Synthesis of New 1,3-Dithiolium Derivatives from Propiophenones

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Novel 4-(3,5-dibromo-2-hydroxyphenyl)-5-methyl-2-(N,N-dialkylamino)-1,3-dithiolium salts have been synthesized by the heterocondensation of the 1-(3,5-dibromo-2-hydroxyphenyl)-1-oxapropan-2-yl dithiocarbamates. The latter compounds have been obtained from the reaction of the corresponding substituted α-halopropiophenone with various salts of dithiocarbamic acids. The structure of 1-(3,5-dibromo-2-hydroxyphenyl)-1-oxopropan-2-yl-morpholine-4-carbodithioate (2b) was unambiguously proved by X-ray crystallography. A strong intramolecular phenol O-H•••O hydrogen bond has been identified in this molecule.

Keywords: propiophenones, dithiocarbamates, 1,3-dithiolium salts, mesionic compounds, X-ray crystallography

1,3-Dithiolium salts are well-known precursors of tetrathiafulvalenes (TTF) [1-4]. The famous charge transfer salts of tetrathiafulvalenes (TTF) with tetracyanoquinodimethane have attracted general interest due to their quasi-metallic electrical conductivity [5, 6]. Recent reports highlighted the TTF's ability to act as donor groups in intramolecular charge-transfer complexes [7, 8]. A variety of acceptor units have been investigated, nitrogen and sulfur containing cations receiving a great deal of attention [9-17]. Of special interest are systems where the donor moiety is linked through a π- or σ-bonded bridge to the acceptor moiety [18-22]. Recent studies on 1,3-dithiolium-2-ylenophenolates systems revealed that 1,3-dithiolium cations can act as acceptor groups in intramolecular charge-transfer processes [24, 25]. Along with the applications in material chemistry [26], 1,3-dithiolium cations exhibit interesting properties for medicinal chemistry. 1,3-Dithiolium systems are known for their reactivity at the C(2)-position towards nucleophiles [27]. Moreover, this type of compounds has been found to exhibit biological activity, in a particular case, against gram-positive and gram-negative bacteria [28-31].

Following our previous investigation on the synthesis of some 4-(hydroxyaryl)-2-(N,N-dialkylamino)-1,3-dithiolium salts from the corresponding α-haloketones [9-11], we wish to extend these studies by presenting a new class of 4-(3,5-dibromo-2-hydroxyphenyl)-5-methyl-2-(N,N-dialkylamino)-1,3-dithiolium salts and the corresponding mesionic 4,6-dibromo-2-(5-methyl-1,3-dithiolim-2-y1)phenolates.

Experimental part

a. Analysis methods

Melting points were obtained on a Mel-Temp II apparatus. IR spectra were recorded on a Bruker Tensor 27 instrument. UV-Vis spectra were recorded on a Varian BioCarry 100 Spectrophotometer. NMR spectra were recorded on a Bruker DPX-300 Spectrometer. Chemical shifts are reported in ppm downfield from TMS. Elemental analyses (C, H, N, S) were conducted using a CE440 Elemental Analyser; the results were found to be in good agreement (±0.35%) with the calculated values.

b. Synthesis

The synthesis of compounds 2, 3 and 4 is described in scheme 1 and 2.

Scheme 1. Synthesis of dithiocarbamates 2 and 1,3-dithiolium perchlorates 3

1-(3,5-Dibromo-2-hydroxyphenyl)-1-oxapropan-2-yl-morpholine-4-carbodithioate (2b) General Procedure

To a solution of 2-bromo-1-(3,5-dibromo-2-hydroxyphenyl)propan-1-one (1, 3.87g, 0.01mol) in acetone (100mL), a solution of morpholinium morpholine-4-carbodithioate (2.5g, 0.01mol) in acetone-water (1:1, 70mL) was added. The reaction mixture was refluxed for 10min, cooled to room temperature and then poured in water. The precipitate was filtered, washed with water and dried off. Recrystallization from EtOH (100mL) gave colorless crystals; yield 3.75g (80%). Analytical and spectral data of carbodithioates 2a, b are presented in table 1.

Scheme 1. Synthesis of dithiocarbamates 2 and 1,3-dithiolium perchlorates 3

4-(3,5-Dibromo-2-hydroxyphenyl)-5-methyl-2-(morpholin-4-yl)-1,3-dithiol-2-ylium perchlorate (3b)

General Procedure

To a mixture of sulfuric acid (98%, 2.35mL) and glacial acetic acid (7mL), 1-(3,5-dibromo-2-hydroxyphenyl)-1-
oxapropan-2-yl-morpholine-4-carbodithioate (2b, 2.35g, 5mmol) was added in small portions. The reaction mixture was heated at 80°C for 10min. After cooling, 70% HClO₄ (1mL) and then water (100mL) were added and the precipitate was filtered and dried off. Recrystallization from EtOH (200mL) gave colorless crystals; yield 2.12g (77%). Analytical and spectral data of 1,3-dithiolium perchlorates 3a, b are presented in table 2.

