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Research Article

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Reductive dechlorination of 4-chloro 3-nitro benzotrifluoride with sodium borohydride

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ABSTRACT

Sodium borohydride, when used as a reductive dechlorinating agent for reducing 4-chloro 3- nitro benzotrifluoide to 3-amino benzotrifluoide in the presence of diglyme and triglyme at higher temperature, leads to the formation of reductive dechlorinating compound (free amine) as well as reductive chlorinating compound (chlorinated amine).

Key words: Sodium borohydride, Reductive dechlorination, Diglyme, triglyme

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INTRODUCTION

From the time immemorial, sodium borohydride has been used for the reagent of choice for reducing various carbonyl compounds and acid chlorides in protic solvents. Over the past decades the utility of sodium borohydride has been greatly expanded and various modifications have been developed. Reductive dechlorination of aromatic halo nitro compounds have a great significance in the field of organic synthesis. Reductive dechlorination of various aromatic halo nitro compounds have been synthesized, several reductive dechlorination compounds are used in several pharmaceuticals and as well as fine chemical industries, synthesizing of these variety molecules have a great concern to the organic chemist.

Baltzley and Philips discloses about removal of halogen atoms during catalytic hydrogenation of organic compounds[1]. The hydrogenation of halogen substituted aromatic nitro compounds to the corresponding amines[2], the process being carried out in the presence of a platinum on carbon catalyst and controlled amounts of magnesium oxide or magnesium hydroxide to suppress dehalogenation. The reductive dechlorination of halo nitro aromatic compounds[3], the process has been employed in the presence of platinum catalyst and a cycloaliphatic acid base such as morpholine[10].

Reductive dechlorination[4,5] of aromatic halo nitro compounds[6-9] can be synthesized by using Pd-c or Pt in the presence of hydrogen in a higher yield[11], it requires high pressure, and the handling of pd-c is an issue in terms of safety. Our present invention is about reductive dechlorination of aromatic halonitro compounds to free amines with sodium borohydride in the presence of diglyme or triglyme and synthetic scheme presented in Scheme-I.

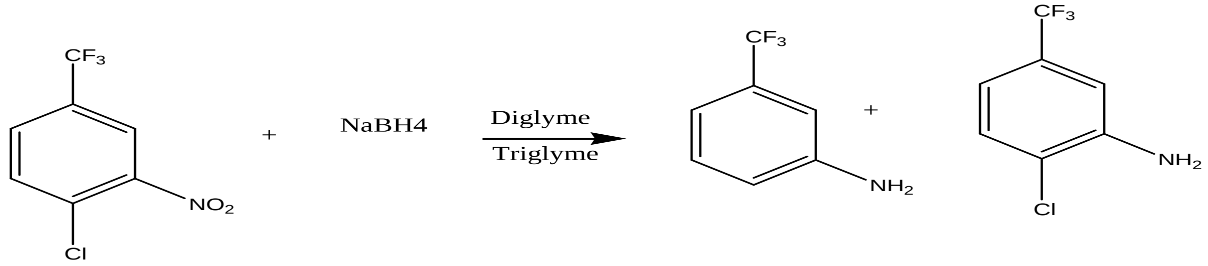
EXPERIMENTAL SECTION

2.1 Reductive dechloination with Diglyme as a solvent:

In a 250ml 4neck RB equipped with condenser and thermopocket, charged 50ml of Diglyme, 10gms of 4-chloro 3-nitro benzotrifluoide (0.04mole), 5gms of Sodium borohydride (0.14mole) is charged at RT. Reaction mass is heated to 160˚C with efficient cooling in condenser , maintained at 160 degree for 12-14 hrs, sample is taken for analysis(GCMS), result of GCMS analysis indicates that 16% conversion of reductive dechlorination product(free amine) and 83% conversion of reductive chlorinated product (chloro amine) is obtained. After 14hrs of maintenance the reaction mass is cooled in to RT and charged water (20ml) at RT, the above reaction mass is extracted with

DCM, the DCM Layer is washed with water three times (3×20ml) for removal of Diglyme, the DCM layer is dried over Sodium Sulphate & concentrated DCM with rotovapour, the crude material contains 17% of free amine and 82% of chloro amine is separated by column chromatography and analyzed by GCMS and NMR Spectra.

