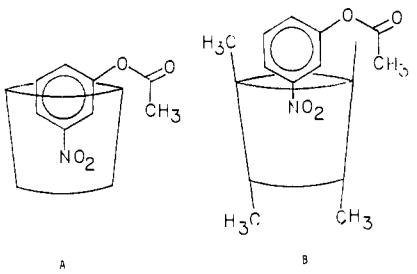

Figure 2. Estimated depth of penetration of 3-nitrophenyl acetate into (A) cyclohexaamylose and (B) dodecakis-2,6-*O*-methylcyclohexaamylose.

of binding of the nitrophenylacetates themselves is similar to that examined here, then the acyl carbonyls would be too far from the DMCD 3-hydroxyls to react with them (Figure 2).

Finally, it is interesting to speculate about the correlations (or lack of) among the thermodynamic binding constants, substrate NOEs, and coupling coefficients, ξ, for cycloamylose substrate binding. Inspection of Table III shows that there is a decrease in K_D through the series of complexes: sodium 4-nitrophenolate/cyclohexaamylose > sodium 2,6-dimethyl-4-nitrophenolate/cyclohexaamylose > sodium 4-nitrophenolate/DMCD $\simeq$ sodium 2,6-dimethyl-4-nitrophenolate/DMCD. Such a sequence suggests that as the hydrophobic character of the substrate and/or host is increased, the binding is increased. However, as the NOEs reflect substrate penetration, this order is reversed; i.e., the magnitude of the binding constant does not correlate directly with the degree of insertion. In contrast, the coupling coefficients show no discernible trends. Thus, the dynamic aspects of molecular association, at least in these complexes, are substantially different from the picture implied by examination of the binding constants. Particularly in the case of the sodium 2,6-dimethyl-4-nitrophenolate/DMCD complex, while the possibility that the substrate methyls could slip between the DMCD rim methyls, drawing the substrate more deeply into the cavity and thereby increasing dispersion interactions between guest and host exists, this does not appear to be occurring here.

Conclusions

For some time, arguments that the 2- and 3-hydroxyls of cycloamylose differ greatly in their degree of involvement in catalytic deacylation have been made. However, in light of our findings, the basis of such arguments must be carefully reconsidered. The alleged difference in catalytic ability between these two hydroxyl groups was based on two lines of evidence: a substantial difference between their respective pK_as implied by a difference in their reactivity with electrophiles under basic conditions, and the loss of catalytic activity on methylation of the 2- and 6-hydroxyls.

With respect to the first of these two suggestions, Laufer has recently shown that the difference in pK_as is virtually nonexistent.[15] Furthermore, Breslow has isolated mixtures of acylcycloamylose intermediates that, based on coupling constants and chemical shift analyses, appear to be substituted at both the 2- and 3-positions.[32] While these findings suggest that the 2- and 3-hydroxyls do not differ substantially in catalytic ability, the curious loss of catalytic activity in 2,6-O-permethylated cycloamylose derivatives remained to be explained. Others have suggested that this loss of activity could not be attributed to steric effects, i.e., the 2-*O*-methyl groups did not hinder the substrate's access to the remaining 3-hydroxyl, and thus concluded the 3-hydroxyl was simply unreactive. However, such suggestions were based solely upon examination of molecular models.[9] In contrast, as a result of our NOE, chemical shift, and dynamic coupling measurements of sodium 4-nitrophenolate and sodium 2,6-dimethyl-4-nitrophenolate/dodecakis-2,6-*O*-methylcyclohexaamylose complexes, we conclude that methylation of cyclohexaamylose does, indeed, provide an effective barrier for access to the remaining 3-hydroxyl. Comparison of these parameters to those obtained for the same substrates' binding to cyclohexaamylose clearly shows that the substrates are prevented from equivalent penetration of the cycloamylose cavity when the 2-hydroxyls are methylated. Thus, this result alone appears to be sufficient to explain Bender's original observations.

Acknowledgment. We acknowledge Dr. Roy King of the University of Florida Chemistry Department for his help in obtaining NMR relaxation measurements on the JEOL FX-100 FT-NMR spectrometer. We further acknowledge Dr. Michael A. Channing of the National Institutes of Health for providing the chemical shift data obtained at 220 MHz.

Registry No. I, 824-78-2; II, 63831-48-1; DMCD, 51166-72-4; cyclohexaamylose, 10016-20-3.

(32) R. Breslow, M. F. Czarniecki, J. Emert, and H. Hamaguchi, *J. Am. Chem. Soc.*, **102**, 762 (1980).

(33) The di-*O*-methylated cyclodextrin was first described by J. Staerk and H. Schlenk. These authors suggested that the unsubstituted hydroxyls are those at C-2 (J. Staerk and H. Schlenk, 149th National Metting of the American Chemical Society, Detroit, Spring, 1965, Abstract 11c). This assignment has since been shown to be incorrect. The methylation occurs at C-2 and C-6, leaving the C-3 hydroxyls unsubstituted.[29]

Cycloaddition of Substituted Allenes with 1,1-Dichloro-2,2-difluoroethene. A Model for the Two-Step, Diradical-Intermediate Cycloaddition of Allenes

