

An efficient synthesis of dithiocarbamates from primary amines, CS₂ and maleic anhydride

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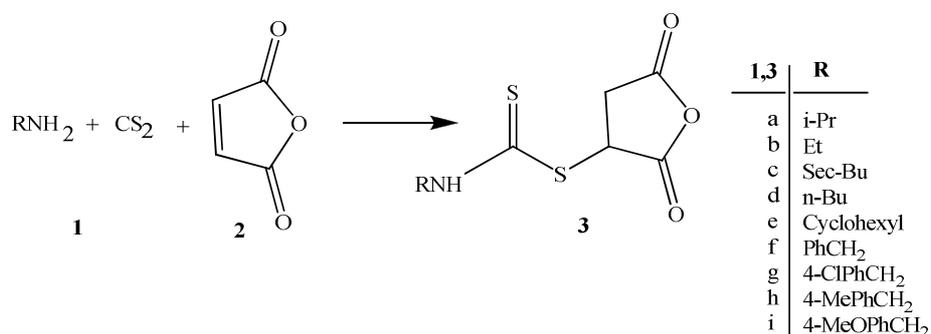
Abstract: An efficient, one-pot synthesis of new dithiocarbamates is described via three component reaction of maleic anhydride, CS₂ and primary amines in good to excellent yields.

Keywords: Dithiocarbamate; Primary amines; One-pot synthesis; Maleic anhydride.

Introduction

Organic dithiocarbamates have received a great deal of attention due to their interesting chemistry and wide utility as radical precursors and intermediates in organic synthesis [1, 2]. They also have a variety of applications in agriculture as pesticides, as well as in the rubber industries as vulcanization accelerators; and antioxidants [3-4]. Because they have strong metal-binding capacity, they can act as inhibitors of enzymes and have a profound effect on biological systems [5-6]. Moreover, they have found application in the treatment of cancer and HIV [7]. Synthesis of

dithiocarbamates by using thiophosgene, chlorothioformates and isothiocyanates [8] which are costly and toxic reagents, is not convenient. Recently, a variety of reagents and catalyst including Mitsunobu's reagent [9a], solid LiClO₄/DMF [9b], DMSO [9c] and Cs₂CO₃/tetrabutylammonium iodide [9d] have been used in the synthesis of them. In this paper, we prepared dithiocarbamate derivatives with different substitutions in a one-pot reaction of amines, carbon disulfide and maleic anhydride without any organic catalyst (Scheme 1).



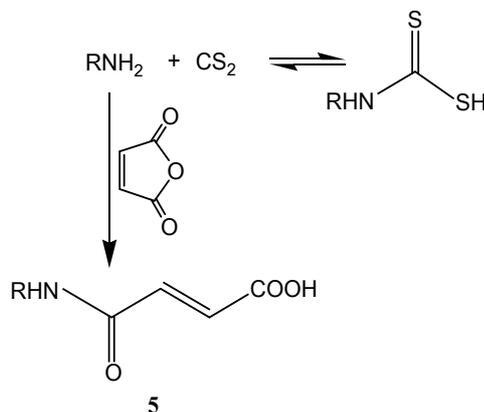
Scheme 1. Formation of tetrahydro-2,5-dioxofuran-3-yl alkylcarbamodithioates (**3**)

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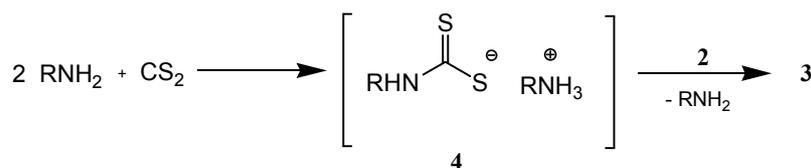
Results and discussion

The above three-component reaction leads to dithiocarbamate derivatives **3** in 70-95% yields at room temperature. These products are stable even under reflux in toluene for 12 h. We had found, although

amines react with unsaturated anhydride in ring-opening process (Scheme 2) but reaction of the xanthate salt **4**, generated from the amine and CS₂, with maleic anhydride is placed without ring-opening reaction (Scheme 3).



Scheme 2. Reaction of the amine with maleic anhydride



Scheme 3. A tentative mechanism for formation of carbamodithioates **3**.

In order to find the best reaction conditions, we first mixed amines with CS₂ without any solvent and then maleic anhydride is slowly added to this mixture in the room temperature. In conclusion, we have described a convenient and efficient protocol for the one-pot, three-component coupling of various aliphatic amines with CS₂ and maleic anhydride. This reaction proceeds via Michael addition of the salt of dithiocarbamic acid **4** to maleic anhydride in high yields and competes with direct addition of amines to maleic anhydride. Structures of compounds **3a-j** were characterized by IR, ¹H NMR and ¹³C NMR. The mass spectra of compounds **3a-i** display molecular ion peaks at appropriate *m/z* values. The ¹H NMR spectrum of **3a-i** exhibited three characteristic systems of the doublet of doublets (ABC) for the CH₂ and CH groups of anhydride with ³J_{HH} of about 18, 8.5 and 3.5 Hz. The proton decoupled ¹³C NMR spectrum of **3** shows two distinct resonances for the C=O groups of anhydride and a distinct resonance for the C=S group.

Structure of compound **3c** is consistent with two diastereomers in the same yields. The ¹H NMR spectra

of **3c** shows two doublets ($\delta = 1.42$ and 1.46 ppm) for CH₃-C-N and two multiples ($\delta = 4.28$ and 5.06 ppm) for CH-S. The ¹³C NMR spectrum of **3c** shows two distinct resonances for every carbon. The methylene protons of the benzyl group in **3f-i** are diastereotopic and exhibit characteristic AB systems. We have also found secondary amines react with maleic anhydride directly under ring-opening process and don't act such as primary amines.

Experimental

Maleic anhydride, CS₂, and amines **1** were obtained from Fluka and were used without further purification. M.p.: Electrothermal-9100 apparatus; IR Spectra: Shimadzu IR-460 spectrometer. ¹H and ¹³C NMR spectra: Bruker DRX-300 AVANCE instrument; in CDCl₃ at 300 and 75 MHz, respectively; δ in ppm, *J* in Hz; EI-MS (70 eV): Finnigan-MAT-8430 mass spectrometer, in *m/z*. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer.

