

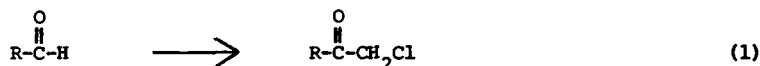
PYROLYSIS OF  $\beta$ -HYDROXY- $\alpha$ -CHLOROSULFOXIDE: A SIMPLE SYNTHESIS OF CHLOROMETHYLKETONES

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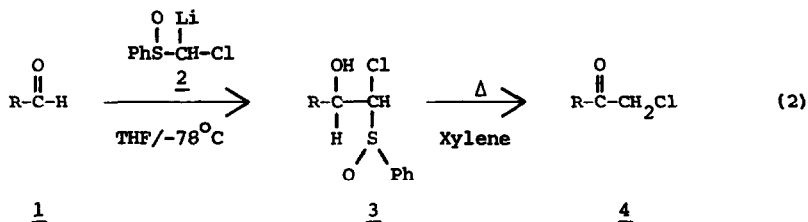
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The pyrolysis of  $\alpha$ -sulfinyl compounds has been a subject of current interest due to their wide applications in organic syntheses. The elimination of the sulfoxide compounds to  $\alpha$ ,  $\beta$  unsaturated carbonyl compounds<sup>1</sup>, to methyl ketones<sup>1</sup>, and to  $\beta$ -ketoesters<sup>2</sup> has been reported. In this communication, we wish to report a novel two-step synthesis of chloromethylketones from the corresponding aldehydes. The overall synthetic transformation is represented by equation (1).



Numerous methods are available for the synthesis of  $\alpha$ -haloketones<sup>3</sup>, but there are very few methods for specific synthesis of halomethylketones<sup>4</sup>. Our reaction sequence (equation 2) is highly convenient to carry out, and chloromethylketone is the only product formed. The reaction of aldehyde 1 with lithio chloromethyl phenyl sulfoxide 2 in tetrahydrofuran at  $-78^\circ\text{C}$  gave the



$\beta$ -hydroxy- $\alpha$ -chlorosulfoxide 3 as crystalline compound (except R = n-C<sub>3</sub>H<sub>7</sub>-) in good yield. The pyrolysis of 3 in xylene gave the chloromethylketone 4 in excellent yield.

The complete sequence is illustrated by the transformation of n-heptanal to chloromethyl hexyl ketone. Addition of n-heptanal (1.0 equiv.) to THF solution of lithio chloromethyl phenyl sulfoxide<sup>5</sup> (1.0 equiv.) at  $-78^\circ\text{C}$  gave a pale yellow homogeneous mixture which was maintained at this temperature for 20 min before being warmed to  $-20^\circ\text{C}$ . After stirring had been continued for an additional 45 min, the reaction was quenched with water. The aqueous solution was extracted with chloroform and the crude product was purified by recrystallization from chloroform-light petroleum (1:3) to give 1-chloro-1-phenylsulfinyl-2-hydroxyoctane (70.0% yield). Pyrolysis, under nitrogen, of the hydroxysulfoxide in xylene ( $160^\circ\text{C}$ ) gave chloromethyl hexyl ketone in 95.0% yield (isolated by preparative thick layer chromatography, PLC, on Merck PF<sub>254</sub> silica gel;

1:9 ether-light petroleum;  $R_f = 0.46$ ). The results are summarized in Table 1.