SCHEME-I:



Column chromatography :60-120 mesh Silica gel is used for loading the column, mobile phase is Hexane and Ethyl acetate

Procedure:
Crude material is absorbed with silicagel, and charged into the column ,initially column eluted with hexane, slowly increased the polarity of the mobile phase, eluents are monitered by TLC, fractions collected separately, concentrated fractions With rotovapour ,isolated pure material and analysed by G.C.M.S and NMR.

Yield – Reductive dechlorinated amine 14% (Free Amine)
Reductive chlorinated amine 76% (Chlorinated Amine)

2.2Reductive dechloination with Triglyme as a solvent:
In a 250ml 4neck RB equipped with condenser and thermopocket, charged 50ml of Triglyme , 10gms of 4-chloro 3-nitro benzotifluoride (0.04mole) and 5gms of sodium borohydride(0.13mole) at 28-30°C, the reaction mass heated to 200°C, maintained 200°C for 14 hrs, the reaction mass analysed by GCMS, and having the composition of reductive dechlorinated amine(free amine 19%), and chlorinated amine is 77%,the reaction mass cooled to 28-30˚C, 20ml of water is added and extracted with dichloromethane, the DCM layer is washed with plenty of water(3×20ml) , the organic layer dried over Sodium sulphate, concentrated organic layer with rotovapour , the crude product contains 19% of free amine and 77% of chlorinated amine, the crude material is separated by column chromatography and analysed by G.C.M.S and NMR

Yield – Reductive dechlorinated amine 16% (Free Amine)
Reductive chlorinated amine 74% (Chlorinated Amine)

NMR Analysis for free amine: (Reductive dechlorinated product)

^{1}HNMR (400MHZ, $CDCl_3$) : 7.213 (1H, dd), 6.9 (1H, dd), 6.82 (1H, dd), 6.86 (1H, dd), 3.7 (1H,S).

NMR Analysis of chlorinated amine: (Reductive chlorinated product)

^{1}HNMR (400MHZ,$CDCl_3$) :7.280 (1H, dd),7.380 (1H, m),6.629(1H, dd), 4.15(1H,dd).

GCMS Analysis for free amine: (Reductive dechlorinated product): m/e 161.1, m/e 114.0,m/e 91.1,m/e 83.1, m/e 75.0, m/e 65.0,m/e 52.0, m/e 39.1.

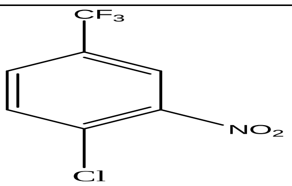
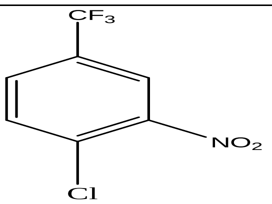
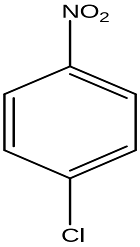
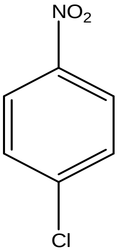
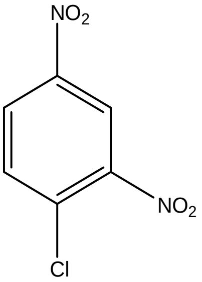
GCMS Analysis for chlorinated amine: (Reductive chlorinated product): m/e 195.0, m/e 176.0, m/e 160.1, m/e 148.0, m/e132.0, m/e 113.0, m/e 99.0, m/e 90.1, m/e 80.0, m/e 63.1, m/e 52.1, m/e 38.0 .

