The Scope of the Synthesis of Tetrahydrothiophenes from *α,β*-Unsaturated Carbonyl Compounds and Sodium Polysulfide

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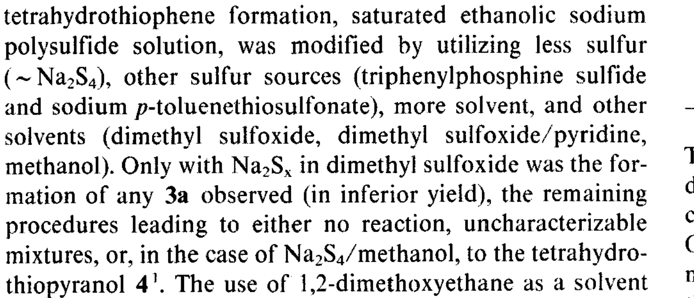
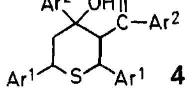
During a recent study[1] of the reactions of *α,β*-unsaturated carbonyl compounds with hydrogen sulfide the structure of the "*γ*-sulfide" obtained from 1,3-diphenylpropenone (chalcone; **1a**) and sodium polysulfide (Na_2S_x) was revised from **2** originally suggested by Fromm and Hubert[2] to the tetrahydrothiophene **3a**. Because of the current interest in the synthesis[3,4] and biosynthesis[5] of such compounds, a study of the scope of the transformation **1**→**3** was undertaken.



Using chalcone **1a** as a substrate, the original[1,2] reagent for tetrahydrothiophene formation, saturated ethanolic sodium polysulfide solution, was modified by utilizing less sulfur (~Na_2S_4), other sulfur sources (triphenylphosphine sulfide and sodium *p*-toluenethiosulfonate), more solvent, and other solvents (dimethyl sulfoxide, dimethyl sulfoxide/pyridine, methanol). Only with Na_2S_x in dimethyl sulfoxide was the formation of any **3a** observed (in inferior yield), the remaining procedures leading to either no reaction, uncharacterizable mixtures, or, in the case of Na_2S_4/methanol, to the tetrahydrothiopyranol **4**[1]. The use of 1,2-dimethoxyethane as a solvent has been reported[5] to yield the monothioketone **5**.



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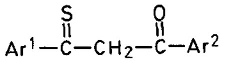
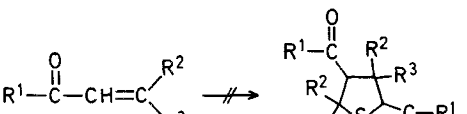


$$Ar^1-\overset{S}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-Ar^2$$

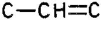
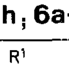
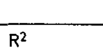
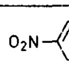
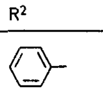
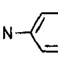
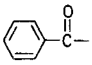
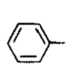
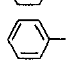
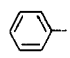
5

The only changes which improved the previous[1] yield of **3a** (47%) were more rigorous drying of the sodium sulfide nonahydrate used in the preparation of the polysulfide reagent (yield of **3a**: 60%). This is consistent with the expected deleterious effect of water on the series of equilibria leading from **1a** to **3a**[1]. The taking of a second crop during recrystallization resulted in an increase of the yield to 74%. The originally reported[2] almost quantitative yield of **3a** could not be reproduced. The resulting "optimized" reagent consisted of a 35-fold excess of a 1 : 4 molar ratio of anhydrous sodium sulfide and sulfur (~Na_2S_5)[6] in absolute ethanol and was used to examine the structural scope of the tetrahydrothiophene synthesis. In those reactions, and only those reactions, where a tetrahydrothiophene **3** was produced, the reaction mixture solidified to a gelatinous mass within 24 h after the chalcones **1a-f** and the reagent had been mixed. Filtration and recrystallization usually gave analytically pure tetrahydrothiophenes **3a-f** although in one case (**3d**), chromatography on silica gel was necessary to remove the last traces of sulfur. The properties and yields of the tetrahydrothiophenes **3a-f** are summarized in the Table.

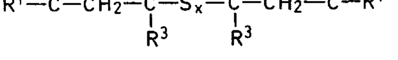
Of the chalcones examined, the nitro derivatives **1g** and **1h** did not yield the corresponding product **3**. Furthermore, a variety of other *α,β*-unsaturated carbonyl compounds **6a-i** and fumaronitrile, with structures very similar to the chalcones, failed to give tetrahydrothiophenes **3** on reaction with polysulfides.



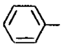
1g,h; 6a-i **3**

1,6	R^1	R^2	R^3
1g			H
1h			H
6a			H
6b	$t\text{-}C_4H_9$		H
6c	H_3C		H
6d	H_3C	H_3C	H_3C
6e	H	H	H
6f		$-(CH_2)_3-$	H
6g		H	H
6h		H_3C	H
6i		$t\text{-}C_4H_9$	H

Those reaction mixtures which did not precipitate a tetrahydrothiophene **3** were evaporated and the residue taken up in chloroform or ether for examination by N.M.R. and/or M.S. Of the compounds examined, most gave uncharacterizable mixtures except for **6b** and **6d**, which showed evidence for the presence of the mono-, di-, and trisulfides **7**, and for phenyl vinyl ketone (**6g**) which polymerized.



$$R^1-\overset{O}{\overset{\|}{C}}-CH_2-\underset{R^3}{\overset{R^2}{C}}-S_x-\underset{R^3}{\overset{R^2}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-R^1$$

