The preparation of methyl benzoate and methyl salicylate on silica gel column

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An investigation of the acid catalyzed esterification of benzoic acid and salicylic acid with methanol on silica gel solid support system was carried out. The method involved distilling continuously or refluxing the alcohol over the packed column. The conventional method of esterification was also carried out to assess the advantages of the packed column method on improved yield and easier work-up procedure. This modified method minimized the lengthy and cumbersome work-up associated with the conventional method. Although the yields obtainable from the packed column methods compared favourably with yields from conventional method, the new method will require further modification to bring about optimal yields of the desired esters.

Key words: Esters, esterification reaction, salicylate, packed column, modification.

INTRODUCTION

Many esters are known today which may either be natural or synthetic. Many of the esters have found use in diverse areas of human needs: 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. For instance, sodium salicylate is the chief ingredient used in the preparation of antirheumatic and antiseptic drugs. It was also used in the manufacture of dyes and in the preparation of preservatives, McGraw – Hill (1997).

Acetyl salicylic acid (aspirin) is an effective analgesic, antipyretic and anti-inflammatory drug, and it also prevents the aggregation of platelets and stroke, (McGraw – Hill 1997; Kurlikarmi et al., 1993) Methyl salicylate, a constituent of wintergreen and other plants such as Ambyoma variegatum and A. hebraeum (Lusby et al., 1991), Lawsonia inermis (Wong and Teng, 1995) is another ester used as a local anesthetic agent and disinfectant commercially used in toothpaste, mouthwash, perfumes as well as flavouring agents, Finar (1993). Methyl salicylate is also useful in synthesis as a generator of reactive intermediates. This was demonstrated when its thermal decomposition generated ortho-quinoketene, a benzene precursor, (Badea et al., 1992).

Sodium benzoate is an ester used in the modification of alkyd resin, (Gwiatek and Zadernowski, 1993), as well as in the treatment of hyperammonemia, (Tremblay and Qureshi, 1993). Similarly, benzocaine, the ethyl ester of p-amino benzoic acid widely used as local anesthetic has demonstrated relief of pain in patients with spontaneous toothache pain from an open tooth cavity, (Hersh et al., 1993). Lactate esters are versatile solvents that are biodegradable, nontoxic and applicable to a wide range of industrial and consumer use, (Hidetoshi et al., 2004). However, the preparation of ester involved lengthy work-ups 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 the one reported by Krbechek, (1993) in which sulphuric acid was employed as a catalyst as well as to remove or immobilize the water produced. Using this method, isooctanoic acid was esterified with methanol in the presence of excess sulphuric acid both as catalyst and as desiccants affording 95% yield of ester.

A method reported by Nelson, et al (1992) involved providing a mixture of a monohydrate alcohol and a lower carboxylic acid in a reaction vessel equipped with a fractionating column connected to a condenser and a collecting
vessel. Heating technique and a device for passing small bubbles of gas through the reactants were incorporated. The alcohol/carboxylic acid mixture was maintained at a temperature of at least about the boiling point of the alcohol, but below the boiling point of the carboxylic acid, a gas inert to the esterification reaction was bubbled through the mixture to remove the esterification product that was formed. The removed vapour was collected and condensed yielding the esterification product with a high percentage conversion and purity. Using this method, they were able to produce ethyl acetate resulting from three cycles of esterification of ethanol with acetic acid at 85°C with air bubbling at a rate not exceeding 200 ml/min resulting in 85 - 90% conversion efficiency in terms of acetic acid consumption.

Similarly, 0.5 mole phthalic anhydride and 1.1 mole butanol had been dropped into a mixture of various ratios of alumina gel, silica gel and or active carbon. The mixtures were then heated at 250°C, and the reaction was maintained for 6 hours. Dibutyl phthalate was obtained in a yield of approximately 30 - 52% with the maximum yield obtained when the mixed catalysts comprise 80% Al₂O₃ gel and 20% SiO₂ gel or active carbon, (Shigeri and Shiro, 1954). In another preparation, n-butanol and butyric acid were esterified in a batch reactor using amberlyst macro porous cation exchange resin as a catalyst. It was observed that the reaction rate increased with increasing catalyst concentration and reaction temperature, (Bhatnagar et al., 1994). In a recent finding, Hidetoshi et al. (2004) reported the use of water – permeable – zeolite T membranes for the esterification reaction of lactic acid. Benzoic acid was purified by recrystallizing from boiling water. From the foregoing, we decided to investigate a modified esterification technique in which the esterification reaction would be carried out on a packed silica gel column with the alcohol being distilled or refluxed over the column. We aimed at minimizing lengthy and cumbersome solvent extraction work-up associated with the preparation of esters by conventional method. Methyl esters of benzoic acid and salicylic acid have hereby been prepared as case studies.

**MATERIALS AND METHOD**

**Materials**

All reagents used in this study were of analytical grade. These include benzoic acid, sodium bicarbonate, sodium carbonate, salicylic acid. Benzoic acid was purified by recrystallizing from boiling water.

