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A New Approach for Preparation of Various Phenylethylamines

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Abstract: A new approach for preparation of various substituted phenylethylamines from the corresponding nitro compounds with iron powder and NH_4Cl in 75% aqueous ethanol solution was developed.

Keywords: Phenylethylamines, nitro compounds, reduction, iron powder.

Phenylethylamines are important intermediates for many biologically active compounds. As known, phenylethylamines can be obtained by reduction of phenylacetonitrile with Raney nickel or 10% Pd/C[1], it also can be prepared from β-nitro-styrene by hydrogenation under high hydrogen pressure[1]or reduction with $LiAlH_4$ [2], borane with catalytic amount of $NaBH_4$[3] and other methods[4]. However, the limits of all above methods are high cost , high toxicity and the need of autoclave apparatus. Additionally, β−nitro-phenylethanes can be reduced to phenylethylamine by $LiAlH_4$, unfortunately, this method is not very attractive because of its high cost and inconvenient work-up. According to literatures, nitroarenes can be easily reduced into aromatic amines by various methods[5,6,7]. but fewer reagents can reduce aliphatic nitro compounds to the corresponding amines.

In this paper, we would like to report a new method to prepare phenylethylamines from aliphatic nitro compounds **(Scheme 1)**. β-Nitro-styrene was reduced with PBI which formed *in situ* from benzaldehyde and *o*-phenylenediamine, to give β-nitro-phenylethanes in high yield[8] . These nitro compounds were reduced with iron powder and NH_4Cl in aqueous ethanol to give the corresponding phenylethylamines in high yield. To our knowledge, the above approach to prepare phenylethylamine is not reported in the literature yet. The advantages of our system are: the reaction was carried out in mild condition, the starting saturated nitro compounds can be purified by distillation in vacuum and the reagents are considerable cheaper.

*Typical procedure for reduction of **4b**:* 35g (0.12 mol) of **4b** , 34g (0.6 mol) of iron powder and 30g (0.6mol) of NH_4Cl, 120 ml 75% aqueous ethanol were added by turns. The mixture was heated to reflux for 4 h and cooled to 20℃, 20g of Na_2CO_3 was added , stirred for 0.5 h. The sludge was filtered off and the filtrate was evaporated to give brown solid. This solid was dissolved in 100 ml water and extracted with ethyl acetate150×4 ml, after drying, cooled over ice-bath, ethanol solution of hydrochloric acid was added

dropwise to give white precipitate of hydrochloride salt of **4c** . It was recrystalized from ethanol . m.p 173-174℃[9d] . yield 79%.

In conclusion, a convenient method for synthesis of various substituted phenylethylamines *via* the β -nitro-phenylethanes have been developed.

Scheme 1

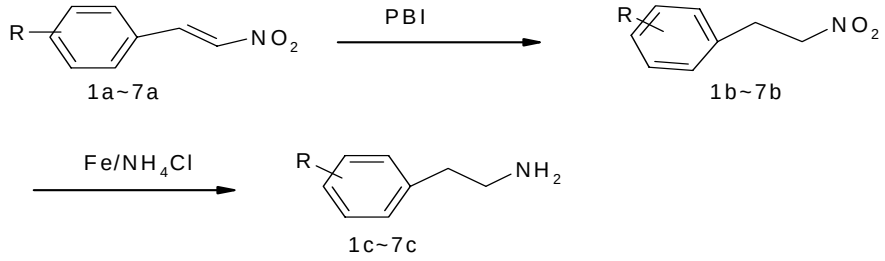

Table 1 The yields of phenylethylamines from the corresponding β -nitro-phenylethanes

Entry	R group	m.p (℃, HCl salt, ethanol)	Yield(%)
1c	3,4-$(CH_3O)_2$	153-154 (154-155)[9a]	85
2c	3,4-OCH_2O	208-210 (210-211)[9a]	82
3c	4-MeO	209-210 (211) [9a]	83
4c	3-MeO-4-$PhCH_2O$	173-174 (173-174)[9d]	79
5c	4-Cl	213-215 (215)[9c]	75
6c	2-Cl	202-203 (204)[9b]	78
7c	2-MeO	140-141 (141)[9a]	80

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