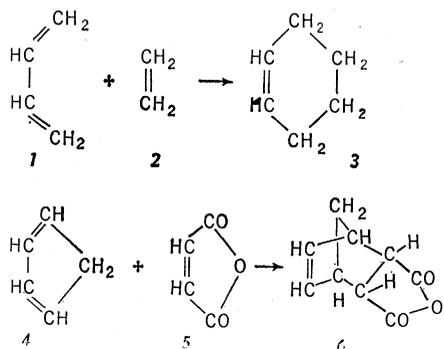


## 1,2- and 1,4-Cycloaddition to Conjugated Dienes

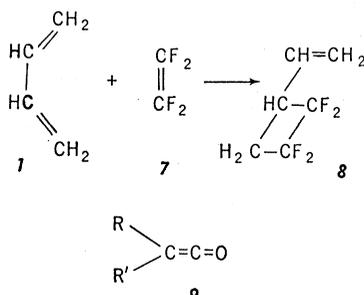
Dependence of products and rates on reactant structure tells something about competing reaction mechanisms.

Paul D. Bartlett

Six-membered rings of carbon atoms are highly favored and abundant in nature, while four-membered rings are not. In the Diels-Alder reaction, six-membered rings (**3**, **6**) are formed with great generality from dienes, such as butadiene (**1**) or cyclopentadiene, (**4**) with other unsaturated molecules (called "dienophiles" for purposes of this reaction only), such as ethylene (**2**) or maleic anhydride (**5**).



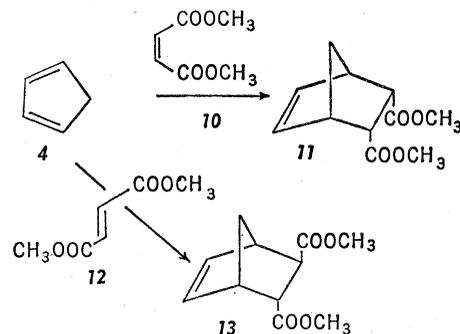
The usual formation of six-membered rings in this way is not surprising. But why then do a few alkenes, chiefly fluorinated ethylenes such as **7**, and ketenes (**9**), react with the same butadiene to yield exclusively products with four-membered rings (**8**)?



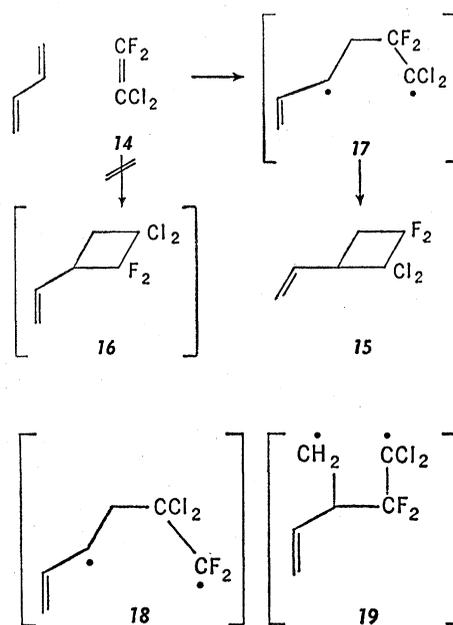
A number of classes of cycloaddition reactions have been comprehensively reviewed (*1*). Their interpretation presents a simple problem of mechanism: What determines the formation of entirely four- or six-membered rings in such a reaction? What other characteristics are associated with these two modes of reaction? Vinylcyclobutanes, such as **8**, are unstable relative to the isomeric cyclohexenes and will always rearrange into them, but only at temperature hundreds of degrees higher than those of the cycloadditions. There is therefore something about the reaction mechanism that forces the less stable isomer to be formed the more rapidly from the fluoroolefin.

Many observations on the Diels-Alder reaction are indicative of a concerted mechanism, in which the passage from reactants to products occurs in a single step without any other molecular species intervening. The alternative to a concerted mechanism is a stepwise reaction with one of the new bonds forming first, and leading to a definite, though short-lived, bifunctional intermediate (biradical or dipolar ion), whose free ends then combine to close the ring. One of the marks of a concerted mechanism is stereospecificity; in the Diels-Alder reaction, for example, cyclopentadiene reacts with a *cis*-dienophile (**10**) to yield a *cis* product (**11**), and with the isomeric *trans* dienophile (**12**) to yield a *trans* product (**13**).

