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THE DIELS-ALDER REACTION OF HETERODIENES CONTAINING SULFUR

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Regio-, site-, peri and stereoselectivity present major challenges in synthesis. For simple Diels-Alder reactions involving a 1,3-diene and a dieneophile, site- and peri-selectivity problems are avoided; and, since these reactions obey the Woodward-Hoffman rules, the stereochemistry is usually *cis*. However, the ability to predict regioselectivity of products when unsymmetrical reagents are utilized remains an arena for continued investigation.[1] Heteroatom substituents have been effective in altering the course of cycloaddition reactions; presumeably by modifying the frontier molecular orbital energies and coefficients. This has been particularly true when sulfur is bonded as a sulfide to the diene.[2]

Thiocarbonyls have been used in Diels-Alder reactions to prepare thiapyranyl systems,[3,4] and generally the carbon-sulfur double bond serves as the dieneophile component. Only in the work of Quiniou, et. al.[4f] has the thiocarbonyl functioned as part of the diene, and then with an apparent effect on regioselectivity. In this work, either highly conjugating substituents were present or the diene was a vinylogous thioamide. We now wish to report the unusual Diels-Alder reaction of a diene containing a carbon-sulfur double bond which is also void of substituents which might attenuate regioselectivity.

Heating at reflux a pyridine solution (20 ml) of methylvinyl ketone [1](2.8 g) and phosphorous pentasulfide(1.3 g) for 20 hr resulted in a brown-colored solution from which 3.2 g of dark oil could be isolated. Analysis by GLC (10% SE-30 on Chromasorb G) indicated five major products, assigned structures [3] - [7] (figure 1).

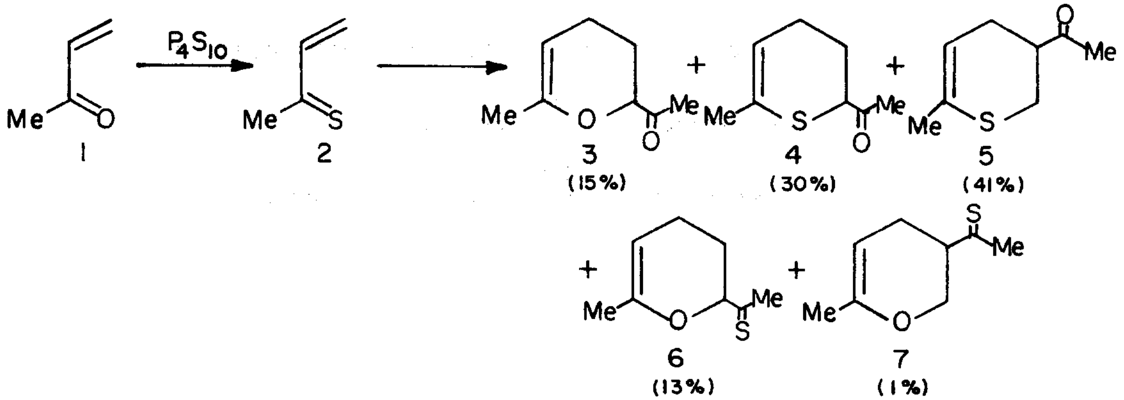


Figure 1

Methylvinyl ketone dimer [3] has been characterized.[5] The remaining four compounds can be separated into two sets: [4], [5] and [6], [7]. The first set exhibit an infrared carbonyl absorption (~1700 cm^{-1}) and a mass spectral fragmentation (m/e = 43) characteristic of methyl ketones. The second set has no carbonyl absorption, but does exhibit a sharp enol ether absorption at ~1600 cm^{-1}. Assignment of the structures for [4] and [6] are confirmed by alternative syntheses (figure 2).

The conversion of [3] to [6] is readily accomplished;[6] and heating [6] at reflux for one hr produces [4] (25% isolated). That [4] is a result of a [3,3] sigmatropic shift rather than a retro- Diels-Alder reaction is based on the lack of [5] as a recombination product. All four isomers exhibit a parent ion of m/e = 156.[7] A more detailed spectroscopic analysis, as well as a discussion of the Cope rearrangement described in figure 2 will be presented elsewhere.

