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Application of hydrazinium monoformate as new hydrogen donor with Raney nickel: a facile reduction of nitro and nitrile moieties

Shankare Gowda and D. Channe Gowda*

Department of Studies in Chemistry, University of Mysore, Manasagangotri, Mysore, Karnataka 570 006, India

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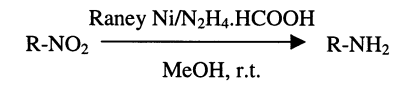
Abstract—The nitro groups in aliphatic and aromatic nitrocompounds also containing reducible substituents such as ethene, acid, phenol, halogen, ester etc., are rapidly reduced at room temperature to corresponding amines by employing hydrazinium monoformate, a new hydrogen donor, in the presence of Raney nickel. It was observed that the nitrile function also undergoes reduction to methylamine ($-CH_2-NH_2$). Hydrazinium monoformate is a more effective donor than hydrazine or formic acid and reduction of nitro and nitrile groups occurs without hydrogenolysis in the presence of low cost Raney nickel, compared to expensive metals like palladium, platinum or ruthenium. The reduction is reasonably fast, clean and high yielding.

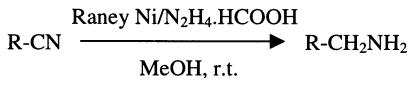
1. Introduction

Rapid and selective reduction of nitrocompounds is of importance for the preparation of amino derivatives in organic synthesis, both practically and industrially, particularly when a molecule has other reducible moieties.[1–4] Numerous new reagents have been developed for the reduction of aromatic nitrocompounds.[5–12] However, little attention has been given to the reduction of aliphatic nitrocompounds,[13–15] which are traditionally reduced by high-pressure catalytic hydrogenation.[10,16,17] Most of the methods, viz., metal/acid reduction,[18] catalytic hydrogenation,[19] electrolytic reduction,[20] homogeneous catalytic transfer hydrogenation,[21] heterogeneous catalytic transfer hydrogenation,[22] etc., are in practice. However, these methods have one or more limitations: (i) metal/acid system lacks selectivity and requires strong acid medium. (ii) Catalytic hydrogenation employs highly diffusible, low molecular weight, flammable hydrogen gas and requires pressure equipment. (iii) Electrolytic reduction requires acidic or alkaline catholite, yields are low and lack practical utility in academic institutions. (iv) Homogeneous catalytic transfer hydrogenation requires expensive complexes as catalysts; work up and isolation of the products are not easy. (v) Heterogeneous catalytic transfer hydrogenation employs expensive bulk or supported metals like palladium, platinum, ruthenium etc., and these supported catalysts require stringent precautions, because of their flammable nature in the presence of air.

Raney nickel is routinely used as a catalyst in the field of catalytic hydrogenation[19,23] as well as in the field of heterogeneous catalytic transfer hydrogenation.[2,12,24–29] It is used for the selective reduction of nitrocompounds, dinitro substituted diphenylsulfones, *O*- and *N*- benzyl containing nitrocompounds, for the conversion of nitro olefins into carbonyl derivatives,[30] and for the synthesis of halo amines from halo nitrocompounds. In all these cases, the commonly used hydrogen donors are hydrazine hydrate, ammonium formate, formic acid and cyclohexene. Further, the use of hydrazine derivatives like methyl hydrazine,[31] unsymmetrical dimethyl hydrazine,[31] phenyl hydrazine,[32] and triethylammonium formate in the presence of various metals are also in practice, but not hydrazinium monoformate.

In this communication, we wish to report a rapid and simple reduction of aliphatic and aromatic nitrocompounds, and nitriles to the corresponding amino derivatives by using Raney nickel and hydrazinium monoformate, a new hydrogen donor, at room temperature (Scheme 1). This new system reduced with ease a wide variety of nitro and nitrile compounds directly to the corresponding amines and many functional groups are tolerated. Hydrazinium monoformate is soluble in solvents like methanol, ethanol,





Scheme 1. R=alkyl or aryl residue substituted with –OH, OR, $-CO_2H$, $-CO_2R$, $-CONH_2$, $-NHCOCH_3$, etc.