4,6-Dibromo-2-{5-methyl-2-(morpholin-4-yl)-1,3-dithiol-2-ylium-4-yl}phenolate (4b);

General procedure
To a saturated sodium hydrogen carbonate solution (20mL), perchlorate 3b (1g, 1.8mmol) was added. Carbon dioxide evolved and the reaction mixture became yellow. After 2h under vigorous stirring at room temperature, the yellow solid was filtered off, washed with water, and dried. Recrystallization from ethanol gave yellow crystals; yield 0.81g (100%). Analytical and spectral data of 1,3-dithiolium phenolates 4a, b are presented in table 3.

c. X-ray structure determination of 2b
Numerical details are presented in table 4. The intensity data of 2b was collected on a Stoe IPDS 2T diffractometer with MoKα radiation. The data were collected with the Stoe XAREA program using ω-scans [32]. The space groups were determined with the XRED32 program [32]. The structures were solved by direct
Results and discussions

Phenacyl carbodiethioates are useful intermediates for the synthesis of 1,3-dithiolium salts and their derivatives. The reactions of α-bromophenones with salts of dithiocarbamic acid, readily available from the reaction of secondary amine with carbon disulfide [35], represent an accessible way to various substituted phenacyl carbodiethioates. Following this synthetic strategy, we obtained phenacyl dithiocarbamates 2a, b by reacting 2-bromo-1-(3,5-dibromo-2-hydroxyphenyl)propan-1-one (1) [36] with sodium N,N-diethyldithiocarbamate and morpholinum morpholine-4-carbodithioate, respectively. These compounds have been obtained as colorless crystals in good isolated yields. The structure of dithiocarbamates 2 has been proved by analytical and spectral data (table 1). The 1H NMR spectra indicate a shift in value for the α-carbonyl proton from around 2.5ppm to ca. 5.76ppm. Also, new signals appear at high fields corresponding to the signals belonging to the rest of the protons in the diethylenimine and morpholine moieties. 13C NMR spectra indicate the appearance of a new signal at 192ppm, attributed to the thiocarbonyl group. The structure of 1-(3,5-dibromo-2-hydroxyphenyl)-1-oxa-propan-2-yl-morpholinium-4-carbodiethioate (2b) has unambiguously proved by X-ray crystallography [37]. Crystal data are presented in table 4. A strong intramolecular phenol O(1)-H(1) ••• O(2) hydrogen bond has been identified in this molecule (fig.1 and table 5). The recorded data confirms the extended π-σ conjugation at the level of dithiocarbamic group [38, 39]; the lenght of N-C(9) bond is 1.338(4)Å, shorter than N-C(10) and N-C(13) that are essentially σ-bonds (1.46(5)Å). The dihedral angle between the plane of the phenol group and that of the planar section of the morpholine-4-carbodiethioate moiety is 71.4(3)°.

Using a concentrated sulfuric acid-glacial acetic acid (1:3 v/v) mixture [40-42] the cyclization of dithiocarbamates 2a, b takes place under mild reaction conditions. After 10min at 80°C the homogeneous reaction mixture was cooled to room temperature and 70% HClO4 and water were added. Filtration and recrystallization of the precipitate gives perchlorates 3 as colorless crystals, in good yields (table 2). The cyclization of dithiocarbamates 2 was accompanied by important spectral changes. The IR spectra revealed the disappearance of the absorption band corresponding to the carbonyl group (ca. 1640cm −1) and the presence of new, strong and broad absorption bands at 1100-1200cm −1, corresponding to the perchlorate anion. Heterocyclization of dithiocarbamates 2 is also supported by the NMR spectra. Thus, the 1H NMR spectra of 1,3-dithiol-2-ylum perchlorate indicate the absence of the α-carbonyl hydrogens from compounds 2 (ca. 5.7ppm). 13C NMR spectra also support the synthesis of 1,3-dithiolium salts 3 by the disappearance of the carbonyl and thiocarbonyl carbon atoms present in the dithiocarbamates spectra and the appearance of a new signal at a very low field (185ppm) which correspond to the electron deficient C(2) atom.

Treatment of perchlorates 3a, b, under heterogeneous conditions, with saturated aqueous sodium hydrogen carbonate solution provides 3,5-dibromo-2-[5-methyl-2-(dialkyalamino)-1,3-dithiol-2-ylum-4-yl]phenolates 4a, b, in quantitative yields as yellow compounds (Scheme 2). The molecular structure of the new compounds was proved by analytical and spectral data (table 3) and by the following chemical transformation: treatment of an acetone suspension of the mesoionic compounds 4 with 70% HClO4, regenerates the 1,3-dithiolium perchlorates 3 in quantitative yields (scheme 2).

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hydroxyphenyl)-1-oxapropan-2-yl-morpholine-4-carbodithioate. Crystallographic data revealed a strong intramolecular phenol O-H•••O hydrogen bond and an extended $p-\pi$ conjugation at the level of dithiocarbamic group.

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References