Transition-State Geometry and Stereochemistry of the Ene Reaction between Olefins and Maleic Anhydride†

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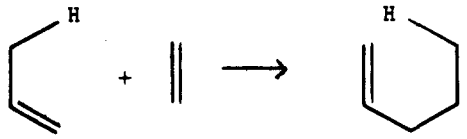
Received March 3, 1986

A systematic study of the ene reaction between linear olefins and maleic anhydride is carried out. High-field (90-MHz) ^{13}C NMR has provided detailed information about the regioselectivity, diastereoselectivity, and cis/trans selectivity of the reaction. It has permitted a quantitative characterization of the reaction products directly, without resorting to isotopic labeling of the starting materials, product transformations, or separation. The product distribution depends on the factors affecting transition-state geometry, including reactant orientation (endo or exo), configuration (cis or trans olefins), and conformation in the transition state. A unified reaction scheme based on these spatial considerations and the distribution of all the observed products is proposed. A mathematical treatment is used to quantify and to predict the steric and the electronic effects occurring in the system.

The ene reaction occurs with the addition of an electron-deficient double bond to an olefin containing an allylic hydrogen.[1] It is thermally allowed ($2n_\pi + 2n_\pi + 2_\sigma$) and is related to the more well-known Diels–Alder reaction and 1,5 sigmatropic hydride shift.[1]



The ene reaction has been well studied, with evidence cited for concerted 6-membered electrocyclic,[2-4] free-radical[5-8], and ionic mechanisms.[9] Recent workers favor the concerted reaction, with other mechanisms occurring in special cases.[1a,c] The different mechanisms have been supported by stereochemical evidence,[10-15] threo/erythro preference in product formation[14], kinetic measurements,[16-18] kinetic isotope effects[19], and high-pressure studies.[20,21]

In spite of the number of studies of this reaction, some stereochemical uncertainties still remain.[22] These uncertainties are significant because of their relationship to the transition-state geometry and their relevance to the reaction mechanisms. They arise from the lack of reliable, quantitative data. Determination of product stereochemistry previously has been accomplished by lengthy transformation to compounds of known stereochemistry[14] or the use of isotopically labeled materials.[10]

This work describes our study of the products from the reaction between a family of linear alkenes and maleic anhydride. We have found that high-field ^{13}C NMR can provide precise information concerning the product stereochemistry directly. By this means, all of the stereoisomers have been assigned and quantified. Our results have permitted a very detailed mechanistic picture to emerge, providing a unified view of regioselectivity, cis/trans stereospecificity, and diastereoselectivity of product formation in the ene reactions under consideration.

Although this is the first time high-field ^{13}C NMR has been used to study ene reaction products, it is well-known that ^{13}C NMR can provide detailed information about the structure and the stereochemistry of geometric isomers and diastereomers. In the characterization of synthetic polymers, for example, many workers for many years have used ^{13}C NMR to successfully distinguish between regioisomers, stereoisomers, and even conformers in some cases.[23-27] A considerable understanding of the ^{13}C shift behavior has been developed.[28-30] The ability to fully characterize ene reaction products by ^{13}C NMR is therefore not surprising.

During the course of this work, some highly stereoselective reaction pathways were observed. Within the proper constraints, these reactions should find application in rational strategies toward the synthesis of optically active target molecules, based on readily available and nonoptically active substrates.

† Hercules Research Center Contribution No. 1792.

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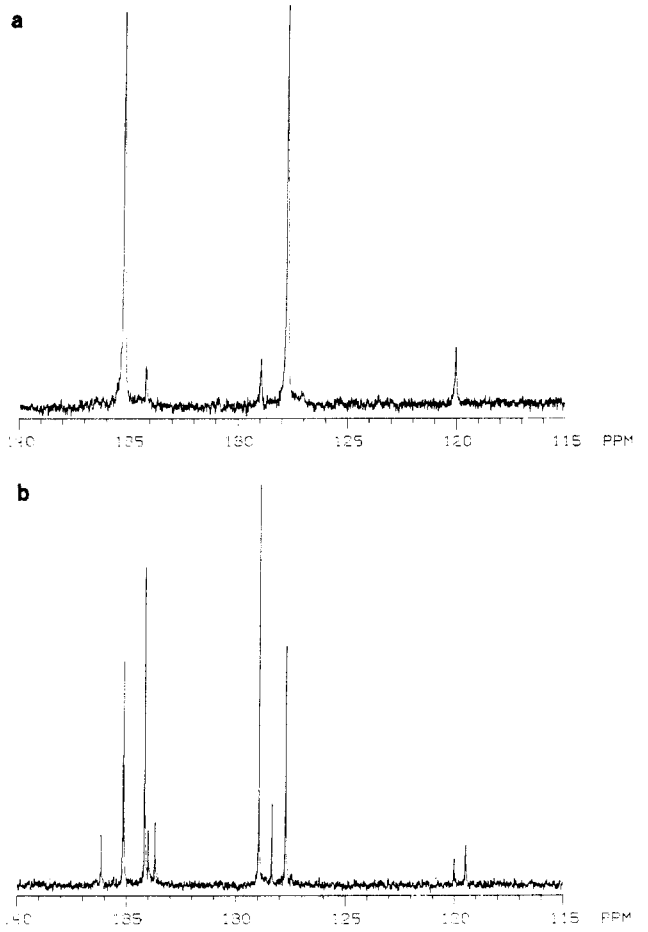
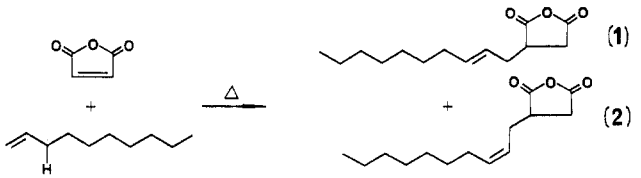


Figure 1. ^{13}C NMR spectra of the reaction products of maleic anhydride with (a) *cis*-2-decene and (b) *trans*-2-decene.

