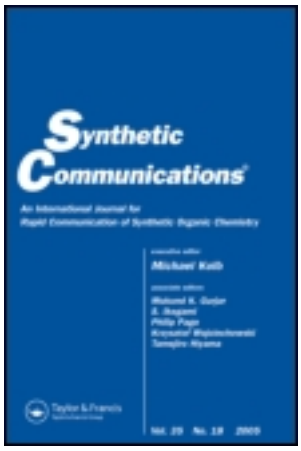

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A SIMPLE AND CONVENIENT ONE-POT SYNTHESIS OF FATTY ACID ESTERS FROM HINDERED ALCOHOLS USING *N*,*N*-DIMETHYLCHLORO-SULFITEMETHANIMINIUM CHLORIDE AS DEHYDRATING AGENT

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ABSTRACT

N,*N*-Dimethylchlorosulfitemethaniminium chloride ($SOCl_2$-DMF) has been found to be an efficient reagent for one-pot synthesis of esters from equimolar amounts of fatty acids and hindered alcohols under mild conditions.

Key Words: Fatty acid esters; Hindered alcohols; *N,N*-Dimethylchlorosulfitemethaniminium chloride

Esterification of alcohols is an important transformation in organic synthesis[1] and a variety of methods have been developed to accomplish it.[2] The classical acid catalyzed esterification methods are of little value for the preparation of esters from sterically hindered alcohols.[3] Acid anhydrides without any catalyst[4] and in the presence of catalysts like *N*,*N*-dimethyl-aminopyridine (DMAP),[5] cobalt (II) chloride,[6,7] magnesium bromide with

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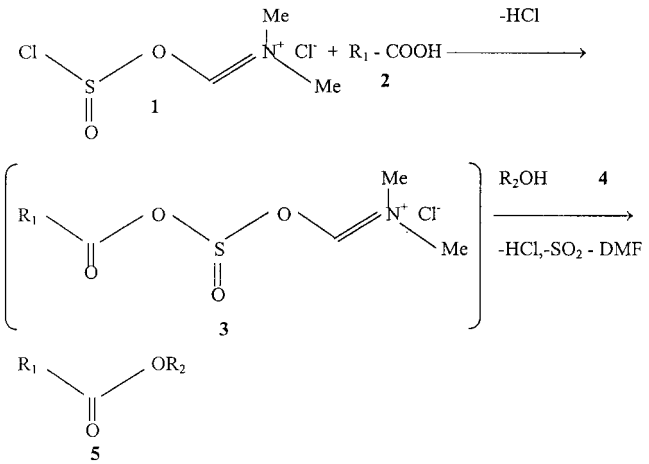
tertiary amines,[8] scandium triflate,[9] trimethylsilyl triflate,[10] indium triflate[11] and bismuth triflate[12] have been extensively used for esterification of hindered alcohols. However, acid anhydride method has limitation for its application in case of acids like fatty acids which do not yield anhydrides easily. Another approach for facile esterification of sterically hindered alcohols has been the use of various type of dehydrating reagents which activates carboxyl group.[1] In this context the use of reagents like *N*-alkyl-2-halopyridinium salts with trialkylamines,[13] di(2-pyridyl) carbonate with DMAP,[14,15] 2-thiopyridyl chloroformate with tertiary amines[16] and *O*,*O*′-di(2-pyridyl) thiocarbonate with DMAP[17–19] has been reported in the literature.

N,*N*-Dimethylchlorosulfitemethaniminium chloride, a versatile dehydrating agent is easily prepared from dimethylformamide and thionyl chloride and has been used for carboxyl group activation in various synthetic transformations.[20–23] However, the literature search indicate that the potential of this reagent for esterification of hindered alcohols has not been exploited.

In connection with one of our ongoing projects we needed a variety of fatty acid esters of hindered alcohols and these could not be prepared by conventional acid catalysed esterification methods. In search of a simple and convenient method we focused our attention on *N*,*N*-dimethylchlorosulfitemethaniminium chloride ($SOCl_2$-DMF) (**1**) due to its easy preparation from readily available reagents, and now report a direct and efficient one-pot procedure for the preparation of esters (**5**) from fatty acids (**2**) and hindered alcohols (**4**) using $SOCl_2$-DMF (**1**) as dehydrating agent (Scheme 1).



Scheme 1.

A variety of hindered primary alcohols (polyols) like dipentaerythritol (Table 1, Entry 1), 1,1,1-trihydroxymethylethane (Table 1, Entry 3), pentaerythritol (Table 1, Entry 5), 2,2-diethyl-1,3-propanediol) (Table 1, Entry 10) and 2-methyl-2-propyl-1,3-propanediol (Table 1, Entry 14) were esterified with C_6–C_{12} fatty acid to give esters in almost quantitative yields with all CH_2OH groups being converted into esters. These results are presented in Table 1.

Similarly a number of different types of hindered secondary alcohols like *end*oborneol (Table 2, Entry 1), isoborneol (Table 2, Entry 3), 4-*tert*-butylcyclohexanol (Table 2, Entry 5) were esterified with C_6–C_8 fatty acids to yield corresponding esters in excellent yields. These results are presented in Table 2.