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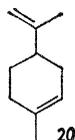
Before it was shown that such stereospecificity is often absent in the formation of four-membered cycloadducts, it was suggested that these adducts arise by way of biradical intermediates (**2**). The original evidence for this was the prevalence of "head-to-head" orientation. The "head" of a reactant molecule in this case is the end most capable of conversion into a free radical. Thus the addition of 1,1-dichloro-2,2-difluoroethylene (**14**) to butadiene yields the product **15** and not **16**, suggesting the intermediate biradical **17**. Other evidence indicates that the biradical **17** is about 8 kcal/mole lower in energy than **18**, and at least 21 kcal/mole lower than **19**.



These energy differences between biradicals, if present in the transition states for their formation, are great enough to guarantee that as little as 0.001 percent of the product will have the reverse orientation if the biradical is an intermediate. Exclusive head-to-head orientation is observed also in the

cyclobutane-forming dimerization of 1,1-dichloro-2,2-difluoroethylene, acrylic acid, styrene, and many other ethylenic compounds, which have one end that forms a better free radical than the other.

There are also preferred orientations in the Diels-Alder reaction, except that they apparently are often strongly influenced by steric effects. The prevalent orientation of dipentene (**20**), the "high temperature" dimer of isoprene, is not derivable from a head-to-head biradical.



In recent years, much more attention has been given to what the biradical reaction mechanism implies. As a result, the biradical mechanism has been placed upon firmer ground, and intensive study has been given to compounds and reactions that appear to

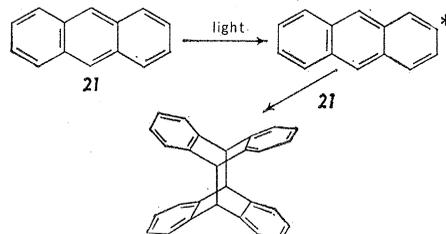
present a meeting ground for the two kinds of mechanisms.

On the basis of molecular orbital symmetries, Hoffmann and Woodward (3) proposed that, in cycloadditions involving ethylenic bonds and conjugated systems, a smooth, concerted cycloaddition can occur when six-membered rings are being formed, but not when the products are four-membered or eight-membered rings. In their communication, the hypothetical concerted reaction of two ethylene molecules to form cyclobutane is followed through from reactant pair to product and is shown to involve, because of symmetry restrictions, an activation energy comparable to that of electronic excitation of ethylene—an energy unavailable to an ordinary thermal reaction. For the interesting, allowed case of formation of a six-membered ring, the full demonstration would be somewhat more complicated than the Hückel molecular orbital treatment of benzene, and Hoffmann and Woodward present in-

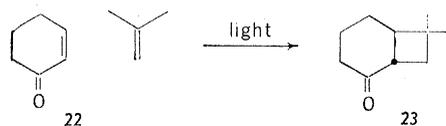
stead a shortcut which omits visualization of the transition state. They state, however, that extended Hückel calculations support the qualitative conclusion. Indeed, the Hoffmann-Woodward selection rules do provide a satisfactory framework for viewing the concerted Diels-Alder reaction and the unconcerted cycloadditions leading to cyclobutanes.

Like other selection rules, those of Hoffmann and Woodward deal with probabilities, usually overwhelming ones, but not with the difference between the possible and the impossible. Any process which is "forbidden" by the selection rules will have a high activation energy by a *concerted mechanism*, but it may occur with great facility as a stepwise process by way of a biradical or an intermediate dipolar ion.

The same considerations which cause cyclobutane formation to be non-allowed by a thermal concerted mechanism predict that it may be concerted as a reaction between an excited and an unexcited ethylene, and likewise for the conjugate addition of an excited to an unexcited diene with formation of an *eight-membered ring*. The latter process is illustrated (4) by the photodimerization of anthracene (**21**) which has been shown to proceed through an excited singlet state as judged by studies of the competition of dimerization with fluorescence.



