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Synthesis and X-ray analysis of butyl and glycosyl (2-arylamino-4,4-dimethyl-6-oxocyclohex-1-ene)carbodithioates and their possible cyclization to 2-thioxo-6,7-dihydro-1*H*-benzo[*d*][1,3]thiazin-5(2*H*)-one derivatives

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ABSTRACT

Variety of butyl [2-arylamino-4,4-dimethyl-6-oxo-cyclohex-1-ene]carbodithioates (**3a–c**), 2-thioxo-6,7-dihydro-1*H*-benzo[*d*][1,3]thiazin-5(2*H*)-one derivatives (**5a–c**), and the glucosyl carbodithioates **6a–c** as well as galactosyl carbodithioates **7a–c** have been synthesized from the reaction of enaminone derivatives **1a–c** with carbon disulfide followed by the alkylation with *n*-butyl bromide and α-D-glycosyl bromides, respectively. The amount of carbon disulfide plays a great role in the mode of reaction. The structures of the synthesized compounds were elucidated by spectral data and X-ray crystallography.

1. Introduction

Much attention has been focused on compounds functionalized with the – CSS-group because of their diversity as represented by industrial chemicals, such as rodent repellents, vulcanization additives in rubber manufacturing, lubricants, and polymers in addition to their metal chelating properties, which are used in analytical chemistry and waste management. These compounds exhibit a wide spectrum of biological activities[1–4] and are used as fungicides in pesticides and fumigants.[4,5] They modulate the function of a number of key proteins involved in apoptosis, oxidative stress, transcription, and proteosome function.[6] Thus, they are of potential therapeutic value for cancer,[7–10] viral infection,[11] antitumor activity,[12] inflammation,[13] immunosuppressive agents,[14] and antioxidants, as well as inhibition of the replication of rhinovirus, influenza virus, and polio virus.[11–15] Their biological effects are dependent on their structural characteristics that influence the stability decomposition and their metabolic products in vivo.[16–20]

A great demand for significant amounts of oligosaccharides and glycoconjugates for biological, medicinal, and pharmacological studies has been generated because of the important roles played by these compounds in biological processes.[21] Therefore, tremendous effort has been made to develop new procedures for the synthesis of glycosides and developing strategies for the formation of glycosidic bonds.[21–24] However, efforts are still directed toward the synthesis of glycosidic bonds, particularly in a stereoselective manner. Glycosyl sulfanyl heterocycles have been regarded as good glycosyl donors in addition to their biological activities such as the inhibition of enzyme activity.[25] Having the above aspects in mind and in addition to the paucity of work that has been reported on the glycosyl carbodithioates and their biological value[26–28] as well as their value as glycosyl donors for glycosyl bond formation, we became interested in the synthesis of new members in this class of compounds. We are also investigating their spectra and X-ray crystallographic data as a continuation of our work,[23,24] and our interest[29–32] in elucidating structures by X-ray crystallography.

2. Results and discussion

The reactivity of enaminones toward some electrophilic reagents was investigated in order to synthesize carbodithioates and benzothiazine derivatives. Thus, the reaction of **1a–c**[33] with carbon disulfide in dimethyl sulfoxide (DMSO) containing sodium hydroxide followed by addition of *n*-butyl bromide afforded butyl [2-arylamino-4,4-dimethyl-6-oxo-cyclohex-1-ene]carbodithioates