The solvents used include, diethyl ether, methanol, ethanol, petroleum spirit, etc, the solvent were redistilled before use.

**Preparation of methyl benzoate**

A column [30 cm; Ø3 cm] was packed with silica gel to about half of the column, then silica gel mixed with 2 drops of concentrated sulphuric acid (H₂SO₄) was packed into the column and separated with some silica gel, and this was followed by silica gel mixed with benzoic acid and packed into the column and finally the column was topped with silica gel. The column was then connected to a flask containing methanol and the other end was connected to a condenser and finally to a receiver. The methanol was heated over water bath until all the excess methanol had been collected in the receiver at the other end (Figure 1). After all the methanol has been distilled over the column and the excess methanol collected in the receiver, the set up was left overnight to allow silica gel embedded methanol drain back in to the flask.

The column was emptied into three beakers viz the upper layer containing the benzoic acid, the silica gel/H₂SO₄ layer and the lower silica gel part of the column. The methanol that had drained into the flask was also collected for TLC analysis.

The silica gel and the silica gel mixtures were extracted with diethyl ether, concentrated and collected in sample bottles labeled 1A-4A. The four samples were spotted on a TLC plate along with benzoic acid and developed with 1:1 mixture of diethyl ether and petroleum ether.

Sample 2A and 3A were combined. The combined sample was washed with water until neutral, dried over anhydrous magnesium sulphate (MgSO₄) and concentrated. It was then spotted on TLC plate along with benzoic acid and developed with 1:2 mixture of diethyl ether petroleum ether.

The esterification reaction was repeated with packed column, but this time around the benzoic acid and concentrated H₂SO₄ were mixed together before packing with silica gel. The column was then fitted with a condenser for refluxing. This was carried out for 3 h (Figure 2).

The set up was then left overnight. The following day, excess methanol was distilled off and the residue was collected. The column was emptied into two beakers viz the mixture of the acid layer and the lower part of the column. The samples were extracted with diethyl ether, concentrated and labeled 1B - 3B. Sample 1B that is, the layer of the mixture of the organic acid and H₂SO₄ was washed with water until neutral before extraction. The samples were spotted, developed with the same solvent system as in the first experi-

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**Figure 1. Distillation of alcohol over silica gel.**
ment. The products were stored in labeled sample bottles.

The esterification reaction was repeated using the conventional refluxing method. This involved refluxing 1 g of benzoic acid, 2 drops of concentrated H_2SO_4 and excess methanol for 3 h. The excess methanol was distilled off, the residue was washed with excess water until neutral and the ester was extracted with diethyl ether. The solvent was removed and the TLC was carried out. The product was stored in a labeled sample bottle.

Preparation of methyl salicylate

Methyl Salicylate was prepared described as previously i.e. in the preparation of methyl benzoate.

However, the preparation of methyl salicylate was repeated with a longer column [50 cm; Ø3 cm] in which anhydrous MgSO_4 (20 g) was incorporated into the lower part of the column, this was refluxed with methanol for 4 h after which it was left overnight. It was also worked up and analyzed as described earlier.

Melting point determination

The melting points of solid acid samples were determined using the Galenkamp melting point apparatus.

Infrared analysis

The infrared (IR) analysis was carried out using Buck Scientific (model 500) i.r. spectrophotometer, at Obafemi Awolowo University, Ile-Ife.

RESULTS AND DISCUSSION

Result of the preparation of methyl benzoate

Experiment A1: Distillation experiment of alcohol over the column

The melting point of the re-crystallized benzoic acid was determined before the commencement of the experiment. The melting point was found to be 123°C.

The acid catalyzed esterification of benzoic acid with methanol can be represented as in Figure 3.

The product of the first experiment in which methanol was continuously distilled over the column gave 2 spots (with poor separation) on the TLC plate, indicating that there was a partial conversion of the acid to the ester (Figure 4).

Spot 1A corresponding to the benzoic acid zone on the column indicates the absence of the ester but only the unreacted benzoic acid. However, 2A and 3A (the extracts from mineral acid layer and the lower part of the column respectively) showed the presence of the ester formed as well as the unreacted acid. The ester being an oil, drained down the column as it was being formed. On combination of samples 2A and 3A and after the work-up followed by TLC (reducing the polarity of the developing solvent system) with benzoic acid as reference, the mineral acid spot disappeared and the spot (with better separation) showed the presence of the ester and trace amount of unreacted benzoic acid (Figure 5).

The percentage yield was 21.04. The low percentage yield can be attributed mainly to the low conversion of the benzoic acid. On investigation, the melting point of the solid substance formed from the extracts of 1A was found to be 119°C.

Experiment A2: Refluxing experiment

The products from the second experiment in which meth-
anol was refluxed over the packed column gave a mixture of spots on TLC indicating also partial conversion of the organic acid (Figure 6).

This TLC result revealed that the ester was formed at the layer containing the mixture of the organic and inorganic acids (i.e. benzoic and sulphuric acids). The percentage yield was 15.23.