The expectation that all light-induced cycloadditions proceed concertedly through the formation of four- or eight-membered rings would be an oversimplification. The photocycloaddition of olefins to cyclohexenone (**22**) (5) may well be concerted; the products, such as **23**, do not represent head-to-head



addition, and they appear to be formed with the strained and unstable *trans* ring junction, which would not be expected from a biradical intermediate. On the other hand, the most general way of

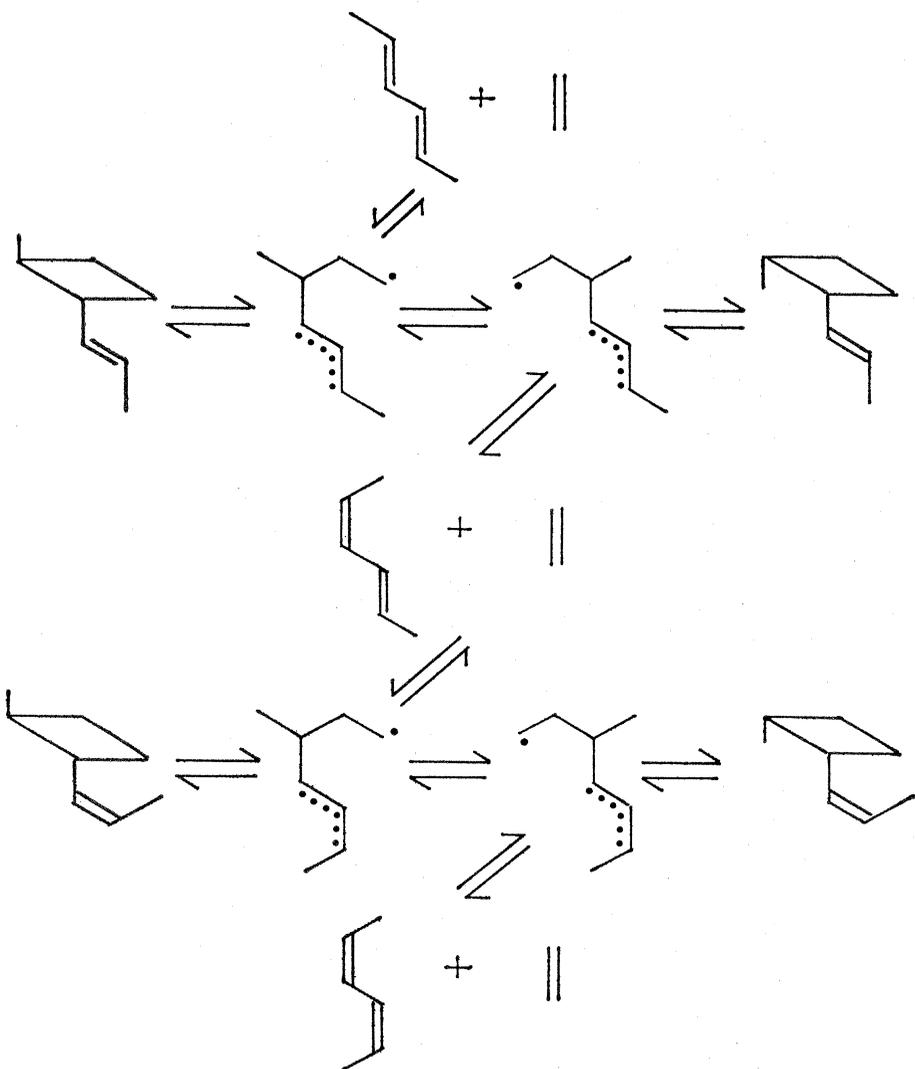
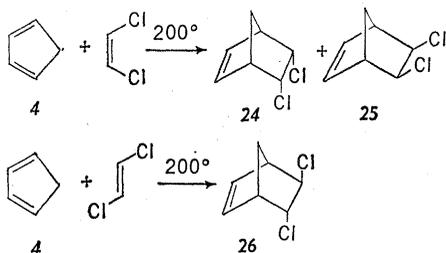


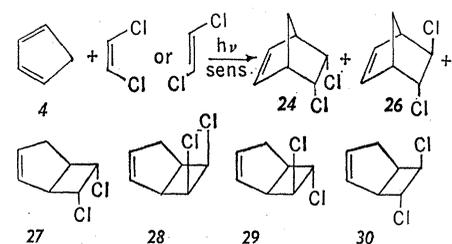
Fig. 1. *Cis-trans* isomerization of diene by redissociation of biradicals.

inducing cycloaddition by light is with photosensitizers, a variety of types of compounds (including many ketones, polynuclear aromatic hydrocarbons, and dyes) which absorb light, go over to triplet excited states, and transfer their triplet energy by collision to one of the reactants. Most cycloadditions which proceed with the aid of a photosensitizer follow the biradical pattern and are head-to-head and nonstereospecific. An example is the cycloaddition of *cis*- and *trans*-dichloroethylenes to cyclopentadiene (6). The thermal addition of *cis*-dichloroethylene leads to two Diels-Alder products (24 and 25) in the ratio of 2 to 1, in which the *cis* configuration of the two chlorine atoms is retained. The thermal addition of *trans*-dichloroethylene leads to the Diels-Alder adduct 26 having exclusively *trans* orientation of the two chlorine atoms. In the presence of a



