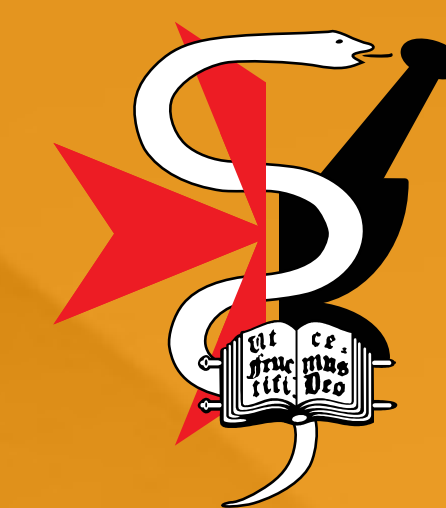


IMPROVING THE YIELD IN ORTHOESTERIFICATION OF STEROIDS

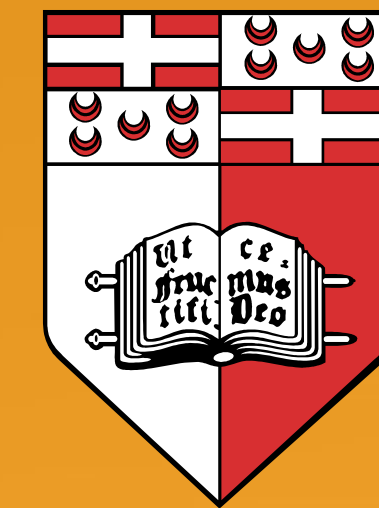
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INTRODUCTION

Steroids are used to treat various conditions from asthma to skin inflammation. Orthoesterification of steroids at C17 and C21 leads to the formation of compounds which are more potent than their parent steroids.¹⁻³

Steroid orthoesters are synthesized by reacting a selected steroid with the respective orthoester. The parent steroid should have two hydroxyl groups situated in close proximity to react with the orthoester, for example at C17 and C21. An acid is used to catalyse the reaction.

AIMS

To synthesise and improve the yield of the orthoesterification of a steroidal compound

METHOD

The parent steroid was dissolved in the polar organic solvent tetrahydrofuran. Dissolution of the steroid was followed by the addition of the respective orthoester reagent.

The catalyst p-toluenesulfonic acid (PTSA) was then added drop-wise and the temperature was increased to reflux.

Another reaction was carried out simultaneously in a separate flask, using the same conditions, except for the catalyst. The catalyst pyridinium p-toluenesulfonate (PPSA) was used as a catalyst, instead of PTSA.

PPSA is the pyridinium salt of PTSA and is less acidic compared to PTSA.

Samples were taken from both reactions at one hour intervals and monitored using HPLC.

