



Studies on N-acetylation of anilines with acetyl chloride using phase transfer catalysts in different solvents

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ABSTRACT

Studies on N-acetylation of anilines with acetyl chloride in the presence of a base like K_2CO_3 and phase transfer catalysts like TBAB, TEAC and D-Glucose in different solvents like DMF, DMSO, acetonitrile, ethyl acetate, chloroform etc at RT have been carried out. Phase Transfer Catalyzed (TBAB) N-acetylation of anilines with acetyl chloride in DMF as solvent and K_2CO_3 as base is considered to be efficient and convenient synthetic methodology.

Keywords: Amines, Acetyl Chloride, phase transfer catalysts.

INTRODUCTION

N-Acetylation of amines is a common important chemical reaction in organic synthesis[1] [2]. Acetic anhydride is commonly used reagent for acetylation of anilines. This reagent bears certain advantages[3][4] as well as some disadvantages[5]. For example, it is a high boiling liquid (=140⁰C), easily distillable under normal atmospheric pressure. However, its use or misuse in manufacture of narcotic drugs like heroin have made it costly and dutiable item. The US Drug Enforcement Administration (USDEA) listed acetic anhydride under list II precursor [6].

Thus, development of an efficient and convenient synthetic methodology in different solvents using acetyl chloride as acetylating agent in the presence of phase transfer catalysts is an important alternate option. In this methodology, N-acetylation of anilines with acetyl chloride requires a base like K_2CO_3 which neutralizes the liberated acid and catalytic amount of PTCs like TBAB, TEAC[7][8] and D- Glucose[9] facilitate the process leading to achievement of high yields.

MATERIALS AND METHODS

Melting points are uncorrected and were obtained in open capillary tubes in sulphuric acid bath. TLC checking was done on plastic sheets coated with silica gel GF-254, supplied by Merck &

Co., and spotting was done using Iodine or UV lamp. IR spectra were recorded using Perkin-Elmer model 1000 instrument in KBr phase.

General Procedure for the synthesis of 2 from 1:

A mixture of the substrate **1** (0.93 g, 10 mmol), K_2CO_3 (2.07 g, 15mmol), catalytic amount of PTC (0.32g, 1mmol) and acetyl chloride (0.71 ml, 10 mmol) in a solvent (20ml) was stirred at room temperature for 10-15 min. After the completion of reaction (as indicated by the disappearance of starting material on TLC) the mixture was poured into crushed ice (20gms). The separated solid was filtered, washed with water (2x 10 ml) and dried. The crude product on recrystallization from aq.methanol gave pure **2**.

2a *M.p* = 113 -114⁰C (*Lit* : 115⁰C.)

2b *M.p* = 153 -154⁰C (*Lit* : 155⁰C.)

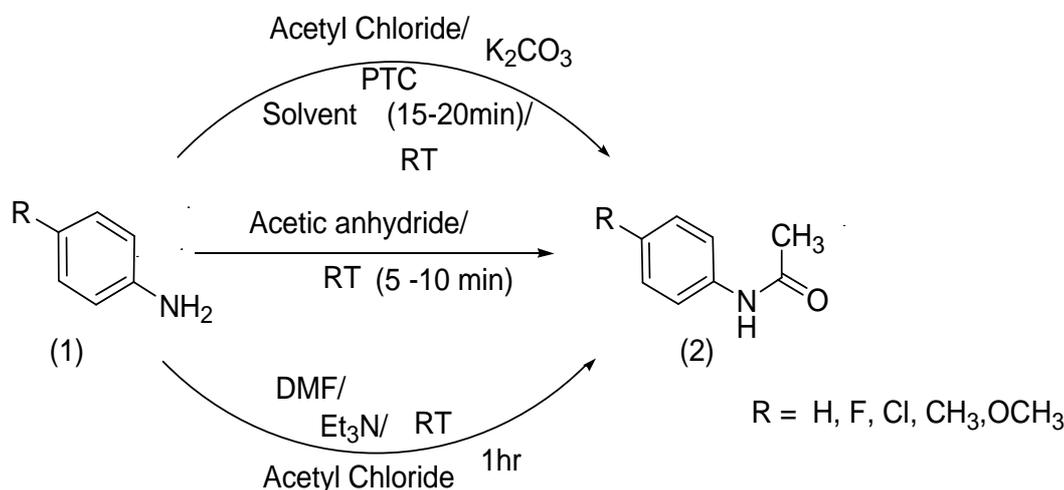
2c *M.p* = 166-168⁰C (*Lit* : 170⁰C.)