Thermal addition

photosensitizer and light which is not absorbed by either cyclopentadiene or dichloroethylene, either isomer of the dichloroolefin leads to a mixture of six products (24 and 26 to 30) that does not retain the original configuration of the chlorine atoms. The relation of this to the biradical mechanism



Photochemical addition

will be discussed below, but it is clear that this photosensitized cycloaddition is not a concerted process. Moreover, the amount of isomerization of the unconverted *cis*- and *trans*-dichloroethylenes attending this reaction is very slight, indicating that the loss of configuration does not occur in any molecule until that molecule becomes involved in the formation of product. Although the reasoning of the Hoff-

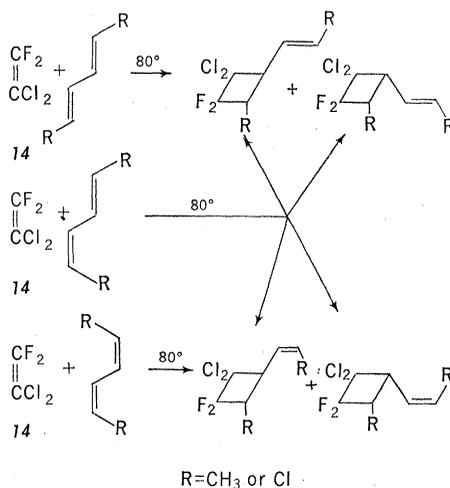
Table 1. Cycloadditions at 120°C, 24 hours; *trans,trans*-hexadiene, 1 mole, with F<sub>2</sub>C=CF<sub>2</sub> or F<sub>2</sub>C=CCl<sub>2</sub>, 7.06 moles.

Reagent	Recovered dienes, (%)				Cycloadducts			
CF <sub>2</sub>    CF <sub>2</sub>		18.2			50.4		12.1	
CF <sub>2</sub>    CCl <sub>2</sub>	0.06	1.4	0.73	0.07	35.6	2.50	12.2	0.39

mann-Woodward rules does not distinguish between singlet and triplet states, the general pattern of photocycloadditions suggests that concerted reaction is limited to singlet states, while triplet states tend to react stepwise via biradicals.

#### Fluorinated Olefins and the Biradical Mechanism

In a stepwise mechanism the intermediate biradical or dipolar ion may have a long enough lifetime for internal rotation to compete with ring closure. In the addition of 1,1-dichloro-2,2-difluoroethylene ("1122") (14) to the *cis* and *trans* double bonds of the isomeric 2,4-hexadienes, the cyclobutane products show stereoisomerization at that double bond that becomes part of the four-membered ring and not at the other one. The stereoequilibrium is incomplete and allows a measurement of the competition between rotation and ring closure (7). The relative rates of the competing processes of rotation and ring closure are consist-



ent with reasonable values assigned on the basis of known rotational barriers and known rate constants for the combination of analogous free radicals. More recently (8), the configurational evidence has been extended to the isomers of 1,4-dichlorobutadiene, the four cycloadducts being isolated and characterized by analysis of their proton and fluorine nuclear magnetic resonance (NMR) spectra. 1,4-Dichlorobutadiene is less reactive than 2,4-hexadiene, but the stereochemical results present exactly the same pattern. The stereochemical patterns also are unchanged when "1122" is replaced by the less reactive tetrafluoroethylene in the addition to 2,4-hexadiene.

#### Diene Isomerization

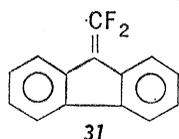
When at a common temperature of 120°C, a direct comparison is made in the addition of tetrafluoroethylene and 1,1-dichloro-2,2-difluoroethylene to *trans,trans*-2,4-hexadiene, striking differences of another sort are observed (8) (Table 1). Between these two reagents an increase is seen in isomerization of the recovered diene. At 120°C, "1122" produces substantial isomerization to the other two geometrical isomers of 2,4-hexadiene, and a detectable amount of hydrogen shift to 1,3-hexadiene as well. Since heating the diene without haloolefin gives no isomerization, these results are interpreted to indicate the formation of the usual biradical, rotation around the new single bond, and then partial reversion to reagent and isomerized diene (Fig. 1). The positional shift of the double bond cannot be a result of simple reversion from the biradical. Although a mechanism could hypothetically in-

Table 2. Cycloadducts from 2-substituted dienes.

