

## A BROAD SCOPE HIGHLY EFFICIENT SYNTHESIS OF BIS(R-THIO)ACETYLENES

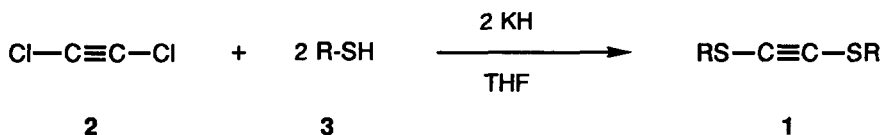
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**Summary:** Treatment of dichloroacetylene with two equivalents of a thiol and two equivalents of potassium hydride in THF solution affords the corresponding bis(R-thio)acetylene in high yield

Acetylene dithioethers (1) are interesting synthetic intermediates possessing a highly electron rich triple bond<sup>1</sup>. Although these substances have been known from a long time ago, and many different approaches to their preparation have been investigated<sup>2</sup>, no synthetic methodology of wide applicability has been yet developed. Thus, whereas the preparation of bis(n-alkylthio)acetylenes is well documented, knowledge on bis(*sec*- or *tert*-alkylthio)acetylenes and bis(arylthio)acetylenes is scarce.

In the course of a research program devoted to the development of efficient acetylene equivalents for Diels-Alder chemistry<sup>3</sup>, the preparation of acetylene dithioethers bearing bulky alkyl groups bonded to sulfur was required. Since the only reported procedure<sup>2b</sup> which seemed to be applicable was characterized by a very low yield, the search for a more convenient alternative was decided.

Some earlier, rather inefficient, procedures<sup>2a,2e</sup> for the preparation of acetylenes 1 involve the reaction of trichloroethylene with metal thiolates. The formation under these conditions of dichloroacetylene (2) as a reactive intermediate has been suggested<sup>1</sup>. Since it is known that dichloroacetylene behaves as a very electrophilic compound, being readily attacked by bulky nucleophiles<sup>4</sup>, it appeared to us that preformed 2 could react with metal thiolates in an aprotic medium, to afford the corresponding acetylene dithioethers in a clean way (Scheme I).



Scheme I

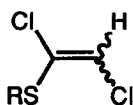
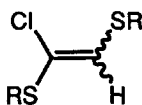
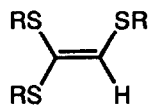
We have studied the reaction of **2**, generated from trichloroethylene in THF solution<sup>5</sup>, with a representative set of alkanethiols and thiophenols (**3a-d**) under two sets of reaction conditions. The results are summarized in the Table.

**Table: Preparation of Bis(R-thio)acetylenes from Dichloroacetylene**

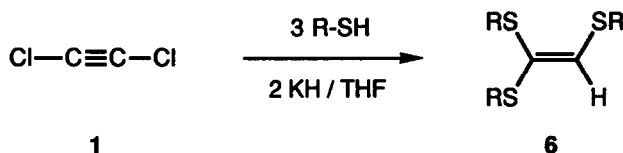
<b>3</b>	<b>R</b>	<b>Reaction Conditions<sup>a</sup></b>	<b>1</b>	<b>Yield (%)<sup>b</sup></b>
<b>3a</b>	CH <sub>3</sub> CH <sub>2</sub> -	B	<b>1a</b>	87
<b>3b</b>	(CH <sub>3</sub> ) <sub>2</sub> CH-	A	<b>1b</b>	93
<b>3c</b>	(CH <sub>3</sub> ) <sub>3</sub> C-	A,B	<b>1c</b>	98
<b>3d</b>	p-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> -	B	<b>1d</b>	43 <sup>c</sup>