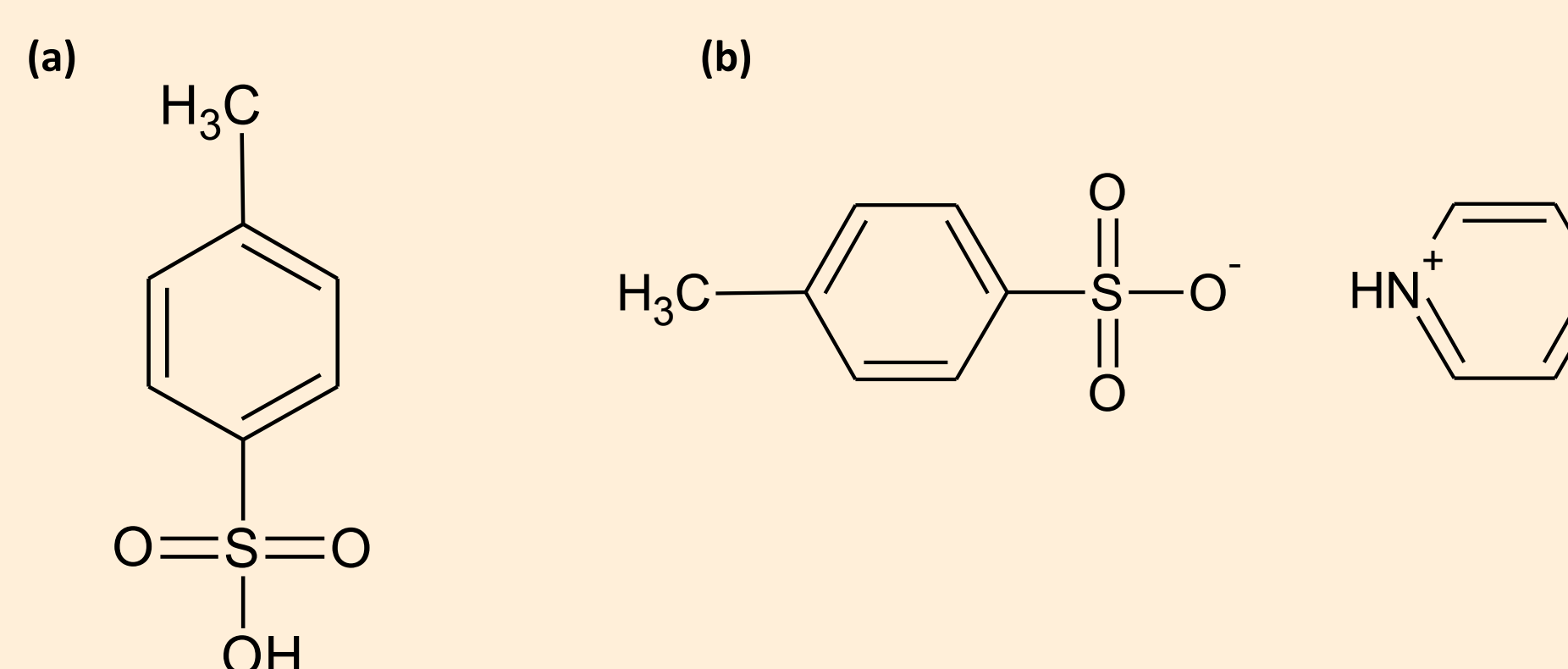


Figure 1: The structure of (a) PTSA and (b) PPSA

RESULTS

Both PTSA and PPSA catalysed the reaction to yield the steroid orthoester. Samples were taken from both reactions at the same time intervals. When comparing the yield obtained with the two different catalysts at the same time interval, that is 2 hours after adding the catalyst (Figure 2), a higher yield was observed when using PPSA as a catalyst. The yield of the reaction catalysed using PPSA was estimated to be 90% (Figure 2a) while that catalysed with PTSA was estimated to be 73% (Figure 2b).

Orthoesters are hydrolysed in acidic conditions. Using a less acidic catalyst may have decreased the hydrolysis of orthoesters leading to a higher concentration of reagent available to react with the starting material.

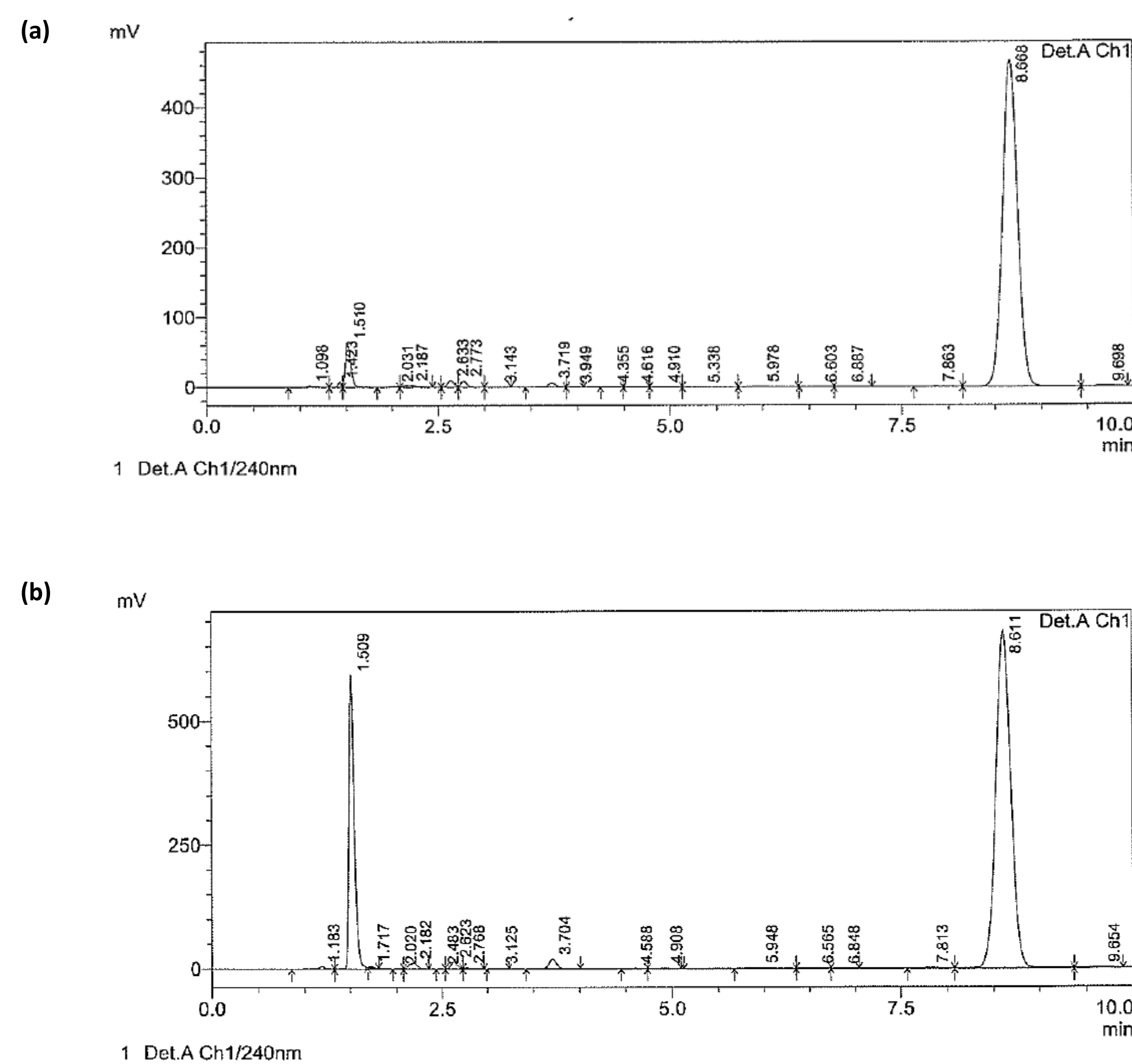


Figure 2: Analysis of a sample taken 2 hours after adding the catalyst (a) PPSA and (b) PTSA. The peak with a retention time of 1.5min corresponds to the starting material while that at 8.6min corresponds to the product.

CONCLUSION

When a less acidic catalyst was used, the yield of the steroid orthoester obtained was improved.

References

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