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SYNTHESIS VIA OXAZOLINES - ONE CARBON HOMOLOGATION OF ALDEHYDES AND KETONES TO THIIRANES AND OLEFINS

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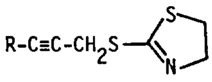
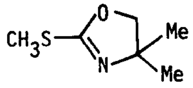
Thiiranes are useful precursors for the synthesis of olefins by phosphine[1a] or phosphite[1b,c] mediated desulfurizations. However, these heterocycles are obtained from multi-step procedures involving intermediate oxiranes[2] derived from carbonyl compounds or olefins. The synthetic utility of oxazolines has been amply demonstrated[3] and we now report a route to thiiranes and olefins using this readily available heterocycle. Recently,[4] the lithio salt of several 2-(propargylthio)-2-thiazolines 1 was condensed with benzaldehyde providing the corresponding 2-propargyl-3-phenylthiiranes, however, the modest yields (~20%) encountered appear to have discouraged further study. Our extensive studies on oxazolines have led us to the 2-(thiomethyl)-2-oxazoline[5] 2 which was found to readily metalate with n-butyllithium (THF, -78°) and may be



1, R=H, Ph



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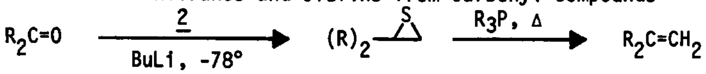
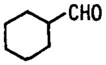
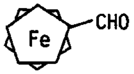
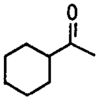
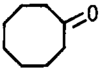
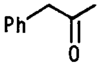
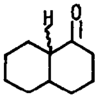
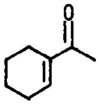
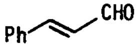
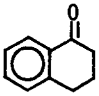
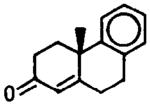
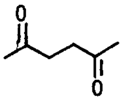
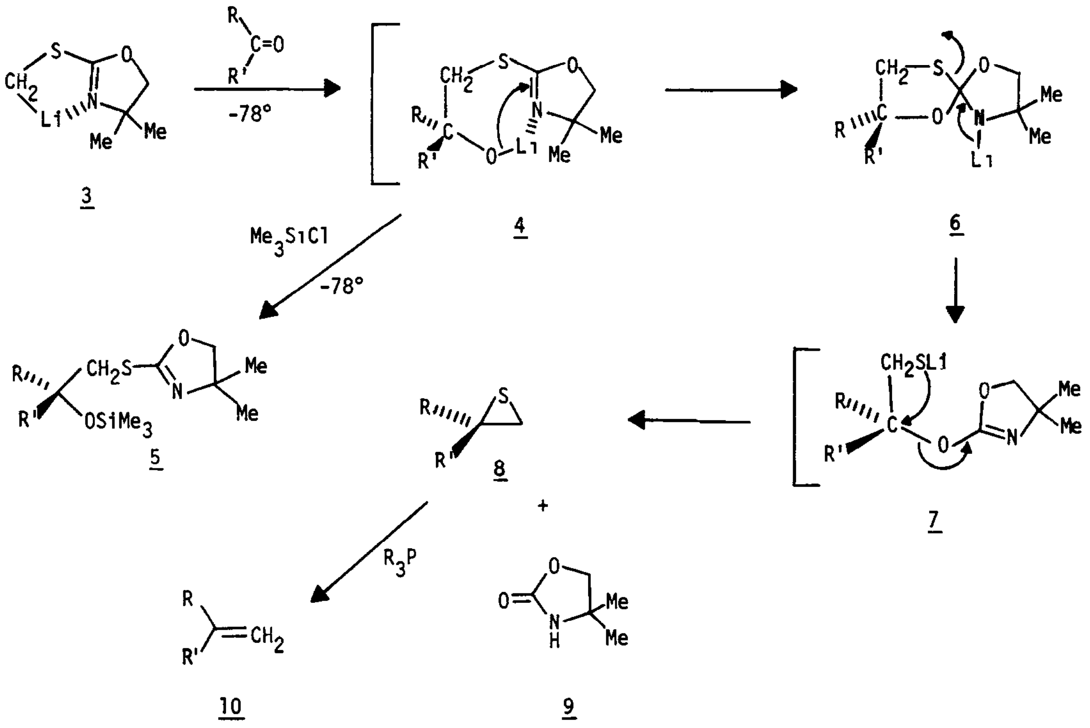
alkylated with various carbonyl compounds furnishing, in a single operation, the homologated thiiranes in 61-78% yields (Table I).[6] Reaction proceeds by rapid addition of the lithio oxazolines 3 to the carbonyl compound producing 4, which was trapped as its trimethylsilyl ether 5 at -78°. However, if the solution of 4 was allowed to slowly warm to ambient, rearrangement and fragmentation takes place via 6 and 7 affording the thiiranes 8 and the oxazolone 9 after hydrolytic treatment. Attempts to trap 7 as its TMS ether were uniformly unsuccessful. The resulting thiiranes are smoothly desulfurized to the olefins 10 using triphenylphosphine (Method A) or the sequence allows for passing over the thiirane and proceeding directly to the olefin by heating the crude products (8 and 9) with P(OEt$_3$) or Ph$_3$P (Method B) The latter method is the procedure of choice when the products are conjugated olefins since the crude material

