Ultrasound-promoted Highly Chemoselective Reduction of Aromatic Nitro Compounds to the Corresponding *N*-Arylhydroxylamines Using Zinc and $HCOONH_4$ in CH_3CN

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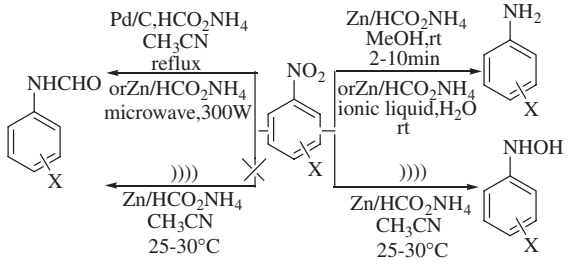
N-Arylhydroxylamines were prepared in high yields through chemoselective reduction of the corresponding aromatic nitro compounds under ultrasound (59 kHz) at room temperature using a convenient $Zn/HCOONH_4/CH_3CN$ system. This method was highly efficient, environmentally benign, especially simple and practical.

Ultrasound, as high frequency sound waves, can create, expand, and crack bubbles in ultrasonically irradiated liquid.[1] This process induces extremely high temperature and pressure which are very beneficial to the chemical reaction. The acceleration of a traditional reaction by ultrasonic was firstly reported by Richards and Loomis[2] in 1927. Since then, more attention has been paid to the ultrasonic field by organic chemists.[3] The results of the former researches indicate that ultrasounds can enhance the rate of the reactions or show positive effects for reactions that otherwise are practically impossible and sometimes improve product yields.

N-Arylhydroxylamines are an important class of compounds frequently used as key intermediates in the synthesis of nitrogen-containing heterocyclic compounds[4] and some promising biologically active compounds such as *N*-aryl-*N*-hydroxyformamides[5] and NO releasing compounds.[6] Hence, various methods have been reported for the preparation of *N*-arylhydroxylamines. The traditional methods are the careful reduction of nitroarenes.[7] However, these methods involve tedious work-up procedures and extra efforts for control of reaction. Ferroud et al. modified the conventional approach (Zn/NH_4Cl) by the introduction of ultrasound.[8] Nevertheless the universal problem, that the zinc dust has to be added slowly by portions, which complicates the experimental step, still exists in their method. In order to overcome these difficulties, hydrogen-transfer methods have been developed. But these methods also suffer from some disadvantages such as the use of toxic heavy metals or hazardous reagents.[9] Recently, Cui and co-workers have reported catalytic reduction of aromatic nitro compounds to the corresponding hydroxylamines by yeast or plant cells.[10] However, their methods either demand very long reaction times (3–5 days), which is exceedingly unfavourable to the proverbially labile *N*-arylhydroxylamines, or have no effect on nitroarenes bearing electron-donating groups. Here, we report a practical, simple, and extremely effective $Zn/HCOONH_4/CH_3CN$/ultrasonic system to prepare *N*-arylhydroxylamines from aromatic nitro compounds.

As part of our ongoing program, initially we were interested in the direct conversion of aryl nitro compounds under ultrasonic conditions for the preparation of *N*-arylformamides which had been prepared with Pd/C and $HCOONH_4$ in CH_3CN at reflux[11] or with $Zn/HCOONH_4$ under microwave irradiation (Scheme 1).[12] For this purpose, a mixture of 1-(4-nitrophenyl)ethanone, commercial zinc dust and $HCOONH_4$ in CH_3CN was sonicated



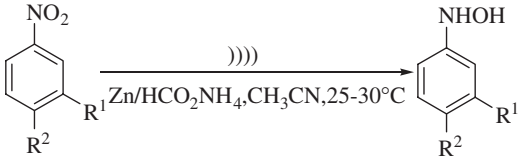
Scheme 1.

at 25–30 °C (water bath temperature) for 50 min. However, after extraction and removal of the solvent, the desired product, N-formylation, was not obtained. To our surprise, the isolated product was identified as 1-(4-hydroxyaminophenyl)ethanone as the result of the selective reduction of the starting aromatic nitro compound. This unexpected result was very interesting because the $Zn/HCOONH_4$ system was usually used as the method of rapid, mild, and highly effective preparation of arylamines (Scheme 1).[13] The only difference in our experiment compared to the literature was the use of CH_3CN as the solvent and application of ultrasound. In consideration of the above result and the fact that, to our knowledge, so far there is no report on the preparation of *N*-arylhydroxylamines using the $Zn/HCOONH_4/CH_3CN$/ultrasonic system by reduction of aromatic nitro compounds, our studies were directed into the preparation of *N*-arylhydroxylamines using commercial zinc dust and $HCOONH_4$ in CH_3CN under ultrasonic conditions.

