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PII: S0040-4039(15)30341-5
DOI: http://dx.doi.org/10.1016/j.tetlet.2015.11.033
Reference: TETL 46973

To appear in: *Tetrahedron Letters*

Received Date: 11 May 2015
Revised Date: 20 October 2015
Accepted Date: 10 November 2015

Please cite this article as: Halimehjani, A.Z., Shayegan, M.H., Poshteh, S.S., Amani, V., Notash, B., Hashemi, M.M., Investigation of the reaction of dithiocarbamic acid salts with trimethyl orthoformate and styrene epoxide, *Tetrahedron Letters* (2015), doi: http://dx.doi.org/10.1016/j.tetlet.2015.11.033

Tetrahedron Letters
journal homepage: www.elsevier.com

Investigation of the reaction of dithiocarbamic acid salts with trimethyl orthoformate and styrene epoxide

Azim Ziyaei Halimehjani,*[,a] Mojtaba Hajilou Shayegan,[b] Shiva Shakori Poshteh,[c] Vahid Amani,[d] Behrouz Notash,[e] Mohammad M. Hashemi[b]

[a] *Faculty of Chemistry, Kharazmi University, 49 Mofateh St., Tehran, Iran. Tel.: +98(21)88848949, Fax: +98(21)88820992. Email address: ziyaei@khu.ac.ir*
[b] *Department of Chemistry, Sharif University of Technology, P.O. Box 11465-9516, Tehran, Iran.*
[c] *Islamic Azad University, Pharmaceutical Science Branch (IAUPS), No. 99, Yakhchal Gholhak, Shariati, Tehran*
[d] *Department of Chemistry, Yadegar-e-Imam Khomeini (RAH) Branch, Islamic Azad University, Tehran, Iran.*
[e] *Chemistry Department, Shahid Beheshti University, G. C., Evin, Tehran 1983963113, Iran.*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

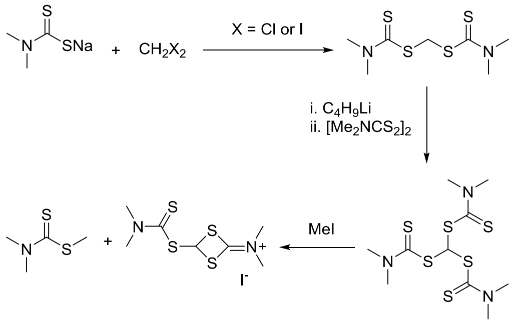
Keywords:
Dithiocarbamate
orthoesters
epoxides
4-(*N,N*-Dialkyldithiocarbamato)-2-dialkyliminio-1,3-dithietane tetrafluoroborate 2-iminium-1,3-dithiolanes

ABSTRACT

The reaction of dithiocarbamic acid salts with trimethyl orthoformate in the presence of $BF_3.OEt_2$ was investigated to give 4-(*N,N*-dialkyldithiocarbamato)-2-dialkyliminio-1,3-dithietane tetrafluoroborates in good yields. Additionally, a one-pot procedure for the synthesis of 2-iminium-1,3-dithiolanes from the $BF_3.OEt_2$ catalyzed reaction of dithiocarbamic acid salts with styrene epoxide is described.