Keywords: hydrazinium monoformate; Raney nickel; catalytic transfer hydrogenation; nitrocompounds; nitriles; reduction; new hydrogen donor.

* Corresponding author. Tel.: +91-0821-515525, ext. 48; +91-0821-344348; fax: +91-0821-421263; +91-0821-518835; e-mail: dcgowda@yahoo.com

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tetrahydrofuran, dimethylformamide and glycols. But with solvents like dichloromethane, chloroform, benzene, etc., it forms a biphasic system and in this system, the reactions are rather slow. This system cannot be employed with ketonic and nitrile solvents, as it forms hydrazones with former and reduces the latter.

Our main intention was to reduce nitrocompounds selectively to the corresponding amines. But surprisingly, we observed that this system reduced nitriles to methylamines, unlike the reduction of a nitrile group to methyl group, using 10% Pd–C/$HCOONH_4$.[33,34] In the case of nitro nitriles, the two moieties are reduced to an amino group and a methylamine group, respectively. This system is not helpful to directly obtain an amino carbonyl compound, due to the formation of a hydrazone derivative with the donor. However, the nitro hydrazones are reduced to the corresponding amino hydrazines by this system. Further, hydrazinium monoformate/Raney nickel system is more effective than either triethylammonium formate/5% Pd–C[35] or cyclohexene/10% Pd–C[36] or hydrazine hydrate/Fe(III)[37] and equally compatible with the systems like $HCOONH_4$/10% Pd–C,[1] $HCOONH_4$/5% Pt–C[11] and $HCOONH_4$/Raney Ni.[12] Though ammonium formate is extensively used in the field of catalytic transfer hydrogenation, it is sparingly soluble in solvents such as methanol; but hydrazinium monoformate is freely soluble in 'methanol-like' solvents. Therefore, this system may find its own application in the field of catalytic transfer hydrogenation.

The reduction of nitro aromatic compounds in the presence of Raney nickel and hydrazinium monoformate was complete within 2–10 min. The course of reaction was monitored by thin layer chromatography (t.l.c.) and IR spectra. The work-up and isolation of the products were easy. Thus, all the compounds reduced (Table 1) by this system were obtained in good yields (90–95%). All the products were characterized by comparison of their t.l.c., IR spectra and melting points with authentic samples. A control experiment was carried out using nitrocompounds with hydrazinium monoformate but without Raney nickel, does not yield the desired product. The t.l.c. and IR spectra could not detect any intermediates such as nitroso or hydroxylamine in the reaction mixture after the completion of reaction. Since the reaction is so fast (2 min), the detection of intermediates is not possible. In order to test the selectivity, the reduction was attempted with *p*-dichlorobenzene, *p*-chloro-*m*-cresol, β-naphthol, cinnamic acid, acetanilide, benzoic acid, anisole, phenyl acetate, etc., at laboratory temperature. However, the reaction failed to give any reduced product. Further, it was observed that hydrazinium monoformate is a more effective donor than either hydrazine or formic acid in the presence of Raney nickel. The reduction was completed within 2–6 min with the present system. The methods reported earlier for the reduction of nitro arenes to amino arenes by using Raney nickel and hydrazine requires longer reaction time as long as 2–10 h at reflux temperature[24,26,28,29] and Raney nickel/formic acid system needs 20–30 min for the completion of reduction.[12] Furthermore, both the systems are unable to reduce nitrile function. Thus, the reduction of nitrocompounds and nitriles can be accomplished with Raney nickel instead of expensive platinum, palladium etc., without effecting the reduction of any reducible or

Table 1. Reduction of nitrocompounds and nitriles using hydrazinium monoformate/nickel

