

Comparative Study of Acetylation of Alcohols and Phenols with Different Acetylating Agents Using Zinc Chloride as Catalyst Under Solvent Free Conditions at Room Temperature

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Efficient acetylation of 1°, 2° and 3°, benzylic alcohols and phenols under solvent free conditions at room temperature in presence of less toxic, easily available and in-expensive catalyst ZnCl₂, using acetic anhydride or acetyl chloride as an acetylating agent. On comparative study of these two acetylating agents, the acetyl chloride seemed to be better acetylating agent.

Key Words: Acetylation, Alcohols, Phenols.

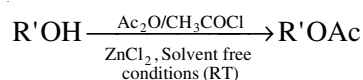
INTRODUCTION

Acetylation of hydroxyl groups is an often used protection technique because of the ease of formation as well as mild conditions for de-protection. Since the hydroxyl groups are present in a number of compounds of biological and synthetic interest, including nucleotides, carbohydrates, steroids and alkaloids *etc.* In general, acylation reactions take place by treatment of alcohols and phenols with hyper active acylating agents such as acetic anhydride or acid chlorides in the presence of tertiary amines such as triethyl amine and pyridine¹. In addition to this various types of catalysts have been used from time to time some of them are: 4-(dimethyl amino) pyridine (DMAP)², COCl₂³, Bu₃P⁴, triflates⁵⁻¹⁰, zeolites¹¹, TaCl₅¹², clays¹³, LiClO₄¹⁴, Mg(ClO₄)₂¹⁵, ionic liquids¹⁶, InCl₃¹⁷, ZrCl₄¹⁸, Cu(BF₄)₂·xH₂O¹⁹, RuCl₃²⁰, P₅O₅/SiO₂²¹, ZrOCl₂·8H₂O²², *p*-toluene sulphonic acid²³, 3-nitrobenzene boronic acid²⁴, alumina²⁵, *etc.*

However use of microwave irradiation technique²⁶ can also brought the acylation reactions. Very recently molecular iodine catalyzed acylation of alcohols has also been reported²⁷.

However, some of these methods are not entirely satisfactory. Triethyl amine and pyridine have unpleasant odours and are not so easy to remove. Tributyl phosphine is an irritant which is highly flammable and expensive and other suffer from low yields of products and long reaction times. Therefore, introduction of new methods and catalysts for the preparation of ester is still in demand.

For the same we choose zinc chloride as catalysts for the acetylation of alcohols and phenols under solvent free conditions using acetic anhydride or acetyl chloride as acylating agents (**Scheme-I**).



where R = aliphatic or aromatic

Scheme-I

EXPERIMENTAL

Melting and boiling points: All boiling and melting points were uncorrected and expressed in °C.

Thin layer chromatography: The thin layer chromatography (TLC) was performed using silica gel 60 F₂₅₄ plates. The spots were made visible by exposing to iodine vapors. Silica gel (230-400 mesh) was used for column chromatography. ¹H NMR spectroscopic analysis was done by using TMS as an internal standard.

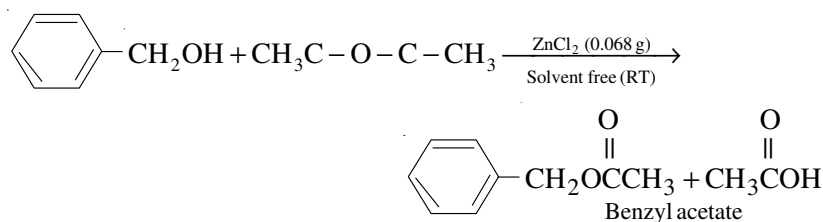
Drying agents: All organic extracts were dried over anhydrous sodium sulphate.

General procedure: To a mixture of ZnCl₂ (dry powder, 0.068 g, 0.5 mmol) and an acid or acid anhydride (1 mmol), alcohol or phenol (1 mmol) was added. The reaction mixture was stirred with magnetic stirrer for a certain period of time as required to complete the reaction (monitored by TLC). The solid mass of ZnCl₂ was then eluted with CH₂Cl₂ (20 mL) and the CH₂Cl₂ extract was then washed with an aqueous solution of sodium bicarbonate and dried over anhydrous sodium sulphate.