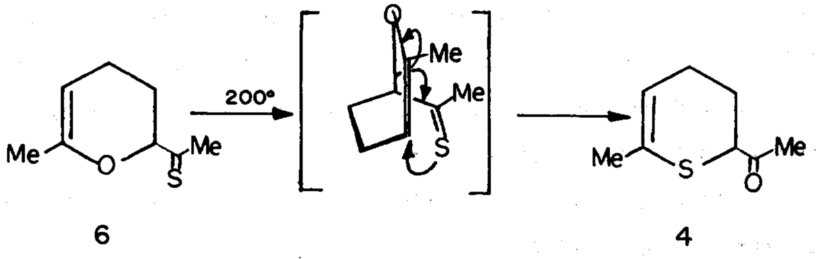


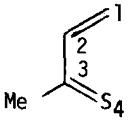
Figure 2

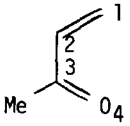
It is of interest to note that thioketone [2] can serve as either a diene or dieneophile, much like its oxygen analog [1]. However, unlike methylvinyl ketone, which regiospecifically forms [3], the thiocarbonyl produces a mixture of regioisomers whether acting as a diene to form [4] and [5] or as a dieneophile to form [6] and [7]. Furthermore, the degree of regioselectivity presented here is not as high as that reported by Quiniou. A comment in this regard is necessary, yet at this time we can not fully assess whether this decreased regioselectivity is primarily a steric or electronic affect.

Unlike Quiniou, who was able to dimerize two thiocarbonyls,[8] we find no thiocarbonyl dimer. It is conceivable that such adducts indeed form but immediately decompose or revert back to starting material.[9] We also point out that no products were isolated which contain more than one heteroatom in the ring.

Product formation and the origin of regioselectivity can be accounted for by frontier molecular orbital theory.[10] Eigenvalues and eigenvectors from CNDO/2 calculations for [1] and [2] are presented in table 1, along with the ΔE for each product. All four frontier orbitals were considered. Transition state resonance integrals used were those calculated by Anh, et. al.[11] at 3 a.u. The predicted and observed results agree quite well, indicating that the CNDO/2 wave functions are reliable in this instance.

Table 1





$HOMO = -.4063$	$LUMO = -.002$		$HOMO = -.5127$	$LUMO = .0944$
-.3844	-.4384	1	.5220	-.5866
-.2066	.1425	2	.4308	.3839
.4060	.5561	3	-.3030	.4645
.7432	-.6122	4	-.6350	-.4940

$$\Delta E = \sum_{r}^{occ} \sum_{s}^{unocc} + \sum_{s}^{occ} \sum_{r}^{unocc} \frac{2(\Sigma_{ab}\, C_{ra} C_{sb} \beta_{ab})^2}{E_r - E_s}$$

Compound	[3]	[4]	[5]	[6]	[7]
ΔE	.0803	.1005	.1237	.0362	.0308

References and Notes:

1. The syntheses of several aggregating pheromones critically depend on the regioselectivity of 1,4-cycloadditions of heterodienes. See B.P. Mundy, K.B. Lipkowitz and G.W. Dirks, Heterocycles, 6, 51 (1977) for a review.

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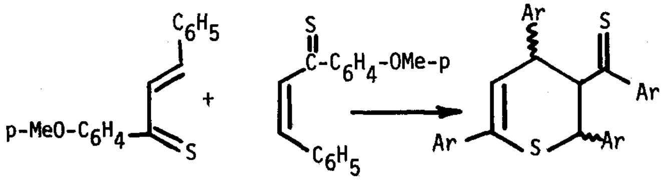
5. K.B. Lipkowitz, B.P. Mundy and D. Geeseman, Synth. Comm., 3, 453 (1973).

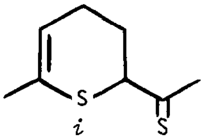
6. Reagents for Organic Synthesis, Vol. 3, M. Fieser and L. Fieser, J. Wiley and Sons, 1972, p. 227.

7. It was not possible to obtain sufficient amounts of [7] for combustion analysis. The instability of [4] and [5], is evidenced by a very rapid deterioration of the sample; glc pure samples changed color from a light yellow to an orange-brown overnight. The nmr, ir, and mass spectra of these samples were consistent with the assigned structures.

8. Specifically:



9. In fact, the calculated ΔE for thiocarbonyl i is .0407.



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11. O. Eisenstein, J. LeFour and N.T. Anh, Tet., 33, 523 (1977), table 6.