

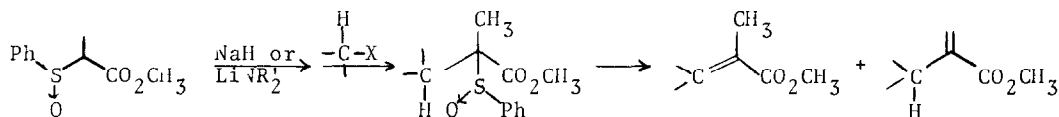
ON THE REGIOSPECIFICITY OF THE SULFOXIDE ELIMINATION

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Recently, the sulfoxide<sup>1</sup> and selenoxide<sup>2</sup> eliminations have become widely used for the introduction of double bonds, especially alpha to a carbonyl group. The one pot alkylative-elimination<sup>3,4</sup> expands the applications of these reactions. A major problem is the factor(s) that determines the regio-specificity of the reaction. Especially noteworthy is the high preference for endocyclic olefin formation in the case of 2-alkylcycloalkanones and 2-alkyllactones. Some of the factors involved, such as steric interactions,<sup>5</sup> have already been recognized. We wish to report that dipole-dipole interactions appear to play an important role in this reaction.

The alkylative-elimination of methyl 2-phenylsulfinylpropionate, a diastereomeric mixture, with various alkylating agents was



explored and is summarized in the Table. In each case, abstraction of a methylene or methine hydrogen is contrasted to that of a methyl hydrogen. The trends indicate the following order of reactivity:  $\text{C}=\text{CCH}_2 \sim \text{C}\equiv\text{C}-\text{CH}_2 > \text{ArCH}_2 \sim \text{CH}_3 > \text{C}-\text{CH}_2 \gg \text{C}-\text{H}$ . For the allyl and propargyl examples, the regio- and stereoselectivity is complete within nmr detectable limits and makes these reactions useful for trisubstituted olefin formation. A slight change in

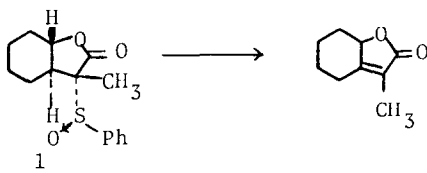
Table Alkylative Elimination with Methyl 2-Phenylsulfinylpropionate

Alkylating Agent	Conditions <sup>a</sup>		Products (Ratio)	% Isolated yield
	Alkylation	Elimination		
$p\text{-XC}_6\text{H}_4\text{CH}_2\text{Pr}$				
X = H	0°, 1 hr <sup>c</sup>	80°, 0.5 hr <sup>e</sup>	$p\text{-XC}_6\text{H}_4\text{CH}=\text{CHCO}_2\text{CH}_3$ (57)	71
	0°, 1 hr <sup>c</sup>	110°, 0.5 hr <sup>e</sup>	(43)	84
X = CN	0°, 1 hr	80°, 0.5 hr <sup>e</sup>	(43) (42)	67
geranyl bromide	0°, 1 hr <sup>b,c</sup>	80°, 1 hr	$\text{CH}_3\text{CH}=\text{CHCH}_2\text{CH}_2\text{CH}(\text{CO}_2\text{CH}_3)\text{CH}_2\text{CH}=\text{CH}_2$	76-83
$n\text{-C}_6\text{H}_{13}\text{C}\equiv\text{CCH}_2\text{X}$	0°, 1 hr (X-I, d OMs <sup>c</sup> )	100°, 0.5 hr <sup>e</sup>	$n\text{-C}_6\text{H}_{13}\text{C}\equiv\text{C}-\text{CH}=\text{CHCO}_2\text{CH}_3$	X = I 64 OMS 53
citronellyl iodide	25°, 44 hr <sup>d</sup>	120°, 1 hr <sup>e</sup>	$(\text{CH}_3)_2\text{CHCH}=\text{CHCH}_2\text{CH}_2\text{CH}(\text{CO}_2\text{CH}_3)\text{CH}_2\text{CH}=\text{CH}_2$ (71)	60
isopropyl iodide	25°, 41 hr <sup>c</sup>	120° <sup>f</sup>	$(\text{CH}_3)_2\text{CHC}(\text{CH}_2)_2\text{CH}=\text{CHCO}_2\text{CH}_3$	40

