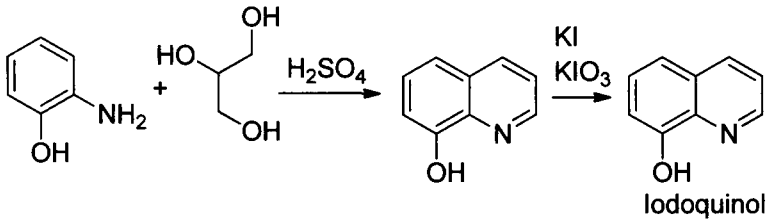
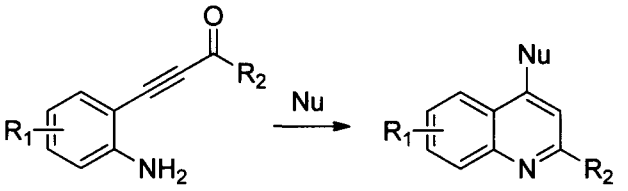


11.3.8 Modern Methods

Except the classical methods described above, modern processes for the construction of quinoline and isoquinoline cores are gaining ground in drug discovery. Although most of them have never been used for the synthesis of specific quinoline drugs, their references are expected to serve as an inspiration for designing more efficient routes for the drugs of the future. Basically these methods can be subdivided in three major categories: i. cyclization of ynones, enones, alkynes and alkenes; ii. cycloaddition and pericyclic reactions and iii. metal-metadiated cyclizations.

Cyclization of ynones and alkynes

Internal ynones and alkynes have been frequently used as starting materials for the synthesis of quinoline compounds. Ynones can act as Michael acceptors with various nucleophiles, affording intermediate enones, which are readily cyclized to quinolines.[101]



Mono-substituted anilines bearing an internal alkyne can be cyclized to quinolines either by metal-mediated hydroarylation of alkynes or through an electrophile-mediated Friedel–Craft type reaction.[102]