Substrate		Substrate mmol	Yield of corresponding amine %[b]		TOF h^{-1} [c]	Time h
1	nitrobenzene		90.0	98.5		529	2.4
2	2-nitrotoluene		84.9	98.7		457	2.6
3	2,4-dinitrotoluene		56.1	84.6[d]		134	5.8
4	3-nitro chlorobenzene		63.5	99.0		434	2.0
5	4-nitro chlorobenzene		63.5	96.2		400	2.2
6	2-nitroanisole		82.0	89.2		450	2.5
7	2-nitroaniline		72.5	98.2		116	8.7
8	4-nitrobenzoic acid		59.8	85.8		393	2.1
9	4-nitro acetophenone		60.0	99.0		208	4.0
10	4-nitrophenyl acetonitrile		61.0	90.1		99	8.5

[a] Reaction conditions: pressure 400 psi; temperature 150 °C; aqueous phase 90 mL; organic phase consists of neat substrate; catalyst $FeSO_4 \cdot 7H_2O$ 0.072 mmol; Fe EDTANa$_2$ 1:5; conversion in all cases was complete. [b] Based on GC analysis. [c] TOF calculated as mol of nitro compound converted per mol of Fe per hour. [d] Monoamino product was 11.5%.

products as observed for the hydrogenation of *p*-nitrobenzoic acid, 4-nitrobenzyl nitrile, and 4-nitro anisole is due to formation of other products, mainly the azo and hydrazo derivatives and high boilers. In these reactions, too, no aniline was formed and no hydrogenation of the nitrile, keto, or carboxylic acid group was observed, which shows the chemoselective nature of the catalyst. The variation in the activity observed for the hydrogenation of the different compounds could be attributed to the influence of the substituents on the ring as well as the solubilty of the substrate in water. In this reduction process, water, apart from being a green solvent, effectively controls the rate of the reaction and hence exothermicity. The limited solubility of the substrate in water maintains sufficient productivity and also prevents reaction runaway. This is an additional advantage since hydrogenation of nitro aromatics is highly exothermic. Due to the use of the aqueous-phase catalyst, organic solvents can be totally avoided, thereby making the process more eco-friendly.

The high chemoselectivity of the biphasic iron catalysts for nitro-group hydrogenation, shown for the first time, is similar to that observed in Bechamp reduction. The simplicity of the catalyst preparation and recycling and the low cost, coupled with the prospect of solvent-free operations, are likely to form the basis for application of such a catalyst in commercial practice in the future.

JO035511T