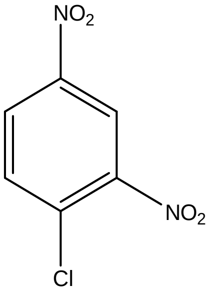
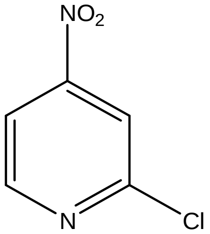
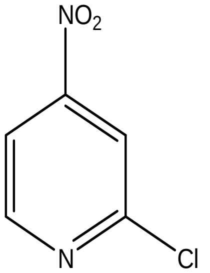
Reductive dechlorination is tried with various substrates which contains nitro and halo substituted aromatic compounds, among all we observed the formation of reductive dechlorinated amine is comparatively less and the formation of reductive chlorinated amine is comparatively more, in this research we are highlighting that reduction of nitro compounds as well as dechlorination is attaining at the same time in single step. Now our concern is how to convert reductive chlorinated amines in to reductive dechlorinated amine.

RESULTS AND DISCUSSION

Reductive dechlorination normally happens in presence of Pd-c, Pt-c and Raney Ni in presence of hydrogen, handling of these reagents requires high pressure for conversion of products. Sodium borohydride is enhanced reagent than other reagents in terms of safety and other issues. Reductive dechlorination with Sodium borohydride is giving lesser yield, we tried to increase the yield of dechlorinated amine by using the various solvents such as Diglyme, and triglyme. When using the high boiler solvents the formation of dechlorinated amine is faintly increased, but chlorinated amine formation is more, when increasing the reaction temp the formation of dechlorinated product is also slightly increased, but we are not able to convert the chlorinated amine into the dechlorinated amine by maintaining the reaction temp with several hours. At one point of time reaction is not in progress, maximum 22% of dechlorinated amine is obtained and 72% of chlorinated amine is obtained, we increased the Sodium borohydride quantity also (9eqs) concluded no further improvement in the reaction. Reductive dechlorination is happening with sodium borohydride with less conversion and lesser yield.

Table 1 Reductive dechlorination with various substrates:

S.NO	Substrate	Reagent	Solvent	Temp˚C	Yield
01		Sodium boohydride	Diglme	160-170˚C	Reductive dechlorinated amine-14% Reductive chlorinated amine 76%
02		Sodium boohydride	Triglyme	200-210˚C	Reductive dechlorinated amine-16% Reductive chlorinated amine 74%
03		Sodium boohydride	Diglyme	160-170˚C	Reductive dechlorinated amine 12% Reductive chlorinated amine 76%
04		Sodium boohydride	Triglyme	200-210˚C	Reductive dechlorinated amine 14% Reductive chlorinated amine 74%
05.		Sodium borohydride	Diglyme	160-170˚C	Reductive dechlorinated amine 13% Reductive chlorinated amine 75%

06		Sodium borohydride	Triglyme	200-210˚C	Reductive dechlorinated amine 14% Reductive chlorinated amine 74%
07		Sodium borohydride	Diglyme	160-170˚C	Reductive dechlorinated amine 12% Reductive chlorinatedamine76%
08		Sodium borohydride	Triglyme	200-210˚C	Reductive dechlorinated amine 14% Reductive chlorinated amine 75%

Reductive dechlorination of aromatic halo nitro compounds with sodium borohydide in diglyme and triglyme as a solvent obtained lower yield, but nitro group reduction and dechlorination is attained at same time, when temp is increases yield also slightly increased. In triglyme yields are improved slightly than diglyme.

CONCLUSION

In the part of our work we also tried with various reducing agents like zinc and acetic acid, zinc and ammonium chloride solution, iron and Hcl solution, iron and acetic acid solution, out of these experiments, nitro group reduction is in progressing well, dechlorination is not happening. Reductive dechlorination with pd-c in presence of hydrogen in protic solvent like ethanol and methanol is progressing well and we achieved good yield, but the process with pd-c in presence of hydrogen is well known and its reported, finally we choosen Sodium borohydride as reductive dechlorinating agent.

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