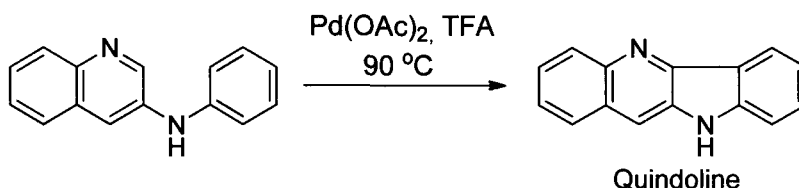


11.2.7 Palladium-Catalyzed Oxidative Coupling

Oxidative cyclizations are generally facilitated by the use of $\text{Pd}(\text{OAc})_2$ in acetic acid under reflux. The initial step in these oxidative cyclization reactions is believed to be the electrophilic palladation of the aromatic ring. An example is presented in the preparation of anti-malarial agent quindoline, isolated from a West African plant *Cryptolepis sanguinolenta*, which was synthesized through an oxidative cyclization of the appropriately 3-substituted quinoline in the presence of two equivalents of $\text{Pd}(\text{OAc})_2$ in trifluoroacetic acid.³³



11.2.8 Cross-Coupling Reactions

Metal-catalyzed cross-coupling reactions have become, in recent years, an important tool in the organic synthetic arsenal. Among the several known cross-coupling reactions that use a quinoline fragment as a coupling partner, Suzuki and Stille are more widespread. On the other hand, only a few precedents exist for Negishi and Hiyama reactions.

Negishi coupling

Quinolinyl moiety has been applied in the Negishi reaction either as an electrophile or as nucleophile. 2- or 4-substituted quinolinyl triflates or bromides have been used extensively for introduction of aromatic rings at the C2 or C4 positions of the heterocycle. In a representative example, Murata et al. employed a Negishi reaction in his effort toward the formal synthesis of antitumor compound camptothecin. In accordance to that, 2-chloropyridine was allowed to react with lithium naphthalenide, followed by zinc chloride, to afford the corresponding zinc pyridine salt. Reaction of the resulting organozinc intermediate with 2-chloro-3-quinoline carboxylate provided the hetero biaryl core of camptothecin.³⁴