Acid-Catalyzed Tandem Hydrolysis–Esterification of Acetylsalicylic Acid from Commerical Asprin Tablets to Form Methyl Salicylate

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Abstract

Methyl salicylate was synthesized from commercial aspirin tablets via an acid-catalyzed tandem hydrolysis–esterification sequence. Acetylsalicylic acid (ASA) was extracted from the tablet matrix into methanol and reacted under reflux with a catalytic volume of H_2SO_4. This one-pot method facilitates simultaneous deacetylation and Fischer esterification, bypassing the isolation of a salicylic acid intermediate. The resulting methyl salicylate was isolated via aqueous quenching and liquid–liquid extraction. Crude product purification was achieved through neutralization with saturated $NaHCO_3$ and drying over anhydrous $MgSO_4$. This synthesis demonstrates an efficient, high-yield conversion of a common pharmaceutical precursor into a high-value fragrance ester, highlighting fundamental principles of equilibrium-driven organic transformations and multistep one-pot synthesis.

Introduction

Acetylsalicylic acid (ASA), $C_9H_8O_4$, is a synthetic organic derivative of salicylic acid and is commonly known as aspirin [1].

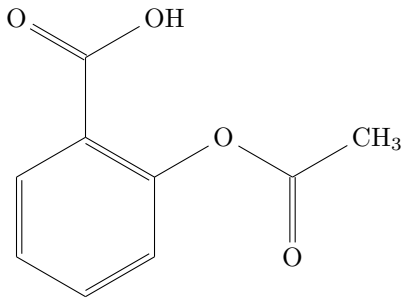

Figure 1: Chemical structure of ASA

Commercial aspirin is commonly synthesized from salicylic acid through Eq 1, and the two molecules differ by an ester group ($-OCOCH_3$) [2].

$$C_7H_6O_3 + C_4H_6O_3 \xrightarrow{H_2SO_4} C_9H_8O_4 + CH_3COOH \tag{1}$$

Another common derivative product of salicylic acid is methyl salicylate, $C_8H_8O_3$, commonly referred to as

wintergreen oil. Methyl salicylate is commonly used in edibles (e.g. gum, mints), perfumes, and pain-relief ointments (e.g. Icy Hot, BenGay) [3]. Methyl salicylate also differs with salicylic acid by a single ester group and has simply been esterified differently than ASA.

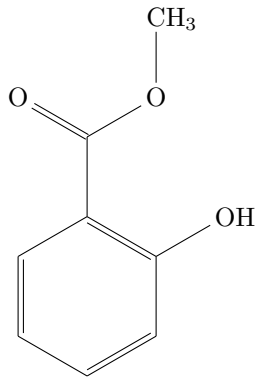

Figure 2: Chemical structure of methyl salicylate

Due to the similarity between the two molecules, ASA can be reacted to synthesize methyl salicylate [4]. The purpose of this experiment was to convert acetylsalicylic acid obtained from commercial aspirin tablets into methyl salicylate through acid-catalyzed esterification in methanol under reflux conditions.

Results and discussion

Extraction and Solvation of ASA

The synthesis began with the mechanical breakdown of commercial aspirin tablets (500 mg ASA/tablet) using a mortar and pestle. The resulting powder was digested in an excess of methanol for one hour with constant stirring.

The heterogeneous mixture was subsequently clarified via filtration through a cellulose-based filter. This step effectively isolated the soluble ASA and miscible plasticizers from the insoluble structural excipients and pigments (Table 1).

Table 1: Methanol Solubility/Miscibility Profile of Tablet Components

Component Category	**Specific Ingredients**	**Solubility in CH_3OH**
Active Ingredient	Acetylsalicylic Acid (ASA)	Soluble
Binders / Fillers	Corn Starch, Powdered Cellulose	Insoluble
Coating Agents	Carnauba Wax, Shellac, Hypromellose	Insoluble / Sparingly
Plasticizers	Propylene Glycol, Triacetin	Miscible
Pigments / Lakes	Titanium Dioxide, D&C Red #7, FD&C Blue #2, FD&C Red #40	Insoluble

Outline

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Table 2: An example table

Header one	Header two
Entry one	Entry two
Entry three	Entry four
Entry five	Entry five
Entry seven	Entry eight

References

References should be given in the normal way in LaTeX. If you are using biblatex (as recommended) then you can use the full range of citation commands it provides. If you choose to use classical BibTeX, the natbib package will be loaded and you can use it's commands.

Floats

New float types are set up in the preamble. The means graphics are included as follows (Scheme 1). As illustrated, the float is "here" if possible.

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Scheme 1: An example scheme

The use of the different floating environments is not required, but it is intended to make document preparation easier for authors. In general, you should place your graphics where they make logical sense; the production process will move them if needed.

Math

If packages such as amsmath are required, they should be loaded in the preamble. However, the basic LaTeX math(s) input should work correctly without this. Some inline material $1 + 1 = 2$ followed by some display.

$$A = \pi r^2$$

It is possible to label equations in the usual way (Eq. 2).

$$\frac{\mathrm{d}}{\mathrm{d}x} r^2 = 2r \tag{2}$$

This can also be used to have equations containing graphical content. To align the equation number with the middle of the graphic, rather than the bottom, a minipage may be used.

As illustrated here, the width of the minipage needs to allow some space for the number to fit in to. (3)

Experimental

The usual experimental details should appear here. This could include a table, which can be referenced as Table 2. Notice that the caption is positioned at the top of the table.

Adding notes to tables can be complicated. Perhaps the easiest method is to generate these using the basic `\textsuperscript` and `\emph` macros, as illustrated (Table 3).

The example file also loads the optional chemformula and mhchem packages, so that formulas are easy to input: `\ce{H2SO4}` gives H_2SO_4. The two have similar syntax but authors may prefer one or the other.

Table 3: A table with notes

Header one	Header two
Entry one[a]	Entry two
Entry three[b]	Entry four

[a] Some text; [b] Some more text.

The use of new commands should be limited to simple things which will not interfere with the production process. For example, `\mycommand` has been defined in this example, to give italic, mono-spaced text: *`some text`*.

Acknowledgements

Please use "The authors thank ..." rather than "The authors would like to thank ...".

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The following files are available free of charge.

- Filename-1: brief description
- Filename-2: brief description

References

(1) Fijałkowski, Ł.; Skubiszewska, M.; Grześk, G.; Koech, F. K.; Nowaczyk, A. *Molecules* **2022**, *27*, 8412.

(2) Sneader, W. *BMJ* **2000**, *321*, 1591–1594.

(3) Guo, J.; Hu, X.; Wang, J.; Yu, B.; Li, J.; Chen, J.; Nie, X.; Zheng, Z.; Wang, S.; Qin, Q. *Frontiers in Pharmacology* **2022**, *13*, DOI: `10.3389/fphar.2022.1015941`.

(4) Hartel, A. M.; Hanna, J. M. *Journal of Chemical Education* **2009**, *86*, 475.

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