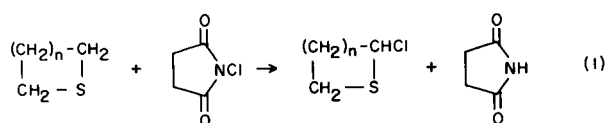


Synthesis of  $\alpha$ -Substituted Cyclic Sulfides

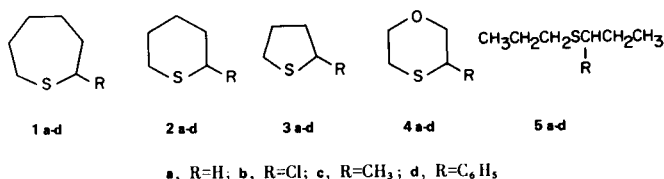
D. L. Tuleen and R. H. Bennett

Department of Chemistry, Vanderbilt University

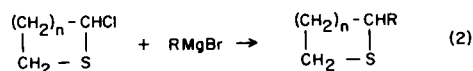
Sulfides **1a-4a** react readily with one mole of *N*-chlorosuccinimide (NCS) in carbon tetrachloride or benzene solution to afford the corresponding  $\alpha$ -chloro sulfides



**1b-4b** (Eq. 1,  $n=2,3,4$ ). Attempted purification of the chloro sulfides by distillation resulted in partial dehydrohalogenation; NMR spectra of these chloro sulfides (particularly the position (6b) and multiplicity of the signal corresponding to methinyl hydrogen) were consistent with the assigned structures.



The reaction of  $\alpha$ -chloro sulfides with Grignard reagents is known to lead to coupling (1-3). Treatment of benzene solutions of chloro sulfides **1b-4b** with an ethereal solution of methylmagnesium bromide or phenylmagnesium bromide gives the desired Grignard-coupling products **1c,d-4c,d** (Eq. 2,  $n=2,3,4$ ; R=CH<sub>3</sub>, C<sub>6</sub>H<sub>5</sub>). The overall yields for the two steps (chlorination and coupling) were greater than 50%. The NMR spectra of substituted cyclic sulfides **1c,d-4c,d** were consistent with the assigned structures. Carbon and hydrogen analyses were obtained for previously unreported substances.



The product of the chlorination of **4a** is identified as 3-chloro-1,4-oxathiane rather than the isomeric 2-chloro-1,4-oxathiane on the basis of its NMR spectrum and the

fact that the physical properties of the methyl and phenyl derivatives are considerably different from those reported for 2-methyl-1,4-oxathiane (**4**) and 2-phenyl-1,4-oxathiane (**5**).

Tetrahydrothiophene is the smallest monocyclic sulfide that can be successfully chlorinated at the  $\alpha$  carbon

TABLE I

NMR Spectra of **1b-5b** in Benzene ( $\delta$ )

|           | CHCl             | Other protons                      |
|-----------|------------------|------------------------------------|
| <b>1b</b> | 5.1 (t, broad)   | 3.1-1.1 (m)                        |
| <b>2b</b> | 5.0 (m)          | 3.0-1.1 (m)                        |
| <b>3b</b> | 5.4 (m)          | 3.0-1.4 (m)                        |
| <b>4b</b> | 4.5 (t, broad)   | 3.9-2.7 (m, 5H)<br>2.0-1.7 (m, 1H) |
| <b>5b</b> | 4.9 (t, J=7 cps) | 2.7-0.7 (m)                        |

TABLE II

NMR Spectra of **1c-5c** in Carbon Tetrachloride ( $\delta$ )

|           | CHCH <sub>3</sub> (d) | Other protons                                                           |
|-----------|-----------------------|-------------------------------------------------------------------------|
| <b>1c</b> | 1.2 (J=7)             | 2.9-2.5 (m, 3H, -CHS)<br>2.0-1.4 (m, 8H)                                |
| <b>2c</b> | 1.1 (J=6.5)           | 2.8-2.4 (m, 3H, -CHS)<br>2.1-1.3 (m, 6H)                                |
| <b>3c</b> | 1.27 (J=6.5)          | 3.4 (q, broad, J=6, 1H, CHS)<br>3.0-2.6 (m, 2H, CHS)<br>2.2-2.4 (m, 4H) |
| <b>4c</b> | 1.1 (J=6.5)           | 4.2-2.2 (m, 7H)                                                         |
| <b>5c</b> | 1.2 (J=7)             | 2.8-2.3 (m, 3H, CHS)<br>1.9-0.8 (m, 10H)                                |

TABLE III

NMR Spectra of **1d-5d** in Carbon Tetrachloride (8,12)

|           | $C_6H_5CH$                     | Other protons                                |
|-----------|--------------------------------|----------------------------------------------|
| <b>1d</b> | 3.9-3.6 (m)                    | 2.9-2.6 (m, 2H, $CH_2S$ )<br>2.2-1.6 (m, 8H) |
| <b>2d</b> | 3.9-3.6 (m)                    | 2.8-2.6 (m, 2H, $CH_2S$ )<br>2.2-1.6 (m, 6H) |
| <b>3d</b> | 4.4 (t, $J=7$ )                | 3.1-2.8 (m, 2H, $CH_2S$ )<br>2.4-1.7 (m, 4H) |
| <b>4d</b> |                                | 4.2-2.2 (m, 7H)                              |
| <b>5d</b> | 3.6 (d of d, $J=7.8$ ,<br>6.8) | 2.3-1.2 (m, 6H)<br>0.9 (t, $CH_3$ , 6H)      |

by NCS. Thietane is cleaved by NCS and forms *N*-(3-chloropropylthio)succinimide (**6a**). Chlorination of rings larger than thiepane (**1a**) would presumably parallel the behavior of acyclic sulfides such as propyl sulfide (**5a**), which is readily chlorinated at the *alpha* carbon. The chloro sulfide **5b** reacts normally with Grignard reagents to form *sec*-butyl propyl sulfide (**5c**) and 1-phenylpropyl propyl sulfide (**5d**).