Results

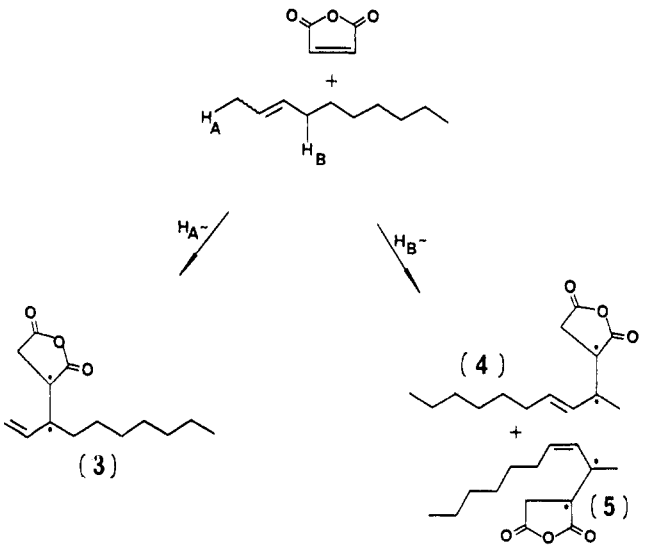
We have subjected all nine linear decene isomers to similar reaction conditions with maleic anhydride. Owing to the formation of a complex mixture of geometric isomers and diastereomers, product analysis and identification were not trivial. Standard ^1H NMR (at 360 and 600 MHz[31]), infrared spectroscopy, gas chromatography (packed or capillary column GC), mass spectroscopy (MS), and gas chromatography/MS techniques were unable to uniquely distinguish between all the isomers and provide the quantification and complete structural details needed for our purposes. However, ^{13}C NMR at high field (90 MHz) readily provided all the requisite information. For illustration, two representative spectra are shown in Figure 1.

The product mixture obtained from the reaction of 1-decene with maleic anhydride was relatively simple to analyze. The two products obtained were the trans and cis isomers 1 and 2. For this type of structure, with two



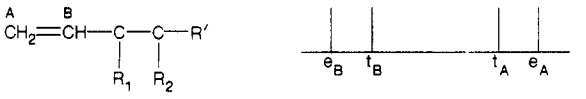
very different allylic substituents, the olefin carbons are the most diagnostic in the ^{13}C NMR spectrum. The spectrum of the product mixture consisted of only four lines in the olefin region at 122.1, 122.8, 135.5, and 136.8 ppm (Table I), corresponding to the expected products. The spectral assignments could be readily made for these 1,2-disubstituted olefins, since the double-bond carbon resonances in trans structures usually occur downfield from the cis.[23,24] The observed cis to trans ratio was 18:82.

A more complex product mixture was obtained from the 2-decenes. The addition of maleic anhydride exhibits some regioselectivity, corresponding to allylic hydrogen transfer from either side of the double bond. We also found that the product distribution depends on whether the starting material was the cis or trans isomer (see Table I).



Two adjacent chiral centers (one at each end of the newly formed C–C bond) are generated in all of the products from 2-decene, resulting in three possible sets of diastereomeric pairs from either 2-decene isomer. All three sets were observed for the *trans*-2-decene/maleic anhydride reaction; the ^{13}C NMR spectrum (Figure 1b) contained 10 resolvable olefin lines. Spectral assignments were made through the use of empirical additivity rules[32-34] and comparisons with model compounds.

In vinyl compounds with the structure



available literature references[34-37] indicate that the olefin resonances of erythro (e) diastereomers occur outside of the lines for the threo (t) diastereomer. Thus, in 2-methyl-2-vinyl-1-cyclohexanol, the A and B resonances for the isomer with anti vinyl and hydroxyl groups occur at 113.65 and 140.44 ppm. For the isomer with syn vinyl and hydroxyl groups, these signals occur at 111.47 and 146.39 ppm.[35] Similarly, in a series of acyclic carbinols ($R_1 = CH_3$, $R_2 = OH$), the erythro signals lie outside the threo signals in almost all cases.[36] Furthermore, in polybutadiene with

(31) Attempted structural verification by standard H–H coupling constant values at 600 MHz were unsuccessful due to signal overlap in the ^1H NMR spectrum, run for us at the NMR Facility for Biomedical Studies, Carnegie-Mellon University, under a grant from NIH (RR 00292).

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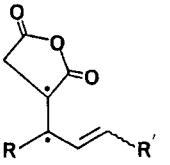
Table I. ^{13}C NMR Assignments and Product Structure Summary for the Ene Reaction between Maleic Anhydride and Linear Olefins

