



Catalytic Acylation of *p*-Toluidine with Acetic Acid and Mercuration Reaction

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ABSTRACT

An easiest and environmentally friendly N-Acylation reaction is reported. In this reaction an effective N-C bond forming reaction takes place to give primary amides, in which primary amines was treated with acetic acid in presence of metal free catalyst benzophenone. The probable mechanism and mercuration reaction with acetamide was discussed.

Keywords: environment friendly; N-Acylation; amides; mercuration; metal free catalyst

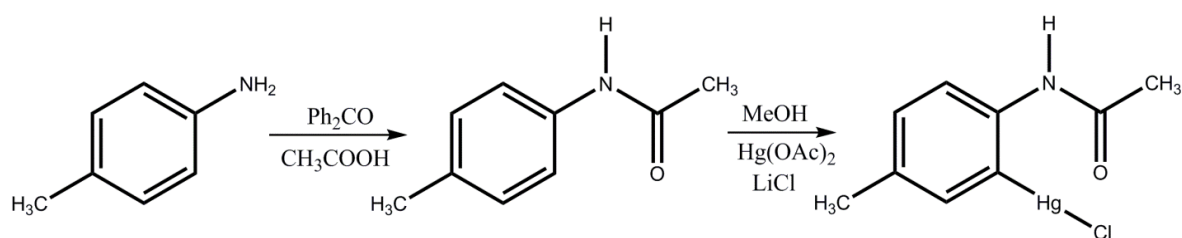
I. INTRODUCTION

Amide derivatives have attracted much attention of researchers due to their widespread applications in the pharmaceutical industry. Amide group are commonly employed as a protective group in synthetic methodology [1,2]. The amide bond generally can be developed through the treatment of primary amines with acyl halides [3], acid anhydrides [4], esters [5] and acids [6] in different conditions. In 2008 Wang and co-workers has reported a simple, convenient, and efficient synthetic method for amides using primary amine and acetic acid/benzoic acid under microwave irradiation in good to excellent yield [7]. Recently Sharley and Williams has developed a cheap and easiest method for acylation of a variety of amines. In this reaction acetic acid was used as catalyst and ethyl acetate/butyl acetate as the acyl source [8]. In 2009 Brahmachari et al. reported that the zinc acetate alone can act as a selective N-acetylation agent without any solvent under closed vessels microwave irradiation [9]. However all these procedure have several limitations. Hence, development of novel and environmental friendly methodologies using organic catalyst is still required for its usefulness in synthetic chemistry. On the basis of these backgrounds, we are reported here an easiest and environment friendly N-acylation reaction between *p*-toluidine and acetic acid is in presence of metal free catalyst benzophenone. Finally we also discussed its probable mechanism and mercuration reaction with N-(*p*-tolyl)acetamide.

