SYNTHESIS OF ISOCRYPTOLEPINE

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Isoneocryptolepine is an isomer, not yet found in nature, of three known alkaloids: cryptolepine, neocryptolepine and isocryptolepine. The core of isoneocryptolepine, 7\(H\)-indolo[2,3-\(c\)]quinoline, has been synthesized now in two steps via a new approach starting from commercially available 3-bromoquinoline and 2-bromoaniline. The new approach consists of two consecutive palladium-catalyzed reactions: a selective Buchwald/Hartwig amination followed by an intramolecular Heck-type reaction.

Alternatively, the same skeleton has also been prepared via the combination of a Suzuki arylation with an intramolecular nitrene insertion starting from 4-chloroquinoline and \{2-[(2,2-dimethylpropanoyl)amino]phenyl\}boronic acid. Selective methylation of 7\(H\)-indolo[2,3-\(c\)]quinoline yielded 5-methyl-5\(H\)-indolo[2,3-\(c\)]quinoline (Isoneocryptolepine) which is an interesting new lead compound in the search for new antiplasmodial drugs [1].