Environmentally benign un-catalyzed esterification of alcohols under solvent-free condition using acetyl chloride.

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Abstract

A general and practical route for un-catalyzed esterification of alcohols using acetyl chloride is described under solvent free and energy efficient conditions. Excellent yields, wide applicability to various alcohols, mild reaction conditions, short reaction time, ease of operation makes this method economic and environmentally benign.

Keywords: Esterification, un-catalyzed, solvent-free, acetyl chloride, alcohol.

1. Introduction

Functional group protection and deprotection is an important in synthetic organic chemistry (Greene 1991). Amongst protecting groups for alcohols the esters are the most important with acetates being simplest and easiest of all. Ester protests the –OH groups particularly during oxidation, peptide coupling and glycocidation reaction (Greene 1991). Also ester groups are highly important in chemistry and can found in bulk chemicals, fine chemicals, natural products and polymers (Octra 2003). Esters are prepared using transition metal catalyzed cross-coupling reactions which involved the carbonylation of aryl halides (Schoenberg 1974; Brennfuhrer 2009) but presence of halide anion and reaction conditions are not environmentally benign. Another way of synthesis of esters is an oxidative esterification of aldehydes with alcohols (Kovi 2008; Yoo 2007; Yoo 2006; Xu 2010; Wu 2009) using stiochiometric amounts of metal salts like $KHSO_5$(oxome) or MnO_2 as an oxidant (Travis 2003; Maki 2008). Many of the esterification reactions were reported using homogeneous basic catalyst such as amine(Zhdanov 1975), DMAP(Hofle 1978; Scriven 1983), tri-butyl phosphine(Vedejs 1993) or acidic catalyst like p-toluene sulfonic acid(Cope 1963), $COCl_2$(Iqbal 1992), $Sc(OTf)_3$(Ishihara 1996) or $Bi(OTf)_3$(Oriata 2000) with acid chloride or acid anhydride as the acetylating agent. However, the use of homogeneous catalyst possesses several problems such as difficulty in the separation and recovery of the catalyst, disposal of the spent catalyst, corrosion problems. Traditionally esters are prepared by the reaction of activated derivatives like acyl chlorides and acyl anhydride in presence of base(Muzler 1991; Trost 1995). Later modifications involve use of lewis acid (Izumi 1995; Vedejs 1996; Iranpoor 1998; Chandrasekahar 1998; Ganesan 1974) in combination with Ac_2O which is inherently wasteful since half of the every acid anhydride molecule looses as a carboxylic acid. Among the various base catalyst used for esterification of alcohols using acid chlorides, the most common are 1,4-diazobicyclo[2.2.2]-octane (DABCO)(Ishihara 1993; Hajipour 2002), N,N,N,N-tetramethylethylenediamine(TMEDA)(Sano 1999) and NaOH(Volker 1979). Few other catalysts are also reported for these syntheses are Al_2O_3 (Yadav 2001; Paul 2003; Yadav 2004), TiO_2 (Pasha 2008), ZnO (Tamaddon 2005; Sarvari 2005; Tayebee 2010), $ZrOCl_2.8H_2O$(Ghosh 2005), $CeCl_3$(Torregiani 2005), Tl (Taylor 1968), $BiCl_3$ (Ghosh 2004) and $BiFeO_3$ (Farhadi 2009). A catalyst free reaction using acid halides and alcohols has been reported using dichloromethane solvent (Strazzolini 1994). Ranu et.al.(Ranu 2003), reported a solvent free esterification of different alcohols reacted with acetyl or propanoyl chloride. Recently catalyst free condensation of acid chlorides and alcohols has been reported by Christian V. Steven (Stevens 2012) using continuous flow for which microwave technology is required.

Some methods using eco-friendly catalysts i.e. commercial HY Zeolites (Ballini 1998) and montmmorillonite K-10 or KSF clay (Li 1998) for the acylation of alcohols and phenols by acetic anhydride also reported.

However most of these methods still have limitations such as use of catalyst and solvent, high power microwave, harsh reaction conditions, long periods of reaction, use of large amount of organic solvents as the reaction medium and air sensitive nature of catalysts, critical product isolation process of high boiling solvents.

Nowadays, the reactions under catalyst and solvent-free conditions are considerably safe, nontoxic, environmentally friendly and inexpensive.

In continuation of our earlier work (Makone 2010) to the best of our knowledge which was first report on un-catalyzed esterification of alcohols under solvent free and energy efficient conditions starting from acid chloride, here we report novel, un-catalyzed esterification of alcohols using acetyl chloride as an acylating agent under solvent free and energy efficient conditions.