To further explore the utilization scope of this reaction, a series of aromatic nitro compounds were examined under similar reaction conditions and the results were summarized in Table 1. From the Table 1, we could see that this method was highly chemoselective and many sensitive functional groups, such as -Cl, $-COCH_3$, -CN, and $-COOC_2H_5$, were tolerated. Furthermore, the yields were excellent. Over-reduction to the corresponding arylamines was prevented by the rapid filtration of the zinc dust. However, as to the known lag of the monitoring of TLC, traces of arylamines were unfortunately observed in Entries 5–7. Nevertheless, in view of the proverbial lability of *N*-arylhydroxylamines during the reaction and disposal, the purity of the crude products (>90%) was still heart-stirring. Furthermore, during the experiment, we found that the reaction temperature almost did not change when the $HCOONH_4$ was added to the reaction mixtures after the zinc dust. Therefore, the careful operation in Ferroud's experiment was not needed in our experiment, which largely simplified the experimental procedure.

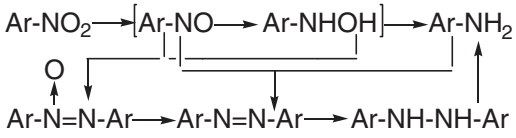
In order to check the effect of the ultrasound in our experiment, 4-nitrotoluene was reduced under the same condition without the use of ultrasound. The reaction proceeded very slow-

Table 1. Reduction of aromatic nitro compounds under ultrasound using $Zn/HCOONH_4/CH_3CN$ system[a]



Entry	R^1	R^2	Time /min	Yield[b] /%	Purity[c] /%
1	H	$COCH_3$	50	97	>98
2	CN	H	100	95	>98
3	H	CN	55	94	>96
4	Cl	Cl	60	97	>93
5	H	$CO_2C_2H_5$	55	98	>93
6	Cl	H	60	94	>92
7	H	CH_3	70	96	>90

[a]Substrate:Zn:$HCOONH_4$ = 2.5:10:25 (molar ratio). [b]Yields of crude products were based on the single experiment and were not optimized. [c]Estimated by ^1H NMR analysis.



Scheme 2.

ly and a small quantity of nitro compound still could be detected by TLC even after 12 h. Therefore, the influence of the ultrasound on enhancing the reaction rate was very obvious.

Scheme 2 gave the known reduction mechanism of a nitro group to an amino group.[8,14] The reduction underwent two middle stages and produced nitroso and hydroxylamine intermediates. The hydroxylamine was converted into amine finally. Moreover the azoxy, azo, and hydrazo compounds could be formed very easily when the reduction was performed under basic condition. Owing to the existence of traces of azoxy, azo, and amine compounds in our reaction mixture, we believed that the reaction mechanism of our experiments was the same as that in the literature[14] (Scheme 2).

In conclusion, we reported here an approach for the preparation of *N*-arylhydroxylamines from the corresponding aromatic nitro compounds using the $Zn/HCOONH_4/CH_3CN$ system under ultrasound. This method was mild, exceedingly efficient, highly chemoselective, environmentally friendly, and especially simple compared to the traditional method in which the careful manipulation was needed. Further studies to optimize reaction conditions and investigate solvent influence on the chemoselective reduction are in progress in our laboratory.

General procedure for the preparation of substituted *N*-arylhydroxylamines is as follows: A mixture of commercial zinc dust (10 mmol) and aromatic nitro compound (2.5 mmol) in CH_3CN was sonicated at 59 kHz under mechanical stirring at room temperature for 30 min. Then, to the suspension, was added all at once $HCOONH_4$ (25 mmol) and the mixture was still stirred under ultrasonic conditions for 50–100 min at 25–30 °C (controlled by adding ice to the water bath). When the starting aromatic nitro compound had completely reacted (monitored by TLC), the suspension was poured into ice water and extracted with dichloromethane (4 × 150 mL). The extract was washed with brine and dried over anhydrous Na_2SO_4. Then, it was concentrated under reduced pressure and a temperature never exceeding 15 °C to give the corresponding *N*-arylhydroxylamine.

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