Asymmetric Synthesis of Thiiranes from Aldehydes and Ketones and *S*-Lithiomethyl *O*-(−)-Menthyl Dithiocarbonate

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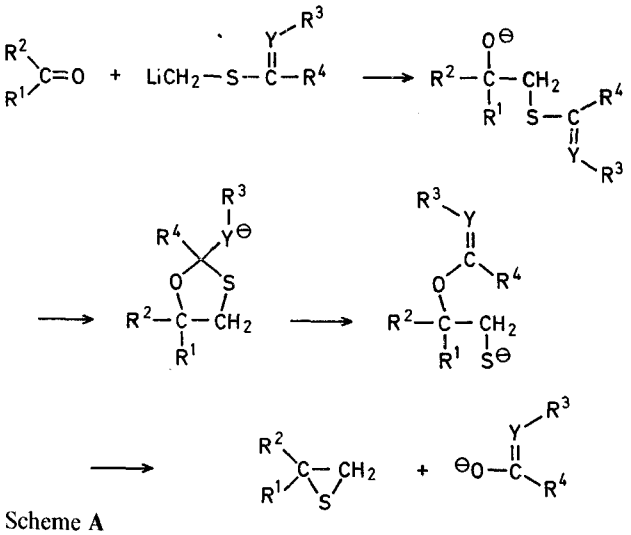
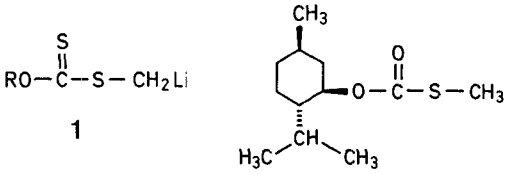
Several new methods for the direct conversion of aldehydes and ketones to homologous thiiranes have been described[1,2,3]. All of these methods involve variants of the reaction generalized in Schema **A**.



Scheme **A**

The group represented as $\geq C{=}Y{-}R^3$ in Scheme **A** has a twofold function. First, it must act as an alkoxide trap

and second it must be capable of converting the oxido function to a leaving group, $^{\ominus}O-\overset{|}{C}=Y-R^3$. Among the various reagents which we have found to be capable of achieving such transformations, the lithium derivatives **1** of dialkyl dithiocarbonates are the most readily accessible. Optically active examples of such reagents are readily made beginning with available optically pure alcohols. It is the use of such chiral reagents in the asymmetric synthesis of thiiranes that we now wish to describe[4].



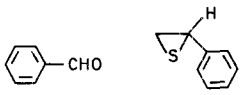
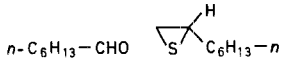
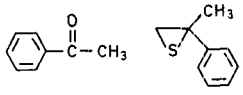
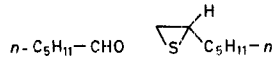
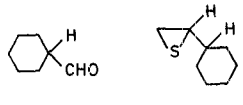
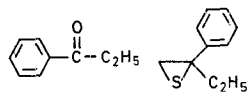
1

2

O-(−)-Menthyl *S*-methyl dithiocarbonate[5] [**2**; m.p. 39–40°, $[\alpha]_D$ −82.3° (c = 1, $CHCl_3$)] is stable, nicely crystalline, readily prepared and easily purified. The *S*-methyl group was lithiated by reaction with lithium diisopropylamide in tetrahydrofuran. Reactions of the lithium reagent with a variety of carbonyl compounds are summarized in the Table. Of all the reagents which we have examined for the transformation described in Scheme **A**, reagent **2** is superior for ease of preparation, stability, and overall yields. We recommend its use even in those cases where asymmetric induction is of no consequence.

The reaction described by the last entry in the Table was repeated using **1** (R = 3β-cholestanyl). The 2-ethyl-2-phenylthiirane thus obtained (53% yield) had $[\alpha]_D$ +0.43° (c = 17, CCl_4).

Table. Formation of Chiral Thiiranes from **2**

Carbonyl Compound	Yield (%)	$[\alpha]_D$ (c, CCl_4)	Optical Purity (%)
	55	−2.22 (23)	2.3[a], ~5[b]
	63	+0.26 (34)	~1.5[c]
	61	+1.08 (18)	--
	61	−0.34 (13)	--
	77	−2.36 (26)	~9[c]
	64	+6.95 (20)	--

[a] Based on reduction to (−)-1-phenylethanethiol, $[\alpha]_D$ = −2.51° (neat); maximum reported for (+)-isomer $[\alpha]_D$ = +108° (neat) [H. M. R. Hoffmann, E. D. Hughes, *J. Chem. Soc.* **1964**, 1244].

[b] E. Chiellini, M. Marchetti, and G. Ceccarelli [*Int. J. Sulfur Chem. Part A*, **1**, 73 (1971)] report $[\alpha]_D$ = −15.7° (heptane) for 2-phenylthiirane which they consider to be 36% optically pure.

[c] Estimated from values provided by A. I. Meyers (reference 4).

Preparation of Thiiranes; General Procedure:

A solution of *O*-(−)-menthyl *S*-methyl dithiocarbonate (**2**; 10 mmol) in tetrahydrofuran (5 ml) was added dropwise to a solution of lithium diisopropylamide (10 mmol) in tetrahydrofuran (20 ml) at −78°. After 30 minutes, the carbonyl compound (12 mmol) in tetrahydrofuran (5 ml) was slowly added. The reaction mixture was stirred at −78° for 1 h, then allowed to warm to room temperature while stirring was continued for an additional 2 h. Methanol (4 ml) was added and the mixture was poured into cold dilute hydrochloric acid (11 mmol) covered with benzene (50 ml). Work-up was completed with additional extractions with benzene and chromatography over silica gel with benzene/hexane as eluent.

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[1] C. R. Johnson, A. Nakanishi, N. Nakanishi, K. Tanaka, *Tetrahedron Lett.* **1975**, 2865.

[2] A. I. Meyers, M. E. Ford, *Tetrahedron Lett.* **1975**, 2861.

[3] K. Hirai, H. Matsuda, Y. Kishida, *Chem. Pharm. Bull.* **20**, 2067 (1972).

[4] A. I. Meyers and M. E. Ford have observed asymmetric induction in the synthesis of thiiranes utilizing chiral oxazoline reagents (private communication).

[5] H. R. Nace, *Organic Reactions* **12**, 57 (1962).