7b x = 1,2,3; $R^1 = t\text{-}C_4H_9$, R^2 =  , R^3 = H

7d x = 1,2,3; R^1, R^2, R^3 = H_3C

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Table. Tetrahydrothiophenes **3a–f** prepared

Product No.	Ar^1	Ar^2	Yield [%][a]	m.p. [°C]	Molecular Formula[b] or Lit. m.p. [°C]	M.S. (70 eV)[c] *m/e*	^{1}H-N.M.R. ($CDCl_3$)[d,e] δ [ppm]	^{13}C-N.M.R. ($CDCl_3$)[d,f] δ [ppm]
3a	C_6H_5	C_6H_5	74	206–208°	206–208°[1] 212°[2]	448, 343, 240, 239, 209, 105 (100%)	4.7 (m, 2H); 5.0 (m, 1H); 5.2 (m, 1H)	54.4; 55.1; 57.0; 65.2
3b	C_6H_5	4-H_3CO—C_6H_4	70	186–187°	$C_{32}H_{28}O_4S$ (508.6)	508, 373, 270, 268, 239, 135 (100%)	3.63 (s, 3H); 3.76 (s, 3H); 4.5–4.9 (m, 2H); 5.0–5.2 (m, 2H)	54.4; 54.8; 55.2; 55.4; 57.0; 64.5
3c	4-H_3CO—C_6H_4	C_6H_5	66	170–171°	$C_{32}H_{28}O_4S$ (508.6)	508, 403, 270, 269, 239, 105 (100%)	3.53 (s, 3H); 3.57 (s, 3H); 4.3–4.9 (m, 2H); 5.0–5.2 (m, 2H)	53.7; 55.0; 56.5; 65.0
3d	C_6H_5	4-Cl—C_6H_4	63	204–205°	$C_{30}H_{22}Cl_2O_2S$ (517.5)	516, 377, 274, 273, 243, 139 (100%)	4.4–4.9 (m, 2H); 5.0–5.2 (m, 2H)	54.4; 55.1; 57.0; 65.5
3e	4-Cl—C_6H_4	C_6H_5	67	196–198°	$C_{30}H_{22}Cl_2O_2S$ (517.5)	516, 411, 274, 273, 243, 105 (100%)	4.3–4.8 (m, 2H); 5.0–5.2 (m, 2H)	53.7; 55.0; 56.2; 64.9
3f	4-H_3C—C_6H_4	C_6H_5	72	229–231°	$C_{32}H_{28}O_2S$ (476.6)	476, 371, 254, 253, 223, 105 (100%)	2.10 (s, 3H); 2.17 (s, 3H); 4.6–4.8 (m, 2H); 5.0–5.2 (m, 2H)	21.0; 54.2; 55.2; 56.9; 65.1

[a] Yield of product after recrystallization from glacial acetic acid.
[b] Satisfactory microanalyses obtained: C ±0.4, H ±0.3, S ±0.2.
[c] Finnigan 1020 OWA instrument.
[d] Only aliphatic resonances given.
[e] Varian EM 390 spectrometer.
[f] JEOL JNM-FX60 spectrometer.

These results suggest that chalcones and only chalcones give tetrahydrothiophenes **3** with sodium polysulfide. The exceptions to this generalization, the nitro compounds **1g** and **1h**, are probably reduced by the reagent perhaps followed by further reactions of the resulting amino ketones[8]. Why only chalcones, and not structurally similar compounds, give tetrahydrothiophenes is not clear, but it is consistent with the observation[1] that small changes in reagents and conditions can alter the course of reactions of sulfide ion with α,β-unsaturated carbonyl compounds.

Tetrahydrothiophenes 3; General Procedure:

Anhydrous sodium sulfide (18.3 g, 235 mmol), prepared by drying the nonahydrate at 130 °C in a vacuum oven until no more water collects in the pump traps, is alternately added with powdered sulfur (30.35 g, 947 mmol) to absolute ethanol (40 ml) with vigorous shaking. After the exothermic reaction has subsided, the chalcone **1a–f**[9] (3 g, ~ 12 mmol) is added to the deep red suspension with continued shaking. The mixture is allowed to stand at room temperature for 24 h at which time the gelatinous precipitate is removed by suction filtration, shaken with 22% aqueous ammonium sulfide solution (40 ml), refiltered, and washed with additional ammonium sulfide solution (40 ml) and water (100 ml). The resulting product can usually be freed from residual sulfur by recrystallization from glacial acetic acid except for **3d** which requires a prior passage through a short silica gel column with acetone as an eluent. A second crop can be recovered from the acetic acid mother liquors.

This research was supported by grants from the Robert A. Welch Foundation and the TCU Research Foundation.

Received: September 27, 1982

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[1] D. Del Mazza, M. G. Reinecke, *J. Org. Chem.* **46**, 128 (1981).
[2] E. Fromm, E. Hubert, *Justus Liebigs Ann. Chem.* **394**, 301 (1912).
[3] S. Kambe, K. Saito, A. Sakuri, H. Midorikawa, *Synthesis* **1980**, 839.
[4] R. A. Sanchez, *Synthesis* **1982**, 148.
[5] R. T. LaLonde, *J. Chem. Soc. Chem. Commun.* **1982**, 401.
[6] T. G. Pearson, P. L. Robinson, *J. Chem. Soc.* **1930**, 1473.
[7] H. K. Porter, *Org. React.* **20**, 455 (1973).
[8] K. V. Rao, *J. Heterocycl. Chem.* **12**, 725 (1975).
[9] E. P. Kohler, H. M. Chadwell, *Org. Synth. Coll. Vol.* I, 78 (1941).

0039-7881/83/0232-0161-02 $ 03.00