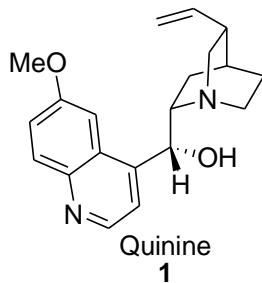


All about Anti-Malarial drugs

In the beginning there was Quinine.....Quinine was the first effective treatment for malaria caused by *Plasmodium falciparum*, appearing in therapeutics in the 17th century.



Quinine has been a target for synthetic chemistry for 150 years

- 1) What class of compounds is quinine from?
- 2) What is the correct numbering order for this compound? Rationalise.
- 3) What are the key features of this compound?
- 4) What is the correct name of the bicyclic ring present in the compound?
- 5) What key disconnections would you make in your attempts of a total synthesis?

The First stereoselective total synthesis of quinine was achieved in 2001 by Gilbert Stork

Questions for Scheme 1

- 6) What are the reagents required in steps a) b) and c) ?
- 7) What is the reaction happening in step d)? Please give reagents and a mechanism
- 8) Account for the stereoselective formation of compound 9 in step e)

Questions for Scheme 2

Once the tetrahydropyridine 9 had been synthesised, Quinine was only four steps away, one of which was the key to the stereoselective nature of this synthesis.

9) Can you elucidate all four steps? Also rationalise and discuss the significance of the key step.

Scheme 2

9) Although we haven't fully discussed the synthesis of azido aldehyde **5**, we know that it was synthesised from butyrolactone **3**, which was in turn synthesised from the commercially available lactone **2**.

Please propose a retrosynthetic analysis and thus forward synthesis of lactone **3** from **2**.