



Reduction of Carboxylic Acids to Alcohols Using Phosphonitrilic Chloride And Borohydride Exchange Resin

Jitendra S. Pulle,*¹ Sanjeev M. Reddy²

¹Department of Chemistry, S.G.B. College, Purna (Jn.), Dist. Parbhani (M.S.), India

²Department of Chemistry, G.M.V. Kotgyl, Dist. Nanded (M.S.) India.

Abstract

The aliphatic carboxylic acids were reduced selectively to corresponding alcohols by activation with Phosphonitrilic chloride (PNT) and subsequently reduced using borohydride exchange resin (BER) as reducing agents under mild conditions. BER was found to be mild and selective reducing agent.

Key words: Phosphonitrilic chloride, borohydride exchange resin, reduction, carboxylic acids, alcohols.

1. Introduction

In organic synthesis, reduction of organic compounds is one of the most important fields of research. In 1874, von Wilde carried out the first catalytic hydrogenation reaction in which ethylene and acetylene were reduced to ethane in presence of platinum block.¹ The most commonly used catalysts for the reduction reactions are platinum, palladium, rhodium, ruthenium, nickel, Raney nickel etc. In organic synthesis, one of the most significant conversions is the reduction of carboxylic acid to alcohols as alcohols are used as precursors for large number of organic compounds. Therefore number of methods were developed.²⁻¹² Carboxylic acids were reduced to corresponding alcohols using metal hydrides such as lithium aluminum hydride,¹³ lithium trimethoxyaluminum hydride,¹⁴ aluminum hydride,¹⁵ mixed hydride,¹⁶ etc.

Polymer supported reagent have significant interest because of their potential use in various organic reactions such as

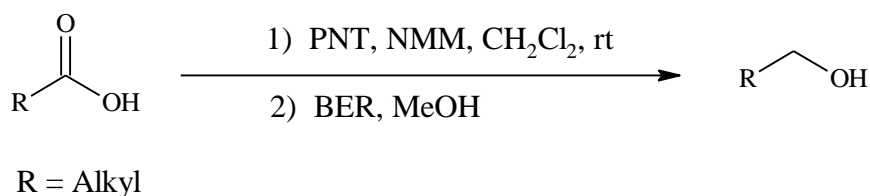
substitution, oxidation and reduction reactions.¹⁷ In 1961, polymer bound borohydride was first reported^{18,19} while the first borohydride supported on ion exchange polymer was published in 1977 by Gibson and Bailey.²⁰ Polymer supported borohydride reagents selectively reduces α , β – unsaturated carbonyl compounds to corresponding allylic alcohols.^{20,21} Aldehydes show more reactivity towards BER than ketones and the reagent was found to be highly chemoselective between the carbonyl groups.²²

BER was used selectively in order to reduce aliphatic carboxylic acids to corresponding alcohols.²³ BER was found to be specific reagent for the reduction of aliphatic carboxylic acids at room temperature, low cost and simple isolation procedure and it is recyclable reagent. Various reducing systems were developed using BER in combination with catalysts.²⁴⁻²⁷ however borohydride exchange resin (BER) was found to be useful reducing agents for the conversion of carboxylic acids to alcohols.

In organic transformations it is always important to search and investigate the new catalysts/reagents for the improvement or development of organic transformations. We have successfully investigated TCT/BER²⁸ and PNT/Sodium borohydride²⁹ system for the reduction of carboxylic acids. Phosphonitrilic chloride trimer (PNT) containing six chloride atoms present over the phosphorous atoms of the stable phosphazine ring, which shows more reactivity towards nucleophiles.³⁰ Therefore, PNT was used for the activation of carboxylic acids similar to cyanuric chloride (TCT). It could activate six equivalents of carboxylic acids which is twice than that of TCT. Importantly PNT is less moisture sensitive and non irritating compound, also it

is easy to handle. Therefore, we investigated the activation of carboxylic acids with PNT and subsequent reduction to alcohols by using BER under mild conditions.

