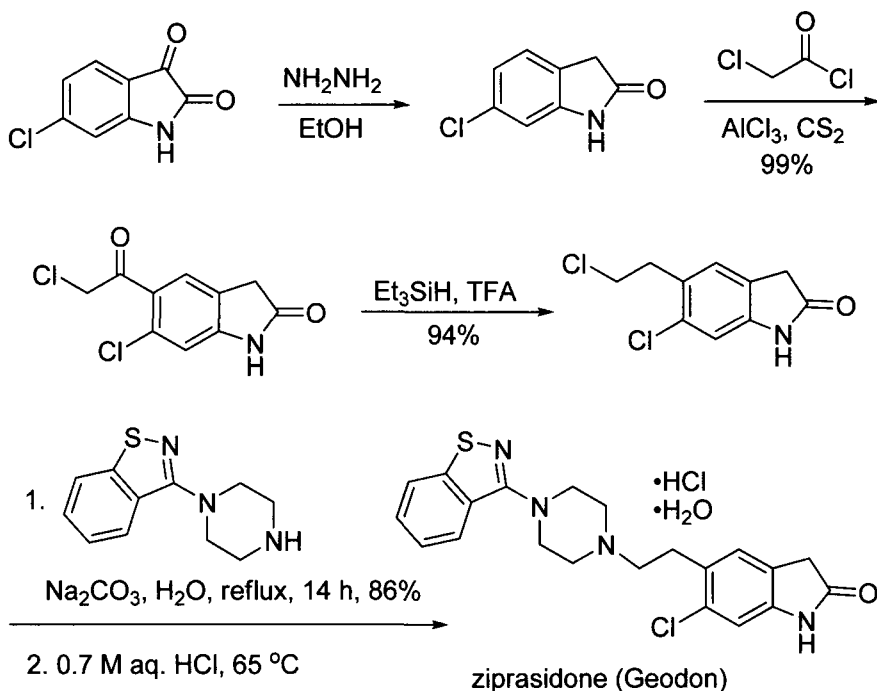


of the coupling step was improved dramatically (86%) when the reaction was conducted in water.



Another oxindole-containing drug is sunitinib (Sutent), discovered by Sugen. Sunitinib, an angiogenesis inhibitor, inhibits a panel of kinases including VEGFR1, VEGFR2, VEGFR3, PDGFR $\alpha$ , PDGFR $\beta$ , Flt-3, and c-Kit. Its core structure 5-fluorooxindole was constructed from 5-fluoroisatin in two steps.<sup>61</sup> Thus, heating a neat mixture of 5-fluoroisatin and hydrazine hydrate to 110 °C effected a Wolff–Kishner reduction and ring-opening to give an acyl hydrazide. The crude material was subjected to an intramolecular acylation reaction by exposure to aqueous HCl at room temperature to afford the oxindole in 73% yield over two steps.