II. RESULT AND DISCUSSION

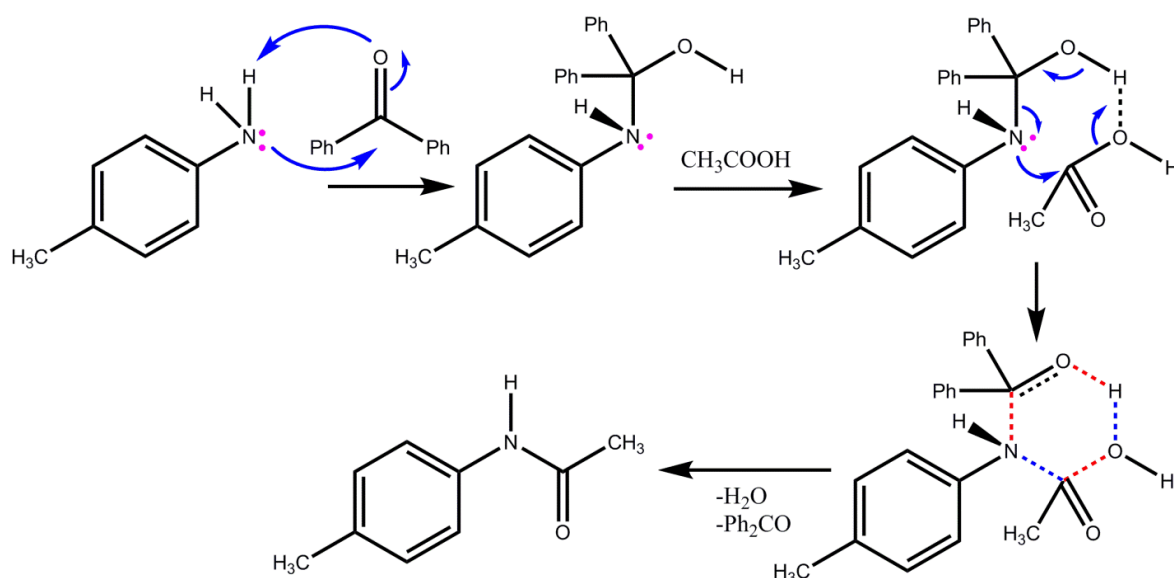
During the experiment *p*-toluidine was treated with acetic acid in presence of benzophenone at 80° C for 12 h. Reaction mixture after 12 h allow cooling to room temperature and poured in distilled water. The organic

phase was extracted with ether and dried over sodium sulphate. The ether solution was evaporate to give a off white colour crystalline solid of *N*-(*p*-tolyl)acetamide in excellent yield. The isolated solid was characterized with the help of melting point (149-150 °C) and ¹H NMR spectrum. (**Figure 1**) In proton NMR spectra of *N*-(*p*-tolyl)acetamide shows two sets of singlet at 2.12 and 2.29 ppm for *p*-methyl and acetyl group respectively. In aryl region we can see a two set of double-doublet of aryl proton at 7.10-7.07 & 7.35-7.38 ppm (for four aryl proton) with coupling constant 2.8 Hz. Along with theses a broad singlet was observed at 7.71 ppm for NH proton. In next reaction we treated *N*-(*p*-tolyl)acetamide with mercuric acetate followed by lithium chloride to give rise a white crystalline solid of (2-acetamido-5-methylphenyl)mercury(II) chloride in good yield. However this compound was less soluble in common organic solvent but good soluble in polar solvent like DMSO. Its proton spectra was recorded in DMSO-d₆ solvent. (**Figure 2**) In proton spectra again we observed here two sets of singlets at 2.00 and 2.21 ppm for *p*-methyl and acetyl group respectively. In aryl region we can see a two sets of double doublet at 7.06-7.09 and 7.51-7.54 ppm (for two aryl proton) with coupling constant 3 Hz along with these we also get two singlet at 7.18 ppm (for one aryl proton) and 9.66 ppm (for NH proton). These two singlet observed in aryl region confirmed that mercuration reaction takes place in tolyl ring. A probable mechanism was sketched in **Scheme 2** in which benzophenone was act as a catalyst.



Scheme 1 Catalytic acylation of *p*-toluidine and mercuration reaction with *N*-(*p*-tolyl)acetamide.