R	Percentage of total			Total yield
CH <sub>3</sub> -	15	83	1.6	95
C <sub>2</sub> H <sub>5</sub> -	23	72	5	48
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> -	23	73	4	99
	38	46	16	71
(CH <sub>3</sub> ) <sub>3</sub> C-	44	11	45	80
(CH <sub>3</sub> ) <sub>3</sub> CCH <sub>2</sub> -	26	64	10	86
C <sub>6</sub> H <sub>5</sub> -	12	76	12	

involve intramolecular hydrogen capture within the biradical, it has proved difficult to eliminate the possibility of catalysis by some acid, arising from the action of traces of water on the 1122.

In some experiments (9) prompted by the biradical reversion hypothesis, it was found that 9-(difluoromethylene) fluorene (31) can effect geometrical



isomerization of *trans,trans*-2,4-hexadiene without producing any detectable amount of stable cycloadduct.

### Biradical 1,4-Cycloaddition?

In connection with a biradical mechanism, one of the problems arising is why a biradical with one allylic end (Fig. 1) leads only to 1,2-cycloaddition instead of giving also some 1,4-addition. The reasonable interpretation pre-

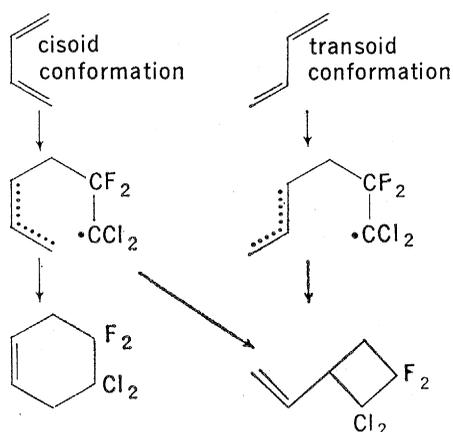
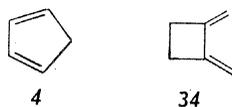


Fig. 2. Diene conformation determines mode of cycloaddition.

sented by Roberts and Sharts (2) proposes that butadiene exists, normally, preferentially in a *transoid* conformation (Fig. 2) because of interference between terminal hydrogens when butadiene is brought around into a *cis* coplanar form. Therefore, the allylic component of the biradical is normally *transoid*; since an allylic radical is coplanar like an olefinic molecule (10), a *trans*-allylic radical is geometrically incapable of closing to a six-membered ring. An implication of this hypothesis is that bulky 2-substituents introduced into butadiene might render the *cisoid* conformation more favorable than the *transoid* (11), thus leading to increasing numbers of *cis*-allylic radicals and increasing amounts of 1,4-addition by the biradical mechanism. Indeed, six 2-substituents larger than the methyl group have this effect—for example, 2-*t*-butylbutadiene leading to 45 percent 1,4-cycloaddition of 1,1-dichloro-2,2-difluoroethylene (8) (Table 2). At the same time, cyclobutanes are produced four times as often by attack at the unsubstituted double bond as at the substituted bond, in contrast to the 15:83 ratio of these product types observed with isoprene. This ratio, however, arises (9) from a preferred 1,4-ring closure of the biradical 32 and a preferred 1,2-ring closure of the biradical 33, as shown by determining the orientations and proportions of the two different 1,4-addition products (Fig. 3).

Even when a diene is constrained to lie in the *cisoid* conformation, there are important factors leading to variety in the relative amounts of 1,2- and 1,4-cycloaddition with 1122. Cyclopentadiene (4) yields over 80 percent 1,4-cycloaddition (1) while 1,2-dimethylenecyclobutane (34) yields at



least 99 percent 1,2-cycloaddition product (10). The distances between carbons 1 and 4 in dienes 4 and 34 lie at opposite ends of the available range (2.40 and 3.35 Å, respectively), and these differences will persist in the allylic radicals. It is probably difficult for attack at the 4-position to compete with attack at the 2-position when the former must occur at a distance that is not ideal.