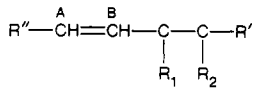


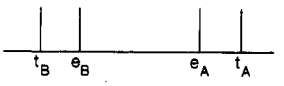
starting matl	R	R′	confign	design	mol %	^{13}C, ppm[a]
1-decene	H	n-C_7H_{15}	trans	1	82	136.8, 122.8
			cis	2	18	135.5, 122.1
trans-2-decene	n-C_7H_{15}	H	threo	3 t	3	135.1, 120.0
			erythro	3 e	4	136.1, 119.4
	CH_3	n-C_6H_{13}	trans-threo	4 t	26	135.1, 127.7
			trans-erythro	4 e	51	134.1, 128.9
	CH_3	n-C_6H_{13}	cis-threo	5 t	8	133.9, 128.3
			cis-erythro	5 e	9	133.6, 128.9
cis-2-decene	n-C_7H_{15}	H	threo	3 t	11	135.1, 120.0
			erythro	3 e	1	~136.1, 119.4
	CH_3	n-C_6H_{13}	trans-threo	4 t	78	135.1, 127.6
			trans-erythro	4 e	9	134.1, 128.9
	CH_3	n-C_6H_{13}	cis-threo	5 t	0	
			cis-erythro	5 e	0	
trans-3-decene	n-C_6H_{13}	CH_3	trans-threo	6 t	13	131.0, 127.5
			trans-erythro	6 e	19	130.6, 128.6
	n-C_6H_{13}	CH_3	cis-threo	7 t	4	129.7, 127.0
			cis-erythro	7 e	5	129.0, 128.3
	C_2H_5	n-C_5H_{11}	trans-threo	8 t	19	136.9, 126.0
			trans-erythro	8 e	30	136.7, 126.9
	C_2H_5	n-C_5H_{11}	cis-threo	9 t	4	136.1, 125.5
			cis-erythro	9 e	6	135.5, 126.7
cis-3-decene	n-C_6H_{13}	CH_3	trans-threo	6 t	39	131.1, 127.5
			trans-erythro	6 e	6	130.7, 128.6
	n-C_6H_{13}	CH_3	cis-threo	7 t	0	
			cis-erythro	7 e	0	
	C_2H_5	n-C_5H_{11}	trans-threo	8 t	49	137.0, 126.0
			trans-erythro	8 e	7	136.8, 126.9
	C_2H_5	n-C_5H_{11}	cis-threo	9 t	0	
			cis-erythro	9 e	0	
trans-4-decene	n-C_5H_{11}	C_2H_5	trans-threo	10 t	15	136.6, 126.1
			trans-erythro	10 e	27	136.3, 127.1
	n-C_5H_{11}	C_2H_5	cis-threo	11 t	3	135.8, 125.7
			cis-erythro	11 e	5	135.2, 127.0
	n-C_3H_7	n-C_4H_9	trans-threo	12 t	13	138.1, 125.2
			trans-erythro	12 e	27	137.8, 126.2
	n-C_3H_7	n-C_4H_9	cis-threo	13 t	5	137.3, 125.1
			cis-erythro	13 e	5	136.6, 126.5
cis-4-decene	n-C_5H_{11}	C_2H_5	trans-threo	10 t	45	136.7, 126.1
			trans-erythro	10 e	7	136.3, 127.1
	n-C_5H_{11}	C_2H_5	cis-threo	11 t	0	
			cis-erythro	11 e	0	
	n-C_3H_7	n-C_4H_9	trans-threo	12 t	42	138.1, 125.2
			trans-erythro	12 e	5	137.8, 126.3
	n-C_3H_7	n-C_4H_9	cis-threo	13 t	0	
			cis-erythro	13 e	0	
trans-5-decene	n-C_4H_9	n-C_3H_7	trans-threo	14 t	38	136.5, 126.4
			trans-erythro	14 e	44	136.1, 127.4
	n-C_4H_9	n-C_3H_7	cis-threo	15 t	9	135.7, 125.9
			cis-erythro	15 e	9	135.0, 127.3
cis-5-decene	n-C_4H_9	n-C_3H_7	trans-threo	14 t	89	136.5, 126.4
			trans-erythro	14 e	11	136.1, 127.4
	n-C_4H_9	n-C_3H_7	cis-threo	15 t	0	
			cis-erythro	15 e	0	

[a] Olefin carbon assignments.

a high level of 1,2 addition,[37] the ^{13}C shifts for the isotactic vinyl carbons (113.5, 143.0 ppm) lie outside the shifts of the syndiotactic vinyl carbons (114.6, 142.5 ppm). Thus, in vinyl groups, e.g. structure **3**, the trend is e_B–t_B–t_A–e_A, with increasing field.

In 1,2-disubstituted olefins with the structure





the resonances for the erythro and threo diastereomers are reversed; the threo signals lie outside of the erythro signals. For example, in data reported by Schmid et al.,[38] the ^{13}C shifts of the threo diastereomers (structures **16** and **17**, ref 38) are consistently found outside the corresponding signals for the erythro diastereomer (structures **14** and **15**). The same trend (t_B–e_B–e_A–t_A) is observed in this work for

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olefins with 1,2-disubstitution, as in structures **4** and **5**. The observed chemical shifts for structures **3–5** are reported in Table I. Although the trends in ^{13}C shifts reported above need not be universal, the internal consistency observed for all the data on the alkene/maleic anhydride products indicates that the chemical shift assignments are correct, at least for this class of compounds.

Using the integrated peak areas of the ^{13}C NMR spectra, we can determine the product distribution. For the *trans*-2-decene starting compound, the product distribution of **3** to **4** to **5** was 7:77:17. The overall threo to erythro ratio was nearly 40:60 (Figure 1b; Table I).

For the corresponding reaction with *cis*-2-decene as starting material, the ^{13}C NMR spectrum (Figure 1a) indicated that the trans-threo adduct **4** was the predominant product,[39] and we were unable to detect any cis products **5**. The product distribution of **3** to **4** to **5** was 12:87:0, and an overall threo to erythro ratio of 90:10 was obtained.