Mechanism



Scheme 2 Probable mechanism for catalytic acylation of *p*-toluidine

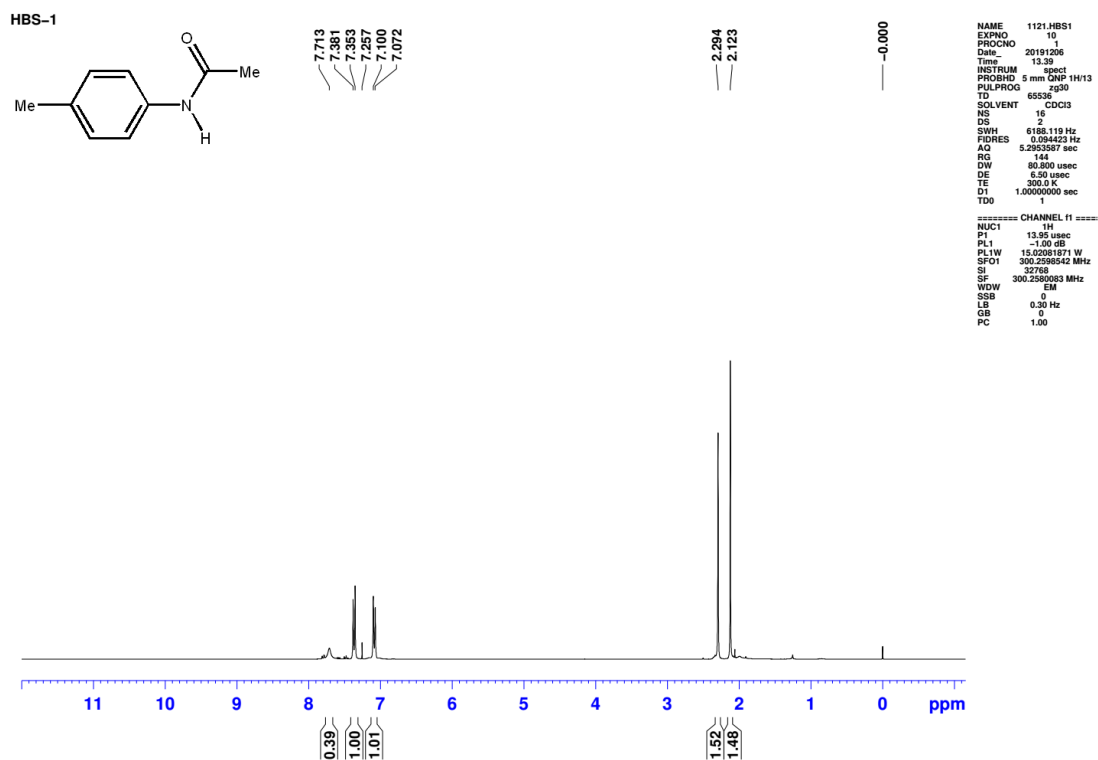


Figure 1 ¹H-NMR spectrum of N-(*p*-tolyl)acetamide in CDCl₃ solvent.

