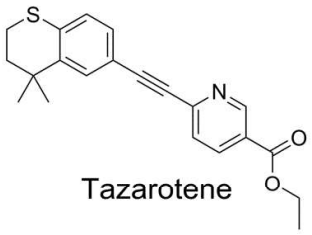
3. This question is about spot cream

The drug tazarotene (sold under the trade names of Zorac® or Tazorac®) can be prescribed as a cream that can be applied to the skin to help to treat acne and certain other skin conditions. It is commonly sold as a 0.05% cream by mass.

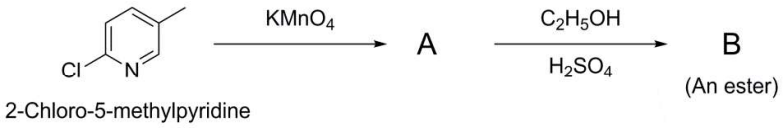


Tazarotene

(a) The molar mass of tazarotene is 351.46 g mol^{-1}. Assuming that tazarotene cream has a density of 0.90 g cm^{-3}, calculate the concentration of tazarotene in the cream in mol dm^{-3}.

The synthesis of tazarotene is shown below. Not all of the reaction by-products are shown.

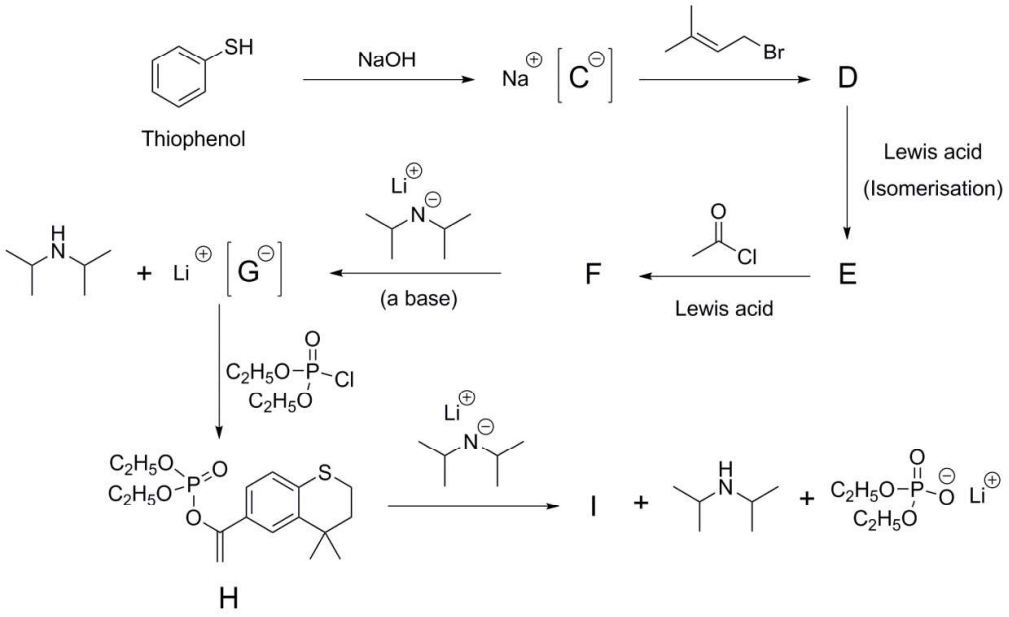
The synthesis begins with the conversion of 2-chloro-5-methylpyridine to Ester **B**.



2-Chloro-5-methylpyridine

(b) Draw the structure of Compound **A** and Ester **B**.

The second part of the synthesis begins with thiophenol, which is converted into Compound **I** by a number of steps.



(c) Draw the structures of Compounds **D**, **E**, **F** and **I**, and anions $\mathbf{C^-}$ and $\mathbf{G^-}$.

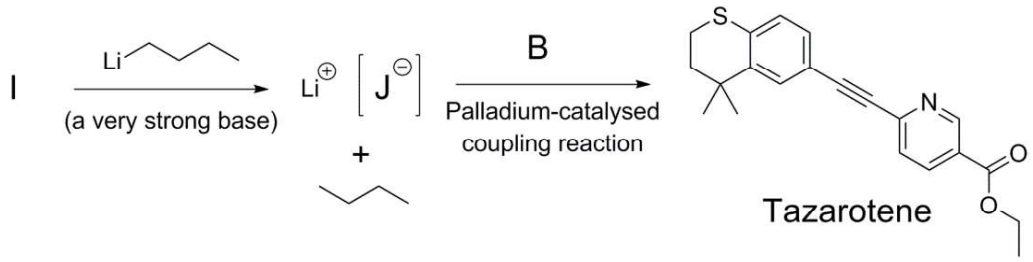
(d) How would you classify the reaction of Compound **H** into Compound **I**?

Circle one of the following answers in the answer booklet.

Oxidation **Reduction** **Addition** **Elimination** **Substitution**

Finally, Compound **I** is treated with a very strong base to form anion **J**.

Anion **J** can be reacted with Compound **B** to form tazarotene.



(e) Suggest a structure for Anion **J**.

(f) How many signals would you expect to see in the ^{13}C NMR spectrum of tazarotene?

Tazarotene is actually a pro-drug, meaning it is metabolised to its active form when inside the body.

The active form has a molar mass of 323.41 g mol^{-1} and two fewer signals in its ^{13}C NMR spectrum than tazarotene.

(g) Suggest a structure for the active form of the drug.