TABLE I Formation of Thiiranes and Olefins from Carbonyl Compounds[a]



Carbonyl Compound	Thiirane, %[b]	Olefin, %[b,c]	
		A	B[d]
	73	64	69
	78		
	68		
	66		
	61	65	47
	31 (62)[e,f]		
	61[g]	52	
	h		42
	h		46
	h		46[i]
	h		48[i]
	(dithiirane)[h]		40

a) All thiiranes and olefins exhibited expected spectral and physical characteristics, b) Chromatrographed or distilled yields; c) Yield based on thiirane, d) Yield based on carbonyl compound, e) Decomposed above 125° on UCW-98 vpc column; f) Parenthetical yield based on recovered ketone, g) Vpc indicated a mixture of isomers which were not separated, h) Thiirane was not purified. A mixture of 8 and 9 was heated with Ph_3P or $P(OEt)_3$, i) The nmr spectrum in benzene-d_6 was totally consistent with the exo-methylene structure. However, if the nmr spectrum is taken in $CDCl_3$, traces of HCl present in this solvent effects a slow isomerization to the endo-isomer.



contains both the olefin and the thiirane Isolation of vinyl thiiranes is difficult due to their instability and propensity for elimination of sulfur.

The present method thus provides an efficient route to thiiranes from carbonyl compounds and a method for forming olefins and polyenes under regiospecific conditions.[7]

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REFERENCES AND FOOTNOTES

1. a) R. D. Schuetz and R. L. Jacobs, *J. Org. Chem.*, **23**, 1799 (1958), *ibid.*, **26**, 3467 (1961), b) M. J. Boskin and D. B. Denney, *Chem. and Ind.* (London), 330 (1959), c) R. E. Davis, *J. Org. Chem.*, **23**, 1767 (1958).
2. M. Sander, *Chem. Rev.*, **66**, 297 (1966).
3. A. I. Meyers, D. L. Temple, D. Haidukewych, and E. D. Mihelich, *J. Org. Chem.*, **39**, 2787 (1974).
4. K. Hirai, H. Matsuda, and Y. Kishida, *Chem. Pharm. Bull.*, **20**, 2067 (1972). Recently Professor C. R. Johnson, Wayne State University, has informed us of his similar approach to thiiranes and we thank him for communicating his results to us which appear in the accompanying article.
5. Prepared by treating 4,4-dimethyloxazolin-2-thione [M. Skulski, D. L. Germaise and A. F. McKay, *Can. J. Chem.*, **34**, 815 (1956)] with sodium hydride and methyl iodide in THF.
6. General Procedure - A 0.2 *M* solution of **2** in THF is treated under N_2 at -78° with 1.1 equiv of *n*-butyllithium. After 2 h, the carbonyl compound (1.0 equiv) is added as a solution in THF and the mixture slowly allowed to reach ambient. The mixture is quenched in saturated brine solution and extracted several times with ether, dried, and concentrated. Column chromatography (benzene, silica gel) provides the pure thiirane. Desulfurization of the pure thiirane or the crude mixture was accomplished by heating at 90° (2 h) with neat Ph_3P or $P(OEt)_3$ (1.15 equiv) and either distilling out the pure olefin or passing the mixture through silica gel with benzene.
7. This method currently possesses a serious limitation in preparing 1,2-disubstituted thiiranes and ultimately internal olefins. If the alkyl group on sulfur is other than methyl, benzyl, cyanomethyl, or carboethoxymethyl (i.e. ethyl, *n*-propyl, *n*-butyl, etc.), the lithio salt could not be generated even though a wide variety of bases, solvents, and temperatures were examined.