

Introduction

Quinine is an important medicine used in treatment of Malaria. The formula of quinine is $C_{20}H_{24}N_2O_2$. The synthesis of quinine launched a thousand research projects.

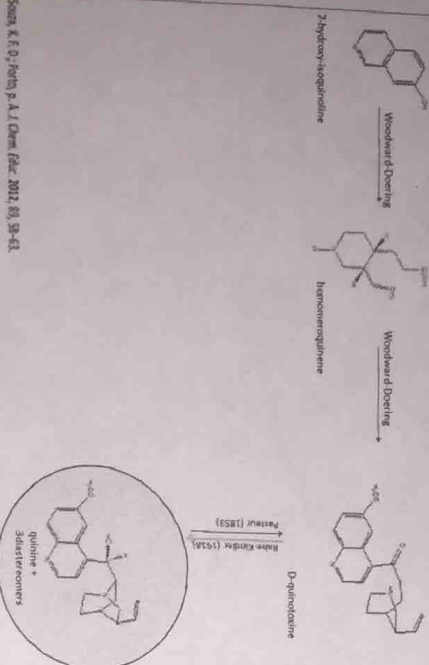
History

Perkin (1856) produced mauveine.
Rabe and Kindler (1918) obtained the partial synthesis with lack of details and stereochemical problems.

A Formal Total Synthesis of Quinine

Woodward and Doering (1944) obtained homomeroquinine in scheme 1, but their process had the lack of stereocontrol, the low yields.

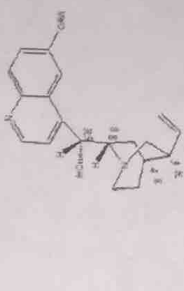
Scheme 1



Souza, K. F. D.; Porto, P. A. L. *Quim. Educ.* 2012, 83, 39-43.

4 stereocenters: C3, C4, C8, C9

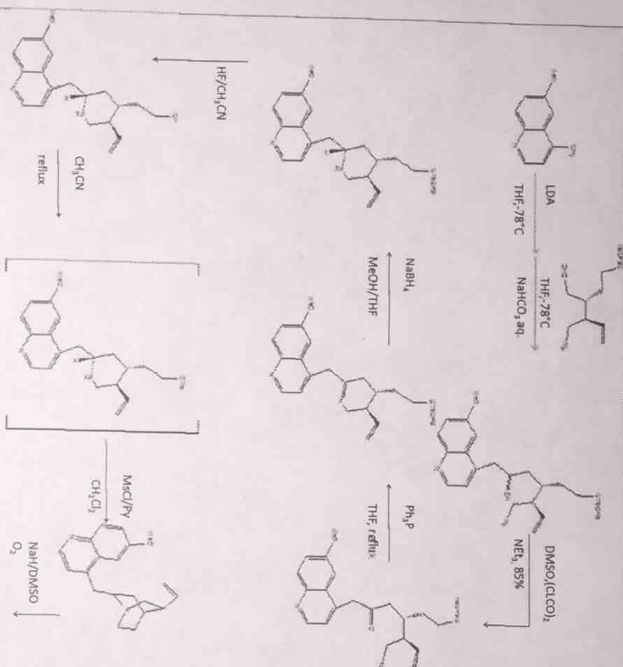
The Stereoselective Synthesis of Quinine



The Stereoselective Synthesis of Quinine

Uskokovic and Gutzwiller (1978) had better yields and poor stereocontrol at C8. Stork (2001) provided the first stereoselective synthesis in scheme 2.

Scheme 2

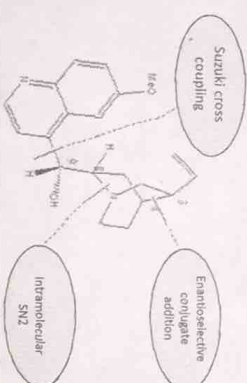


Stork obtained somewhat higher stereoselectivity quinine with 78% yield.

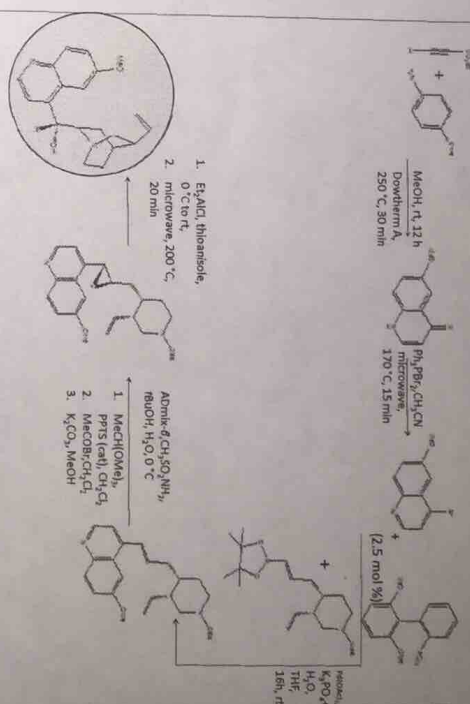
Stork, G.; Wu, D.; Fujimoto, A.; Kofu, E. R.; Balkovec, J. M.; Tara, J. R.; Dake, G. R. *J. Am. Chem. Soc.* 2001, 123, 3239-3242.

A Catalytic Enantioselective Total Synthesis

Jacobsen 2004



Scheme 3



Jacobsen was able to control the C8 and C9 stereocenters

Rahem, T. J.; Goodman, S. N.; Jacobsen, E. N. *J. Am. Chem. Soc.* 2004, 126, 705.

The Latest Total Synthesis

Kobayashi (2004) provided the most efficient total syntheses. Smith and Williams (2008) revisited Rabe and Kindler's syntheses.

References

1. Kaufman, T. S.; Ruveda, E. A. The Quest for Quinine: those Who Won the Battles and those Who Won the War. *Angew. Chem. Int. Ed.* 2005, 44, 854-885.
2. Rahem, T. J.; Goodman, S. N.; Jacobsen, E. N. Catalytic Asymmetric Total Syntheses of Quinine and Quinidine. *J. Am. Chem. Soc.* 2004, 126, 706-707
3. Souza, K. F. D.; Porto, P. A. History and Epistemology of Science in the Classroom: The Synthesis of Quinine as a Proposal. *J. Chem. Educ.* 2012, 89, 58-63.
4. Stork, G.; Niu, D.; Fujimoto, A.; Kofu, E. R.; Balkovec, J. M.; Tara, J. R.; Dake, G. R. The First Stereoselective Total Synthesis of Quinine. *J. Am. Chem. Soc.* 2001, 123, 3239-3242.
5. Uskokovic, M.; Gutzwiller, J.; Henderson, T. Stereoselective Total Syntheses of Quinine and Quinidine. *J. Am. Chem. Soc.* 1970, 92, 203-204.
6. Woodward, R. B.; Doering, W. E. The Total Synthesis of Quinine. *J. Am. Chem. Soc.* 1945, 67, 860-874.