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First Selective Reduction of Aromatic Nitro Compounds Using Water Soluble Catalysts

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Abstract: A new methodology has been developed which involves the reduction of substituted nitro aromatics to substituted anilines using a two phase system with water - soluble palladium catalysts. The nitro group was reduced selectively to an amine in up to 85% yield whereby other functional groups i.e., ketone, nitrile, chloride and alkene were untouched.

Aromatic amines are important intermediates in the fine chemical, dyes and pigment industry.¹ Reductive carbonylations of nitro compounds with CO using metal complexes have gained considerable importance due to the potential application for the manufacture of urea² and amines³ and for the synthesis of carbamates⁴ and isocyanates⁵, thus bypassing the toxic phosgene route.⁶ The reduction of nitroarenes to anilines using CO is known.⁷ So far, Rh₄(CO)₁₂ catalyst and CO, as well as the ruthenium cluster Ru₃(CO)₁₂ and methyl formate, used as a source of CO, have been disclosed in the literature.^{8,9} Unfortunately, other functional groups are reduced under the reaction conditions i.e., chloride, ketones.⁹ Also, often the selective reduction of aromatic nitro groups using hydrogen in the presence of sensitive functional groups i.e., ketones, nitrile, chloride and alkene is difficult, because these sensitive functionalities are reduced faster by hydrogenation than the nitro group.¹⁰ Recent work by Kaneda¹¹ describes selective reduction of conjugated nitroaromatics to conjugated aromatic amines under homogeneous conditions using Rh carbonyl clusters. This work prompted us to disclose our results on a highly selective method for reductive carbonylation of nitro aromatics using a two phase system.

Despite the advantages of using CO for the functionalization of nitroaromatics, the large amount of catalyst necessary and the lack of efficient catalyst recycling methods have prevented the widespread use of such methodology. Two phase catalysis with water soluble catalysts offers the most elegant principle for catalyst recycling in homogeneous catalysis.¹² Thus, we investigated for the first time reductive carbonylation of nitroaromatics with water soluble catalysts. As ligands we used trisulfonated triphenylphosphine (TPPTS, 3) and a mixture of tetra-, penta- and hexa-sulfonated 2,2'-bis diphenylphosphinomethylene binaphthyl which we call BINAS 4 (scheme 1).¹³

As a model of the reaction we studied the reduction of 5-trifluoromethyl-2-chloronitrobenzene (7) to 5trifluoromethyl-2-chloroaniline (8). During our investigation of the reaction we found a strong effect of the amount of ligand on the yield of the reaction. When the TPPTS/palladium ratio of 3, 5, or 10 was used, then it produced $\underline{8}$ in 40, 70, and 30% yield respectively. On the other hand, when BINAS/palladium ratio of 1, 3, or 5 was used then it produced $\underline{8}$ in 30, 85, and 50% yield respectively. If, the temperature and pressure were dropped from 100 to 50 °C and pressure from 120 to 60 bar, the conversion and yield of $\underline{8}$ dropped from 85% to 45% yield. The reaction produced diazaoxide $\underline{2b}$ as a byproduct which is formed in significant amount if the temperature and pressure are lowered (10-15%). Thus, when the pressure and temperature are lowered from 100 to 50 °C and pressure from 120 to 60 bar, $\underline{2b}$ was formed in 15% yield.



Scheme 1

The bi-phasic CO reduction methodology is summarized in table 1: it allows reduction of the nitro group to an amine in the presence of chlorides (entry 1-4). In addition, ketones which are normally reduced to alcohols in the presence of hydrogen, are preserved using this methodology (entry 1). Moreover, the CO reduction method was selective in the presence of nitrile function (entry 3). To our surprise, the methodology was also found to be selective to nitro-styrene. Thus, when 3-nitrostyrene **13** was subjected to bi-phasic CO reduction 3-aminostyrene **14** was recovered in 50% isolated yield (entry 5). In most of the runs which were conducted using bi-phasic reduction conditions, it was found that BINAS is a better ligand than TPPTS for the reduction of nitro compounds to amines. This probably can be explained on the basis of substituents on phosphorus. BINAS containes methylene groups on the phosphorus thus making the ligand more basic and the bidentate complex of BINAS/palladium more active toward CO reduction. In the cases where an electron donating group is present in the molecule i.e., OH group, the reduction was somewhat disappointing. The reduction of 2-nitro-4-chlorophenol (**15**) using TPPTS or BINAS produced 2-hydroxy-5-chloroaniline (**16**) in 5% and 10%, respectively. Further studies are underway to overcome this problem.¹⁴

As far as the mechanism is concerned, it is presumed that the amine is formed by the deoxygenation of the nitro group to the corresponding nitrene species. The nitrene can either be converted to an amine by abstracting a proton from the water or it can react with CO to give isocyanates which react further with water to give phenyl carbamic acid. Hydrolysis affords the desired amine (Scheme 2).³

Entry	Nitro compound	Ligand	Yield%	Amine
	¥°			\searrow°
(1)	\wedge	TPPTS =	65%	\wedge
(-)		BINAS =	70% ^b	
(2)	CF ₃	TPPTS =	45%	
		BINAS =	85%	
(3)	CN	TPPTS =	60%	
	CI NO2	BINAS =	60%	
	NO ₂	TPPTS =	40%	
(4)		BINAS =	50%	
(5)		BINAS =	50% ^b	NH2 14
(6)		TPPTS = BINAS =	5% 10%	

Table -1. CO - Reduction of substituted nitro aromatic compounds^a

b Yield refers to an isolated, pure material.

In conclusion, our two phase system using water soluble ligands (TPPTS $\underline{3}$, BINAS $\underline{4}$) for the reductive carbonylation of nitro aromatic is unique. We have developed conditions where the nitro group can be selectively reduced to an amine in good yield in the presence of other sensitive functional groups i.e., ketone, nitrile, chloride, alkene. Furthermore, our methodology ensures good product separation, due to the high solubility of catalyst in water, whereas product remains in the organic phase. These attributes of a catalyst system are of paramount importance when large-scale application is considered.



Scheme 2

a Instrumental analysis data including ¹H NMR, ¹³C NMR, IR and Ms spectra were fully consistent with the assigned structure.

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- 14. A general description using either of the ligands can be summarized as follows: A degassed solution of 40 ml xylene and the nitro aromatic substrate (40 mmol) was added to a 200 ml autoclave. BINAS (14.5 g, 2.5 mmol from a solution of 173 mmol/kg), 60 mmol of 32% NaOH and 30 ml H₂O were added to the autoclave followed by the addition of PdCl₂ (1mmol). The pH at this stage was measured to be 11-12. The autoclave was closed and was subjected to a degassing procedure by vacuum and refill with nitrogen followed by CO three times. The autoclave was pressurized to a pressure of 120 bar CO and the temperature was set to 100 °C. The reaction was allowed to run for 20 h and at the end of the reaction, the mixture was cooled down to room temperature and the autoclave was opened. The organic layer was separated from the water layer and was filtered to remove traces of palladium. The reaction mixture was concentrated under vacuum to give the desired raw product. The product was purified by crystallization.

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