<sup>a</sup>**Experimental procedures. Reaction Conditions A:** To a solution of dichloroacetylene in anhydrous THF containing KH (2.2 eq.), the thiol (2.0 eq.) was added at 0°C and the mixture was stirred at room temperature for 20 h under N<sub>2</sub>. After pentane dilution and aqueous work-up, the crude material was purified by flash chromatography on SiO<sub>2</sub>/Et<sub>3</sub>N (97.5% v/v), eluting with hexane/CH<sub>2</sub>Cl<sub>2</sub> mixtures. **Reaction Conditions B:** To a solution of dichloroacetylene in THF containing a small amount of KH (0.1 eq.), the thiol (2.0 eq.) was added at 0°C and the mixture was stirred at room temperature for 3h. The solution was then transferred *via* canula to a reaction flask containing KH (2.2 eq.) and a small volume of THF under N<sub>2</sub>, and the mixture was stirred for 20h at room temperature. Work-up and product isolation as in conditions A. <sup>b</sup>Yields in pure isolated compounds are referred to dichloroacetylene. <sup>c</sup>A 15% yield of **4d** was obtained as well.

When the less acidic secondary and tertiary alkanethiols **3b** and **3c** are involved in the reaction, the process can be performed as a single, one pot operation (reaction conditions A), the corresponding acetylene dithioethers **1b** and **1c** being obtained in essentially quantitative yield<sup>6</sup>. However, when the same reaction conditions are used with **3a** and **3d**, complex reaction mixtures of the expected **1a** or **1d** with the presumed intermediate olefins **4** and **5** and the tris(R-thio)ethene (**6**) are obtained.

**4****5****6**

Much probably, the tris(R-thio)ethenes **6** arise from a base catalyzed addition of thiol to the triple bond of the corresponding acetylene dithioethers. Thus, the use of excess thiol (3 eq.) in these reactions, together with more energetic reaction conditions (heating under THF reflux for 20h), allowed the isolation of **6a** and **6d**<sup>2d,7</sup> with synthetically useful yields (Scheme II).



R	<b>6</b>	Yield (%)
CH <sub>3</sub> CH <sub>2</sub>	<b>6 a</b>	87
p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	<b>6 d</b>	62

Scheme II

The differential behaviour of thiols **3a** and **3d** vs. **3b** and **3c** in these processes could be clarified through an experimental observation: whereas the reaction of **3b** and **3c** with KH is slow under the usual reaction conditions, taking up to 2 hours to completion, in the cases of **3a** and **3d** a fast evolution of hydrogen is observed. This led us to think that, with the secondary and tertiary alkanethiols, addition to **2** could take place faster than reaction with KH, and that this fact could be responsible for the precise course of the reaction recorded with these thiols.

In order to test this hypothesis, **2** was reacted with 2 eq. of **3c** in THF in the presence of a small amount (ca. 0.1 eq.) of KH. After 3 hours, the NMR analysis of the reaction mixture revealed the exclusive formation of **4c**, as a single stereoisomer. Subsequent treatment of the reaction mixture with KH allowed the isolation in high yield of **1c**.

Application of this simple modification (Table, reaction conditions B) finally allowed the extension of the developed methodology to the preparation of acetylene dithioethers derived from primary alkanethiols and thiophenols.

In summary, the reported procedure represents the first broad scope methodology for the preparation of acetylene dithioethers derived from thiols of very different types. Moreover, our results strongly suggest that the dichloroolefins **4** occupy a strategic position along the complex mechanistic pathway leading from dichloroacetylene to acetylene dithioethers. Thus, only when the intermediate **4** can be properly formed (i.e., when free thiol exists in the reaction medium), the corresponding dithioether **1** is obtained in good yield as the final product.

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### References and Notes.

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5. Denis, J.N.; Moyano, A.; Greene, A.E. *J. Org. Chem.* **1987**, *52*, 3461. **Warning!** Dichloroacetylene is toxic and explosive. Although this procedure appears to be completely safe, it is strongly recommended that all work with dichloroacetylene be conducted in a hood and behind appropriate shielding.
6. Selected spectral data (<sup>13</sup>C NMR, 50 MHz, CDCl<sub>3</sub>) of the prepared acetylene dithioethers: **1a**: δ 14.22, 30.44, 86.02 ppm. **1b**: δ 22.60, 40.21, 86.60 ppm. **1c**: δ 29.97, 48.40, 88.52 ppm. **1d**: δ 20.99, 87.91, 126.20, 129.69, 130.04, 136.87 ppm.
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