An informative reexamination of the cycloaddition of 1,1-dichloro-2,2-di-

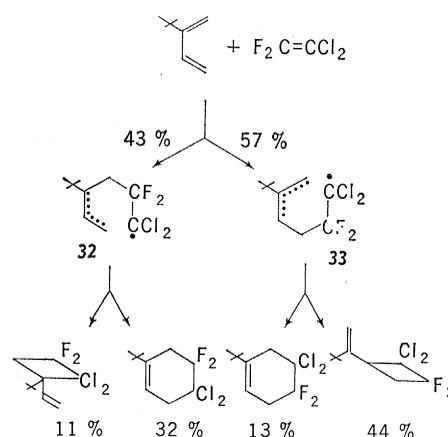


Fig. 3. Biradical cycloaddition mechanism for 2-*tert*-butylbutadiene.

fluoroethylene to butadiene was made by Swenton (12). Apart from the 1,2-cycloadduct which was obtained in high yields, a small amount of a material convertible by strong base into *ortho*-chlorofluorobenzene was formed. This cycloadduct, obviously the missing 1,4-addition product, amounted to only 1 percent of the product at 80°C. An examination of cycloadducts over the temperature range from 60° to 176°C showed the temperature dependence indicated in Fig. 4. With the 1,4-adduct varying from 0.8 percent at the lowest temperature to 2.3 percent at the highest temperature, it was possible to make a direct comparison between these 1,4-adduct yields and the fraction of butadiene existing in the *cisoid* conformation as deduced

Table 3. Products of cycloaddition of trifluoroethylene to butadiene at 215°C.

Product	%
	26.7
	30.2
	15.2
	13.7
	14.2

from thermodynamic data (13). The curve of the conformational equilibrium constant ( $[cisoid]/[transoid]$ ) is shown on the same graph, and it has exactly the same temperature dependence. In fact, the ratio of the percentage of *cisoid* conformation to the percentage of 1,4-adduct is approximately constant—about 6.7 over the entire temperature range. The conclusion appears reasonable that *cis* biradical formed from butadiene and 1122 normally closes to a six-membered ring about 14 percent of the time and to a four-membered ring 86 percent of the time. Thus the substitution of an alkyl group at the 2-position of butadiene affects not only the conformation of the diene and the relative reactivities at its two ends, but also the relative probabilities of the occurrence of two modes of ring closure of the *cis* biradical.

The possibility also exists that some or all of the 1,4-adducts observed arise from the concerted cycloaddition mechanism, which of course is also favored by *cisoid* conformation of the diene.

#### Cases of Ethylene and $\alpha$ -Acetoxyacrylonitrile

It has not been obvious why ethylene and tetrafluoroethylene behave totally differently toward butadiene (1,4- and 1,2-addition, respectively). A careful reinvestigation of the case of ethylene (14) has revealed 0.02 percent of vinylcyclobutane in a product consisting otherwise entirely of cyclohexene. Thus the 1,2-addition mechanism and the Diels-Alder mechanism proceed in this case at rates in the ratio of 2 to  $10^4$ .

A favorable case has not yet been found for demonstrating the simultaneous occurrence of stereospecific 1,4- and nonstereospecific 1,2-cycloaddition between the same pair of reactants. Even with the minute amount of 1,2-cycloadduct resulting from ethylene and butadiene, if there had been a comparable amount of 1,2-addition of ethylene to *trans,trans*-2,4-hexadiene, it

Table 4. Modes of cycloaddition to butadiene.

Reagent	Temp. (°C)	Yield (%)	
		1,2-	1,4-
1122	79	99	1
Trifluoroethylene	215	85.8	14.2
1,1-Difluoroethylene	250	35	65
Allene	180	25	75
Ethylene	175	0.02	99.98

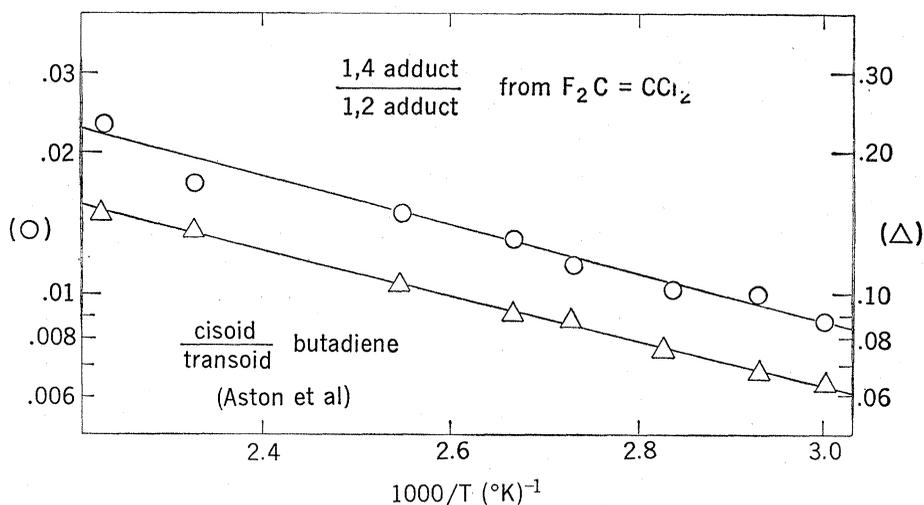


Fig. 4. Butadiene conformational populations and ratio of cycloaddition products.