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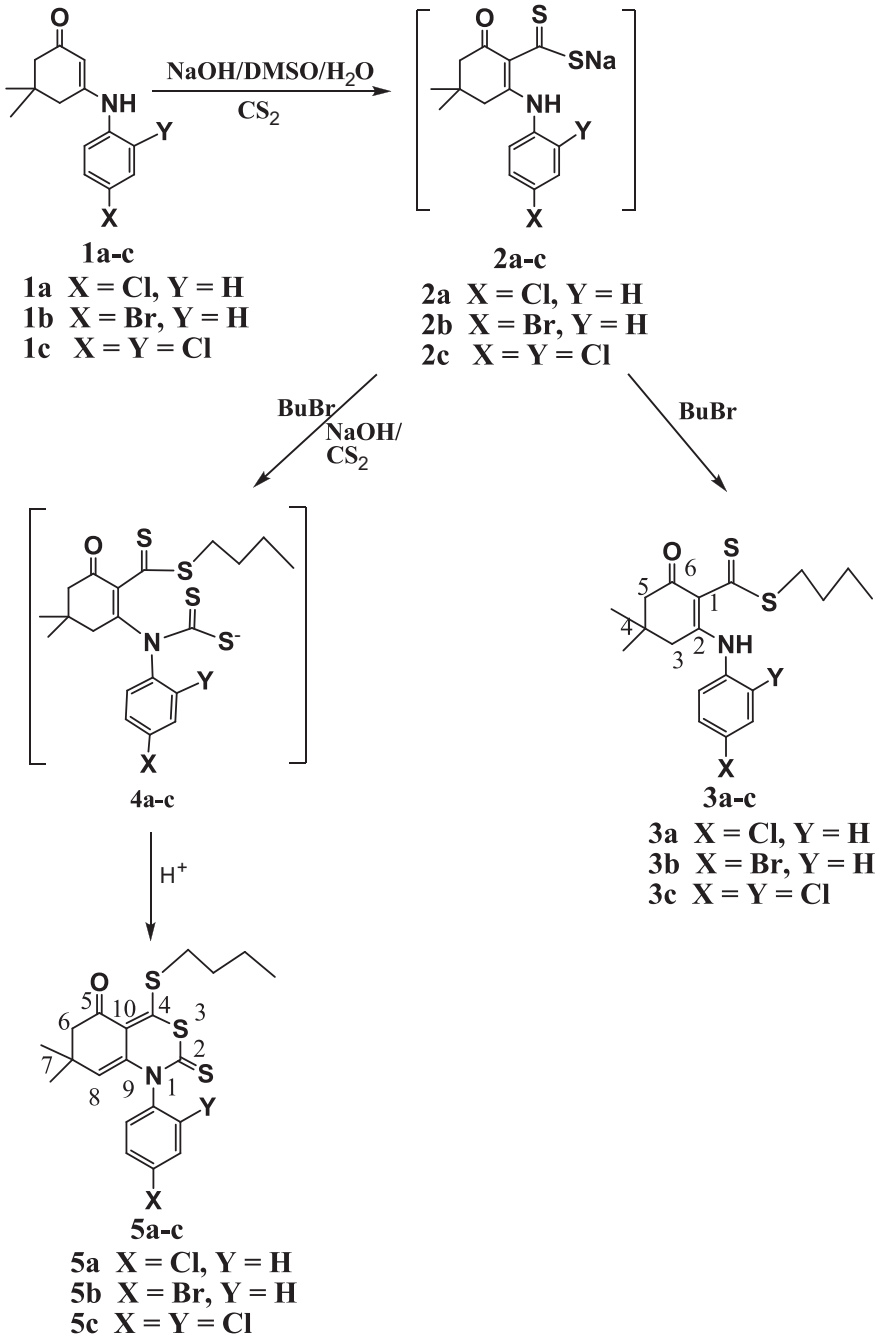
(**3a–c**) via the loss of a molecule of HBr from the nonisolable intermediates **2a–c**.

On the other hand, the reaction of enaminones **1a–c** with an excess of carbon disulfide in DMSO containing a catalytic amount of NaOH followed by addition of *n*-butyl bromide furnished benzothiazine derivatives **5a–c**, (Scheme 1). These thiazinones have been presumably formed via the heterocyclization of the nonisolable intermediates **4a–c**. The conditions for the reactions are critical, probably due to the ready loss of carbon disulfide from the reaction mixture whose amount has a great role in the formation of an intermediate such as **4a–c**. The introduction of a carbodithioate on the nitrogen of **2** before alkylation may be unlikely. The reported[34] methylation of similar analogs did not give good results in our hands. The structural assignments of the butyl derivatives have been considered as model study to be used in assigning the glycosyl derivatives as alkylating agents.

The structures of **3** or **5** can be readily differentiated by their ^{1}H NMR spectra where **3** shows a signal at the low-field region at δ 14.73–15.44 that is exchangeable with D_2O and is due to the NH proton. Such a signal at low field does not appear in the spectra of compounds **5**. On the other hand, the ^{13}C NMR spectra of **3** showed a C=S resonance at δ_c 191.3, whereas the C=S of **5** appeared at δ_c 182.5–183.6. Moreover the H-8 appeared at δ_c 4.49–4.55, which is in agreement with an olefinic proton rather than a methylene group.

Applying the above synthetic scheme, we further explored the synthesis of thioglycoside analogs from the enaminones. Thus, the reaction of enaminones **1a–c** with carbon disulfide in the



Scheme 1.