**Experiment A3: conventional method experiment**

The TLC results of the third experiment (that is, the conventional method of preparing the ester) also showed that benzoic acid was only partially converted to its methyl ester, (Figure 7).

The low yield from this experiment, (10.35%), can be explained, since the esterification was not carried out with concurrent removal of water example, azeotropic distillation.

The i.r. spectrum (Appendix 1) of the product showed absorptions characteristics of the important stretching frequencies of the functional groups in the ester, John, (1965). There is sharp band at 1722.2 accounting for C = O (aryl esters) stretching and a medium band at 1250.9 and 1190 accounting for C – O (aryl esters) stretching.

**The results of the preparation of methyl salicylate**

**Experiment B1: Continuous distillation**

The melting point of recrystallized salicylic acid was determined and found to be 160°C. Methanol and salicylic acid react according to Figure 8.
Figure 8. Reaction of methanol and salicylic acid

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\begin{align*}
\text{H}_3\text{C} & \text{OH} + \text{HO} & \text{H}^+ & \text{CH}_3 \text{O} \text{C} \text{H} & \text{H}_2\text{O} + \text{HO} \\
\text{Methanol} & \text{Salicylic acid} & & \text{Methyl salicylate} & \text{Water}
\end{align*}
\]

The TLC analysis result for the continuous distillation of alcohol over packed, column indicates partial conversion of the acid to its ester (Figure 9).

The organic acid was packed at the upper part of the column and as such the esterification was expected to take place at that point. But the fact that the ester was found from the extracts of the lower part of the column and in the residue in the flask indicates that the ester drained down the column along with the embedded alcohol. The yield (10.23%) was rather low and unsatisfactory. The crystals that formed from the extracts of 1 G melted at 158°C, which meant that it was the unreacted salicylic acid.

**Experiment B2: Refluxing experiment**

The result of the reflux experiment showed that the organic acid was partially converted to its ester. The ester as well as the unreacted acid washed down the column into the distillation flask and no product was found on the column as shown by the TLC analysis result, (Figure 10). The yield was very low (2.82%).

Comparing the two methods adopted for the esterification reaction (that is, continuous distillation and refluxing) the yield of the ester produced from the continuous distillation experiment was higher than that of the refluxing experiment. This can be explained on the assumption that the bulk of the reaction in the refluxing experiment was in the distillation flask (the contents of the column was washed down by the methanol), and as such, the water as by-product impeded further formation of the ester. Whereas, in the continuous distillation experiment the reaction occurred on the column, and water formed as by product was entrained in the lower segment of the silica gel packing.

**Experiment B3: conventional method**

The conventional method of preparation gave slightly improved (13.45%) yield, though still lower than would have been the case with continuous removal of water (Figure 11).
The crystalline residue obtained from this experiment melted at 162°C, confirming that it is the unreacted organic acid.

The incorporation of anhydrous MgSO_4 into the silica gel packing (experiment B4) as a way of trapping the water produced as by product failed to improve the yield of the ester and the TLC analysis of the results (Figure 12) indicates that the conversion and yield were low with the bulk of the products found in the distillation flask.

The reversibility of the esterification reaction is a factor contributing to the low yields of the ester. Once the reaction attains equilibrium, the rate of forward reaction equals that of the backward reaction, and the overall success of the reaction seems therefore contingent on the continuous removal of the by–products. This was the basis of incorporating anhydrous MgSO_4 into the system, which did not achieve the desired result.

The i.r. spectrum (Appendix 2) of the product showed absorptions characteristics of the important stretching frequencies of the functional groups in the ester, John (1965). The band at 3200 - 3600 cm\(^{-1}\) on the i.r spectrum accounts for the presence of hydrogen bonded hydroxyl (-OH) group characteristic of phenolic compounds. Similarly, the presence of the carbonyl (-C=O) functional group is shown on the i.r spectrum as a strong, sharp band at wavelength 1646 cm\(^{-1}\) indicating that it is in conjugation with an aromatic system. The -C-O- stretching characteristics of aromatic ester is depicted on the i.r. spectrum at wavelength 1241 cm\(^{-1}\), but was weak. Also, a weak band at 1380.9 cm\(^{-1}\) could be as a result of O-H bending, and C-O stretching characteristic of phenols, John (1965).

### Conclusion and Recommendation

Some methods have been tried to improve the yield in esterification reaction. These include the use of mineral acid in excess of the catalytic amount required, Krbach-ek (1993) employing different catalysts and catalyst mixture, (Shigeri and Shiro, 1954; Bhatnagar et al., 1994; Jessop et al., 1995; Fermin and Bruno (1993), as well as the use of enzymes such as immobilized lipase catalyst, (Rizzi et al., 1992; Berghund et al., 1995). Esters have also been produced in the presence of microorganism or their products, Garcia et al., (1993).

These ideas prompted the present investigation of esterification on a silica gel column.

The results obtained as far as percentage conversion and yields are concerned would suggest that the method may be suitable for micro – scale preparation. Other solid support systems or their combination may bring about some improvement as shown by the report of Shigeri and Shiro (1954) for the esterification of phthalic anhydride.

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