9-Amino-9-Deoxyepicinchona Alkaloids

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Introduction

9-Amino-9-deoxyepicinchona alkaloids constitute the newest generation of the family of cinchona alkaloids. The last few years have witnessed a special interest in this kind of cinchona alkaloids derivatives. As bifunctional organocatalysts combine a Brønsted acid and Lewis base in one molecule, they are capable of promoting many asymmetric reactions and provide access to chiral building blocks of high enantiopurity. In addition, they can be easily prepared in one pot from inexpensive alkaloid starting materials in either of pseudo-enantiomeric forms (Scheme 1).2

Abstracts

(A) The highly enantioselective direct α-amination of aryl ketones was reported to be catalyzed by 9-amino-9-deoxyepicinchonine (C1).3 Excellent enantioselectivities (93–99% ee) have been achieved for a broad spectrum of aryl ketones.

(B) The first enantioselective organocatalytic Friedel–Crafts alkylation of indoles with simple α,β-unsaturated ketones catalyzed by C1 was investigated by Chen and co-workers.4 The reactions were smoothly conducted and moderate to good ee values have been achieved.

(C) Deng and List have reported the successful enantioselective epoxidation of α,β-unsaturated ketones catalyzed by 9-amino-9-deoxyepiquinine (C2), respectively.5,6 In List’s paper, the C2 chiral amine salt was employed to convert the substituted cyclohexenones into their corresponding epoxides in good yields and excellent enantioselectivities. It’s the first report on the highly asymmetric epoxidation of simple cyclic enones.6

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(D) Further, Deng and Chen reported the asymmetric direct vinylogous Michael addition of \( \alpha,\alpha' \)-dicyanooalkenes and \( \alpha,\beta \)-unsaturated ketones in the presence of \( \text{C}_2 \).\(^7\) The reaction scope was quite substantial and excellent stereoselectivity was observed.

(E) The Michael addition of nucleophiles to nitrolefins catalyzed by cinchona alkaloids derivatives is an efficient strategy for the synthesis of chiral nitroalkane adducts.\(^8,9\) Stephen reported the high-yielding addition of a variety of ketones (cyclic/acyclic) or aldehydes (straight-chain/\( \alpha,\alpha \)-disubstituted) and \( \text{trans} - \beta \)-nitrostyrene in the presence of 9-amino-9-deoxy-epihydroquinine (\( \text{C}_4 \)). Up to 99% ee and a dr of 99:1 were obtained in high yields.\(^{10}\)

(F) The asymmetric Diels–Alder reaction of \( \alpha,\beta \)-unsaturated ketones and 2-pyrones catalyzed by \( \text{C}_2 \) or \( \text{C}_3 \) was introduced by Deng and co-workers.\(^{11}\) Both catalysts gave excellent results and the primary amine functionality was proved to be critical to its catalytic activity.

(G) \( \text{C}_2/\text{C}_3 \) in combination with acid smoothly catalyzed the 1,3-dipolar cycloaddition of 2-cyclohexen-1-one and azomethine imine to give the desired tricyclic product with excellent diastereoselectivity (dr > 99:1), although low to moderate ee values were obtained. Fortunately, another novel multifunctional primary amine 6'-hydroxy-9-amino-9-deoxyepiquinidine can give promising results (dr > 99:1, up to 95% ee).\(^{12}\)

References