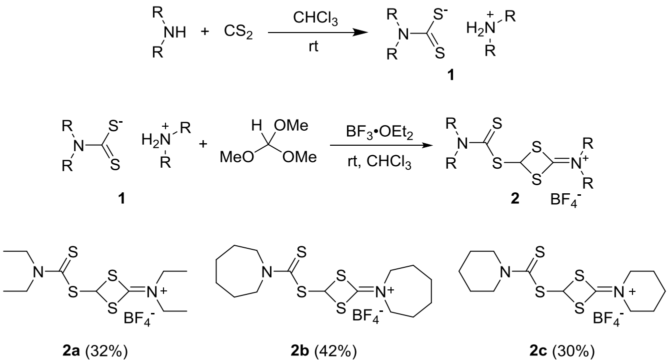
The chemistry of dithiocarbamates is well known and has widespread application in different branches of chemistry, agriculture and medicinal chemistry.[1] Dithiocarbamic acids are good nucleophiles and react with various electrophiles such as alkyl halides,[2] epoxides,[3] carbonyls,[4] electron-rich alkenes,[5] α,β-unsaturated carbonyl compounds,[6] and many others.[7] Although dithiocarbamic acids are unstable, their esters and complexes are stable and have found widespread application as intermediates in synthetic organic chemistry,[8] as NO_x trapping agents in analytical chemistry,[9] sulfur vulcanization agents in rubber manufacturing,[10] radical chain transfer agents in reversible addition-fragmentation chain transfer (RAFT) polymerization,[11] fungicides and pesticides[12] and as drugs.[13]

To the best of our knowledge, the only route for the synthesis of 4-(*N,N*-dialkyldithiocarbamato)-2-dialkyliminio-l,3-dithietane cations was reported by Schumaker and co-workers proceeding in three steps from dithiocarbamic acid salts (Scheme 1).[14] It was shown that these compounds underwent ring-opening, ring-closing tautomerism. Herein, we report a simple, and straightforward route for the synthesis of 4-(*N,N*-dialkyldithiocarbamato)-2-dialkyliminio-l,3-dithietane tetrafluoroborate from amines, CS_2 and trimethyl orthoformate.



Scheme 1. Schumacher's route for the synthesis of 4-(*N,N*-dialkyldithiocarbamato)-2-dialkyliminio-l,3-dithietane cations

We began our investigation with the one-pot, three-component reaction of diethylamine, CS_2 and trimethyl orthoformate in chloroform. At room temperature under catalyst-free conditions, no product was obtained. According to our previous experience utilizing the reactions of dithiocarbamic acid salts with carbonyl compounds in the presence of $BF_3.OEt_2$,[4a] we next performed the reaction using $BF_3.OEt_2$ as a catalyst, however once again no product was obtained. Therefore, an alternative strategy was pursued. Dithiocarbamic acid salt **1**, prepared from the reaction of diethylamine and CS_2 in $CHCl_3$, was added to a solution of trimethyl orthoformate and $BF_3.OEt_2$ in $CHCl_3$ at room temperature furnishing 4-(*N,N*-diethyldithiocarbamato)-2-diethyliminio-1,3-dithietane tetrafluoroborate **2a** in moderate yield. Performing the reaction with trimethyl orthovalerate and trimethyl orthobenzoate were not successful, however the reactions with other secondary amines such as hexamethyleneamine and piperidine were similar to diethylamine (Scheme 2). The isolated yields are based on trimethyl orthoformate.



Scheme 2. Synthesis of 4-(*N,N*-dialkyldithiocarbamato)-2-dialkyliminio-1,3-dithietane tetrafluoroborates

The structures of products **2a-c** were confirmed by ^1H and ^{13}C NMR spectroscopy and CHN analysis. The ^1H NMR spectra of the products showed a singlet peak between 5.50-6.00 ppm for the CH resonance. Three peaks were observed between 3.50-4.20 ppm for the four methylenes attached to the nitrogens; two for methylenes attached to the dithiocarbamate nitrogen due to the restricted rotation around the C-N bond and another for both methylenes attached to the nitrogen in the 2-iminium moiety. The distinctive carbons of the dithiocarbamate and the iminium moieties on the dithietane ring were observed between 190.0-195.0 ppm and 185.0-188.0 ppm, respectively. Additionally, a peak near -153 ppm in the ^{19}F NMR was assigned to the tetrafluoroborate anion.