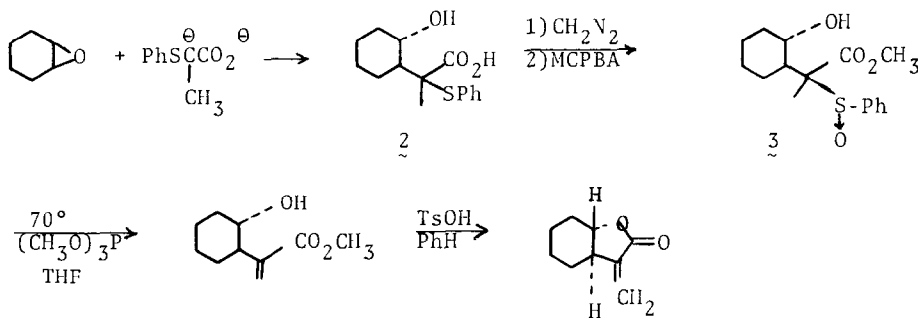
a) All reactions were carried out in HMPA as solvent unless otherwise noted. b) DME employed as solvent c) Lithium N-isopropyl-N-cyclohexyl amide as base d) Sodium hydride as base e) Trimethyl phosphite added prior to raising temperature for elimination f) Elimination performed on crude sulfoxide during distillation in a Kugelrohr g) All compounds have spectral properties in accord with the assigned structure and new compounds have correct elemental compositions

proton acidity, i.e. benzyl versus 4-cyanophenylmethylene, has no effect

A very interesting aspect of the data is the absence of any proton abstraction from a methine relative to a methyl carbon. This observation contrasts to that in cyclic cases such as the lactone 1.<sup>6</sup> To probe whether

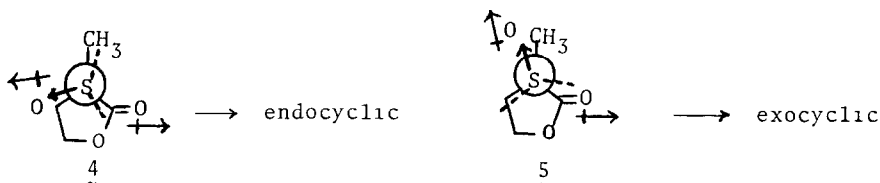


this result was a function of the substitution pattern or of the ring, we synthesized the acyclic version of 1, i.e., 3, as a diastereomeric mixture,<sup>7</sup> by esterification and oxidation of 2 prepared by the method of Iwai et al. Elimination in the presence of trimethyl phosphite as a sulfenic acid trap led exclusively to the  $\alpha$ -methylene ester [nmr  $\delta$  6.14 and 5.57, s, 1H each, 5.06, bs, 1H, 3.52, m, 1H, 2.38, m, 1H]. Lactonization gives the  $\alpha$ -methylene- $\gamma$ -butyrolactone reported previously.<sup>7</sup> Thus, the substitution pattern does not change the intrinsic preference for abstraction of the proton on the primary versus tertiary carbon. In this way,  $\alpha$ -methylene lactones can be available regardless of stereochemistry at the  $\alpha$  carbon if the lactone is simply hydrolyzed prior to elimination



The preference for endocyclic double bond formation appears to be dictated by the conformational rigidity of the ring system. If an examination of the conformation for the two syn eliminations is made, we may note

that minimum dipole-dipole repulsion results in 4 relative to 5. Such a



factor may also account for the regioselectivity seen in the presence of other polar groups such as alcohols<sup>4,8</sup> and may account in part for the rate acceleration seen in the elimination of  $\beta$ -ketosulfoxides (and selenoxides) relative to simple cases. Thus, dipole-dipole effects should be considered in addition to steric interactions, proton acidity, and double bond stability.

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