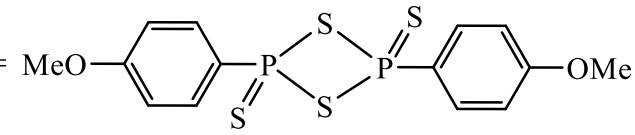
7.2) Synthetic methods:

7.2.1) From 1,4-dicarbonyl compounds and a source of sulfide (Paal – Knorr thiophene synthesis or Paal thiophene synthesis):

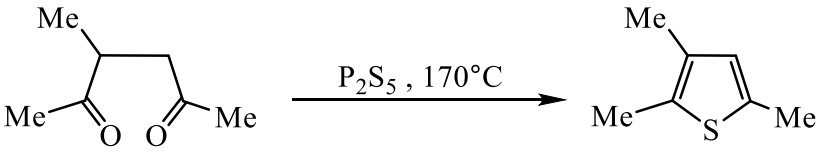
This method allows the generation of thiophene by condensation of a 1,4-dicarbonyl compound in the presence of a source of sulfur such as phosphorous pentasulfide P_2S_5 or Lawesson's reagent (LR).

Note: P_2S_5 present as a dimer P_4S_{10}

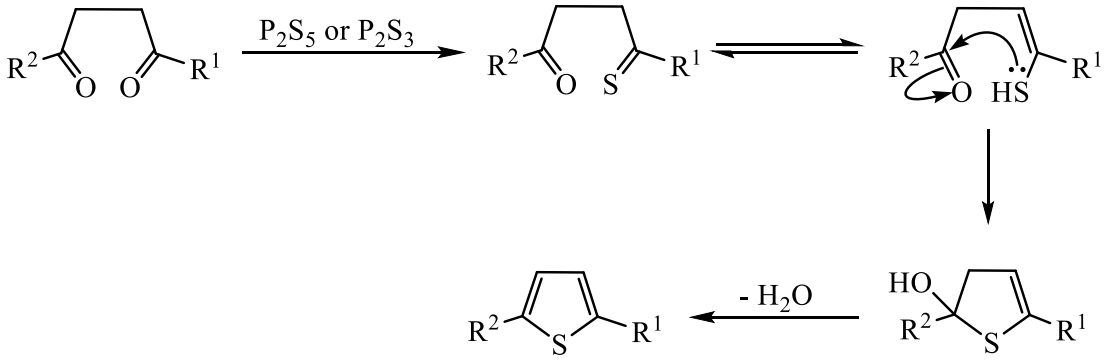
Lawesson's reagent (LR) =



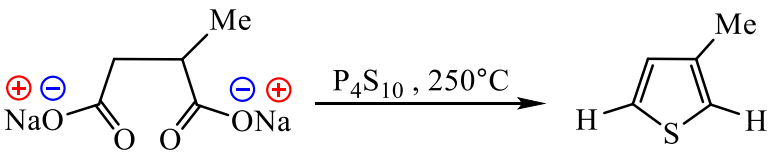
e.g.



Phosphorous pentasulfide act as sulfurizing and dehydrating agent, the reaction proceed presumably, but not necessarily via thioketone since it could proceed via bis(thioketone).



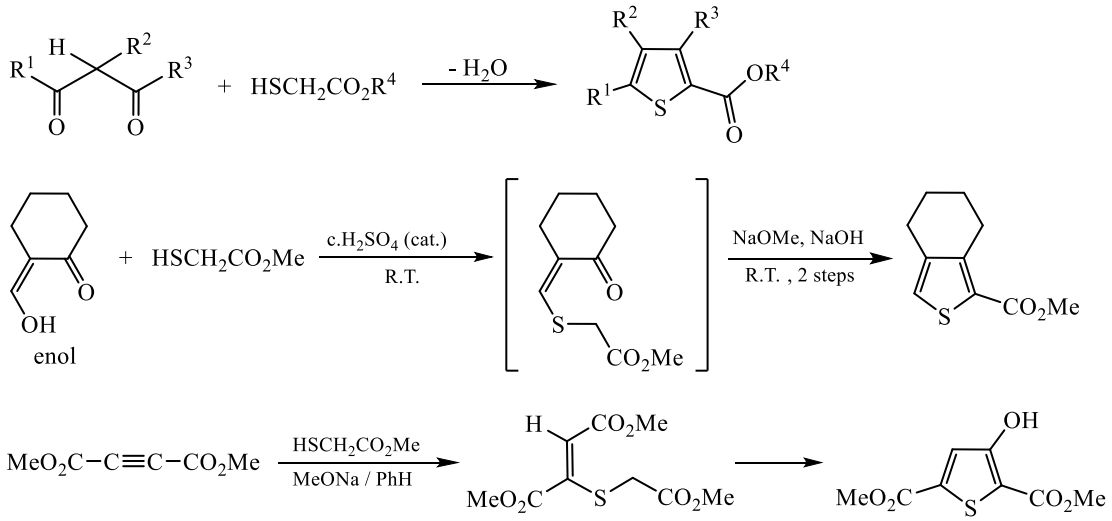
P_2S_5 or P_2S_3 reduce the carboxyl group if it was a part of 1,4-dicarbonyl compound.



7.2.3) From 1,3-dicarbonyl compounds:

Thiophene can be prepared by the reaction of mercaptoacetic ester (thioglycolic ester) with 1,3-dicarbonyl compounds or acetylinic esters.

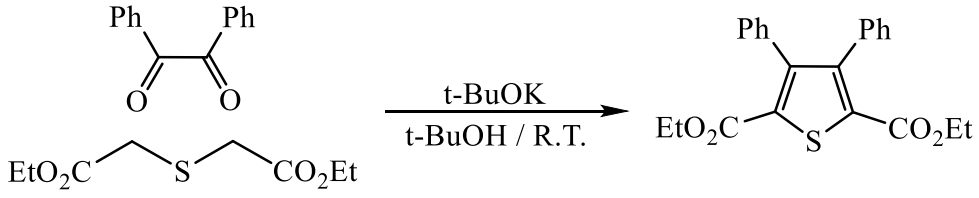
examples



Note: The reaction between acetylinic ester and thioglycolic ester proceed via nucleophilic addition of thiolate anion followed by cyclization through Claisen condensation.

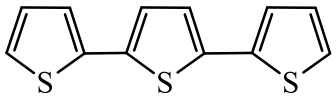
7.2.3) From 1,2-dicarbonyl compounds (the Hinsberg synthesis):

1,2-Dicarbonyl compounds condense with thio-diacetate to give substituted thiophenes. The reaction proceed through two consecutive aldol condensation with the carbonyl groups.

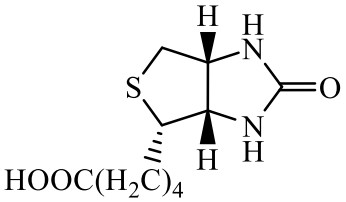


7.3) Naturally occurring thiophene compounds:

There is no clear evidences for the presence of thiophene or tetrahydrothiophene in nature inspite the fact that it do exist in different fractions of crude oil (petrol). However, thiophene derivatives exist in a number of natural products like:



α–Terthienyl
in flowers of indian marigold plant



Biotin, vitamin H