might have been possible to compare the stereochemical courses of these two modes of addition. However, it has been shown that the rate of cycloaddition by the biradical mechanism is affected adversely (by factors of 10 to 20) when, as with 2,4-hexadiene, the initial attack must be on a secondary, rather than on a primary, olefinic carbon atom. At the same time, the Diels-Alder reaction of maleic anhydride with *trans,trans*-2,4-hexadiene proceeds 11 to 12 times faster than that with butadiene. This could mean that the fraction of 1,2-cycloadduct of ethylene to *trans,trans*-2,4-hexadiene would be less than in the butadiene case by a factor of 200! Indeed, Schueller has found that, under conditions permitting isolation of some vinylcyclobutane from ethylene and butadiene, the only product from ethylene and *trans,trans*-2,4-hexadiene is *cis*-3,6-dimethylcyclohexene. This is a new demonstration of stereospecificity of the Diels-Alder reaction under conditions where intermolecular complexing forces must be minimal (Fig. 5).

A more promising case appeared to be that of  $\alpha$ -acetoxyacrylonitrile, which has been shown (15) to add to butadiene and to yield 86 percent of 1,4-addition product and 14 percent of 1,2-addition product (Fig. 6). We have confirmed this result but still could not obtain useful amounts of 1,2-cycloadduct when  $\alpha$ -acetoxyacrylonitrile is added to either *trans,trans*-2,4-hexadiene or cyclopentadiene. In the former case the product consists (to at least 99.6 percent) of two isomers of *cis*-3,6-dimethyl-4-cyano-4-acetoxy-cyclohexene (35 and 36), the two isomers differing according to whether

the CN group or the acetoxy group is *cis* to the two methyls. This result makes improbable any suggestion that the two products from butadiene arise by two branches of a common stepwise mechanism. If the addition had been stepwise in the first place, retention of the *cis* configuration of the two methyl groups in the 2,4-hexadiene adducts would not be expected.

#### Borderline Fluoroolefins

Nevertheless, a middle ground does exist, and there are compounds which will yield 1,2- and 1,4-addition to dienes with comparable facility. Trifluoroethylene reacts with dienes to give predominantly cyclobutanes, but the reaction also yields accompanying 1,4-addition in amounts varying from 2 percent with *cis*-piperylene to 29.7 percent with 2,3-dimethylbutadiene (16) (Table 3).

Unlike 1122, trifluoroethylene reacts with butadiene yielding comparable amounts of the 1,2-addition products with different orientations; and, since

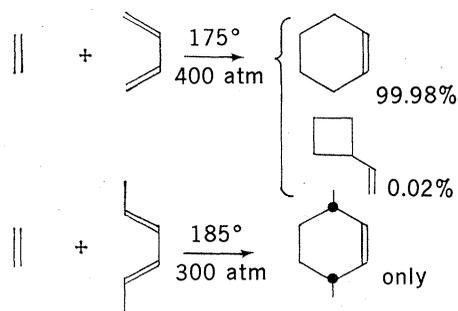


Fig. 5. 1,2- and stereospecific 1,4-addition of ethylene.