The results with both sets of 3-decene adducts were similar to the 2-decene cases. Four geometric isomers are possible (as diastereomeric pairs), resulting in up to a total of eight species in each product mixture. Similarly, both 4-decenes gave rise to as many as eight products, while both 5-decene isomers gave up to four products because of symmetry. The high-field ^{13}C NMR spectra can readily distinguish these various product distributions. Their spectral assignments are similar to the 2-decene products: since all these products are 1,2-disubstituted olefins, the ^{13}C lines of the threo adducts lie outside the lines of the erythro isomers. The observed ^{13}C chemical shifts and their intensities are summarized in Table I.

While no kinetic data were collected, we observed that both 2-decene isomers reacted more slowly than the other corresponding isomers under our experimental conditions, and all trans isomers reacted faster than the same positional cis isomers.

Discussion

The preferred geometry in the transition state for the ene reaction has been a subject of some controversy, especially in relation to the endo/exo orientation of the addends.[14,17] From the reaction of *cis*- and *trans*-2-butene with maleic anhydride, Berson et al.[14] concluded that an endoid transition-state geometry is favored for these reactants. This conclusion was based on the product stereochemistry: *trans*-2-butene gave primarily erythro products, and *cis*-2-butene gave primarily threo products. Berson was careful in interpreting his data: he did not attempt to generalize his conclusions, and he used the term "endoid" (i.e. endo-like) for the transition state.

Benn, Dwyer, and Chappell,[17] on the other hand, devised a different scheme based on their product analysis. From the reactions of maleic anhydride with a series of alkenes, only trans products were observed.[17] They concluded that for 1-alkenes and *trans*-5-decene the reaction proceeded through an exo transition state, whereas for *cis*-5-decene either exo or endo would be possible.

In this work, the complete product analysis obtained from high-field ^{13}C NMR has permitted a detailed and unified picture to emerge concerning the stereochemistry of the products formed in an ene reaction. This information has enabled us to draw certain conclusions concerning possible transition-state geometries. These are described separately in the following sections.

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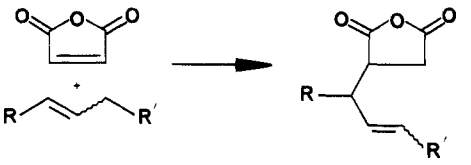
Table II. Summary of Product Distribution



starting matl	R	R′	total cis:trans	total erythro:threo	R/(R + R′)[a]
1-decene	0	7	0.22		100
trans-2-decene	1	6	0.22	1.6	93
cis-2-decene	1	6	0.00	0.12	88
trans-3-decene	2	5	0.24	1.5	59
cis-2-decene	2	5	0.00	0.15	56
trans-4-decene	3	4	0.22	1.8	50
cis-4-decene	3	4	0.00	0.14	47
trans-5-decene	4	5	0.22	1.1	50
cis-5-decene	4	5	0.00	0.12	50

[a] This column describes product regioselectivity expressed as a percent of the total reaction product mixture where the new C–C bond has occurred at the R end of the ene double bond as illustrated.

Chart I

	product stereochem	
starting matl	diastereoselectivity	cis/trans selectivity
cis olefin	threo >> erythro	trans >> cis
trans olefin	erythro/threo ~ 1.5	cis/trans ~ 0.22

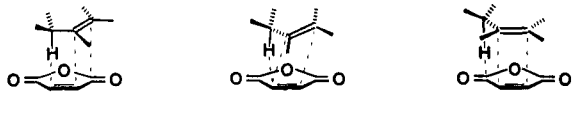
Observed Stereochemistry of the Ene Reaction. From the data provided in Table I, three different stereochemical features can be distinguished: regioselectivity, cis/trans stereoselectivity, diastereoselectivity. For the purposes of this discussion, we use the following definitions: Regioselectivity is the preference of the dienophile to form a new bond at one end or the other of the double bonds. Cis/trans stereoselectivity refers to the double-bond configuration of the reaction products. Diastereoselectivity indicates the preference for either threo or erythro product formation.

The cis/trans selectivity in these reactions was determined by comparing the integrated areas of the resonances corresponding to the cis and the trans products. These are summarized in Table II. In all cases the trans products predominated. This result is in agreement with that of Benn et al.[17] We were able to detect the minor cis isomers because of the more sensitive ^{13}C NMR method. The product distribution profile was found to depend on the configuration of the starting material (as cis or trans). For cis starting materials, the products were exclusively trans. For trans starting materials, however, the cis to trans product ratio stayed at 0.22, being relatively insensitive to chain length.

Similarly, the erythro/threo selectivity was determined by comparing the overall integrated areas corresponding to the erythro and threo products. The results are also summarized in Table II. In the case of trans starting materials, the erythro diastereomers were formed preferentially. With the cis starting materials, diastereomer preference was reversed with threo products strongly favored. These results are generally consistent with Berson's findings.[14] In addition, our data indicate that diastereomer preference is also essentially independent of chain length (Chart I).

Proposed Reaction Scheme. After reviewing our extensive stereochemical data, we devised a general reaction scheme that is consistent with our results and is also compatible with the earlier data of both Berson et al.[14] and Benn et al.[17]

Three orientations that can be assumed by an olefin and maleic anhydride as they approach each other prior to reaction are given in the structures **A–C**. Each set con-



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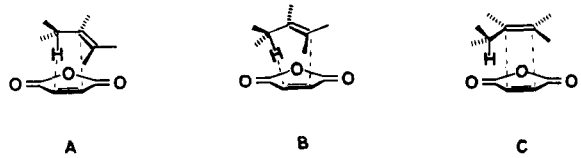


17

tains rotamers about an imaginary axis that passes through the parallel planes of the addends. For clarity, we propose a transition-state nomenclature specifically for the ene reaction. This new convention then describes the orientation of the ene with respect to the enophile (maleic anhydride in this case).