2d *M.p* = 148-150⁰C (*Lit* : 151⁰C.)

2e *M.p* = 132-134⁰C (*Lit* : 132⁰C.)

RESULTS AND DISCUSSION

Reaction of aniline (**1**) with acetyl chloride in the presence of base like Et_3N in DMF at room temperature for 60 min gave **2** in moderate yield. When the same reaction was carried out in the presence of a weak base like K_2CO_3 and catalytic amount of phase transfer catalysts (TBAB, TEBAC and D-Glucose) in a suitable solvent at room temperature for 15-30 min, **2** was obtained in high yields (**Scheme**). N-acetylation of anilines with acetyl chloride leads to the production of one equivalent acid, which will form salt with unreacted aniline. The addition of an equivalent of base like K_2CO_3 neutralises the liberated acid and catalytic amount of PTC leads to achieve high yields in shorter period.



PTCs used= TBAB,
TEBAC,
D-Glucose

Solvents used= DMF,
DMSO,
CH₃CN,
CHCl₃,
Ethyl acetate

Scheme

DMF seems to be the best choice among the solvents used for N-acetylation of anilines. The details of the reactions done in different solvents and PTCs are described in **Table-I**. Thus, when acetyl chloride was added to the reaction mixture in the absence of phase transfer catalysts, no acetylation occurred. However, upon addition of phase transfer catalysts to the above reaction media, N-acetylation took place. The optimised N-acetylation reaction was performed by adding (1 equivalent) to the substrate aniline dissolved in different solvents. It is interesting to note that in most of these cases the product precipitates in less than 20 minutes.

In summary, the N-acetylation of substituted anilines with acetyl chloride in different solvents under in the presence of various phase transfer catalysts like TBAB, TEBAC and D-Glucose and K_2CO_3 as base has been studied. The best results are obtained with DMF as solvent, K_2CO_3 as base, TBAB as PTC.

Table-I PhaseTransfer Catalyzed N-acetylation of anilines

S.No	Anilines used	Product Obtained	Solvent Used	PTC Used	Yield (%)
1	1a (R = H)	2a (R = H)	Acetyl Chloride K_2CO_3 , DMF	TBAB	78
				TEBAC	70
				D-Glucose	70
2	1b (R = F)	2b (R = F)	Acetyl Chloride K_2CO_3 , DMSO	TBAB	75
				TEBAC	70
				D-Glucose	70
3	1c (R = Cl)	2c (R = Cl)	Acetyl Chloride K_2CO_3 , $CHCl_3$	TBAB	75
				TEBAC	72
				D-Glucose	72
4	1d (R = Me)	2d (R = Me)	Acetyl Chloride K_2CO_3 , CH_3CN	TBAB	81
				TEBAC	78
				D-Glucose	78
5	1e (R = OMe)	2e (R = OMe)	Acetyl Chloride K_2CO_3 , Ethylacetate	TBAB	60
				TEBAC	55
				D-Glucose	60

CONCLUSION

In conclusion, this method represents Phase Transfer Catalyzed carbon – nitrogen bond formation of anilines with acetyl chloride is considered to be efficient and is convenient synthetic methodology. The notable advantages of this method are rate of reaction carried out in different solvents under various phase transfer catalytic conditions. Acetonitrile and TBAB are the best choice among all the solvents as well as phase transfer catalysts for N-acetylation of anilines.

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