

A SIMPLE SYNTHESIS OF 5-SUBSTITUTED-THIOPHENE-2 (3H)-THIONES

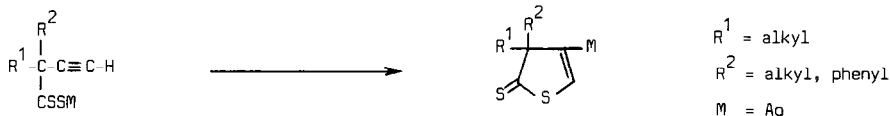
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**Summary** : Treatment of 1-alkyne and allene derivatives successively with two equivalents of n-Buli, one equivalent of CS<sub>2</sub> and then an electrophile yielded novel 5-substituted-thiophene-2 (3H)-thiones 4.

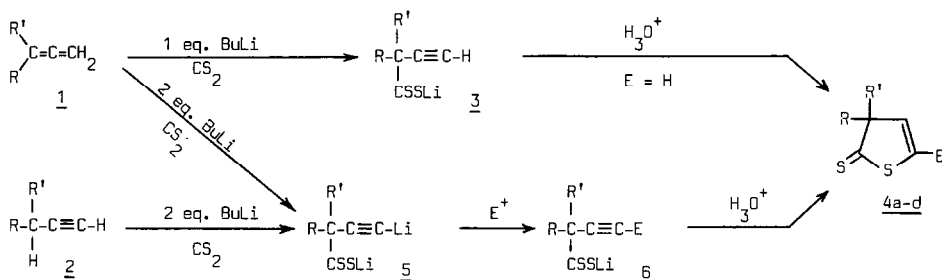
Few thiophene-2 (3H)-thiones have been described in the literature<sup>1</sup> and we wanted to find a general synthesis which allowed the introduction of new substitutions.

Meijer et al.<sup>2,3</sup> showed that silver 3-alkynedithioates cyclised spontaneously to give 4-substituted-thiophene-2 (3H)-thiones, whereas the corresponding lithium salts did not.



Since aliphatic dithioacids were known to add to alkynes<sup>4,5</sup> we thought that the above cyclisation should occur when M = H.

A preliminary experiment showed that this cyclisation did take place : the treatment of 3-phenyl-1,2-butadiene 1a with 1 eq. of n.Buli (-60°C, 1h) and CS<sub>2</sub> (-60°C, 10 min.) followed by protolysis with an aqueous NH<sub>4</sub>Cl solution afforded the known compound 4a<sup>3</sup> (R = CH<sub>3</sub>, R' = C<sub>6</sub>H<sub>5</sub>) in 40 % yield, probably through 3a.



Then we applied this reaction to the substituted analogues 6 in order to obtain thiophene-2 (3H)-thiones bearing various substituents on carbon-5.

Intermediates 6 proved to be accessible by the selective reaction of electrophiles with the lithium acetylide 5. The precursor acetylenic compounds 5 were prepared from the allenes 1<sup>3</sup> or the alkynes 2.

The compounds 4 thus obtained are described in table I and their NMR data are shown in table II.

**General experimental procedure** : the compound 1 or 2 (0.05 mole) is added to a solution of n.butyllithium (0.1 mole, 1.6 M in hexane) in THF (60 ml) at 0°C and under nitrogen. The mixture is stirred for 0.5 h at 0°C and then cooled at -60°C and carbon disulphide (0.05 mole) is added. After stirring for 15 min. at this temperature the electrophile (0.05 mole) is added and the stirring is maintained 0.5 h at -60°C. Then the temperature is allowed to rise to 0°C before protolysis with an aqueous ammonium chloride solution (200 ml). The thiophene-2 (3H)-thiones 4 are isolated by extraction with methylene chloride (3 X 100 ml). The combined organic extracts are

dried with magnesium sulphate, concentrated and purified by column chromatography on silica gel.

