α-Formylketene dithioacetals are versatile starting materials for the synthesis of number of heterocyclic compounds such as pyridones and nicotinonitriles. The methods for the synthesis of such formyl derivatives of ketene dithioacetals are very few. They are usually obtained indirectly from the corresponding bis(methylsulfanyl)ethylene esters via a reduction-oxidation process. This is shown by the oxidation of β-hydroxyketene dithioacetal 2, synthesized by the lithium aluminium hydride reduction of bis(methylsulfanyl)ethylene ester 1 to afford formylketene dithioacetal 3 (Scheme 1).

Rudorf et al have reported the synthesis of formylketene dithioacetals 6 from aroyl acetaldehydes 4 using usual procedure for the synthesis of α-oxoketene dithioacetals (Scheme 17). In their reactions the formylketene dithioacetals 6 were obtained in 40-50% yields. Using various alkylating agents like methyl iodide, ethyl iodide, dibromoethane, phenacyl bromide, bromoacetone etc they synthesized a variety of formylketene dithioacetals.
As sulfur is known to stabilize both positive and negative charges, the double bond in aroylketene dithioacetals 7 should be susceptible to electrophilic attack by Vilsmeier-Haack reagent. The Vilsmeier-Haack reaction, which involves electrophilic substitution of a suitable carbon nucleophile with a chloromethyleneiminium salt, provides one of the widely used methods for formylation. A large number of aromatic and aliphatic substrates undergo iminoalkylation by the Vilsmeier-Haack reagent. Earlier reports from our laboratory have proved the synthetic utility of functionalized halomethyleneiminium salts in the synthesis of carbocyclic and heterocyclic compounds. Asokan et al have also reported some interesting transformations of acylketene dithioacetals and ß-oxodithiocarboxylates under Vilsmeier-Haack reaction conditions. As a continuation to this Asokan and Anabha treated ketene dithioacetals with chloromethyleneiminium salt to afford 2-aroyl-3,3-bis(alkylsulfanyl)acrylaldehydes 8 (Scheme 3).

![Scheme 3](image_url)

The doubly activated 2-aroyl-3,3-bis(alkylsulfanyl)acrylaldehydes (α-formylketene dithioacetals) 8 are unique building units because of the presence of both ketonic and aldehyde functional groups in addition to the ketene dithioacetal moiety at the α-position. As each of these three groups has varying reactivity towards condensing agents, their selectivity can be utilized effectively for the synthesis of a wide variety of substituted and annulated heterocycles. In an earlier report Asokan et al have described the formation of 2-aroyl-2-[(3,3-bis(methylsulfanyl)-2-propyldene]malononitriles 9 from 2-aroyl-3,3-bis(methylsulfanyl)acrylaldehydes 8 and their cyclization reactions in the presence of hydrochloric acid in tertiary butanol to afford
5-aroyl-6-(methylsulfanyl)-2-oxo-1,2-dihydro-3-pyridinecarbonitriles 10 (Scheme 4).  

![Scheme 4](image)

When the dithiolate anion 5 was alkylated by Rudorf and coworkers with two equivalents of α-haloketones or α-halonitriles, the resulted formylketene dithioacetals were in situ cyclized to form corresponding substituted thiophenes 11 and thienothiophenes 12 (Scheme 5).

![Scheme 5](image)

Rudorf et al have attempted to explore the synthetic utility of these compounds in the synthesis of functionalized heterocycles such as pyridinethiones 13 which could then be converted into imidazolinyl substituted heterocycles 15 and 16 (Scheme 6).
Asokan’s group has also developed facile methods for the synthesis of functionalized nicotinonitriles 18 and 19 from 2-aroyl-3,3-bis(methylsulfanyl)acrylaldehydes 8 in good yields (Scheme 7).\(^1\)

![Scheme 7](image)

In this chapter we have discussed the various methods for the synthesis of α-formylketene dithioacetals and their synthetic applications. The methods reported so far for this versatile synthon are very few and the synthetic potentials of this reagent are rarely explored. Therefore the syntheses of various compounds starting from α-formylketene dithioacetals described in this thesis are highly relevant.

References


