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SYNTHESES OF THIIRANES FROM ALDEHYDES OR KETONES AND SULFUR-STABILIZED CARBANIONS

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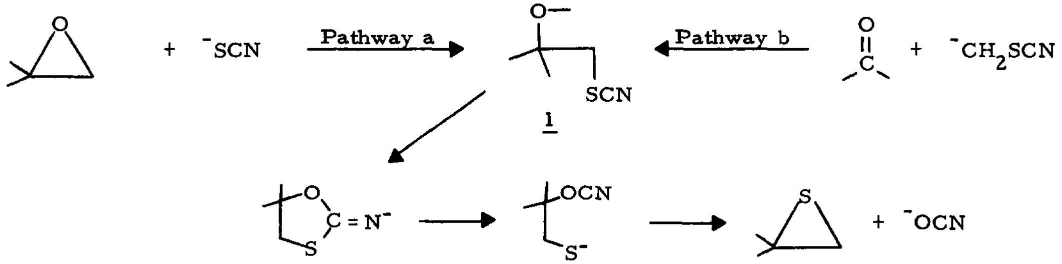
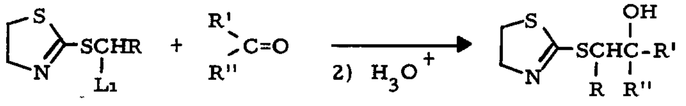
The reaction of thiocyanate ion with oxiranes is the most widely recognized method for the synthesis of thiiranes (Scheme 1, Pathway a).[1] The first intermediate in this reaction is a β-oxidothiocyanate (1). In theory intermediate 1 should be accessible by an independent route involving the combination of a carbonyl group of an aldehyde or ketone and an anion derived by α-deprotonation of an alkyl thiocyanate (Scheme 1, Pathway b). This latter pathway, if successful, could provide a one-step transformation of aldehydes or ketones to thiiranes.

Scheme 1



Treatment of methyl and other alkyl thiocyanates with a variety of bases, including proton-specific bases such as lithium diisopropylamide (LDA) in various solvents, followed by addition of carbonyl compounds failed to produce any detectable thiiranes. Color tests revealed the presence of cyanide ion but the absence of cyanate ion in the final reaction mixture.

It appeared that an alteration of the reagent design was needed, the CN group should be replaced with a system that was less prone to act as a leaving group but which retained an electrophilic multiple bond to serve as an "alkoxide trap." Our first choice was the heterocycle 2. A literature search revealed that Hirai and coworkers had observed a transformation of the type desired although their study did not emphasize the preparative possibilities for the reaction; the lithium reagents 3 and 4 were condensed with benzaldehyde to provide low yields of the corresponding 2-phenyl-3-(2-propynyl)thiiranes mixed with the related alkenes (from elimination of sulfur).[2,3,4]



(1)

2 = R = H

3 = R = C ≡ CLi

4 = R = C ≡ CPh

5 = R = Ph

6 = R = R' = H, R'' = Ph (75%)

7 = R = R' = Ph, R'' = H (80%)

8 = R = Ph, R' = R'' = CH_3 (100%)

We have found 2 and 5 react with aldehydes and ketones to give, after workup, isolable alcohols (eq. 1). These alcohols when treated with base, acid or heat gave thiiranes (eq. 2 and 3)

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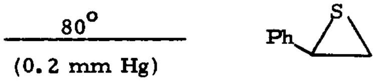
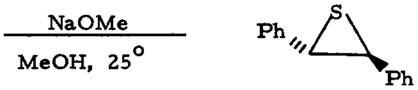


(73%) (2)

