Selective reduction of aromatic nitro groups in the presence of amide functionality

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Pressure mediated selective reduction of aromatic nitro groups in the presence of amide functionality has been achieved by use of hydrazine hydrate.

Keywords: aromatic nitro groups, amide functionality, hydrazine hydrate

Reduction of nitro group is important both for academic research and industrial application. Nitro group can be easily introduced[1,2] into an aromatic ring, and subsequently can be reduced to an amine, which, in turn, can be converted to a host of other compounds such as primary and secondary amines, imine, azo, diazo, amide, phenol, halides and olefins by application of well established chemistry.[3]

Reduction of a nitro group in the presence of amide functionality is a difficult proposition because of the higher reactivity of the latter.[4] Attempts to reduce nitro group in the presence of amide functionality usually result in the formation of diamino compounds. Reducing systems such as catalytic reduction, dissolving metal in an acid or a base, complex metal hydrides cannot be employed for the reduction of aromatic nitro group in the presence of an amide function because all these reagents also reduce amide function to amine. Thus selective reduction of the aromatic nitro group in the presence of amide functionality is highly constrained by limited availability of reagents. Here we report our findings in the selective reduction of aromatic nitro group in the presence of amide functionality by use of hydrazine hydrate.

Hydrazine hydrate is a widely used reducing agent[5,6] and its use in the reduction of aromatic nitro group has been reported[7-11] and reviewed.[12] In all these publications hydrazine as a reducing agent has been used in the presence of catalysts such as iron powder[7], iron (III) oxide hydroxide[8], Raney Ni[9], palladised charcoal[10], graphite[11], *etc.* These reports do not mention the selective reduction of nitro group in the presence of amide functionality. In a recent publication[13] two examples of selective reduction of nitro group in the presence of other functionality, *viz.* nitro group in *p*-nitrobenzaldehyde and *p*-nitroacetanilide, have been reported by use of hydrazine hydrate in the presence of zinc.

All the products shown in Table 1 respond positively to azo dye test thus confirming the presence of aromatic amino group. Proton NMR spectra are in conformity with the structure of the products. Observed melting points of the products are also in conformity with their melting points reported earlier (Table 1). Melting points of *N*-methyl-*m*-aminobenzamide (entry 5) and *N*-benzyl-*p*-aminobenzamide (entry 6) could not be traced in literature. To our knowledge, these two compounds are not yet reported. Spectral (^{1}H NMR and IR) and microanalytical data (for C, H and N) for these two compounds are recorded in the experimental section.

The carbonyl stretching frequency of the parent compounds (nitro compound) varies widely from that of the corresponding products (amino compound). Reductions of the *o*-nitro amides (entries 3, 9, 12 and 15) are invariably slow thus responsible for the low yield as compared to the corresponding *m*- and *p*-nitro compounds. Substantial amount of unreacted starting compounds are recovered in all these cases. Reduction of a few other N-alkyl derivatives of *o*-nitrobenzamide did not yield enough quantity of products for proper characterisation. Low yields in case of *ortho*-nitro compounds can probably be attributed to slow reaction rate due to steric hindrance.

Experimental

All the amides (entries 1 to 9) were prepared from the corresponding acids, and the acetanilides (entries 10 to 12) and benzanilides (entries 13 to 15) were prepared from the corresponding anilines following standard procedures.[14] Reductions were carried out in a medium pressure desk top autoclave made by BERGHOF GmbH, Germany with intake capacity ranging from 75 to 250 ml. Reaction conditions mentioned in the generalised procedure given below were not optimised.

Table 1 Selective reduction of aromatic nitro group in the presence of amide functionality

Entry	Nitro amide	Yield/%	Product*	Melting point/°C	
				Obs.	Lit.[15]
1	*p*-$O_2NC_6H_4CONH_2$	90	Light brown crystals	182	183
2	*m*-$O_2NC_6H_4CONH_2$	83	Light brown crystals	114	115
3	*o*-$O_2NC_6H_4CONH_2$	24	Light brown flakes	110	109–111.5
4	*p*-$O_2NC_6H_4CONHMe$	81	Light yellow crystals	145	143–145
5	*m*-$O_2NC_6H_4CONHMe$	82	Pale yellow crystals	88–90	–
6	*p*-$O_2NC_6H_4CONHBn$	53	Brown crystals	90	–
7	*p*-$O_2NC_6H_4CONHPh$	71	Pale yellow crystals	137–139	138–140
8	*m*-$O_2NC_6H_4CONHPh$	70	Light brown crystal	123–124	124–125
9	*o*-$O_2NC_6H_4CONHPh$	37	Light yellow needles	125	126
10	*p*-$O_2NC_6H_4NHCOCH_3$	59	Grey needles	163–165	165–167
11	*m*-$O_2NC_6H_4NHCOCH_3$	59	Brown needles	85	86.5–87.5
12	*o*-$O_2NC_6H_4NHCOCH_3$	38	Yellowish brown crystals	130	132
13	*p*-$O_2NC_6H_4NHCOPh$	61	Brownish yellow crystals	129	129
14	*m*-$O_2NC_6H_4NHCOPh$	64	Grey crystals	123	125
15	*o*-$O_2NC_6H_4NHCOPh$	39	Light brown crystals	148	150

* The product is the corresponding amine resulting from the reduction of the nitro group.

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Calculated quantities of nitro compounds (3 mmol), 26 ml of ethanol (90%), and 13 ml of hydrazine hydrate (80%) were introduced into a PTFE-liner. The liner was placed into the autoclave, the autoclave was closed and it was then purged with nitrogen. 0.5 MPa of nitrogen pressure was then applied from N_2-cylinder and the temperature of the reaction mixture was raised to 150 °C. The autoclave was maintained at this temperature for 4 h while the reaction mixture inside was stirred the whole time. During this period maximum reaction pressure recorded was 1.8 MPa. After 4 h the autoclave was allowed to cool down to room temperature, and the reaction mixture was made strongly alkaline with 1N sodium hydroxide solution (10 ml). The alkaline mixture was extracted with diethyl ether (3×25 ml). From the organic phase the product was separated from the starting material by acid–base extraction process. The purity of the products and their identity were ascertained by ^{1}H NMR, IR, melting point and elemental analysis.

N-Methyl-m-aminobenzamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ : 2.95 (d, ^3J = 4.8 Hz, 3H, NMe), 3.5 (broad s, 2H, NH_2), 6.28 (broad and unresolved 1H, NH), 6.7–7.2 (complex m, 4H, aromatic). IR (KBr) ν cm^{-1} : 3841, 3743, 3458, 3338, 2949, 1627, 1545. $C_8H_{10}N_2O$ requires C 63.98%, H 6.71%, N 18.65%. Observed C 63.91%, H 6.6%, N 18.59%

N-Benzyl-p-aminobenzamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ : 3.98 (broad s, 2H, NH_2), 4.69 (broad and unresolved 1H, NH), 4.81 (d, ^3J = 4.7 Hz, 2H, CH_2), 6.6–8.3 (complex m, 9H, aromatic). IR (KBr) ν cm^{-1} : 1541, 1635, 3442. $C_{14}H_{14}N_2O$ requires C 74.31%, H 6.24%, N 12.38%. Observed : C 74.11%, H 6.12, N 12.32%

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