Synthesis and applications of xanthate esters

ABSTRACT

We herein present a base induced cycloaddition of active methylene isocyanides like tosylmethyl isocyanide and ethyl isocyanoacetate with xanthate esters for the synthesis of 5-(alkoxy)-4-(tosyl/ethoxycarbonyl)-1,3-thiazoles in DMF. In addition, we have explored xanthate esters as alkylating agents for amines in the presence of acid catalyst. Finally, reaction between xanthate esters and arylmethyl isocyanides produced carbonodithioates in the presence of a base in DMF.

1. INTRODUCTION

Xanthate esters are an important class of organosulfur compounds used in Claisen rearrangements [1], Barton–McCombie [2] and Tschugaeff reactions [3]. They are also involved in the synthesis of natural products [4]. Besides, they are useful key intermediates in the syntheses of photosensitizers [5], carbanions [6], thiocarbonates [7] and thiols [8].

We are actively engaged in organic synthesis [9-16], bioorganic and medicinal chemistry [17-30]. In the last decade, we have developed many organo sulfur substrates such as α-oxodithioesters [31-34], α-oxothioamides [35-38], thioimidates [39-42], α-ketothioesters [43], *S*-methyl thiouronium salts [14], alkyl 2-(methylthio)-2-thioxoacetates [13], alkyl 2-amino-2-thioxoacetates [13], 2-oxo-2-(amino)ethanedithioates [12]. Besides, we are also involved in academic writings like reviews [44-49] and book chapters [50-53]. In continuation of these works, in this chapter we present the synthesis and synthetic applications of xanthate esters.

2. SYNTHESIS OF XANTHATE ESTERS

The required xanthate esters **2** were synthesized from alcohol **1** as illustrated in Table 1. Thus, various arylmethyl/alkyl/cycloalkyl alcohols reacted with carbon disulfide in the presence of

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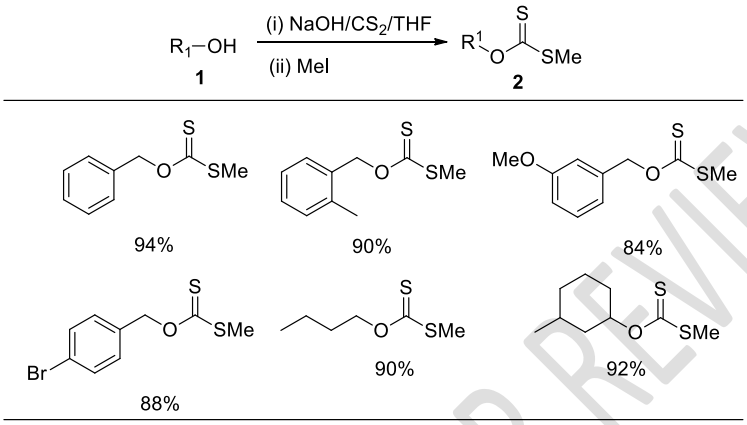
Optical and electrical properties of nickel xanthate thin films, Bulletin of Materials Science 37, 553-561, 2014
Cobalt xanthate thin film with chemical bath deposition, Journal of Nanomaterials 2013 (1), 139864
Optical properties of cobalt xanthate films on different substrates, International Journal of Minerals, Metallurgy, and Materials 21, 736-740, 2014

sodium hydroxide in THF, followed by treatment with methyl iodide afforded xanthate esters **2** in 84-94% yields [54].