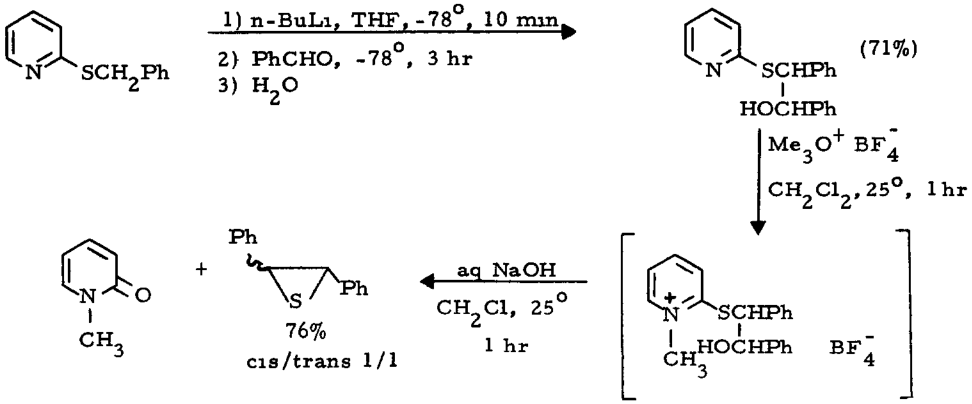
7



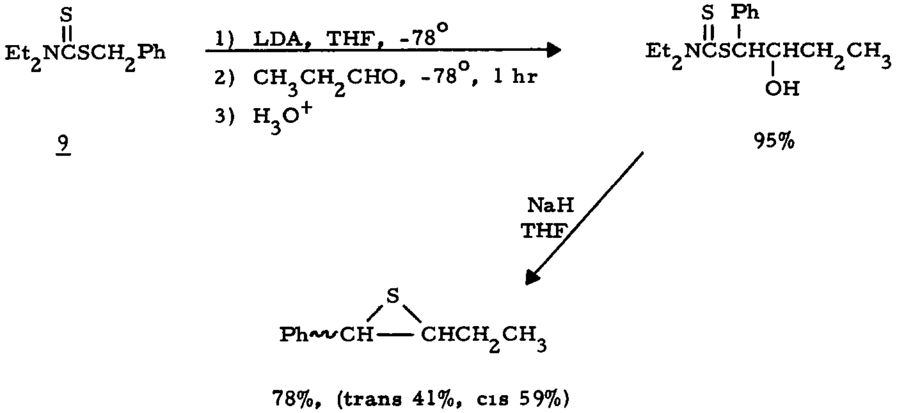
(100%) (3)

A variety of other types of sulfur stabilized carbanionic reagents should be capable of effecting such transformations. In Scheme 2 the utilization of a metalated 2-alkylthiopyridine[5] is illustrated.

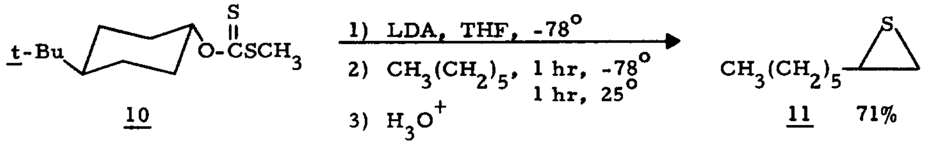
Scheme 2



Reagents derived by lithiation of dithiocarbamates[6] (eq. 4) and O-alkyl S-alkyl dithiocarbonates (eq. 5) have also been found effective for the synthesis of thiiranes.



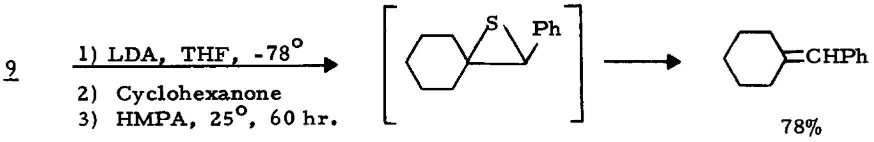
(4)



(5)

When O, S-dimethyl dithiocarbonate is used in place of 10 the thiirane 11 is obtained in 50% yield. Apparently such lithio derivations with secondary O-alkyl groups are somewhat more stable than those with primary.

It should be noted that thiiranes are readily desulfurized to alkenes by reagents such as phosphines[7] and phosphites.[7,8] Many thiiranes, especially those with vinyl or phenyl substituents extrude sulfur on heating or standing.



All of the reagents illustrated have a severe structural limitation, regardless of the base and solvent systems chosen, α-metalation was successful only when the S-alkyl group was methyl, benzyl, allyl, etc.

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REFERENCES AND FOOTNOTES

1. H. R. Snyder, J. M. Steward and J. B. Ziegler, J. Amer. Chem. Soc., 69, 2672 (1947), C. C. Price and P. F. Kirk, ibid., 75, 2396 (1953).
2. K. Hirai, H. Matsuda, and Y. Kishida, Chem. Pharm. Bull., 20, 2067 (1972).
3. K. Hirai and Y. Kishida [J. Synth. Org. Chem., 32, 20 (1974)] have also shown that 2-p-chlorophenylthiirane is produced when 2-(2-p-chlorophenyl-2-oxoethyl)thiazoline is reduced with lithium aluminum hydride.
4. Professor A. I. Meyers, Colorado State University, has informed us of a similar approach to thiiranes using lithium reagents derived from 2-(alkylthio)-2-oxazolines. We thank him for making his results available to us. See accompanying paper by A. I. Meyers and M. E. Ford.
5. For other uses of these reagents see K. Narasaka and T. Mukaiyama, Chem. Lett. (Japan), 259 (1972).
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