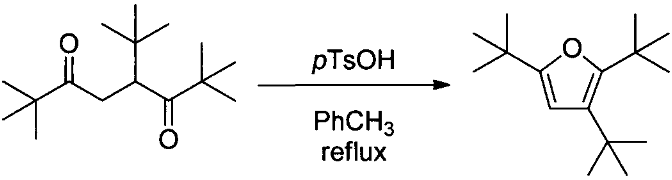
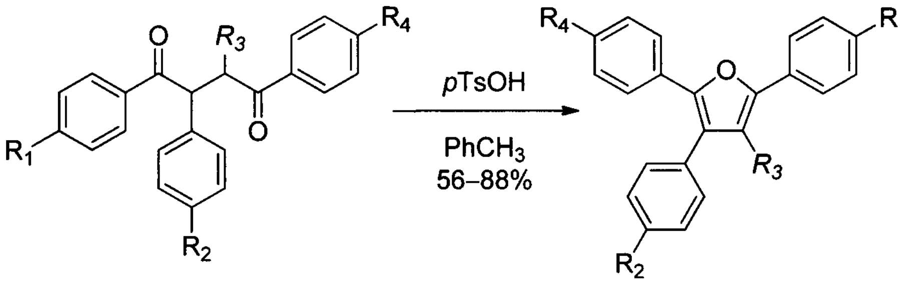
Another interesting example of the use of the Paal–Knorr synthesis is in the preparation of trialkylfurans. General compounds of this class have been shown to play important roles in biological signalling. Weirsum and co-workers used *p*-toluenesulfonic acid in refluxing ether to produce a sterically congested tri-*t*-butylfuran from the corresponding dione.[44]



Tetrasubstituted furan derivatives have also been synthesized via the Paal–Knorr synthesis. In one example, Katzenellenbogen and co-workers prepared numerous alkyl triarylfurans in modest to high yield by treating the corresponding 1,4-dione precursors with *p*-toluenesulfonic acid.[45,46] These compounds, which were designed to mimic estradiol, were evaluated for activity toward the estrogen receptor (ER) α, and it was shown that analogues with basic side chains on the *C*4 phenol were high-affinity antagonists.



Diels–Alder/retro-Diels–Alder Reactions

Combination Diels–Alder/retro-Diels–Alder reactions have been used to prepare substituted furan derivatives from furans and oxazolidinones. Reaction of a furan or oxazolidinone derivative with a disubstituted alkyne (usual dimethyl acetylenedicarboxylate or diethyl acetylenedicarboxylate) produces the Diels–Alder adduct, which can undergo a retro-Diels–Alder reaction to give the desired furan derivative.