In the present work, we developed efficient reducing systems PNT /BER for the reduction of carboxylic acids under mild conditions. Selective reduction of carboxylic acids to corresponding alcohols were also carried out in presence of PNT, NMM, BER in methanol under mild conditions at room temperature (Scheme 1)



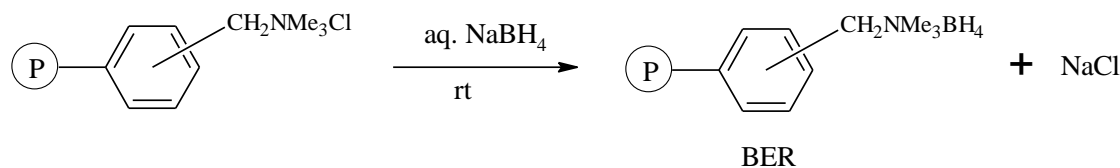
Scheme 1

2. Materials and Methods

1. Preparation of Borohydride Exchange Resin (BER)

An aq. solution of sodium borohydride (0.5 M, 100 ml) was stirred with 10 g wet chloride form resin (Amberlyst A-26 anion exchange resin) for 1 hr. The resin formed, was washed thoroughly with distilled

water until it was free from excess sodium borohydride. The resin was then dried in vacuum at 65 °C for 5 hrs. The dried resin was analyzed for borohydride content by hydrogen evolution on acidification with 0.05 N HCl, the average capacity of BER was found to be 2.5 mmole of BH₄⁻ per gram of resin. The dried resin was stored under nitrogen at room temperature [7] M.



ii) Reduction of carboxylic acids to alcohols using phosphonitrilic chloride and sodium borohydride exchange resin

To a solution of PNT (86.9 mg, 0.25 mmol) in dichloromethane (30 ml) NMM (151 mg, 1.5 mmol) was added at room temperature under stirring. To the suspension, a solution of carboxylic acid (1.5 mmol) in dichloromethane (10 ml) was added. After 3 hrs., BER (1 g) in methanol (15 ml) was added and continued the stirring of heterogeneous mixture for about 1-2 hours at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered to remove BER, dichloromethane and methanol was evaporated under reduced pressure. Diethyl ether was added to this flask. The solution was acidified with HCl (10 %). The organic layer was separated and washed with sodium bicarbonate (10 %) and brine and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give corresponding pure alcohol.

3. Results and discussion

New methods were developed for the reduction of carboxylic acids to corresponding alcohols in good to excellent yields (Table 1). Initially, we found that PNT activates double

equivalents of carboxylic acid compared to TCT. Working with PNT is easier than moisture sensitive and irritating TCT. We used PNT-BER as a reducing system (Scheme 1). In this case PNT activates carboxylic acid and BER being very mild in nature reduces only aliphatic carboxylic acids without reducing aromatic carboxylic acids. At the same time the above system reduces aliphatic carboxylic acids without affecting the olefinic double bond (entry 8) thereby giving excellent yields. Finally we found that PNT-BER system has many advantages over TCT-NaBH₄, ³¹TCT-BER²⁸ and PNT-NaBH₄.²⁹

4. Conclusions

PNT-BER reduces aliphatic carboxylic acids in good to excellent yields at room temperature. PNT activates double equivalent of carboxylic acids compared to TCT thereby reducing half equivalent amount of catalyst loading to the reaction. Whereas PNT in combination with BER is a versatile system gives excellent yields without affecting olefinic substrates under mild conditions.

Table 1: Reduction of carboxylic acids using PNT/BER

Entry	Carboxylic acids	Alcohols	Yield (%)	M.P./B.P [°C] [Lit] ²³
1			95	48-49 [49]
2			94	217-219 [219]
3			93	145-146 [146]
4			94	96-97 [97-98]

5			95	233-235 [235]
6			93	57-58 [56-58]
7			94	229-231 [232]
8			95	248-249 [250]
9		----	----	----
10		----	----	----
11		----	----	----
12		----	----	----
13	 + 		93	217-218 [219]
14	 + 		96	156-157 [158]

15		94	57-58 [59]
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