Nitro or nitrile compounds.	Reaction time (in min)	Product	Yield[a] (%)	Melting point (°C)	
				Found	Lit.
m-Nitrophenol	2	*m*-Aminophenol	94	121–123	123[38]
o-Nitrotoluene	3	*o*-Toluidine[b]	93	142–144	144[38]
p-Nitrotoluene	2	*p*-Toluidine	94	44–45	45[38]
α-Nitronaphthalene	2	α-Naphthylamine	92	50–51	50[38]
p-Nitroanisole	2	*p*-Anisidine	95	56–57	57[38]
m-Nitroaniline	3	*m*-Phenylenediamine	94	64–65	64[38]
m-Nitrobenzyl alcohol	3	*m*-Aminobenzyl alcohol	91	96–98	97[38]
p-Nitrobenzamide	3	*p*-Aminobenzamide	92	115–116	114[38]
p-Nitrophenyl acetate	3	*p*-Aminophenylacetate[c]	93	148–151	150[38]
m-Nitrobenzoic acid	3	*m*-Aminobenzoic acid	94	174–176	174[38]
m-Nitrochloro benzene	3	*m*-Chloroaniline[b]	92	120–123	122[38]
m-Nitrobromo benzene	3	*m*-Bromoaniline[b]	94	118–121	120[38]
p-Nitrocinnamic acid	3	*p*-Aminocinnamic acid[d]	90	265–268	265-270[39]
p-Nitroacetanilide	3	*p*-Aminoacetanilide	93	163–165	163[38]
Nitromethane	2	Methylamine[d]	80	230–233	232–234[39]
Nitroethane	2	Ethylamine[d]	81	106–108	107–108[39]
1-Nitropropane	2	1-Aminopropane[d]	84	158–160	160–162[39]
1-Nitrobutane	3	1-Aminobutane	75	78–80[e]	78[38]
Acetonitrile	3	Ethylamine[d]	75	106–108	105–106[39]
Propiononitrile	3	*n*-Propylamine[d]	76	158–160	159–160[39]
Benzonitrile	5	Benzylamine[b]	80	105–108	105[38]
Phenylacetonitrile	5	2-Phenylethylamine[b]	80	115–118	116[38]
p-Chlorobenzonitrile	6	*p*-Chlorobenzylamine	70	88–90	90[38]
m-Methoxybenzonitrile	6	*m*-Methoxybenzylamine	72	110–112	110[38]

[a] Isolated yields are based on single a experiment and the yields were not optimised.
[b] Isolated as benzoyl derivative.
[c] Isolated as acetyl derivative.
[d] Isolated as hydrochloride salt.
[e] Boiling point at 710 mm.

hydrogenolysable substituents except the nitrile group. The yields are virtually quantitative and the compounds obtained are analytically pure. The obvious advantages of the proposed method over previous methods are: (i) selective reduction of nitro and nitrile compounds, in the presence of other reducible or hydrogenolysable groups, (ii) easy to operate, (iii) rapid reduction, (iv) high yields of substituted amines, (v) avoidance of strong acid media, (vi) no requirement for pressure apparatus and (vii) inexpensive. This procedure will therefore be of general use, especially in the cases where rapid, mild and selective reduction is required. Further investigations of other useful applications related to the deblocking of protecting groups in peptide synthesis are in progress.

2. Experimental

Hydrazinium monoformate was prepared by slowly neutralizing equal moles of hydrazine hydrate and 85% formic acid in an ice water bath, with constant stirring. The hydrazinium monoformate solution thus obtained was used as such for reduction. A suspension of an appropriate nitrocompound or nitrile (5 mmol) and Raney nickel (100 mg) in methanol or in any suitable solvent (3 mL) was stirred under nitrogen atmosphere with hydrazinium monoformate (2 mL), at room temperature. The reaction was exothermic and effervescent. After the completion of reaction (monitored by t.l.c.), the reaction mixture was filtered through celite. The organic layer was evaporated and the residue was dissolved in chloroform or dichloromethane or ether was washed with saturated sodium chloride solution to remove excess of hydrazinium monoformate. The organic layer after drying and evaporation gave the desired amino derivative.

In order to get a good yield of volatile aliphatic amines, the reaction was carried out by controlled addition of hydrazinium monoformate, through the top of a condenser circulated with ice water and by immersing the reaction flask in a cold-water bath. After filtration, the whole reaction mixture was neutralized with HCl. The solvent was evaporated under reduced pressure. The residue was lyophilized or subjected to column chromatography. Aliphatic amines were obtained as their hydrochloride salts up to 80% yield.

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