Standard rules of nomenclature assign sp^2 carbons higher priority than sp^3 carbons. Accordingly, we have numbered the three carbons of the ene component undergoing reaction as carbons 1, 2, and 3, starting with the olefin carbon remote from the reacting hydrogen (as shown above). The proposed convention specifically lists the carbon numbers of the ene component that spatially overlap the double bond of the enophile. Thus, structures **A–C** are respectively (2,3), (1,3), and (1,2) orientations. To further distinguish the two orientations with a given overlapped set, we use "inside" and "outside". As illustrations, **16A** would be 2,3-inside and **17A** 2,3-outside. Similarly, structures **16C** and **17C** would be 1,2-inside and 1,2-outside. (An unsymmetrical enophile would require additional terms to specify overlap orientations completely.) Orientations **16B** and **17B** are closely allied to exo and endo as used for the Diels–Alder reaction. We have designated these 1,3-exo and 1,3-endo.

On the basis of our analysis (vide infra), we believe the transition states responsible for the products we have observed to more closely resemble structures **B** than either **C** or **A**. Furthermore, the ene double bond should tilt slightly away from the maleic anhydride (as drawn).

Our proposed transition-state scheme for the ene reaction is shown in Scheme I. One consequence of this scheme is the geometry acquired by the newly formed double bond. This depends entirely on which allylic hydrogen (H′ or H″) is transferred during the reaction. In turn, this depends on the rotamer population of the allylic C–CH_2Z bond. The four limiting cases of transition-state orientations are shown in Scheme I. In the scheme, 1 or 2 designates the transfer of H′ or H″ during reaction and X or N designates an exo or endo orientation (i.e., structures **16B** or **17B**).

Qualitative Treatment. One can observe how Scheme I works by taking into account all the interactions occurring in the transition state. In the scheme, the starting olefin and the maleic anhydride can react through any one of the four transition states shown, whose relative abundances are dictated by two effects: (1) steric interactions between the substituent groups; (2) orbital overlap. We believe these two effects to be the driving forces for the

Chart II

notation	gps involved	description
s_1	Z ↔ R′	intramolecular, across dbl bond (R′ ≠ H)
s_1'	Z ↔ H	intramolecular, across dbl bond (same as s_1, except R′ = H)
s_2	Z ↔ ring ctr	intermolecular; Z over ring
s_2'	Z ↔ ring side	intermolecular; Z over C=O on maleic anhydride ring
s_3	R ↔ ring or R′ ↔ ring	intermolecular; interactn prob with C=O on ring
s_4	Z ↔ ring	intermolecular; endo addn only; interactn either with C=O on ring (neg sign) or with olefinic H (pos sign)

Chart III

SM	route	product	steric terms
cis olefin	1X	trans-erythro	$s_2 + s_3$
	2X	cis-erythro	$s_1 + s_2 + s_3$
	1N	trans-threo	s_4
	2N	cis-threo	s_1

Chart IV

SM	route	product	steric terms
trans olefin	1X	trans-threo	s_2
	2X	cis-threo	$s_1' + s_2$
	1N	trans-erythro	$s_3 + s_4$
	2N	cis-erythro	$s_1' + s_3$

observed product stereochemistries. (It may be noted that the role of steric effects has been widely cited.[1,4,10,13] The effect of orbital overlap has also been previously noted.[6,14])

Six types of steric interactions can be identified from the transition states shown in Chart II.

For simplicity, we set $s_2 = s_2'$. A study of molecular models suggests tht $s_1 \gg s_1' > s_2 > s_3 \gg s_4$.

If we take the cis olefin starting material (SM) and work through Scheme I, the steric effects can be deduced for the four reaction pathways in Chart III. The product stereochemistries of these pathways are also indicated.

Because of the large steric interaction between R′ and Z in the transition state (the s_1 effect), both the cis-erythro and cis-threo products are predicted to be disfavored; in fact, only trans products were observed (Table II). The steric effects s_2 and s_3 are larger than s_4. This leads to the prediction that the trans-threo product should predominate; this was indeed the case (erythro:threo ~0.12, Table II).

A similar examination of the trans olefin starting material (trans SM) produces Chart IV.

Since the steric effects s_1', s_2, and s_3 are comparable in magnitude, all four pathways are possible in this case. Since s_1' is the largest effect, the trans products are expected to dominate; the product mixtures all contained trans populations about 4 times larger than cis (Table II). Similarly, since $s_2 > s_3$, we should expect a slight preference for erythro over threo products; the observed erythro to threo ratio was 1.5 (Table II).

Our model is consistent with the stereochemical results of the reaction. The reaction pathways in general consist of both exo (structure **17B**) and endo (structure **16B**) additions. It may also be noted that since the transition-state geometry depends upon the crowding in the immediate environment of incipient bond formation, functional groups far away have only minor effects on the stereochemical outcome. Indeed our results (Table II) show little or no dependence of product stereochemistry on alkyl chain lengths.