2. Experimental

2.1. General.

All alcohols and acetyl chloride used were commercially available (Sigma Aldrich).Melting point and boiling points were uncorrected and recorded on Veego melting/boiling point apparatus. ^{1}H NMR spectra were recorded on a Bruker Avance II 400MHz spectrometer with TMS as internal standard. IR spectra were determined on a Perkin Elmer Spectrum RX FTIR spectrometer.

2.2. General procedure for esterification of alcohols.

In a 100 ml two-neck round bottom flask a magnetic stir bar and alcohol (10mmol) were placed. To this alcohol acetyl chloride (20mmol) was added slowly through side neck of round bottom flask. To this round bottom flask reflux condenser was attached through which continuously ice cold water is circulated to trap the fumes of HCl generated during the reaction, which gets condensed and dissolved in distilled water to form dil. HCl in the receiver. The reaction mixture was stirred continuously until corresponding esters are formed. For complete conversion of corresponding alcohols into corresponding esters appropriate proportion of acetyl chloride was added (Table 1). The progress of the reaction was monitored by using TLC. The product formed in the round bottom flask was collected by simple distillation and conversion of alcohols to esters was confirmed by taking following confirmative test of ester group.

A little quantity of formed product of ester was taken in a test tube in which 1-2 drops of phenolphthalein was added. To this mixture 5-6 drops of dil. NaOH was added. Then this mixture was heated in water bath. The pink color of the mixture slowly disappears. This confirms the presence of ester group in the product. The authenticity of the products was established by comparing their melting points and spectral data with the literature.

2.3. *Spectral data information*

Ester of Trigol (entry m):

IR in cm^{-1} : 1739 cm^{-1} (for ester group).

^{1}H NMR : 2.01(s, 6H); 3.45 (t, 4H); 3.65 (t, 4H); 4.2 (t, 4H).

Ester of 1,6-Hexanediol(entry i):

IR in cm^{-1} : 1740 cm^{-1} (for ester group).

^{1}H NMR : 1.30 (quintet, 4H); 1.60 (quintet, 4H); 2.01 (s, 6H); 4.08 (t, 4H).

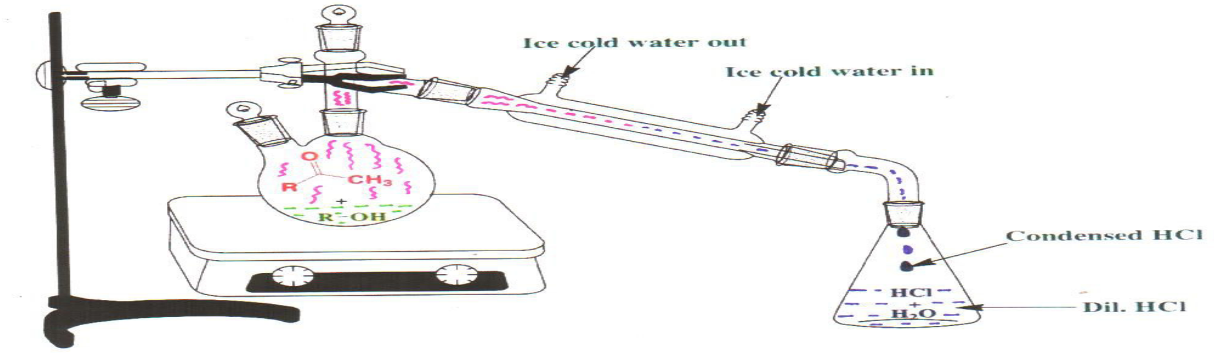
Ester of Glycerol (entry n): IR in cm^{-1} : 1747 cm^{-1} (for ester group)

^{1}H NMR : d 2.01 (s, 9H); 4.32 (d, 4H); 5.20 (quintet, 1H)

3. Result and Discussion

In continuation to our previous work (Makone 2010) as there was no earlier report on the application of acetyl chloride as an acetylating reagent for un-catalyzed esterification of alcohols under solvent free conditions, here we wish to report an efficient and environmentally benign method for the synthesis of an ester from alcohols using acetyl chloride.

In order to study the scope and generality of this method a variety of alcohols were subjected to the esterification using acetyl chloride as an acetylating agent. The reaction was carried out under catalyst free and solvent free conditions using following reaction setup (fig.1).



