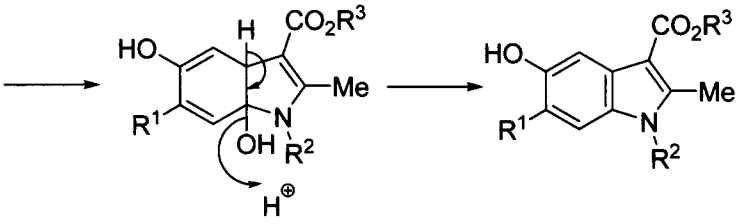
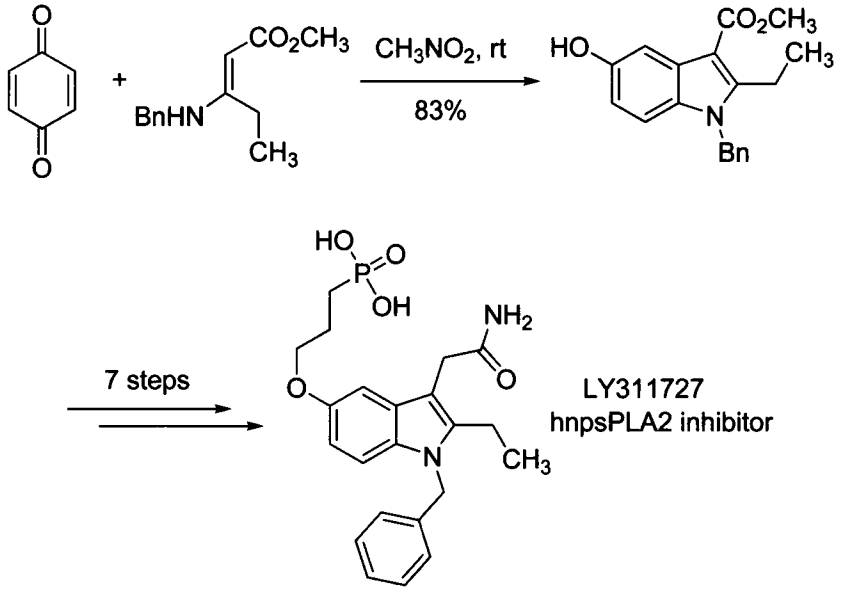


The Nenitzescu indole synthesis was employed to synthesize LY311727, an indole acetic acid-based selective inhibitor of human non-pancreatic secretory phospholipase A2 (hnpsPLA2) by Eli Lilly as a potential treatment for sepsis.[37] The Nenitzescu condensation of benzoquinone with the β-aminoacrylate was carried out in CH_3NO_2 to provide the desired 5-hydroxylindole. An additional seven steps then afforded LY311727.



A Nenitzescu indole synthesis was applied to synthesize benzoxazines as highly selective antagonists at M_4 muscarinic receptors.[38] Ammonia was bubbled into the methanolic solution of the β-keto-ester to give the enamine, which was coupled with 1,4-benzoquinone to give the Nenitzescu indole in 6% yield! The low yield is often acceptable in drug discovery where the key is to make potent, bio-available, and safe compounds. The synthesis could be improved only after the compounds showed desirable profiles. The Nenitzescu indole underwent a Vilsmerier reaction en route to deliver a benzoxazine as a potent and selective M_4 muscarinic antagonist. These selective M_4 muscarinic antagonists may