A single crystal of **2b** was prepared in $CHCl_3$, and X-ray crystallographic analysis confirmed the proposed structure. An ORTEP representation is shown in Figure 1 (CCDC no. 1025387; for details of the crystal structure data and refinement of **2b** see the ESI). Compound **2b** crystallized in the monoclinic space group $P2_1/c$. Fluorine atoms appeared as disorder in the tetrafluoroborate anion. The $S\cdots B^i$ (distance 3.088(5)Å) interaction and intra and intermolecular C-H···F and C-H···S hydrogen bonds (Fig. 2 and Table 3 in ESI) were effective in the stabilization of the crystal structure and formation of a 3D supramolecular network. The C7-N1 bond distance (1.328 Å) was much closer to the C=N double bond length (typical C-N and C=N bond distances are 1.47 and 1.28 Å, respectively) which indicated that the π electron density was delocalized over the dithiocarbamate moiety. As shown in Figure 1, the observed bond distances of C(9)-S(3), 1.7314(19) Å and C(9)-S(4), 1.7432(19) Å, were virtually equal and shorter than C(8)-S(3), 1.832(2) Å and C(8)-S(4), 1.827(3) Å due to incorporation of the sulfur atoms in resonance with the iminium group. The X-ray crystal analysis also showed that the molecular structure in the solid state was favorably oriented for rearrangement in solution.

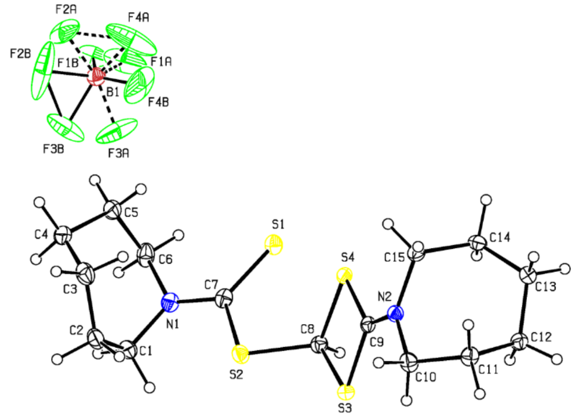
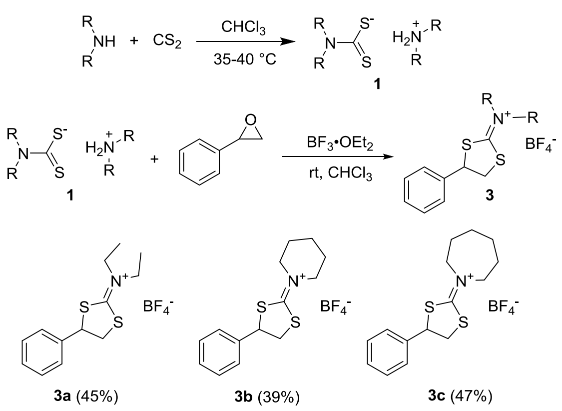


Fig 1. Molecular structure of **2b** with 30% probability displacement ellipsoids. Selected bond lengths (Å): C(7)-N(1), 1.328 (2); C(7)-S(1), 1.683 (2); C(7)-S(2), 1.774 (2); C(8)-S(2), 1.793 (2); C(8)-S(3), 1.832 (2); C(8)-S(4), 1.827 (2); C(9)-N(2), 1.288 (2); C(9)-S(3), 1.7314 (19); C(9)-S(4), 1.7432 (19).

The reaction of dithiocarbamic acid salts with epoxides for the preparation of β-hydroxy dithiocarbamates has been well documented by our group and others.[3a,15] The formed β-hydroxy dithiocarbamates can be converted to 2-iminium-1,3-dithiolanes *via* treatment with a strong acid or activation of the hydroxide group by tosyl chloride, followed by intramolecular ring closure.[16] In a continuation of our efforts regarding the chemistry of dithiocarbamates, we examined a straightforward method for the reaction of dithiocarbamic acids with epoxides to form 2-iminium-1,3-dithiolanes. For this purpose, diethyldithiocarbamic acid was reacted with styrene epoxide under the previously optimized conditions. We observed that 2-iminium-1,3-dithiolane tetrafluoroborate **3a** was obtained in 45% isolated yield. The reaction with hexamethyleneamine and piperidine were similar to diethylamine (Scheme 3). The isolated yields are based on styrene epoxide. These products were only obtained using styrene epoxide and β-hydroxy dithiocarbamates were obtained using aliphatic epoxides. The ^1H NMR spectra of the products showed a peak between 5.50-6.00 ppm for the benzylic hydrogen while the CH_2N and CH_2S signals appeared between 3.50-4.50 ppm. Additionally, the ^{13}C of the iminium moiety in the dithiolane ring of the products was observed between 189-195 ppm in the ^{13}C NMR spectra.