Scheme I

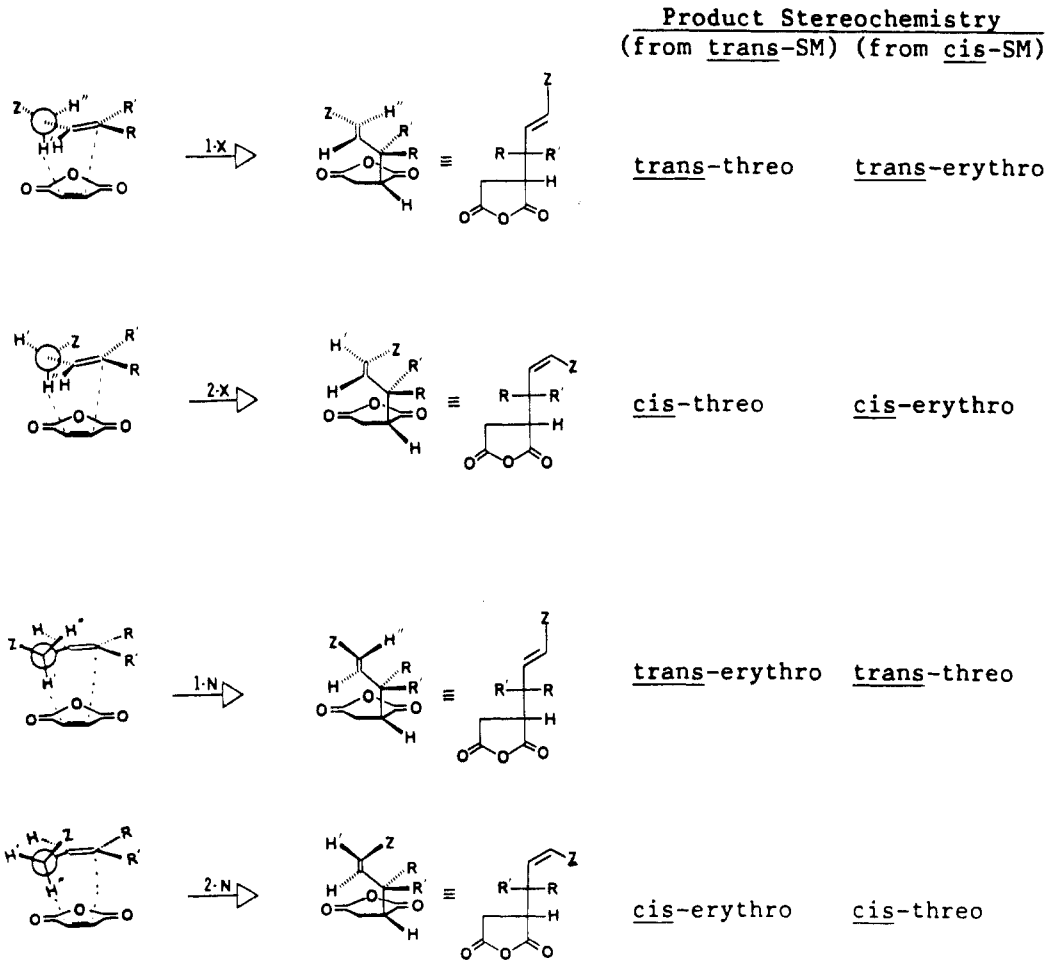


Table III. Quantitative Determination of Orbital Overlap and Steric Effects

starting matl	product	e	s_1	s_1'	s_2	s_3	s_4	c_{av}	log c_{av}
cis	trans-erythro	0	0	0	1	1	0	0.117	−0.9318
cis	cis-erythro	0	1	0	1	1	0	0[a]	−3.000
cis	trans-threo	1	0	0	0	0	0	0.882	−0.0545
cis	cis-threo	1	1	0	0	0	0	0[a]	−2.000
trans	trans-threo	0	0	0	1	0	0	0.310	−0.5086
trans	cis-threo	0	0	1	1	0	0	0.085	−1.0706
trans	trans-erythro	1	0	0	0	1	1	0.505	−0.2967
trans	cis-erythro	1	0	1	0	1	0	0.100	−1.0000

[a] For these values arbitrary intensities approximately corresponding to the noise level in the spectra were given.

Quantitative Treatment. A further step can be made to quantify our reaction scheme. Drawing analogy to linear free energy relationships, we can write

$$\log (c_i/c_0) = e + \sum_i s_i$$

where c_i is the percent of species i and s_i are the steric terms involved. The term e is added to account for the orbital overlap occurring in the endo transition state. The value c_0 is a reference state and for computational purposes is set equal to 1.0. The percent values used are normalized separately for cis or trans starting materials. Where regioisomers are possible, each pathway is separately normalized. The average results for all the olefins are given in Table III. Special cases not included in the regression calculations occur where the double bond is terminal, either in the starting materials (structures **1** and **2**) or in the products (structures **3t** and **3e**).

A linear regression of the data in Table III provided the values $e = 0.014$, $s_1 = -2.0$, $s_1' = -0.583$, $s_2 = -0.521$, $s_3 = -0.399$, and $s_4 = 0.009$. The standard deviation is 0.0919. Predicted results, based on these parameters, are fully consistent with the observed product stereochemistries for all the olefins.

Chart V

SM	route	products	parameters	pred results ratio	pred results %
1-decene	1X	trans	$s_2 = -0.521$	0.30	18.1
	2X	cis	$s_1' + s_2 = -1.104$	0.08	4.8
	1N	trans	$e + s_4 = +0.005$	1.01	60.8
	2N	cis	$e + s_1' = -0.569$	0.27	16.3

As an illustration, consider the special case of 1-decene, which the linear regression did not take into account. Here R = R′ = H, and the scheme is simplified (Chart V).

