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THE DIELS-ALDER REACTION OF METHYL PROPIOLATE WITH 1-VINYLCYCLOALKENES[1]

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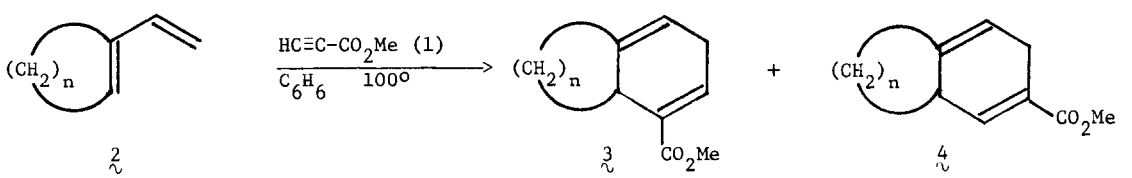
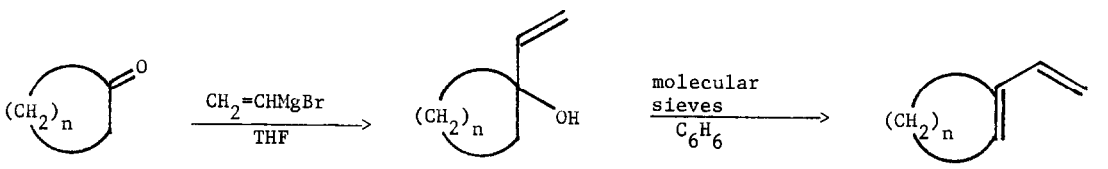
Abstract: The Diels-Alder reaction of methyl propiolate with 1-vinylcycloalkenes was used to assess the influence of ring strain on the regioselectivity of such cycloadditions: the ratio of 1,2,3- to 1,2,4-adducts increased with increasing size of the cycloalkene.

When both components of a Diels-Alder reaction are unsymmetrical a pair of structurally isomeric products can result. In most cases one isomer predominates and this preferential orientation has been the subject of recent theoretical interpretations.[3] Such regioselectivity also continues to receive attention for its synthetic utility[4] and the use of propiolate esters as dienophiles is, in particular, an application of current interest.[5] Previous studies from this laboratory have focused on the synthesis of benzocyclobutenes under mild conditions[6] and on the influence of fused strained rings on heterocyclic systems.[7] Since the cycloaddition of methyl propiolate (1) with 1-vinylcyclobutene (2c) is a route to functionalized benzocyclobutenes, we have explored the regioselectivity of this reaction. The influence of ring strain on the orientation of the Diels-Alder reaction has not previously been reported, and in this Letter we assess such affects for the following system:



2 3 4

The dienes (2) were prepared by the addition of vinylmagnesium bromide to a cyclic ketone and dehydration of the resulting 1-vinyl-1-cycloalkanol. The allylic alcohols derived from cyclohexanone and cyclopentanone were dehydrated in quantitative yield by a new, mild procedure: treatment of a benzene solution of the alcohol with molecular sieves (5A) at room temperature for five days. In the case of 1-vinyl-1-cyclobutanol this process resulted in incomplete conversion and the dehydration was effected by iodine.[8]



Cycloadditions were carried out with equimolar amounts of dienophile (1) and diene (2) in benzene at 100°C under an argon atmosphere in sealed ampoules. Product analysis, performed with capillary gas chromatography (GC) and GC/mass spectrometry within one minute of opening each tube, gave the relative amounts of the isomeric Diels-Alder adducts (3 + 4). Yields ranged from 10% to 40% over the observed time periods. These products (which exhibited the correct molecular weights for dihydro derivatives of methoxycarbonyl-substituted tetralins, indans, and benzocyclobutenes) were purified by preparative GC. Each sample was then re-injected on the capillary GC to confirm peak identities. Time series runs were conducted to determine whether or not the observed adducts were kinetically controlled. The invariance of the product ratios (3:4) over periods of 6 to 72 hours is consistent with the absence of retro Diels-Alder reactions followed by adduct formation under thermodynamic control. It was also demonstrated that product ratios remained constant in the presence of excess dienophile. The results are summarized in Table I.

Product identities were determined by conversion of each purified dihydro adduct to the corresponding aromatic system by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). The structures of the six aromatic esters thus obtained were established by comparison with GC, IR, and NMR spectra of authentic samples. 6-Tetralincarboxylic acid (5) was prepared by diazotization of 6-aminotetralin in the presence of cuprous cyanide and hydrolysis of the resulting nitrile. The product mixture from series a was dehydrogenated to methyl 5- and 6-tetralincarboxylates, which were separated by preparative GC. Hydrolysis of the latter ester afforded material identical to 5. Indan was nitrated, the product mixture was catalytically reduced, and the amino derivatives were converted as above to a mixture of 4- and 5-indancarboxylic acids; treatment with diazomethane afforded the methyl esters. The latter acid was commercially available and esterification gave authentic methyl 5-indancarboxylate which, together

Table I

Diels-Alder Reactions of 1-Vinylcycloalkenes with Methyl Propiolate

$$\underset{\sim}{1} + \underset{\sim}{2} \xrightarrow[100°]{C_6H_6} \underset{\sim}{3} + \underset{\sim}{4}$$

Series	n	Time, hr.	3:4	Average
a	4	6	2.08	
		12	1.95	
		24	2.09	
		72	2.11	
				2.06 ± 0.05
b	3	6	1.40	
		12	1.38	
		24	1.39	
		72	1.40	
				1.39 ± 0.01
c	2	6	0.977	
		12	0.984	
		72	0.976	
				0.98 ± 0.01

with the pair of esters, served to identify the aromatic esters derived from series b. Each product from series c was converted to the known methyl 3- and 4-benzocyclobutenecarboxylates.[9]

The present work establishes that strain effects influence the regioselectivity of [4 + 2] cycloadditions. If the dienes ($\underset{\sim}{2}$) are viewed as 1,2-disubstituted-1,3-butadienes, then the products ($\underset{\sim}{3}$ and $\underset{\sim}{4}$) can be considered cyclohexadienes substituted in 1,2,3- and 1,2,4- patterns, respectively. Increasing the ring size (i.e., decreasing the ring strain) of the cycloalkene moiety of $\underset{\sim}{2}$ results in increased proportions of adduct $\underset{\sim}{3}$. These studies are being extended to cycloadditions with heterodienophiles as a route to strained heterocyclic systems.

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References and Notes

(1) This paper is dedicated to Professor William von Eggers Doering on the occasion of his 65th birthday.

(2) This work is based, in part, on the Honors Thesis of W. J. Zaks, Williams College, 1980.

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