

FULL TEXT LINKS



Review Alkaloids Chem Biol. 2019;82:29-145. doi: 10.1016/bs.alkal.2018.11.001.

Epub 2019 Feb 22.

Cinchona Alkaloids–Derivatives and Applications

Przemysław J Boratyński¹, Mariola Zielińska-Błąjet¹, Jacek Skarzewski²

Affiliations

PMID: 30850032 DOI: [10.1016/bs.alkal.2018.11.001](https://doi.org/10.1016/bs.alkal.2018.11.001)

Abstract

Major Cinchona alkaloids quinine, quinidine, cinchonine, and cinchonidine are available chiral natural compounds (chiral pool). Unlike many other natural products, these alkaloids are available in multiple diastereomeric forms which are separated on an industrial scale. The introduction discusses in short conformational equilibria, traditional separation scheme, biosynthesis, and de novo chemical syntheses. The second section concerns useful chemical applications of the alkaloids as chiral recognition agents and effective chiral catalysts. Besides the Sharpless ethers and quaternary ammonium salts (chiral PTC), the most successful bifunctional organocatalysts are based on 9-amino derivatives: thioureas and squaramides. The third section reports the main transformations of Cinchona alkaloids. This covers reactions of the 9-hydroxyl group with the retention or inversion of configuration. Specific Cinchona rearrangements enlarging [2.2.2]bicycle of quinuclidine to [3.2.2] products are connected to the 9-OH substitution. The syntheses of numerous esterification and etherification products are described, including many examples of bi-Cinchona alkaloid ethers. Further derivatives comprise 9-N-substituted compounds. The amino group is introduced via an azido function with the inversion of configuration at the stereogenic center C9. The 9-epi-amino-alkaloids provide imines, amides, imides, thioureas, and squaramides. The syntheses of 9-carbon-, 9-sulfur-, and 9-selenium-substituted derivatives are discussed. Oxidation of the hydroxyl group of any alkaloid gives ketones, which can be selectively reduced, reacted with Grignard reagents, or subjected to the Corey-Chaykovsky reaction. The alkaloids were also partially degraded by splitting C4'-C9 or N1-C8 bonds. In order to immobilize Cinchona alkaloids the transformations of the 3-vinyl group were often exploited. Finally, miscellaneous functionalizations of quinuclidine, quinoline, and examples of various metal complexes of the alkaloids are considered.

Keywords: Asymmetric synthesis; Chiral ligands; Chiral recognition; Cinchonidine; Cinchonine; Organocatalysis; Quinidine; Quinine.

© 2019 Elsevier Inc. All rights reserved.

[PubMed Disclaimer](#)

Related information

[PubChem Compound \(MeSH Keyword\)](#)

LinkOut – more resources

Full Text Sources

[Elsevier Science](#)

Research Materials

[NCI CPTC Antibody Characterization Program](#)

Miscellaneous

[NCI CPTAC Assay Portal](#)