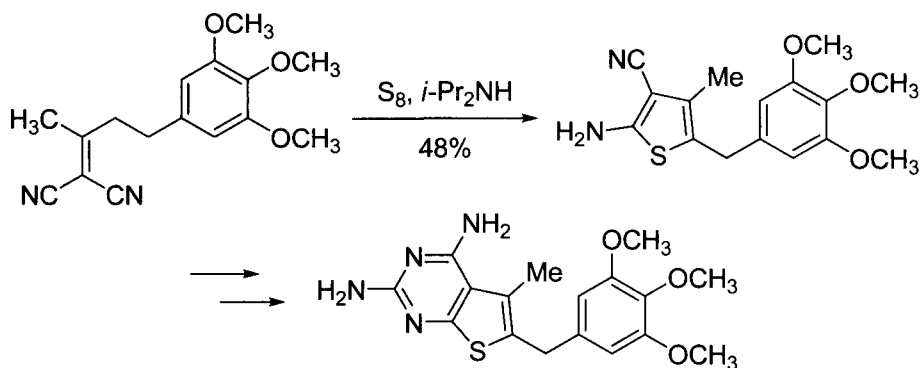


Rosowsky and co-workers sought to synthesize thiophene-containing derivatives of trimetrexate and piritrexim in their search for potential inhibitors of *Pneumocystis carinii* and *Toxoplasma gondii* dihydrofolate reductase.¹⁰⁹ Their goal was to improve selectivity and limit the potential side effects found in trimetrexate and piritrexim. The thiophene moieties were installed by means of a Gewald aminothiophene reaction similar to those used in the creation of the *C*-nucleosides shown previously. Desired substitution patterns were accessed by the use of appropriate substrates as shown below.



The synthetic versatility of the Fiesselman and Gewald reaction is further highlighted in the synthesis of both 2-amino- and 3-aminothiophene derivatives by Romagnoli and co-workers.^{110,111}

