



Efficient Esterification of Carboxylic Acids with Alcohols by Hydrogen Peroxide as a Novel Condensing Agent[†]

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Esterification of carboxylic acids with different alcohols has been achieved in presence of catalyst hydrogen peroxide and sulphuric acid. This method is free from disadvantages of base catalyst and high temperature. Hydrogen peroxide with sulphuric acid increases the yield up to 98 % with minimum side products. Several esters were synthesized by this method by condensing carboxylic acids (1) with alcohols (2) in presence of hydrogen peroxide and sulphuric acid.

Key Words: Esterification, Carboxylic acid, Alcohol, Hydrogen peroxide.

INTRODUCTION

Many esters are known today are either natural or synthetic. Esters have found use in diverse areas of human needs viz., medicine, ointments, foods, preservatives, lacquers, etc. Many of the important esters include the salicylates, which are useful in the preservation of foods, pain control and fever control. They have also been found to inhibit aldose reductase in the lens of the eye and as such they can retard the development of cataracts. Acetyl salicylic acid (aspirin) is an effective analgesic, antipyretic and antiinflammatory drug and it also prevents the aggregation of platelets. Stroke¹, methyl salicylate, a constituent of wintergreen and other plants such as *Amygdalifolia* and *A. hebraeum*², *Lawsonia inermis*³ is another ester used as a local anesthetic agent and disinfectant used commercially in toothpaste, mouthwash, perfumes as well as flavouring agents, methyl salicylate is also useful in synthesis as a generator of reactive intermediates. Similarly, benzocaine, the ethyl ester of *p*-amino benzoic acid widely used as local anesthetic has demonstrated relieve of pain in patients with spontaneous tooth ache from an open tooth cavity⁴.

Several synthetic routes are available for obtaining organic esters, most of which have been briefly reviewed by Yadav and Mehta⁵. The preparation of ester involved lengthy workups and sometimes the products may contain some certain impurities. Several modifications have been under-taken for the preparation of esters in order to minimize lengthy work-ups and to improve yields. One of such methods is reported in

which sulphuric acid⁶ was employed as a catalyst as well as to remove or immobilize the water produced. Using this method, iso octanoic acid was esterified with methanol in the presence of excess sulfuric acid both as catalyst and as desiccants affording 95 % yield of ester⁷.

The most used methodology for ester synthesis is direct esterification of carboxylic acids with alcohols in presence of acids catalysts. Strong mineral acids, such as H₂SO₄, HCl and HI, are effective for the esterification of carboxylic acids. These homogeneous acid catalysts and others have been the subjects of extensive studies. It has been well documented that using this type of catalyst, the slow step of the reaction is the nucleophilic attack of the alcohol on the protonated carbonyl group of the carboxylic acid⁸. This mechanistic route first involves protonation of the carboxylic acids, which activates it for reaction with non protonated methanol to yield a tetrahedral intermediate that, on decomposition, produces the products of reaction, ester and water.

In this paper, we described the new method of synthesis of different esters by using hydrogen peroxide as a catalyst. It involves easy work up, less time, eco friendly side product and improved yield.

EXPERIMENTAL

Methanol (99.9 wt % Merck), benzoic acid, 98 % (Merck); cinnamic acid, 98 % (Merck); salicylic acid, 98 % (Merck); *p*-toullic acid, 98 % (Merck); *p*-nitro benzoic acid, 98 % (Merck); conc. sulphuric acid, 98 % were used without further

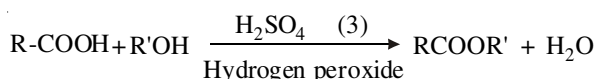
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purification. Hydrogen peroxide 30 % (Merck) (100 mL by volume), was obtained from Upper India Scientific Company.

In a typical experimental procedure the substrate of a carboxylic acid 0.1 mmol was dissolved in methanol (0.3 mmol) and 0.1 M H₂SO₄ was also added drop wise with constant shaking and cooling followed by slow addition of 0.3 M H₂O₂ was added slowly at room temperature. The mixture was refluxed in an oil bath and monitored for completion by TLC. After the completion of reaction it is cooled at room temperature. The product was washed 2-3 times with water and finally with 10 % NaHCO₃ solution followed by again water and dried over anhydrous Na₂SO₄. Product was then confirmed by spectral data.

Detection method: NMR spectra were recorded on a Bruker Avance-II (400 MHz) NMR spectrometer. The chemical shifts (δ) are reported in parts per million (ppm) and *J* values in Hz using CDCl₃ as a solvent for ¹H NMR and TMS as an internal standard. IR spectra were recorded on Shimadzu Dr-8031 FT-IR spectrometer instrument. Mass spectra were determined (LC-MS) making water, model. Q-TOF Micro mass. Elemental analysis was carried out using a Perkin-Elmer, CHN elemental analyzer model 2400.

