Zinc-Catalyzed Ammonium Formate Reductions: Reduction of Nitro Compounds

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Abstract

Aliphatic and aromatic nitro compounds are selectively and rapidly reduced to their corresponding amino derivatives in good yields using Ammonium Formate and commercial Zinc dust. This system is found to be compatible with several sensitive functionalities including halogens, -OH, -OCH_3, -CHO, -$COCH_3$, COC_6H_5, -COOH, -$CO_2C_6H_5$, -$CONH_2$, -CN, -CH=CHCOOH, -$NHCOCH_3$. The reduction can be carried out not only with $HCOONH_4$ but also with HCOOH.

TABLE 1. Zinc catalyzed reduction of nitro compounds

Nitro compound	**Reaction Time (minutes)**		Yield[a]
	$HCOONH_4$	**HCOOH**	
Nitromethane	2	2	45%[b,c]
Nitroethane	5	7	50%[b,c]
1-Nitropropane	5	7	55%[c]
1-Nitrobutane	2	4	60%[c]
1-Nitroethylethanoate	5	5	65%
4-Nitromethylbutanoate	5	7	80%

Nitrobenzene	8	10	90%[d]
o,m,p-Nitrophenol	3-5	3-5	92-93%
2,4-Dinitrophenol	5	5	92%
o,m,p-Nitrotoluene	3-5	3-5	89-91%[d]
2,4-Dinitrotoluene	5	5	90%
o,m-Dinitrobenzene	4-6	4-6	90-91%
o,p-Nitrobenzaldehyde	8-10	10-15	89-90%
o,p-Nitroacetophenone	8-10	10-15	92-93%
p-Nitrobenzophenone	10	10	92%
p-Nitrobenzamide	8	10	90%
p-Nitrophenylacetate	5	5	91%[e]
o,m,p-Nitrobenzoic acid	3-5	5-6	93-94%
o,m,p-Nitrochlorobenzene	5-6	5-6	94-95%
o,m,p-Nitrobromobenzene	5-6	5-6	91-92%
p-Nitroiodobenzene	5	5	89%
p-Nitrocinnamic acid	5	7	90%
p-Nitrobenzonitrile	10	15	93%
p-Nitrophenylacetonitrile	10	15	93%
p-Nitrophenylethylalcohol	15	20	90%
3,5-Dinitrosalicylic acid	6	6	89%
p-Nitroacetanilide	5	5	90%

Notes:
a) Isolated yields, based on a single experiment and not optimized.
b) The low yield of aliphatic amines is due to their volatility.
c) Isolated as hydrochloride salts.
d) Isolated as benzoyl derivatives.
e) Isolated as acetyl derivative.
d) All nitro groups are transformed to their corresponding amine, with no other functional groups affected.

In this communication we wish to report a selective, rapid and simple reduction of aliphatic and aromatic nitro compounds to the corresponding amino derivatives using commercial zinc dust and ammonium formate at room temperature. This new system reduced a wide variety of nitro compounds directly to the corresponding amines and many functional groups can bee tolerated. When ammonium formate is replace by formic acid the reduction proceeds effectively and the products were obtained in almost comparable yields.

The reduction of nitro group in the presence of activated zinc (pretreated with HCl and throughly washed with

water and ether prior to use) and $HCOONH_4$ or HCOOH was complete in 2-10 min. The course of this reaction was monitored by TLC and IR. The work-up and isolation of the products were easy. Thus all compounds reduced (**Table 1**) by this system were obtained in good yield (90-95%). All products were characterized by comparison of their TLC, IR and melting points with authentic samples.

Thus the reduction of nitro compounds can bee accomplished with commercial zinc dust instead of expensive Pt, Pd etc., without affecting the reduction of any reducible substituents including halogen and carbonyl compounds. The yields were virtually quantitative and analytically pure.

The obvious advantages of the proposed method over previous methods are:

i. Selective reduction of nitro compounds in the presence of other reducible groups like halogens and carbonyls
ii. Ready availability and easy to operate
iii. Rapid reaction
iv. High yields of substituted anilines
v. Avoids strongly acid media
vi. No requirement for pressure apparatus
vii. Less expensive

This procedure will be of general use especially in cases where rapid, mild and selective reduction are required.

Typical Procedure

A suspension of an appropriate nitro compound (5 mmol) and Zn dust (6 mmol) in methanol or in any suitable solvent (5 ml) was stirred with ammonium formate (0.5 g) or 90% HCOOH (2.5 ml) at room temperature. After completion of the reaction (monitored by TLC), the mixture was filtered off. The organic layer was evaporated and the residue dissolved in $CHCl_3$ or ether and washed with saturated NaCl to remove ammonium formate. The organic layer upon evaporation gave the desired amino derivatives.

Barium: Proving the above method

Reduction of 1-(2,4,5-Trimethoxyphenyl)-2-nitropropane to 2,4,5-Trimethoxyamphetamine

3g (11.7 mmol) 1-(2,4,5-trimethoxyphenyl)-2-nitropropane was dissolved in 20ml MeOH containing 2.5g (38.2 mmol) zinc powder (activated by stirring in 20ml 5% aq. HCl for two minutes then washed with 3x50ml water and finally 20ml MeOH). To the stirred mixture 1.9g (30 mmol) ammonium formate was added in one portion. The mixture became warm to the touch within one minute. After 15 minutes the mixture was filtered to remove the residual zinc and the solvent removed by distillation. The residual oil was dissolved in 25ml EtOAc and neutralized with dry HCl in IPA. The solution was heated to 60°C and vacuum applied to remove about 10ml EtOAc. The residual solution was slowly cooled to room temp and the walls of the flask scratched with a glass rod. Crystals begun to grow very quickly and within 1 minute the solution was a thick slurry. The crystals was isolated by filtration, washed with 50ml acetone and dried to constant weight.

Yield: 2.1 grams (8.0 mmol, 68%) of 2,4,5-Trimethoxyamphetamine Hydrochloride (TMA-2·HCl)