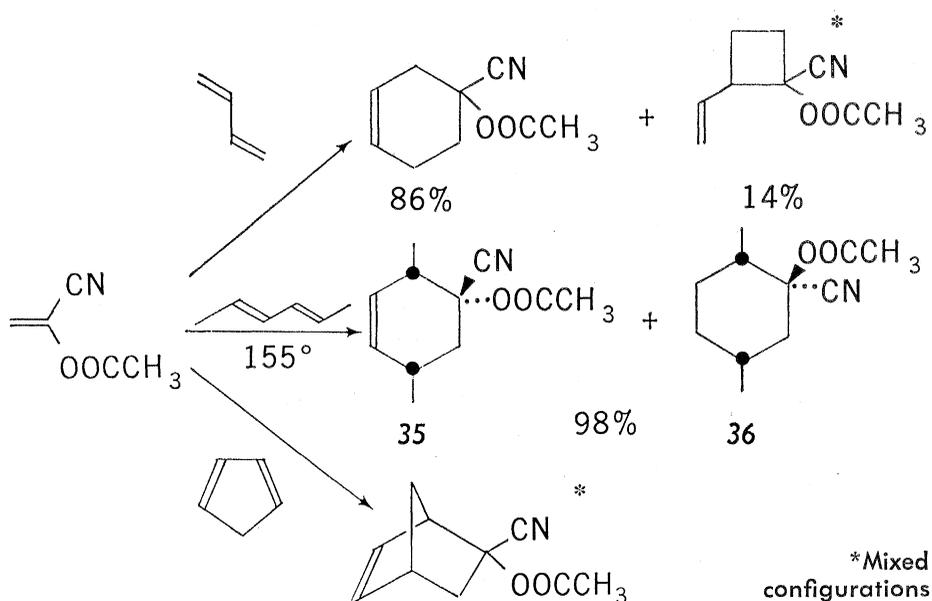


Fig. 6. 1,2- and concerted 1,4-addition of  $\alpha$ -acetoxyacrylonitrile.

each of these exists in two geometrical isomers, five cycloadducts are found. These have been separated by vapor chromatography. Configurations have not been definitely assigned to the third and fourth isomers shown in Table 3, although their orientations have been established by relating them to the adducts of trifluorovinyl chloride and, through these, to the conjugated vinyl-trifluorocyclobutene.

A range from 1 to 99.98 percent 1,4-cycloaddition, covered by the five reagents shown in Table 4, destroys the apparent dichotomy of reagents.

Table 5. Approximate rate constants (liter mole<sup>-1</sup> sec<sup>-1</sup>) for 1,2- and 1,4-cycloaddition to butadiene at 212°C.

Reagent	$k_{1,2}$	$k_{1,4}$
H <sub>2</sub> C=CH <sub>2</sub> *	$2 \times 10^{-9}$	$1 \times 10^{-6}$
H <sub>2</sub> C=CF <sub>2</sub>	$4 \times 10^{-7}$	$2 \times 10^{-6}$
F <sub>2</sub> C=CHF	$4 \times 10^{-5}$	$7 \times 10^{-6}$
F <sub>2</sub> C=CCl <sub>2</sub>	$2 \times 10^{-2}$	$6 \times 10^{-4}$

\* Rate constants calculated for gas phase. Comparison with liquid phase reactions introduces some uncertainty (see 14, p. 47).

When the same reagent shows both 1,2- and 1,4-cycloaddition, is the latter mode of reaction due to *cis* biradical, or is it an outcropping of the universal ability of alkenes to undergo concerted 1,4-addition?

Although the conditions of these cycloadditions, involving high temperatures, sealed tubes, and partition of reactants between liquid and vapor phases are not favorable for accurate study of reaction kinetics, some approximate rate determinations have been made (16) by measuring the competition between dimerization of butadiene and cross-cycloaddition of fluoroolefins to butadiene. Such studies yield a ratio between the two bimolecular rate constants  $k_d$  and  $k_a$  for dimerization and addition. By the use of values of  $k_d$  already determined (17), values of  $k_a$  can be assigned. Since the additions of butadiene to ethylene, to 1122, and to itself have all been found to have an entropy of activation  $\Delta S^\ddagger$  equal to  $-29 \pm 1$  calories per degree (18), this value has been provisionally used for the purpose of extrapolating the  $k_a$

of 1,1-difluoroethylene to the temperature where trifluoroethylene was measured. Finally, use of the observed product ratios leads to the approximate rate constants shown in Table 5.

From Table 5 it appears that 1,4-cycloaddition of ethylene, 1,1-difluoroethylene, trifluoroethylene, and 1,1-dichloro-2,2-difluoroethylene to butadiene cover a range of 300-fold in rate constant, while the rates of 1,2-addition of the same series of reagents cover a range of 10,000,000. Thus, the varying behavior of these compounds must be attributed largely to their varying capacity for entering into the biradical mechanism. For ethylene, which forms biradicals far more slowly than its normal rate of concerted Diels-Alder addition, cyclohexene is almost the sole product, while the biradical mechanism for trifluoroethylene rises appreciably above the almost constant concerted rate level.

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19. Supported by NSF, NIH, the Petroleum Research Fund of the American Chemical Society, and B. F. Goodrich Company.