The ratios shown in Chart V are obtained by taking the antilog of the parameter values; normalization gives the respective percentages. This treatment predicts a product distribution of trans:cis = 0.79:0.21. The observed product

Chart VI

SM	route	products	parameters	pred results ratio	%
cis-2-decene	1X	erythro	$s_2 + s_3 = -0.92$	0.12	7.8
	2X	erythro	$s_2 + s_3 = -0.92$	0.12	7.8
	1N	threo	$e = 0.014$	1.03	66.9
	2N	threo	$e + s_1' = -0.569$	0.27	17.5
trans-2-decene	1X	threo	$s_2 = -0.521$	0.301	21.1
	2X	threo	$s_2 = -0.521$	0.301	21.1
	1N	erythro	$e + s_3 = -0.385$	0.412	28.9
	2N	erythro	$e + s_3 = -0.385$	0.412	28.9

distribution was trans:cis = 0.82:0.18 (1 and 2, Table I). Thus, 1-decene undergoes *all four pathways*, although only two products (cis and trans) are observed.

The other special case not included in the parameter regression was 2-decene, where the new carbon–carbon bond of one regioisomer forms at the 3-position, giving products containing terminal vinyl groups (structures **3e** and **3t**). In this case, Z = H, and the scheme is also simplified (Chart VI). Thus, starting with *cis*-2-decene, the predicted erythro to threo ratio is 16:84. The observed ratio was 12:88. For *trans*-2-decene, the predicted erythro to threo ratio is 58:42. The observed ratio was 57:43. The excellent agreement between prediction and experiment in these special cases *not included in the regression* is most gratifying and lends strong support to the validity of the quantitative approach outlined here.

A comparison of the numerical values of the s_i parameters indicates that $s_1 \gg s_1' > s_2 > s_3 \gg s_4$, in agreement with our qualitative assessment based on studies of molecular models. Furthermore, there is only a small effect due to orbital overlap for an endo transition state. The size of e (0.014) translates to a slight endo preference of 3% (endo:exo = 1.03).

Regioselectivity. Regioselectivity is influenced by the relative sizes of Z, R, and R′. The data in Table II clearly indicate that there is a preference for addition to the less hindered end of the double bond. As the difference in size between the two groups (flanking the double bond) in the starting olefin decreases, the regiospecificity also decreases. This steric differentiation is slightly less pronounced in the cis olefins than in the trans olefins as the transition state in the former case is more crowded.

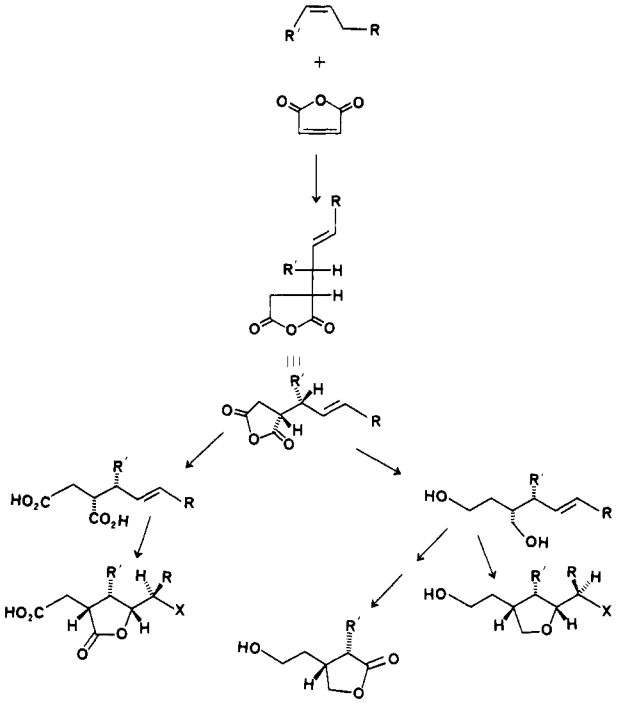
While product regioselectivity is strongly dependent on the size of the alkyl groups flanking the double bond in the reactants, cis/trans selectivity and diastereoselectivity are not. We can imagine the progress of the ene reaction as the reactants approach the transition state, where C–C bond formation occurs:

reactants → transition state → products

The reactant trajectories depend on the size and the orientation of the alkyl groups, where the more hindered approach is disfavored; this introduces the effects on regioselectivity as shown in Table II. Once the transition state geometry is "locked in", substituents in the immediate vicinity of the atoms reacting have only small effects on stereochemical outcome. Thus, cis/trans selectivity and diastereoselectivity are relatively independent of the sizes of Z, R, and R′ (as long as Z, R, and R′ = H).

Retro Ene Reactions. Some workers have reported products derived from retro ene reactions.[9,40] The effect of kinetic instability on the observed product distribution had to be assessed in order for our conclusions to be valid.

Scheme II



This could be done by observing the product distribution as a function of time in one system.

Within the limits of our detection (<0.5%), cis olefins do not produce cis products and show a marked threo selectivity. On the other hand, trans olefins give 20–30% cis products, in addition to showing some erythro selectivity. The principle of microscopic reversability[41] says some crossover from cis to trans olefin can be expected if any retro reaction is occurring. Readduction of the trans olefin produced by such a process will result in (a) a decrease in threo selectivity and (b) formation of some cis products.

cis-5-Decene was chosen as the model system since it was the simplest substrate we examined that could show evidence of retro reaction. Reaction mixtures were maintained at 200 ± 5 °C for up to 120 h. The product mixtures were examined by ^{13}C NMR, and no differences in product distribution were observed. Thus, it appears that retro ene reactions proceed at a negligible rate in these cases; the product distributions we observed were kinetically controlled.