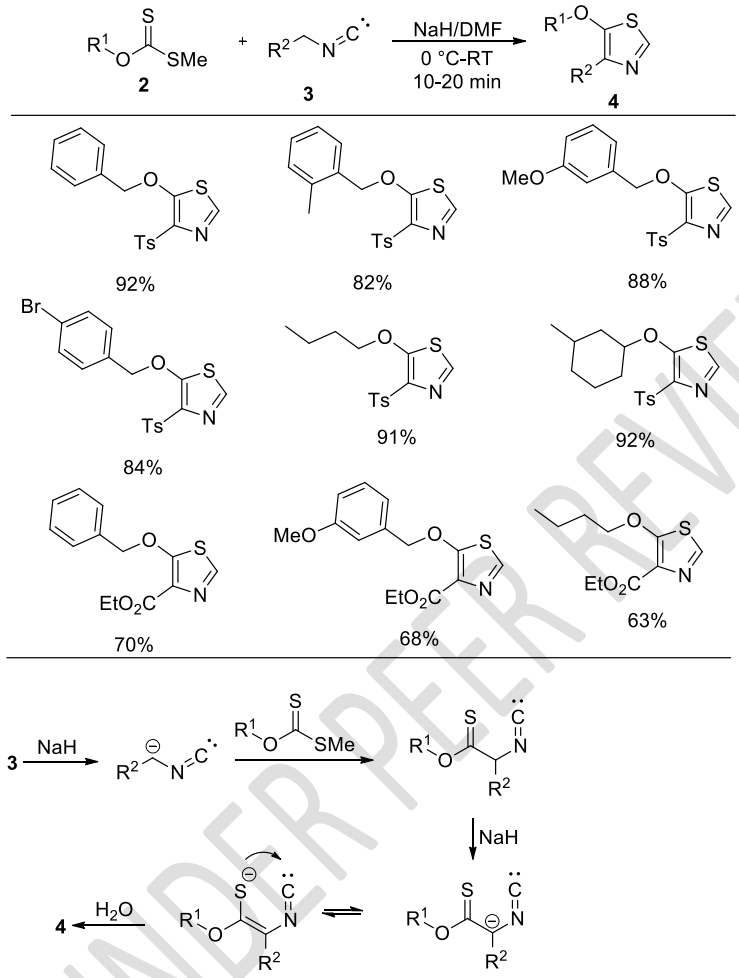
Table 1. Synthesis of xanthate esters



3. SYNTHESIS OF THIAZOLES

With the key intermediates in hand, we next explored their application for the synthesis of thiazoles (Table 2) by base induced cycloaddition with active methylene isocyanides. We screened a reaction in various solvents like dioxane, DMSO, toluene, acetonitrile, THF and DMF in the presence of sodium hydride as a base of choice. The optimization data indicated that DMF was found to the best solvent in the presence of sodium hydride with respect to yield and reaction time. Under this optimal reaction condition, active methylene isocyanides such as tosylmethyl isocyanide and ethyl isocyanoacetate (**3**) reacted smoothly with structurally diverse xanthate esters **2** to produce 5-(alkoxy)-4-(tosyl/ethoxycarbonyl)-1,3-thiazoles in 82-92% and 63-70% yield respectively. The possible mechanism of formation of thiazoles is presented in Scheme 1 [54].