The representative reaction of un-substituted benzyl alcohol was studied to evaluate the results. In a 100 ml two-neck round bottom flask a magnetic stir bar and benzyl alcohol (10mmol) were placed. To this benzyl alcohol acetyl chloride (10mmol) was added slowly through side neck of round bottom flask. To this round bottom flask reflux condenser was attached through which continuously cold water is circulated to trap the fumes of HCl generated during the reaction. The reaction mixture was stirred for 1hr, completion of reaction was monitored by TLC. It was found that the reaction completes to produce 71% formation of corresponding product. For complete conversion of benzyl alcohol into benzyl acetate the percentage of acetyl chloride was increased (20mmol) and progress of reaction was evaluated. During reaction instead of cold water ice cold water was circulated continuously through reflux condenser (Scheme 1). The maximum conversion of benzyl alcohol in to benzyl acetate was observed when 20mmol of acetyl chloride was added and fumes of generated HCl during the reaction gets condensed when ice cold water was circulated continuously through reflux condenser. The reaction was completed in 1hr to produce 98% yield of the product (Table 1, entry a).

Subsequently, various aliphatic alcohols were reacted with acetyl chloride (Table 1, entry b, c, d) to produce corresponding esters with excellent yields. With increasing number of aliphatic carbon chain of various aliphatic alcohols such as heptanol, octanol, decanol were treated with acetyl chloride using 1:4 proportions under optimized reaction set-up conditions, the reaction proceeded successfully producing high yields of desired esters (Table 1, entry e, f, g). The applicability of this process was the investigated using diol substrates such as 1,4-butanediol and 1,6-hexanediol, the desired esters were formed using acetyl chloride in 1:4 proportion (Scheme 2) producing high yields of desire esters (Table 1, entry h, i).

After successful application of esterification to various alcohols we tried to extend the newly developed protocol to long chain aliphatic diols. When 1,12-dodecanediol was introduced with acetyl chloride in 1:6 proportion desired ester was formed with 95% yield (Table 1, entry j). In addition we also investigate the reactions using trigol and glycerol as a substrates with acetyl chloride in 1:4 and 1:6 proportion to form the corresponding esters of trigol and glycerol with excellent yields (Table 1, entry m, n). The trigol and glycerol smoothly undergo the un-catalyzed esterification under solvent-free conditions.

With these results in hand, we set out to examine the scope of these reactions to phenolic –OH groups using simple un-substituted phenol. When phenol (10mmol) was stirred with acetyl chloride (20mmol) up to 1hr, no reaction was observed. The results are confirmed using 4-hydroxy benzyl alcohol substrate with acetyl chloride. To our surprise when 4-hydroxy benzyl alcohol (10mmol) reacted with acetyl chloride in 1:4 proportion at solvent free conditions only benzylic –OH group underwent conversion of ester and corresponding ester of 4-hydroxy benzyl alcohol is formed with 96% yield (Table 1, entry o), where as phenolic –OH remains intact. The results show that the generality of present protocol is effective for the alcoholic –OH groups present the alcoholic substrates.

4. Conclusion

In summary we have developed an efficient un-catalyzed esterification of alcohols under solvent-free and energy efficient conditions using acetyl chloride. Method is applicable to various aromatic as well as aliphatic alcohols such as benzyl alcohol, diols, trigols, glycerols. This protocol also gives results to propargyl and allyl alcohols to give their corresponding esters in high to excellent yields. The advantages of this methodology, solvent free, catalyst free, energy efficient and environmentally benign conditions, simple work-up procedure and easy separation of the formed HCl will lead to this protocol a green technique for practical organic synthesis. However this method is limited to phenolic –OH group. Efforts are underway to elucidate the scope and limitations of this method to more variety of alcohols.

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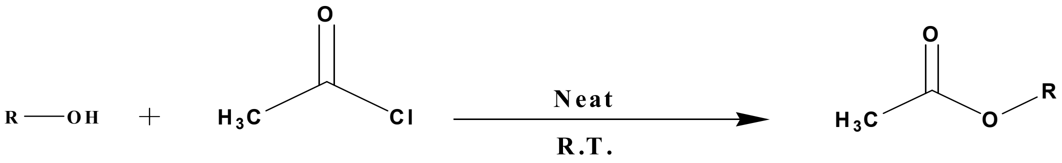
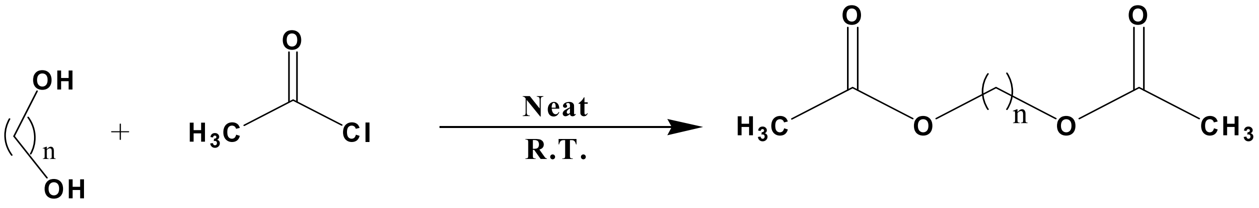