Table 1

Aldehydes	Products <u>3</u> (Yield %)	m.p. °C	Products <u>4</u> (Yield %)
$n\text{-C}_3\text{H}_7\text{CHO}$	$  \begin{array}{c}  \text{OH} \quad \text{H} \quad \text{O} \\    \quad   \quad   \\  n\text{-C}_3\text{H}_7\text{C} - \text{C} - \text{S} - \text{Ph} \\    \quad   \\  \text{H} \quad \text{Cl}  \end{array}  $ (68.0)	liquid <sup>a</sup>	$  \begin{array}{c}  \text{O} \\     \\  n\text{-C}_3\text{H}_7\text{CCH}_2\text{Cl}  \end{array}  $ (76.4)
$n\text{-C}_4\text{H}_9\text{CHO}$	$  \begin{array}{c}  \text{OH} \quad \text{H} \quad \text{O} \\    \quad   \quad   \\  n\text{-C}_4\text{H}_9\text{C} - \text{C} - \text{S} - \text{Ph} \\    \quad   \\  \text{H} \quad \text{Cl}  \end{array}  $ (71.4)	88-89	$  \begin{array}{c}  \text{O} \\     \\  n\text{-C}_4\text{H}_9\text{CCH}_2\text{Cl}  \end{array}  $ (81.0)
$n\text{-C}_5\text{H}_{11}\text{CHO}$	$  \begin{array}{c}  \text{OH} \quad \text{H} \quad \text{O} \\    \quad   \quad   \\  n\text{-C}_5\text{H}_{11}\text{C} - \text{C} - \text{S} - \text{Ph} \\    \quad   \\  \text{H} \quad \text{Cl}  \end{array}  $ (66.5)	91-92	$  \begin{array}{c}  \text{O} \\     \\  n\text{-C}_5\text{H}_{11}\text{CCH}_2\text{Cl}  \end{array}  $ (80.0)
$n\text{-C}_6\text{H}_{13}\text{CHO}$	$  \begin{array}{c}  \text{OH} \quad \text{H} \quad \text{O} \\    \quad   \quad   \\  n\text{-C}_6\text{H}_{13}\text{C} - \text{C} - \text{S} - \text{Ph} \\    \quad   \\  \text{H} \quad \text{Cl}  \end{array}  $ (70.0)	104-105	$  \begin{array}{c}  \text{O} \\     \\  n\text{-C}_6\text{H}_{13}\text{CCH}_2\text{Cl}  \end{array}  $ (95.0)
$n\text{-C}_7\text{H}_{15}\text{CHO}$	$  \begin{array}{c}  \text{OH} \quad \text{H} \quad \text{O} \\    \quad   \quad   \\  n\text{-C}_7\text{H}_{15}\text{C} - \text{C} - \text{S} - \text{Ph} \\    \quad   \\  \text{H} \quad \text{Cl}  \end{array}  $ (69.3)	99-100	$  \begin{array}{c}  \text{O} \\     \\  n\text{-C}_7\text{H}_{15}\text{CCH}_2\text{Cl}  \end{array}  $ (91.0)

<sup>a</sup>Isolated by PLC; 4:1 chloroform-light petroleum;  $R_f = 0.16$ .

Further study on the application of this elimination reaction is in progress.

#### References

1. J. Nokami, N. Kunieda and M. Kinoshita, Tetrahedron Lett., 2841 (1975) and references therein; B.M. Trost and K.K. Leung, ibid., 4197 (1975); B.M. Trost and A.J. Bridges, J.Org.Chem., 40, 2014 (1975); B.M. Trost, T.N. Salzmann and K. Hiroi, J.Amer.Chem.Soc., 98, 4887 (1976) and references therein.
2. J. Nokami, N. Kunieda and M. Kinoshita, Tetrahedron Lett., 2179 (1975) and references therein.
3. J. Villieras, C. Bacquet and J.F. Normant, J.Organometal. Chem., 97, 325 (1975); H. Taguchi, H. Yamamoto and H. Nozaki, Tetrahedron Lett., 4661 (1972); L. Blanco, P. Amice and J.M. Conia, Synthesis, 194, 196 (1976); F. Reinach - Hirtzbach and T. Durst, Tetrahedron Lett., 3677 (1976) and references therein.
4. W. Bradley and G. Schwarzenbach, J.Chem.Soc., 2904 (1928); J. Cason, J.Amer.Chem.Soc., 68, 2078 (1946); J.F. Bunnett and D.S. Tarbell, ibid., 67, 1944 (1945); D.V.C. Awang and S. Wolfe, Can. J. Chem., 47, 706 (1969); J.F. Keana and R.R. Schumaker, Tetrahedron, 26, 5191 (1970).
5. T. Durst, J.Amer.Chem.Soc., 91, 1034 (1969); T. Durst and K.C. Tin, Tetrahedron Lett., 2369 (1970).