We believe that this method of chlorination by NCS followed by coupling with Grignard reagents should prove useful for the synthesis of other sulfides. Discussion of the probable mechanistic course of the chlorination has appeared elsewhere (6).

## EXPERIMENTAL (7)

## Reagents.

*N*-Chlorosuccinimide, obtained from the Arapahoe Chemical Co., was purified by recrystallization from eight times its weight of hot water, followed by rapid filtration. Thiophene-free benzene was dried over sodium before use. The sulfides were all commercially available and were distilled prior to use.

2-Chlorothiepane (**1b**). General method for chloro sulfides **1b-5b**.

*N*-Chlorosuccinimide (6.75 g., 0.05 mole) was added in three portions over a 15 minute period to a solution of thiepane (**1a**) (5.80 g., 0.05 mole) in 60 ml. of benzene. The temperature of the reaction was maintained at 20-25° by intermittent external cooling. The mixture was stirred magnetically for one hour and rapidly filtered to remove succinimide (the completion of the reaction can be determined readily with potassium iodide-starch indicator paper). The NMR spectrum of the chloro sulfides are recorded in Table I.

2-Methylthiepane (**1c**). General method for sulfides **1c,d-5c,d**.

A benzene solution of **1b** was added to a solution of methylmagnesium bromide (0.09 mole) in 60 ml. of ethyl ether. The rate of addition was such that the temperature of the reaction was maintained between 10-15°. The resultant mixture was stirred overnight and was decomposed by the addition of ice and a 20% aqueous solution of sulfuric acid. The organic layer was washed twice with water, once with 10% sodium hydroxide solution, then

three times with water, and was dried over magnesium sulfate. Removal of the solvent, followed by distillation, gave 4.30 g. (66%) of the desired sulfide, b.p. 94-96° (52 mm.),  $n_D^{26}$  1.5007.

*Anal.* Calcd. for  $C_7H_{14}S$ : C, 64.55; H, 10.83. Found: C, 64.40; H, 10.90.

2-Methyltetrahydrothiopyran (**2c**).

This compound was similarly prepared in a 51% yield, b.p. 71-73° (54 mm.),  $n_D^{25}$  1.4914 (Lit. (9) b.p. 68-69° (45 mm.),  $n_D^{20}$  1.4906).

2-Methyltetrahydrothiophene (**3c**).

This compound was synthesized similarly in a 50% overall yield, b.p. 129-132°,  $n_D^{25}$  1.4905 (Lit. (10) b.p. 132°,  $n_D^{20}$  1.4920).

3-Methyl-1,4-oxathiane (**4c**).

This compound was prepared as above (51%), b.p. 71-72° (38 mm.),  $n_D^{25}$  1.4912.

*Anal.* Calcd. for  $C_5H_{10}OS$ : C, 50.81; H, 8.53. Found: C, 50.75; H, 8.62.

*sec*-Butyl *n*-Propyl Sulfide (**5c**).

This compound was synthesized in 60% yield, b.p. 77-79° (54 mm.),  $n_D^{25}$  1.4477.

*Anal.* Calcd. for  $C_7H_{16}S$ : C, 63.56; H, 12.19. Found: C, 63.25; H, 12.17.

NMR spectral data for **1c-5c** are recorded in Table II.

2-Phenylthiepane (**1d**).

2-Phenylthiepane was prepared in 56% yield from the chlorination of thiepane followed by reaction with excess phenylmagnesium bromide, b.p. 100-101° (0.35 mm.),  $n_D^{25}$  1.5748.

*Anal.* Calcd. for  $C_{12}H_{16}S$ : C, 74.94; H, 8.39. Found: C, 75.26; H, 8.48.

2-Phenyltetrahydrothiopyran (**2d**).

This compound was similarly prepared (56%), b.p. 76-79° (0.3 mm.). This material solidified on cooling, and was recrystallized from methanol to afford white needles, m.p. 50.5-51.5°.

*Anal.* Calcd. for  $C_{11}H_{14}S$ : C, 74.10; H, 7.91. Found: C, 73.95; H, 7.88.

2-Phenyltetrahydrothiophene (**3d**).

This compound was formed in 52% yield, b.p. 104-106° (3 mm.),  $n_D^{25}$  1.5855 (Lit. (11) b.p. 97° (0.2 mm.), 82° (0.05 mm.),  $n_D^{25}$  1.5676).

3-Phenyl-1,4-oxathiane (**4d**).

This compound was formed in 75% yield, b.p. 89° (0.05 mm.),  $n_D^{25}$  1.5794.

*Anal.* Calcd. for  $C_{10}H_{12}OS$ : C, 66.63; H, 6.71. Found: C, 66.58; H, 6.78.

1-Phenylpropyl *n*-Propyl Sulfide (**5d**).

This compound was formed in 50% yield, b.p. 90-91° (2.0 mm.),  $n_D^{25}$  1.5289.

*Anal.* Calcd. for  $C_{12}H_{18}S$ : C, 74.16; H, 9.34. Found: C, 74.99; H, 9.38. NMR spectral data for **1d-5d** are recorded in Table III.

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Nashville, Tennessee 37203