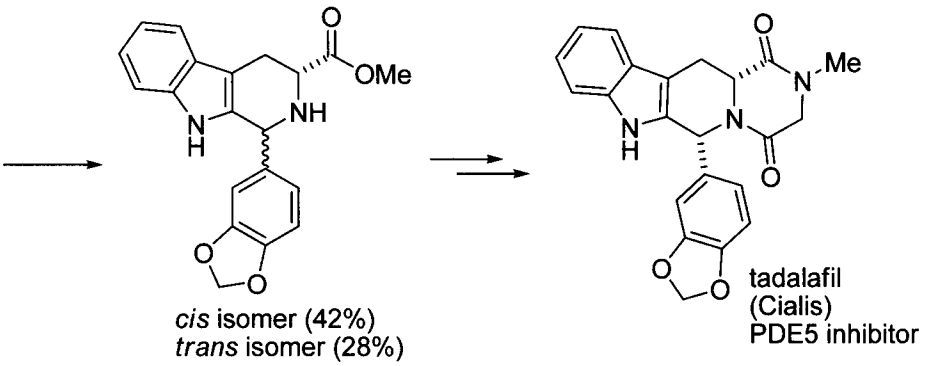
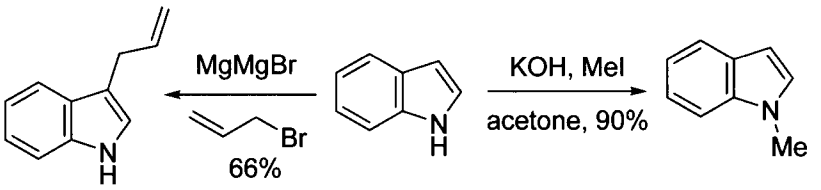


3.2.4 Metallation

The outcome of metallation of indoles depends on many factors, but the base is a crucial player. For instance, indole treated with NaH followed by addition of MeI undergoes an S_N2 reaction at N1 to give 1-methyl-1*H*-indole exclusively. On the other hand, indole treated with a Grignard reagent and then quenched by allyl bromide produced 3-allyl-1*H*-indole predominantly.



As far as N1 protected indoles are concerned, metallation primarily takes place at the C2 position. As a consequence, a "dummy protective group" could be engineered to steer the metallation to the C2 position. Indole is treated with *n*-BuLi and then carbon dioxide is added. The *N*-carboxylated intermediate is then treated with another equivalent of *t*-BuLi and quenched with an electrophile.