Table 2. Synthesis of 5-(alkoxy)-4-(tosyl/ethoxycarbonyl)-1,3-thiazoles

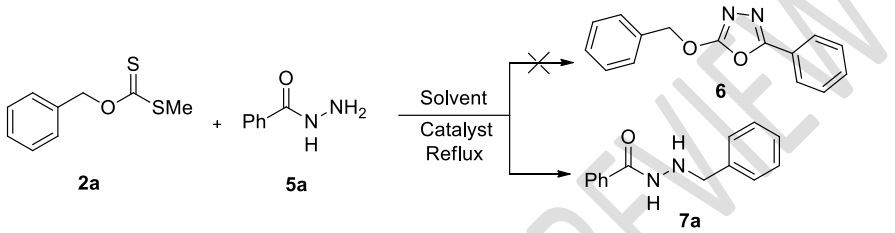


Scheme 1. Possible mechanism of formation of thiazoles

4. ALKYLATION OF AMINES

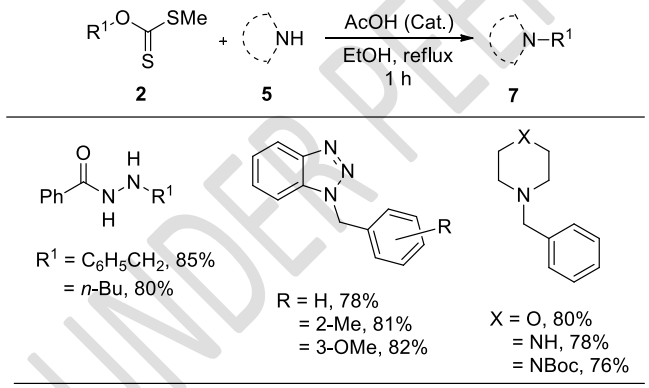
With an objective of synthesizing 2-(benzyloxy)-5-phenyl-1,3,4-oxadiazole **6** we conducted the reaction between *O*-benzyl *S*-methyl carbonodithioate **2a** and benzohydrazide **5a** in the presence of an acid catalyst in a solvent (Scheme 2). A careful characterization of isolated product indicated that *N*'-benzylbenzohydrazide **7a** has formed. We conducted this reaction in various solvents like

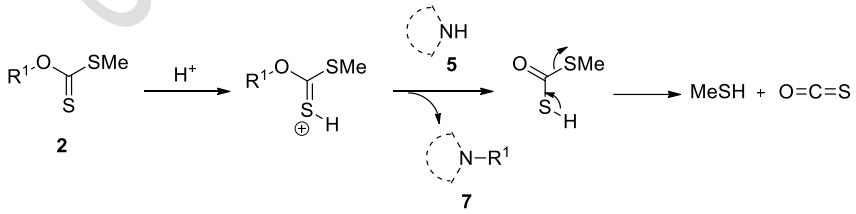
DMF, DMSO, EtOH, acetonitrile and THF and acid catalysts like *p*-toluenesulfonic acid (*p*-TSA), trifluroacetic acid and acetic acid. Amongst, acetic acid in ethanol was found to be the best combination to achieve alkylation. Under this optimal reaction condition, various amines **5** were *N*-alkylated by structurally diverse xanthate esters **2** to afford *N*-alkylated amines **7** in 76-85% yields (Table 3). The plausible mechanism of alkylation is depicted in Scheme 3 [55].



