A SIMPLE AND CONVENIENT PROTOCOL FOR THE SELECTIVE MONO DEBENZYLATION OF DIBENZYLAMINES USING 10% Pd/C AND HCOONH₄

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ABSTRACT

Simple and practical method for partial debenzylation of a dibenzylamine to corresponding monobenzylamine have been achieved by catalytic transfer hydrogenation employing 10% palladium on carbon as catalyst and ammonium formate as hydrogen source.

Keywords: Debenzylation, Catalytic Transfer Hydrogenation, Ammonium formate

INTRODUCTION

The benzyl group is commonly employed for the protection of amino and hydroxyl groups. The simple and practical method for partial debenzylation of a dibenzylamine to corresponding monobenzylamine resulting N-benzyl amines are key component in peptides synthesis and general organic synthesis. This N-benzyl group has found wide application in synthesis because of its remarkable stability towards acidic and basic conditions. Many other functional groups can be easily deprotected keeping the benzyl group intact. Monobenzyl amine has got wide scope in the synthesis of asymmetric N-substituted amines, peptide mimetic and homochiral β-amino acid derivatives over the dibenzyl amines which have valuable the racemic amines.

Generally dibenzyl amines were prepared by alkylation of amine with excess of benzyl halide. Monobenzylated amines are obtained by either one of the methods; direct alkylation of amine with benzyl halide, most commonly benzyl bromide or benzyl chloride and the other method involves the formation of a Schiff base followed by reduction with a hydride or catalytic hydrogenation. These Schiff bases may also be reduced using Zn reagents. Both the methods suffer from drawbacks such as, direct alkylation yields mixture of mono, dibenzylated and esterified products. On the other hand, condensation and reduction requires additional workup and involve expensive reagents or a special apparatus.

Application of catalytic transfer hydrogenation has increased in recent years. Large number of functional groups are reduced using variety of hydrogen donors such as Cyclohexene, Ammonium formate, Formic acid, 1,4-Cyclohexadiene, and Hydrazine. Debenzylation of N-benzyl amine derivatives by catalytic transfer hydrogenation to corresponding amines under drastic condition also are reported in literature. Partial debenzylation of tertiary and dibenzyl amines can also be achieved by oxidising agent such as ceric ammonium nitrate.

Here we wish to report simple and practical method for partial debenzylation of a dibenzylamine to corresponding monobenzylamine by catalytic transfer hydrogenation using 10% Pd/C as catalyst and ammonium formate as hydrogen donor (Scheme-1).

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\begin{align*}
\text{Bn} & \quad \text{HCOONH}_4 / 10\% \text{Pd-C} \quad \text{RT (10-20 min)} \quad \text{R}^\text{H} \quad \text{Bn}
\end{align*}
\]

Scheme 1: Mono debenzylation of dibenzylamines where R = various substituents as shown in Table-1

MATERIALS AND METHODS

The IR spectra were recorded on Shimadzu FTIR-9300 spectrometer. The melting points were determined by using Thomas-Hoover melting point apparatus and are uncorrected. 1H-NMR spectra were recorded at 400 MHz in DMSO-d₆ and the chemical shifts were reported in ppm (Table 2) using DMSO singlet at 2.5 ppm as the reference. Thin layer chromatography was carried out on silica gel plates obtained by Merck (India). Dibenzyl derivatives were prepared by using established method by Goff and co-worker. All the melting points were matched with reported value (Table 1). All other chemicals were purchased from Sigma-Aldrich chemical company (St. Louis, USA) and Spectrochem, India. All chemicals were used as received without any further purification and the reaction was monitored by TLC, visualized in UV chamber and ethanolic ninhydrin.

General procedure for selective mono debenzylation of dibenzenylamines

The substrate dibenzyl compounds (1 mmol), ammonium formate (3 mmol), 10% Pd/C (100 mg) and methanol (20 mL) were charged in to a 50 ml reactor. Reaction was stirred for 15-20 min at room temperature under nitrogen. After completion of the reaction (monitored by TLC) catalyst was removed by filtration, catalyst was washed with 5ml of methanol. The combined filtrate was concentrated to dryness. Then the residue was stirred with methyl tert- butyl ether and filtered to yield desired product.

RESULTS AND DISCUSSION

The reaction conditions are quite mild (RT) and the reactions are fairly fast (less than 20 min), the yields are also quite good. The products have been isolated in all cases except the entry 1 and 10 by simple filtration of the catalyst followed by concentration. The residue was stirred in methyl tert- butyl ether and again filtered. In the case of entry 1 and 10, the products were purified and isolated by column chromatography. All isolated products were characterized by IR and 1H-NMR spectroscopic techniques. The appearance of a strong absorption band between 3400 and 3200 cm⁻¹ for the –NH group clearly confirms its presence.

A control experiment was carried out using dibenzylamine with ammonium formate, but without palladium carbon catalyst which did not yield the desired product. This clearly indicates the requirement of palladium carbon catalyst to catalyze the reaction. Further, mono debenzylation of dibenzylamine was also attempted with palladium carbon and methanol but without ammonium formate. Even after long duration we could not obtain any debenzylated product. This confirms that methanol serves only as solvent and not as hydrogen source.
CONCLUSION

In summary, we have developed a method to selective mono debenzylation of dibenzylation amines using ammonium formate as hydrogen source and palladium carbon as catalyst, under normal laboratory condition. The major advantages of this method are clean work up, catalyst recovery and high yield.

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REFERENCES


