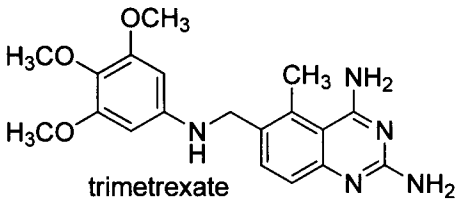
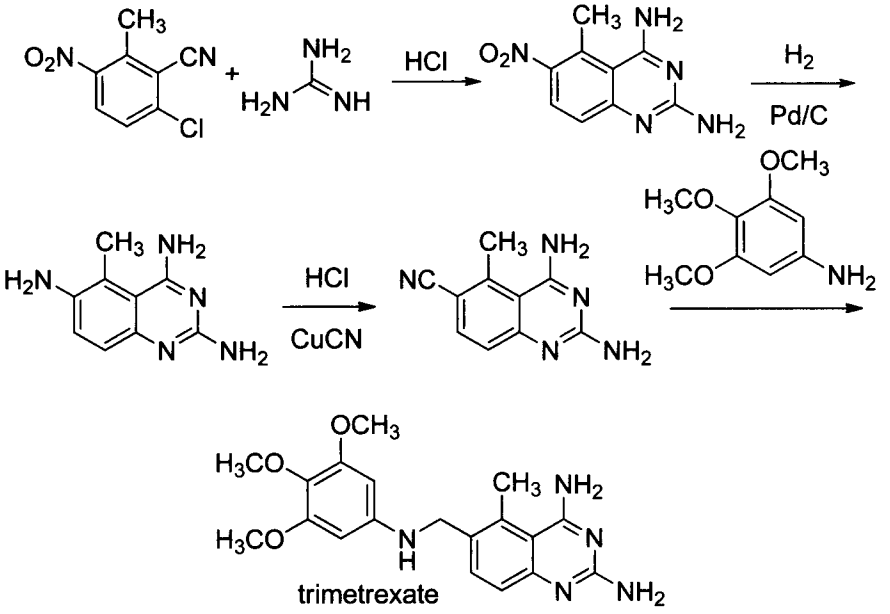


trimetrexate

The synthesis of trimetrexate, reported by Davoll and Johnson,[44] began with an acid-catalyzed condensation reaction between 1-nitro-4-chloro-*o*-toluonitrile and guanidine to produce 2,4-diamino-5-methyl-6-nitro-quinazoline as an intermediate for further functionalization. Hydrogenation of 2,4-diamino-5-methyl-6-nitro-quinazoline produced the corresponding 2,4,6-triamino-quinazoline, which was readily converted the corresponding nitrile upon treatment with hydrochloric acid and cuprocyanide. Condensation of the nitrile with 2,3,4-trimethoxyaniline produced trimetrexate in 26% overall yield.



trimetrexate

Although never commercially marketed, nifurquinazole has been shown to be a powerful nitrofuran-based bactericidal. Nitrofuran-based antibiotics function by a complex set of mechanisms that result in the degradation of bacterial macromolecules. Rapid reduction of nitrofurans via flavoproteins, specifically nitrofuran reductase, occurs inside the bacterial cell. The highly reactive species that are generated in this process are ultimately responsible for damage to ribosomal proteins and DNA, and they