Scheme 2. Unexpected alkylation

Table 3. *N*-alkylation by xanthate esters

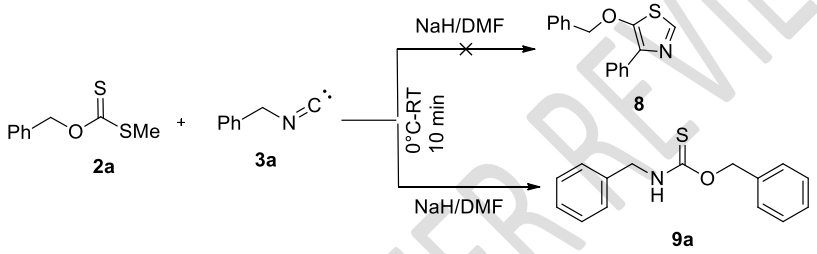




Scheme 3. Possible mechanism of *N*-alkylation

5. SYNTHESIS OF CARBAMOTHIOATES

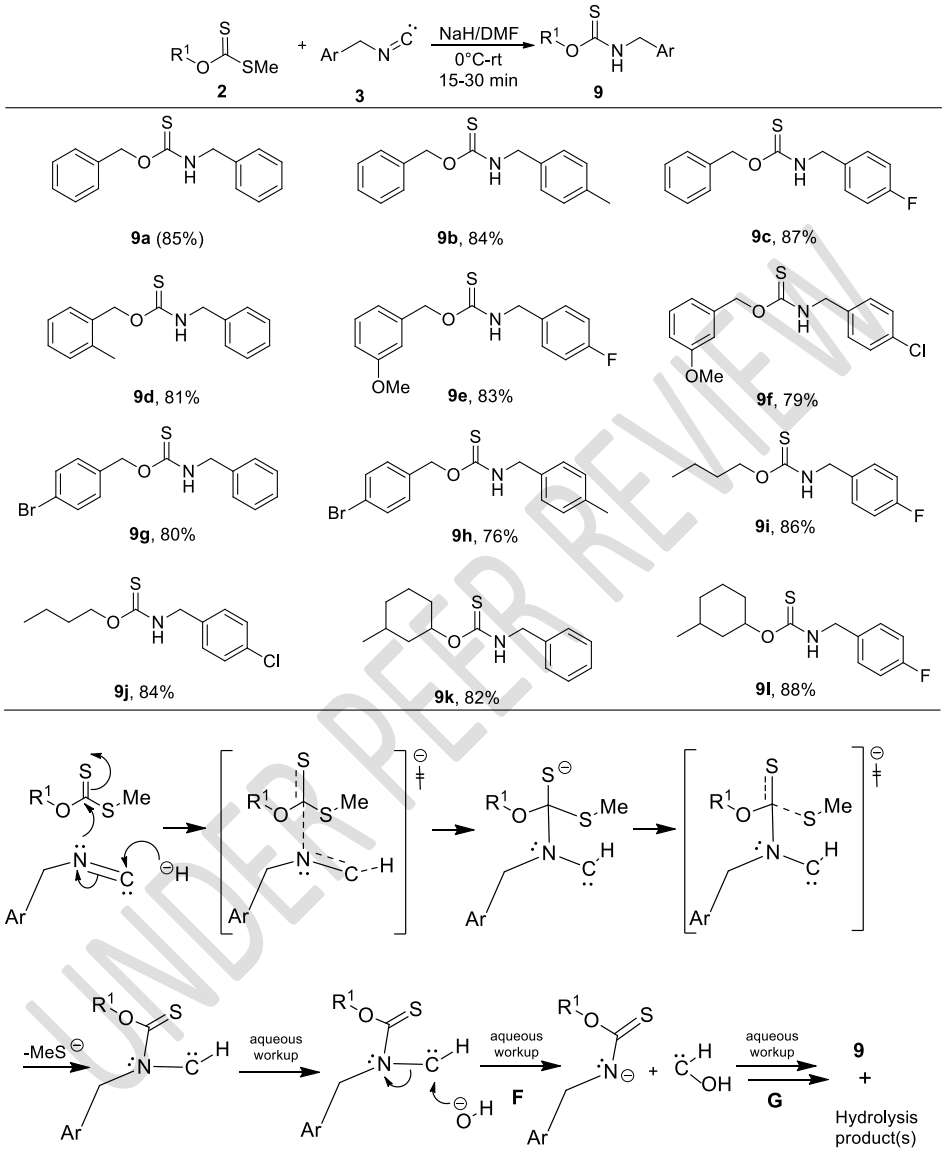
With an objective of getting 5-(benzyloxy)-4-phenylthiazole **8**, we conducted the reaction between *O*-benzyl *S*-methyl carbonodithioate **2a** and benzyl isocyanide **3a** in the presence of sodium hydride in DMF similar to Table 2, Scheme 1 (Scheme 4). Unexpectedly, we observed the formation of *O*-benzyl benzylcarbamothioate **9a** base on careful analysis of spectral data. Analysis of NMR spectra of **9a** indicated that it exists as geometrically isomeric rotamers [56].



Scheme 4. Synthesis of 5-(benzyloxy)-4-phenylthiazole

We conducted the above reaction in other various solvents like THF, acetonitrile, dioxane, DMSO and toluene in the presence of sodium hydride as a base of choice. Among the screened solvents, DMF was found to be the best. Under this optimal reaction condition, we next explored the generality of the reaction by conducting the reaction between diverse xanthate esters **2** and arylmethyl isocyanides **3**, which furnished corresponding carbonodithioates **9** in 76-87% yield (Table 4). The possible mechanism of formation of carbonodithioates **9** is presented in Scheme 5, which is supported by DFT-calculations [56].

Table 4. Synthesis of carbonodithioates



Scheme 5. Possible mechanism of formation of carbonodithioates

6. CONCLUSION

In summary, we have presented the synthesis of 5-(alkoxy)-4-(tosyl/ethoxycarbonyl)-1,3-thiazoles by the reaction between xanthate esters and active methylene isocyanides like tosylmethyl isocyanide and ethyl isocyanoacetate in the presence of sodium hydride in DMF. Besides, in the presence of acid catalyst, xanthate esters behaved as alkylating agent for amines. Finally, we have shed light on an unexpected formation carbonodithioates by the reaction between xanthate esters and arylmethyl isocyanides in the presence of sodium hydride in DMF.

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DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during the writing or editing of manuscripts.

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