Evaporation of solvent furnished, practically pure, the corresponding product. The identity of these compounds was established by comparison of their melting and boiling points and ¹H NMR spectra with those of authentic samples 2).

Preparation of benzyl acetate from acetic anhydride and benzyl alcohol (entry 6, Table-1): To a mixture of ZnCl₂ (dry powder, 0.068 g, 0.5 mmol) and acetic anhydride (1 mmol, 0.094 mL) add benzyl-alcohol (1 mmol, 0.103 mL). The reaction vessel/conical flask was then placed on magnetic stirrer for about 1.5 h, as required to complete the reaction (Monitored by TLC) at room temperature nearly 30 °C, under solvent free conditions.

The solid mass (ZnCl₂) was then eluted with CH₂Cl₂ (20 mL) and the CH₂Cl₂ extract was then washed with aqueous solution of sodium bicarbonate and then dried over anhydrous sodium sulfate evaporation of the solvent furnished practically pure corresponding acetate-benzyl acetate.

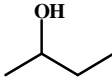
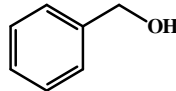
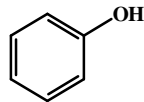
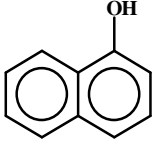


In order to identify our product the boiling point and infrared spectra measured and was then compared to the authentic (actual) sample. The observed boiling point was very much comparable to that of actual.

RESULTS AND DISCUSSION

Using $ZnCl_2$ as a catalyst we have been successful in acylating the 20 or 30 alcohols. The results of various alcohols have been listed in the Table-1: The corresponding acetates are obtained in a handsome quantity both by the use of acetic

TABLE-1

Entry	Substrate	Acetylating reagent	Time (min)	Yield (%)
1	$CH_3CH_2CH_2CH_2CH_2OH$	Ac_2O	120	62
		CH_3COCl	90	68
2	$CH_3CH_2CH_2CH_2OH$	CH_3COCl	90	63
		Ac_2O	55	60
3		Ac_2O	150	55
		CH_3COCl	120	60
4	2-Butanol	CH_3COCl	180	53
5	$CH_3CH_2CH_2OH$	Ac_2O	80	62
		CH_3COCl	50	52
6		Ac_2O	300	65
		CH_3COCl	180	63
7	<i>t</i> -Butanol	Ac_2O	300	58
		CH_3COCl	180	52
8		Ac_2O CH_3COCl	150	40
9	Cyclo hexanol	Ac_2O	300	67
10		Ac_2O	240	59
11	3-Pentanol	Ac_2O	120	61
		CH_3COCl	53	63
12	Isobutanol	Ac_2O	95	65
		CH_3COCl	65	63
13	Isopentanol	Ac_2O	80	55
		CH_3COCl	55	51
14	Cyclopentanol	Ac_2O	150	60
		CH_3COCl	73	65
15	Octanol	Ac_2O	120	61
		CH_3COCl	75	63
16	2-Nitro phenol	Ac_2O CH_3COCl	390	60

anhydride as well as acetyl chloride. But in most of the cases acetyl chloride seemed to be better acylating agent as compared to acetic anhydride. Our catalyst was very much effective in bringing acylation of 20, 30 and also deactivated phenols. The main features of our catalyst is (i) low inexpensive (ii) less toxic, (iii) easily available.

Conclusion

We have presented a mild, simple and efficient protocol for the acetylation of alcohols and phenols under solvent free conditions at room temperature (30 °C). Reaction time of our procedure was very less. 20, 30 alcohols, sterically hindered or deactivated phenols were efficiently acetylated by our procedure. High yield and suppression of by product is reported. Use of inexpensive less toxic easily available catalyst (ZnCl₂) makes our procedure more economical.

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