Synthetic Implications. Any asymmetrically biased reaction has potential applications in the synthesis of optically active natural products. Within certain constraints, this is true of the ene reaction. For example, to minimize separating regioisomers, a symmetrical olefin would be required. To maximize diastereoselectivity, a cis olefin is necessary. Fulfilling these two criteria will provide products of high diastereospecificity starting from simple, symmetrical materials in a predictable manner without resorting to chiral auxilliaries. Alternatively, use of asymmetric olefins with high regiochemical bias built in, for example, cis olefins containing only one set of readily transferable allylic hydrogens,[9] can provide additional control over product composition. The ene product represents a differentially functionalized synthon, looking especially attractive for stereospecific access[42] to certain 5-membered oxygenated heterocycles.[43–45] Some possible

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synthetic pathways are noted in Scheme II.

Experimental Section

Olefin/Maleic Anhydride Reactions. Reactants and solvent were used as received. A magnetic stirring bar and a heterogeneous mixture consisting of 750 mg of olefin (Wiley Organics), 500 mg of maleic anhydride (Aldrich), and 50 mg of phenothiazine (Aldrich) in 3 mL of Decalin (J. T. Baker) were sealed under nitrogen in a heavy-walled tube. The mixture was brought to 200 ± 5 °C in a thermostated oil bath and held at this temperature overnight (16 h). After cooling, the homogeneous mixture was transferred to a distillation flask for removal of solvent and unreacted starting materials under reduced pressure. The crude product was distilled (bulb-to-bulb) under vacuum and obtained as a colorless oil.

In a similar manner, *cis*-5-decene was reacted with maleic anhydride for 6-, 12-, 24-, 48-, and 120-h periods, and the products were isolated as above.

Instrumental Setup. The ^{13}C NMR spectra were recorded at 90.55 MHz at ambient temperature on a Nicolet NT 360 WB spectrometer equipped with Nicolet 1280 computer. Instrumental conditions used: pulse angle, 60°; pulse delay, 5 s; sweep width, 20 000 Hz. Under these conditions, the olefin region should be quantitative. The T_1's for most of these olefin carbons are in the range of 2 s. The only long T_1's are the terminal carbons of the vinyl groups ($RCH{=}CH_2$). These carbons have not been used in the calculations.

Acknowledgment. We are gratefully indebted to E. Laletas for excellent experimental work and Dr. R. W. Harrell and Elizabeth A. Demgar for the ^{13}C NMR spectra given in Figure 1. Thanks are also due to Professor Stephen R. Wilson for ^{13}C NMR spectra of resolved diastereoisomers related to **3**, **4**, and **5**.[39] We also thank Professor J. A. Berson for his helpful comments on the paper.

Registry No. 1, 81949-64-6; **2**, 81949-63-5; **3t**, 104947-44-6; **3e**, 104947-45-7; **4t**, 104947-46-8; **4e**, 104947-47-9; **5t**, 104947-48-0; **5e**, 104947-49-1; **6t**, 104947-50-4; **6e**, 104947-51-5; **7t**, 104947-52-6; **7e**, 104947-53-7; **8t**, 104947-54-8; **8e**, 104947-55-9; **9t**, 104947-56-0; **9e**, 104947-57-1; **10t**, 104947-58-2; **10e**, 104947-59-3; **11t**, 104947-62-8; **11e**, 104947-63-9; **12t**, 104947-60-6; **12e**, 104947-61-7; **13t**, 104975-79-3; **13e**, 104975-80-6; **14t**, 104947-64-0; **14e**, 104947-65-1; **15t**, 104947-66-2; **15e**, 104947-67-3; maleic anhydride, 108-31-6; 1-decene, 872-05-9; (*E*)-2-decene, 20063-97-2; (*Z*)-2-decene, 20348-51-0; (*E*)-3-decene, 19150-21-1; (*Z*)-3-decene, 19398-86-8; (*E*)-4-decene, 19398-89-1; (*Z*)-4-decene, 19398-88-0; (*E*)-5-decene, 7433-56-9; (*Z*)-5-decene, 7433-78-5.

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Addition Reactions of (Phenylsulfonyl)propadiene with 1-Pyrrolidinyl Enamines of Cyclic Ketones: Syntheses and Reactions of 1,3-Dienes Possessing an Allyl Sulfone Moiety

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Received May 30, 1986

Addition reactions of (phenylsulfonyl)propadiene (**1**) with various 1-pyrrolidinyl enamines have been investigated. Allene **1** and enamines of cyclic ketones (**2**, **7–14**) readily underwent the Michael-type addition reactions at −50 °C to give the adducts **3**, **15–20**, and/or their isomers **4** and **21–26**, which apparently arose by base-catalyzed isomerization of the former. These adducts were conveniently converted into the corresponding 1,3-dienes possessing allyl sulfone moiety (**28**, **38–45**) through allyl acetates (**27**, **30–37**) by base-promoted (*n*-BuLi, −50 °C) 1,4 elimination of acetic acid to vinyl sulfones followed by deconjugation to allyl sulfones. The synthetic versatility of these dienes was revealed by the Diels–Alder reactions with dimethyl acetylenedicarboxylate (DMAD) and alkylation reactions via α-sulfonyl carbanions.

Recently we reported[1] that (phenylsulfonyl)-1,2-propadiene (**1**), a readily preparable and stable crystalline compound,[2-4] proved to be the useful synthetic equivalent of allene[5] as a dienophile in the Diels–Alder reaction due to its enhanced reactivity as well as the easy removal of phenylsulfonyl group from the adducts. Compound **1** might be also activated toward nucleophilic addition because of its markedly lowered LUMO energy level compared with allene.[1] While the reactions with heteronucleophiles have been well investigated,[6-13] much less attention has been paid to the carbon–carbon bond-forming reactions of **1** with the C nucleophiles.[14] Therefore, we

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