



CHEMISTRY 4000

Problem Set #6: Tazarotene (aka Tazorac[®])

Spring 2022

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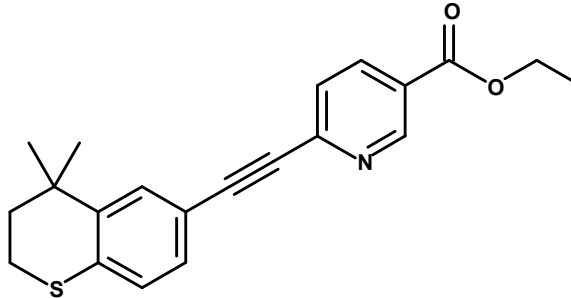


Tazarotene (aka Tazorac®)

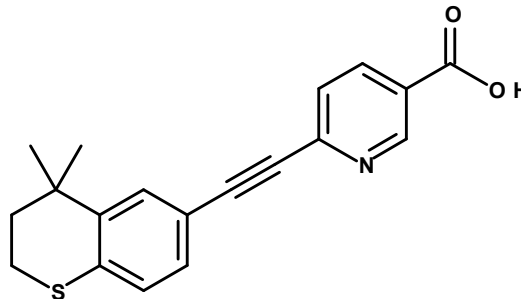
- Tazarotene (Tazorac®) is used to treat skin conditions such as acne and psoriasis.
- It is a prodrug, containing an ester that is hydrolysed into a carboxylic acid to give the active species, tazarotenic acid.
- Tazarotenic acid functions by binding strongly to retinoic acid receptors (RARs, where retinoic acid is a metabolite of Vitamin A). The RARs are also bound to DNA and can bind to other proteins, promoting or repressing transcription of nearby regions of DNA. When tazarotenic acid (or similar drugs) bind to a RAR, that changes the shape of the RAR, affecting which proteins can bind to it and which regions of DNA are transcribed.
- This is a similar mechanism of action to isotretinoin (Accutane®); however, isotretinoin is taken orally while tazarotene is applied directly to the skin. Tazarotene also breaks down more quickly. This can help to reduce side-effects – though pregnant women should still refrain from taking any drug of this nature (RAR-binding drugs are teratogenic).

Tazarotene (aka Tazorac®)

- The structure of tazarotene is:



- *In vivo*, tazarotene is metabolised to tazarotenic acid:



- Tazarotenic acid is further metabolized, converting the sulfide to a sulfoxide then sulfone, increasing the polarity of the molecule and facilitating its excretion (so that it doesn't build up to toxic levels).