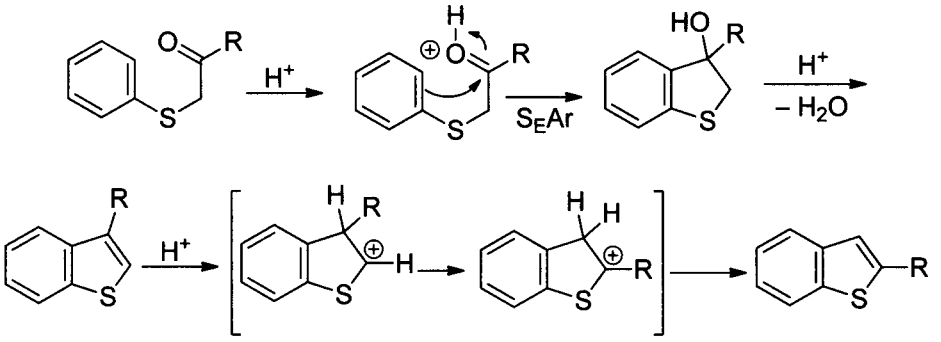
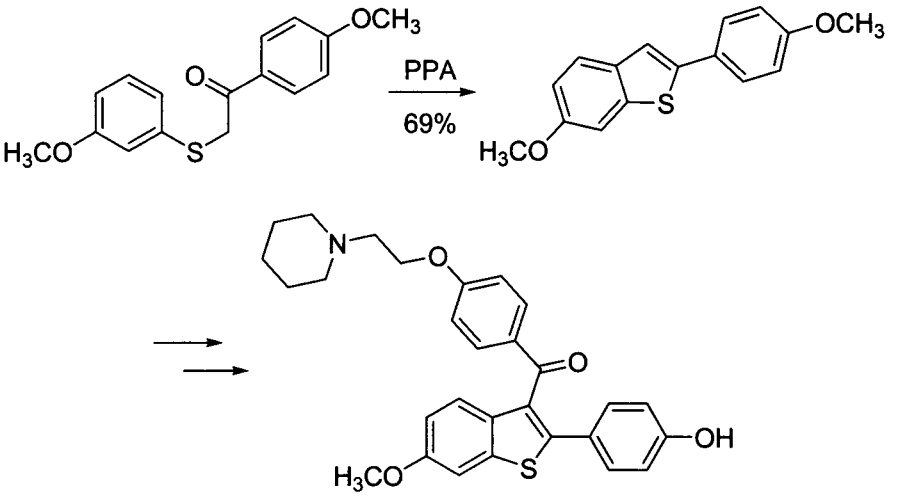


This methodology was used by researchers at Eli Lilly to generate benzothiophene derivatives of tamoxifen.[88] The cyclization and rearrangement reaction to produce the desired 2-aryl benzothiophene derivatives were promoted by polyphosphoric acid (PPA). These 2-aryl benzothiophene were then subjected to several additional transformations to produce LY156758 (raloxifene).



LY156758 (raloxifene)

In pursuit of additional derivatives, Eli Lilly scientists sought to synthesize constrained analogues of raloxifene.[117] The synthesis of these analogues used a unique method of constructing the benzothiophene ring system through an acid-promoted "dehydrative carbocationic cyclization" of the hydroxythioacetamide using methanesulfonic acid as illustrated below.