Scheme 3. A direct route for the synthesis of 2-iminium-1,3-dithiolanes from styrene epoxide

A single crystal of **3b** was prepared in $CHCl_3$, and X-ray crystallographic analysis established the proposed structure. An ORTEP representation is shown in Fig. 2 (CCDC no. 923256; for details of the crystal structure data and refinement of **3b** see the ESI). Crystallographic analysis showed that compound **3b** crystallizes as both (*R*) and (*S*) enantiomers which were located in a similar position in the triclinic crystal system (centrosymmetric space group $P\bar{1}$). The $S\cdots B^i$ (distance 2.986(8) Å) interaction and intra and intermolecular C-H···F and C-H···S hydrogen bonds (see Fig. 4 and Table 3 in the ESI) were effective in the stabilization of the crystal structure and the formation of a 3D supramolecular network. The observed bond distances of C(6)-S(2), 1.743(7) Å and C(6)-S(1), 1.735(7) Å were shorter than typical C-S bond lengths (*ca.* 1.82 Å), but longer than C=S double bonds and could be attributed to the resonance of the sulfur atoms with the iminium group.

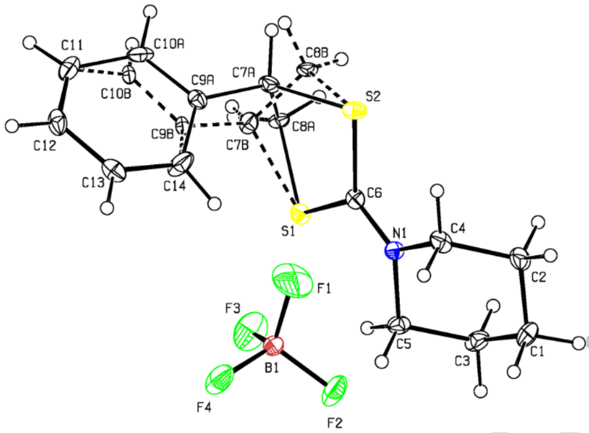


Fig 2. The molecular structure of **3b** with 30% probability displacement ellipsoids. Selected bond lengths (Å): C(6)-N(1), 1.289 (8); C(6)-S(1), 1.735 (7), C(6)-S(2), 1.743 (7); C(7A)-S(2), 1.918 (11); C(8B)-S(2), 1.761 (11); C(8A)-S(1), 1.770 (10); C(7B)-S(1), 1.921 (12).

In conclusion, for the first time, a simple and straightforward method for the preparation of 4-(*N,N*-dialkyldithiocarbamato)-2-dialkyliminio-l,3-dithietane tetrafluoroborates from the reaction of dithiocarbamic acid salts with trimethyl orthoformate in the presence of $BF_3.OEt_2$ is reported. The X-ray analysis showed that these compounds have a suitable orientation for rearrangement, which makes these compounds suitable candidates for molecular switching in information storage devices. Additionally, a direct procedure for the synthesis of 2-iminium-1,3-dithiolane tetrafluoroborates from amines, CS_2 and styrene epoxide catalyzed by $BF_3.OEt_2$ is described.

Acknowledgment

We are grateful to the Research Council of the Sharif University of Technology for financial support. We also thank the Faculty of Chemistry of Kharazmi University for supporting this work.

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Weyl Methods of Molecular Transformations Vol. 30: Acetals:O/N, S/S, S/N, and Higher heteroatom analogues, Thieme 2014.

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