Table I : Examples of compounds 4

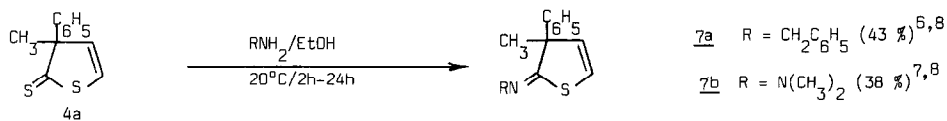
Starting allene or alkyne	Electrophile $E^+$	<u>4</u>	Yield <sup>8</sup> (%)
$\begin{array}{c} \text{C}_6\text{H}_5 \\   \\ \text{C}=\text{C}=\text{CH}_2 \\   \\ \text{CH}_3 \end{array} \quad \underline{1a}$	$\text{H}_2\text{O}$	 <u>4a</u>	60
$\begin{array}{c} \text{C}_6\text{H}_5 \\   \\ \text{C}=\text{C}=\text{CH}_2 \\   \\ \text{CH}_3 \end{array} \quad \underline{1a}$		 <u>4b</u>	81
$\begin{array}{c} \text{CH}_3 \\   \\ \text{C}=\text{C}=\text{CH}_2 \\   \\ \text{CH}_3 \end{array} \quad \underline{1b}$		 <u>4c</u>	58
$\begin{array}{c} \text{C}_6\text{H}_5 \\   \\ \text{CH}_3\text{O}-\text{C}-\text{C}\equiv\text{C}-\text{H} \\   \\ \text{H} \end{array} \quad \underline{2a}$	$\text{CH}_2=\text{N}(\text{CH}_3)_2, \text{I}^-$	 <u>4d</u>	45

Table II : NMR data of compounds 4b-d

<u>4</u>	mp (°C)	<sup>1</sup> H-NMR [CDCl <sub>3</sub> /200 MHz/TMS] δ ppm]
<u>4b</u> <sup>a</sup>	oil	1.42 (s,1H) ; 1.4-1.2 (m,11H) ; 1.68 (s,3H) ; 6.11 (s,1H) ; 7.18 (s,5H).
<u>4c</u>	170 <sup>b</sup>	1.30 (s,6H) ; 5.7 (s,1H) ; 6.1 (s,1H) ; 7.35 (dd,1H) ; 7.85 (br.d,1H) ; 8.40 (br.d,1H) ; 8.50 (br.s,1H).
<u>4d</u>	95	2.30 (s,6H) ; 3.30 (s,3H) ; 3.40 (br.s,2H) ; 6.10 (br.s,1H) ; 7.30 (m,3H) ; 7.45 (m,2H).

a) 60 MHz, CCl<sub>4</sub>. b) hydrochloride.

Compounds 4 proved to be very reactive towards nucleophiles as shown as follows :



Acknowledgement : we thank Mr. A. RENAUDON for his technical assistance.

#### References and Notes :

- 1 - 5-Alkyl-3-(dialkylaminomethylene)-thiophene-2 (3H)-thiones were prepared by Ya L. Gol'dfarb and M.A. Kalik, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2072 (1973) ; *Chem. Abstr.*, **80**, 27 130 f (1974).
- 2 - H. Westmijze, K. Ruitenbergh, J. Meijer and P. Vermeer, *Tetrahedron Letters*, **21**, 1771 (1980).
- 3 - J. Meijer, K. Ruitenbergh, M. Westmijze and P. Vermeer, *Synthesis*, 551 (1981).
- 4 - G. Levesque and A. Mahjoub, *Tetrahedron Letters*, **21**, 2247 (1980).
- 5 - T. Takeshima, M. Muraoka, N. Fukada, A. Takayama and T. Yamamoto, *J. Org. Chem.*, **42**, 3383 (1977).
- 6 - Oil, <sup>1</sup>H-NMR [60 MHz, CDCl<sub>3</sub>] δ ppm ; J Hz : 1.68 (s,3H) ; 4.35 (s,2H) ; 5.92 (d,J=6.5,1H) ; 6.45 (d,1H) ; 6.95-7.50 (m,10H)].
- 7 - mp : 59°C, <sup>1</sup>H-NMR [60 MHz ; CDCl<sub>3</sub>] δ ppm ; J Hz : 1.80 (s,3H) ; 2.50 (s,6H) ; 5.90 (d,J = 6.5, 1H) ; 6.40 (d,1H) ; 7.40 (m,5H)].

8 - Yields are calculated on analytically pure compounds.

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