Where, R= Akyl, benzyl groups

Scheme 1



Where n= number of carbon atoms

Scheme 2

Reaction mechanism of the esterification reaction

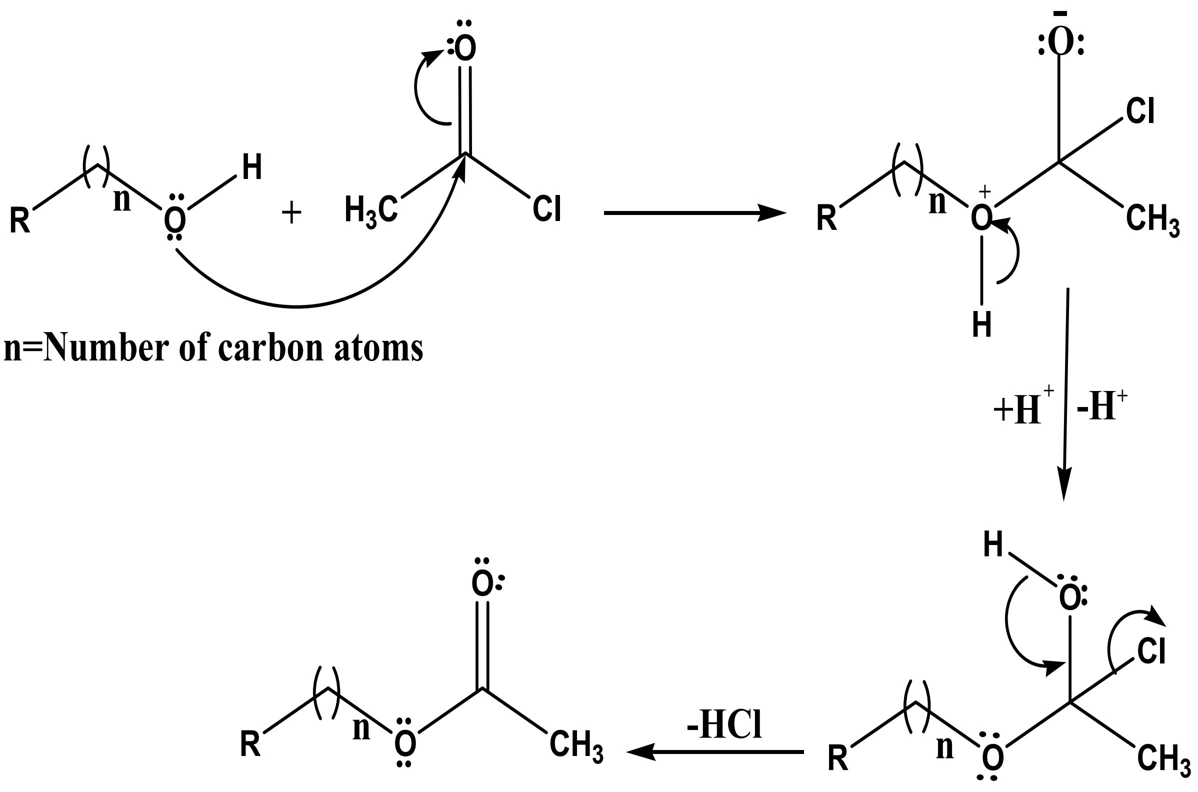


Table 1. Un-catalyzed esterification of alcohols under solvent free and energy efficient conditions.

Entry	R	Alcohols : Acetyl Chloride	Reaction time(hr)	Yield[%][a]
a	$C_6H_5CH_2$	1:2	1	98
b	$CH_3CH_2CH_2$	1:2	1.5	95
c	$CH_3(CH_2)_4$	1:2	1.5	95
d	$CH_3(CH_2)_5$	1:2	1.5	97
e	$CH_3(CH_2)_6$	1:4	2	96
f	$CH_3(CH_2)_7$	1:4	2	96
g	$CH_3(CH_2)_9$	1:4	2.5	95
h	$CH_2(CH_2)_2CH_2$	1:4	2	97
i	$CH_2(CH_2)_4CH_2$	1:4	2	98
j	$CH_2(CH_2)_{10}CH_2$	1:6	2.5	95
k	C_3H_3	1:2	1	96
l	C_3H_5	1:2	1	97
m	$CH_2CH_2OCH_2CH_2OCH_2CH_2$	1:4	1.5	95
n	$CH_2CH(OH)CH_2$	1:6	2	97
o	$4OHC_6H_5CH_2$	1:4	4	96

[a] Yield refer to the pure isolated product.

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