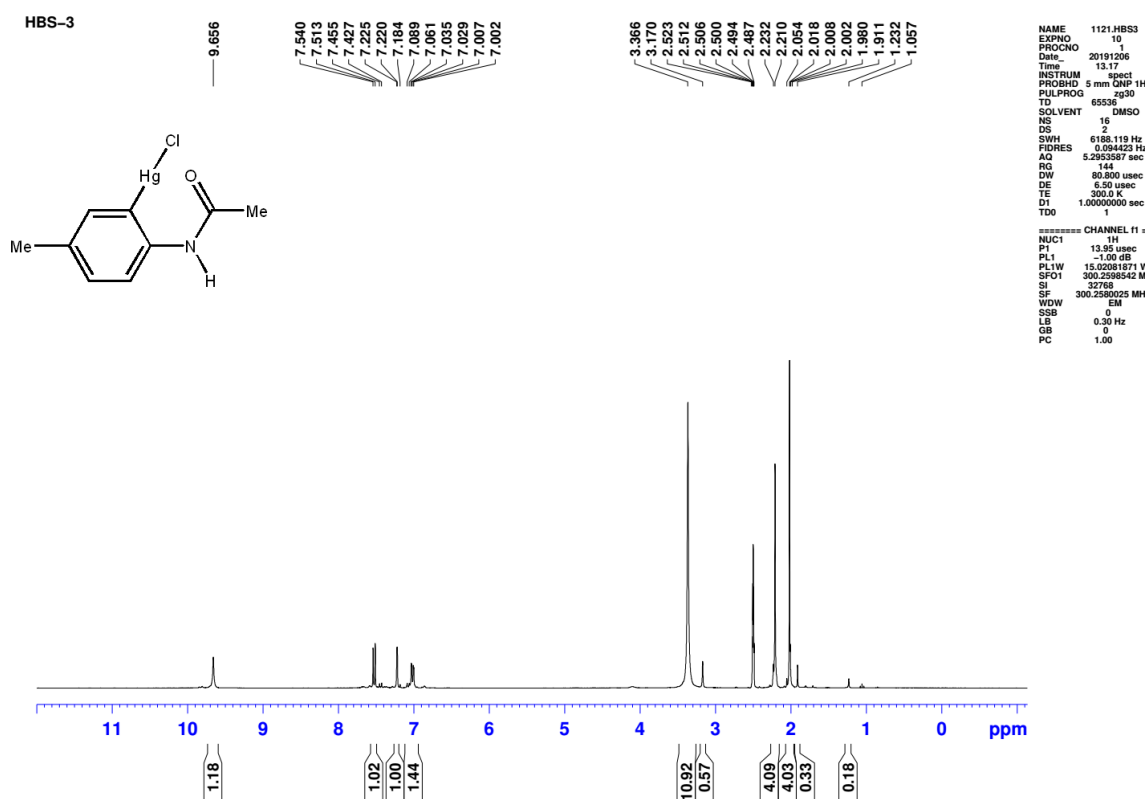


Figure 2 ¹H-NMR spectrum of (2-acetamido-5-methylphenyl)mercury(II) chloride in dmsO-d₆ solvent.

III. EXPERIMENTAL

Melting points were determined with a micromelting-point apparatus. Proton NMR spectra were recorded on a Bruker AMX 300-MHz spectrometer, using CDCl₃ and DMSO-d₆ as solvent. Chemical shifts are reported in parts per million (δ) relative to TMS as an internal standard. *p*-toluidine, benzophenone, Mercuric acetate, Lithium chloride, acetic acid and methanol were purchased from standard sources and purified using literature procedures.

Synthesis of N-(*p*-tolyl)acetamide:

A 50 mL round-bottomed flask was charged with *p*-toluidine (5.35 g, 50 mmol) in acetic acid (50 mL). Under vigorous stirring benzophenone (9.11 g, 50 mmol) was added. The mixture was stirred for 12 h at 80° C. The reaction mixture was allowed cooling to room temperature. For workup reaction mixture was poured in 100 ml distilled water. The organic phase was extracted with ether and dried over sodium sulphate. The ether solution was evaporate to give a off white colour crystalline solid of N-(*p*-tolyl)acetamide in excellent yield. Yield: 7.00 g (94%). Mp. 149-150 °C.

Mercuriation reaction of N-(*p*-tolyl)acetamide:

A 250 mL round-bottomed flask was charged with N-(*p*-tolyl)acetamide (1.49 g, 10 mmol) in methanol (100 mL). Under vigorous stirring mercuric acetate (3.18 g, 10 mmol) was added. The mixture was stirred for 24 h at 80° C. The reaction mixture was allowed cooling to room temperature and added 1 g lithium chloride in the reaction mixture to replace acetate ion with chloride ion afforded white precipitate. The precipitate was filtered and washed with dry methanol to give white powder solid of (2-acetamido-5-methylphenyl)mercury(II) chloride in good yield. Yield: 3.10 g (89%).

IV. CONCLUSION

In conclusion we have reported synthesis characterization of N-(*p*-tolyl)acetamide and (2-acetamido-5-methylphenyl)mercury(II) chloride in excellent yield. Both compounds were characterized with proton NMR spectrum.

V. ACKNOWLEDGMENT

Dr. Puspendra Singh is obliged to the Science and Engineering Research Board, New Delhi, India for Teacher Associateship for Research Excellence Fellowship (Project No.TAR/000075/2021) and heartily grateful to Central Drug Research Institute Lucknow for recording analytical data.

VI. REFERENCES

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