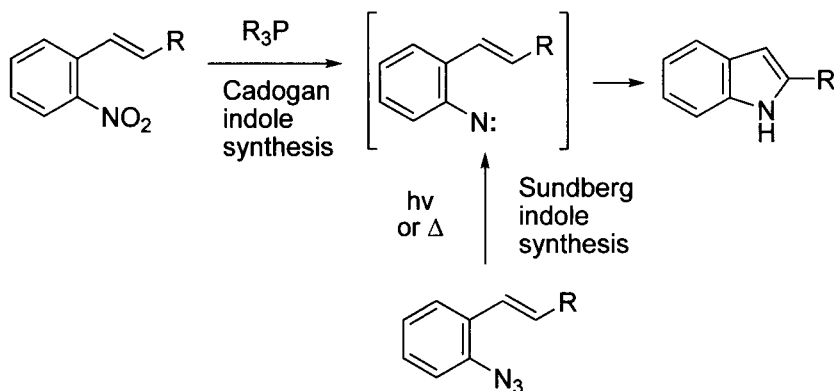


with trialkyl phosphite and subsequent cyclization of the resulting nitrene to form indoles.^{54,55} The mechanism of the Cadogan–Sundberg indole synthesis is similar to that of the Sundberg indole synthesis, which involves a nitrene as the key intermediate.



The Cadogan–Sundberg indole synthesis has recently found utility in medicinal chemistry. It was employed to prepare a novel class of kinase domain receptor (KDR) inhibitors.⁵⁶ The KDR kinase is a tyrosine kinase that has a high affinity for vascular endothelial growth factor (VEGF) and is believed to be a primary mediator of tumor induced angiogenesis. Compounds that inhibit, modulate, or regulate the KDR receptor are useful for the prevention and treatment of tumor induced angiogenesis. Reductive cyclization of the nitrostyrene with $P(OEt)_3$ afforded the indole intermediate. The deprotection of the masked quinolin-2-one moiety of chloroquinoline was accomplished by hydrolysis of chloroquinoline in a 1:1 mixture of $AcOH/H_2O$ to give the freebase of the final product.