RESULTS AND DISCUSSION

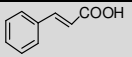
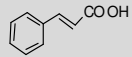
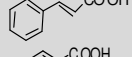
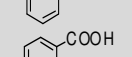
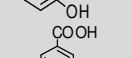
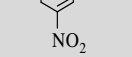
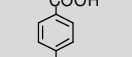
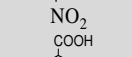


Esterification of carboxylic acids with alcohols using H₂SO₄ in the presence of catalyst hydrogen peroxide gave the corresponding esters in excellent yields (Table-1). According to our preliminary experiment; hydrogen peroxide is more favourable than catalyst enlisted in⁸. Especially, the esterification for aliphatic carboxylic acids^{9,10} (**1a**, **1b**, **1c** and **1d**) and aliphatic alcohols (**2a**, **2b**) using sulfuric acid in absence of hydrogen peroxide was not given the good yield. Primary and secondary alcohol was also esterified in excellent yield with cinnamic acid. (**4a**, **4b**, **4c** in the Table-1) salicylic acid (**4d**, **4e** in Table-1). The reaction of methanol, ethanol and isobutyl alcohol with *p*-nitro benzoic acid (**4f**, **4g**, **4h**) in presence of hydrogen peroxide gave the excellent yield.

Compound **4a** was obtained as colourless white crystalline needle like solid with the formula C₁₀H₁₀O₂ based on HR mass spectrum. The IR spectrum showed carbonyl frequency at 1740 (C=O) cm⁻¹ confirmed the ester group. ¹H NMR spectrum showed a 3H singlet (δ 3.59) indicating the presence of methyl group attached to carboxyl ester group. Additionally two olefinic proton signals were observed at δ 7.53 (d, 1H, *J* = 16.0 Hz) and δ 6.28 (d, 1H, *J* = 16.0 Hz) indicating an E disubstituted double bond. Also two multiplets are observed at δ 7.17 (m, 3H) and δ 7.30 (m, 2H) indicating two different types of aromatic proton).

Similarly compound **4f** was also obtained as pale yellow coloured solid with the formula C₈H₇NO₄ based on HR mass spectrum. IR spectrum showed carbonyl frequency at 1735 (C=O) cm⁻¹ confirmed the ester carbonyl group. Similarly IR frequency at 839 cm⁻¹ indicating *p*-disubstituted aromatic benzene ring. ¹H NMR spectrum showed a 3H singlet (δ 3.97) indicating the presence of methyl group attached to carboxyl ester group (-OCH₃). Two doublet at δ 8.29 (d, 2H) and δ 8.21 (d, 2H) indicating two aromatic proton.

TABLE-1
YIELD AND CONDITION FOR THE ESTERIFICATION OF
CARBOXYLIC ACID (0.1 mol) AND ALCOHOL (0.3 mol)
USING 3 IN PESENCE OF HYDROGEN PEROXIDE

Entry	RCOOH	R'OH	Time	Temp.	RCOOR'	
1	R	2	R'	(h)	(°C)	4 (Yield, %)
1a		2a CH ₃ OH	0.5	85-95	4a (90)	
1a		2b C ₂ H ₅ OH	0.5	85-95	4b (80)	
1a		2c C ₃ H ₇ OH	0.5	85-95	4c (80)	
1b		2a CH ₃ OH	0.5	85-95	4d (82)	
1c		2a CH ₃ OH	1	85-95	4e (80)	
1d		2a CH ₃ OH	1	110-120	4f (98)	
1d		2b C ₂ H ₅ OH	2	120-130	4g (91)	
1d		2c C ₄ H ₉ OH	1	100-110	4h (90)	

Methyl cinnamate (4a): Solid; m.p. 36 °C; IR (KBr, ν_{max} , cm⁻¹) 1740 (C=O); ¹H NMR (CDCl₃) δ = 3.59 (s, 3H, -OCH₃), 7.53 (d, 1H, *J* = 16.0 Hz), 7.17 (m, 3H), 7.30 (m, 2H), 6.28 (d, 1H, *J* = 16.0 Hz).

Methyl salicylate (4d): Liquid; IR (KBr, ν_{max} , cm⁻¹): 1678 (C=O), ¹H NMR (CDCl₃) δ = 3.87 (s, 3H-OCH₃), 6.96 (t, 1H), 6.84 (t, 1H), 7.78 (d, 1H) 7.42 (d, 1H), 10.76 (s, 1H).

Methyl *p*-nitro benzoate (4f): Solid; m.p. 96 °C; IR (KBr, ν_{max} , cm⁻¹): 1718 (C=O); ¹H NMR (CDCl₃) δ = 3.97 (s, 3H, -OCH₃), 8.29 (d, 1H), 8.21 (d, 1H).

Ethyl *p*-nitro benzoate (4f): Solid; m.p. 60 °C; IR (KBr, ν_{max} , cm⁻¹) 1735 (C=O); ¹H NMR (CDCl₃) δ = 4.40 (q, 2H, -OCH₂), 1.39 (t, 3H-CH₃), 8.22 (D, 1H), 8.15 (d, 1H).

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