The protocol developed consist of adding equimolar quantities of *N*,*N*-dimethylchlorosulfitemethaniminium chloride to a suspension of fatty acid in dichloromethane, stirring the mixture for about 15 min, then addition of equivalent quantities of alcohol followed by addition of excess pyridine, stirring the mixture at room temperature for six hours and usual work-up.

The reaction proceed through the formation of activated carboxylic acid species (**3**) which react with the hindered alcohols (**4**) to give carboxylic esters (**5**). As the reactions were conducted at room temperature there is no possibility for the formation of carboxylic acid chlorides.[20]

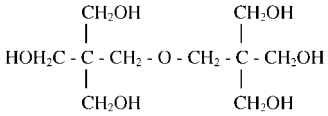
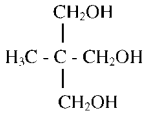
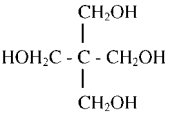
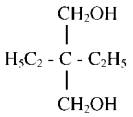
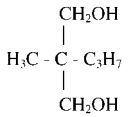
In conclusion, easy preparation of *N*,*N*-dimethylchlorosulfitemethaniminium chloride from readily available and low cost reagents, mild reaction conditions, wide applicability make this method to be simple and convenient for one-pot synthesis of esters from fatty acids and hindered alcohols.

EXPERIMENTAL

N,*N*-Dimethylchlorosulfitemethaniminium chloride was prepared from dimethylformamide and thionyl chloride following the procedure reported by C. Palomo et al.[20]

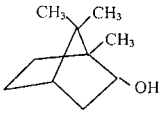
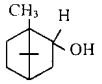
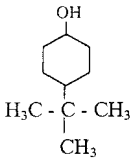
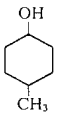
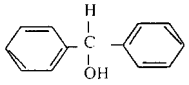
A typical procedure for the preparation of ester from fatty acid and hindered alcohol is as follows: To a solution of hexanoic acid (4.64 g, 40 mmol) in anhydrous dichloromethane (75 mL) was added freshly prepared *N*,*N*-dimethylchlorosulfitemethaniminium chloride (9.6 g, 50 mmol) at 0–5°C. After stirring the mixture at this temperature for 15 min, pentaerythritol (1.36 g, 10 mmol) was added followed by drop wise addition of anhydrous pyridine (12.1 mL, 0.15 mol) in dichloromethane (30 mL). The resulting mixture was stirred at room temperature for 6 h, washed with water (3 × 50 mL), organic layer separated and dried over anhydrous sodium sulphate. Evaporation of the solvent gave pure ester (5.17 g, 98%). Similarly, other

Table 1. Esterification of Hindered Primary Alcohols (Polyols) with Fatty Acids Using *N*,*N*-Dimethylchlorosulfitemethaniminium Chloride

Entry	Alcohol (Polyol)	Fatty Acid	Yield (%)[a]
1		CH_3-$(CH_2)_6$COOH	94
2		CH_3-$(CH_2)_8$COOH	93
3		CH_3-$(CH_2)_4$COOH	96
4		CH_3-$(CH_2)_6$COOH	96
5		CH_3-$(CH_2)_4$COOH	98
6		CH_3-$(CH_2)_6$COOH	97
7		CH_3-$(CH_2)_8$COOH	96
8		CH_3-$(CH_2)_{10}$COOH	96
9		CH_3-$(CH_2)_3$-CH-(C_2H_5)COOH	98
10		CH_3-$(CH_2)_4$COOH	96
11		CH_3-$(CH_2)_6$COOH	95
12		CH_3-$(CH_2)_8$COOH	96
13		CH_3-$(CH_2)_{10}$COOH	96
14		CH_3-$(CH_2)_4$COOH	96
15		CH_3-$(CH_2)_6$COOH	98
16		CH_3-$(CH_2)_8$COOH	96
17		CH_3-$(CH_2)_{10}$COOH	97
18		CH_3-$(CH_2)_3$-CH(C_2H_5)COOH	98

[a]Isolated yields.

Table 2. Esterification of Hindered Secondary Alcohols with Fatty Acids Using *N,N*-Dimethylchlorosulfitemethaniminium Chloride

Entry	Alcohol	Fatty Acid	Yield (%)[a]
1		$CH_3(CH_2)_4COOH$	96
2		$CH_3(CH_2)_6COOH$	93
3		$CH_3(CH_2)_4COOH$	97
4		$CH_3(CH_2)_6COOH$	99
5		$CH_3(CH_2)_4COOH$	97
6		$CH_3(CH_2)_6COOH$	99
7		$CH_3(CH_2)_4COOH$	97
8			97
9		$CH_3(CH_2)_6COOH$	97
10		$CH_3(CH_2)_4COOH$	98
11			97

[a]Isolated yields.

esters were prepared and their yields obtained are shown in Tables 1 and 2. The products were identified by comparing their physical and spectral data with those of authentic compounds reported in the literature.

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