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Abstract: The stereoselectivities, chemoselectivities, relative reactivities, and kinetic isotope effects have been determined in the cycloaddition reactions of substituted allenes with 1,1-dichloro-2,2-difluoroethene (1122). The stereoselectivity observed about the exocyclic double bond in the cycloadducts is governed by steric interactions generated in the formation of the stereosiomeric diradical intermediates **13** and **16**, the rate of formation of the latter decreasing with increasing size of R. The chemoselectivity is also determined by steric interactions generated in the transition states for ring closure, favoring closure to the least substituted end of the allyl radical as the degree of substitution and size of the alkyl groups increase. The relative reactivity sequence for the substituted allenes is mono- < 1,1-dialkyl- < 1,1,3-trialkylallene. Within the mono- and 1,1-dialkylallene series, the relative reactivities decrease as the size of the alkyl groups increases. The observed relative reactivity sequence is discussed in terms of steric factors and changes in the energies of the π MO's. The trends discovered in the present study provide an excellent model for comparison with other cycloaddition reactions of allenes whose mechanisms are still in question.

Recent investigations in our laboratories have focused on the possible mechanisms of allene cycloaddition and cyclodimerization reactions.[1] The results of a theoretical study suggested that a $[_\pi 2_s + (_\pi 2_s + _\pi 2_s)]$ concerted process, which involves interactions

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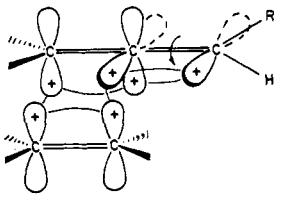
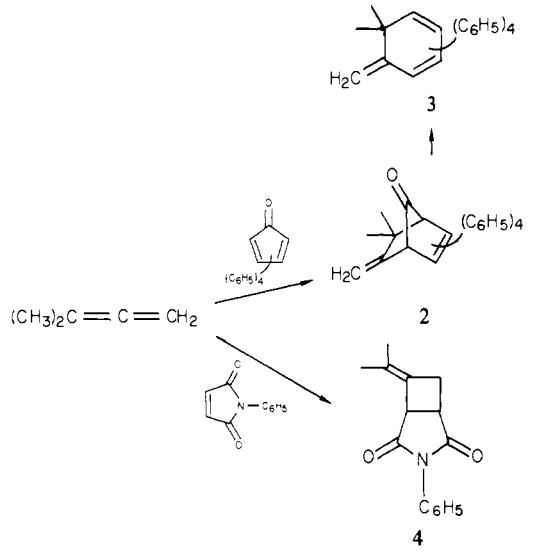


Figure 1. Orbital interactions in the $[{}_{\pi}2_s + ({}_{\pi}2_s + {}_{\pi}2_s)]$ cycloaddition transition state.

of the dienophile with both π systems of the allene in the transition state (**1** in Figure 1), should be more favorable than a $({}_{\pi}2_s + {}_{\pi}2_a)$ concerted process.[2] Furthermore, the calculations predicted a difference in chemoselectivity in the cycloadditions with unsymmetrically substituted allenes, the six-electron process favoring addition across the least substituted double bond and the four-electron $({}_{\pi}2_s + {}_{\pi}2_a)$ process and cycloaddition with an electron-deficient four π-electron system [i.e., a $({}_{\pi}4_s + {}_{\pi}2_s)$ process] favoring addition across the more highly substituted double bond.[2] Preliminary[3] and more detailed studies[4] on the cycloaddition of substituted allenes with tetraphenylcyclopentadienone (TPCP) gave results in accord with the prediction. For example, 1,1-dimethylallene reacts with TPCP to form **2**, which under the reaction conditions expels carbon monoxide with formation of **3**. In contrast, cycloaddition with *N*-phenylmaleimide (NPMI) gives essentially only **4**.[4]



Consideration of steric effects in the transition state **1** for the six-electron process and the required direction of rotation of the substituted terminus of the allene[2] suggested that the stereochemistry about the exocyclic double bond in the product should be that shown in **5** and that as the size of R increases the ratio of **5**:**6** should increase.[2]

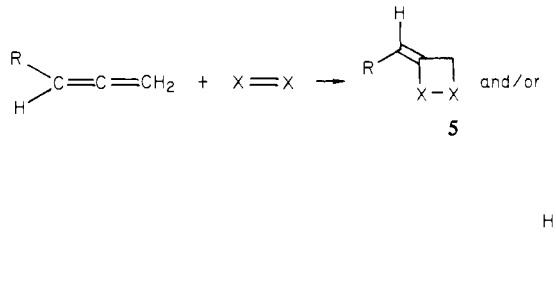
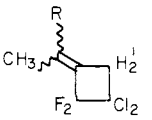


Table I. Chemical Shifts (δ) in Adducts 7 and 8



	H^1		CH_3		R^a		
R	7	8	7	8	R	7	8
CH_3	3.25		1.70	1.94	CH_3	1.70	1.94
CH_3CH_2	3.25	3.25	1.90	1.67	CH_2	2.01	2.29
					CH_3	1.03	1.09
						(8.2)	(8.2)
$(CH_3)_3C$	3.51	3.26	1.89	1.65	$(CH_3)_3C$	1.10	1.23

[a] Coupling constants between sets of hydrogen atoms are given in parentheses.

Although the theoretical studies predicted a difference in the chemoselectivities of the two concerted processes and the preferred stereoselectivity about the exocyclic double bond in the six-electron process, they provided no insights as to the chemo- and stereoselectivities expected to be observed in a two-step, diradical intermediate process.

Studies were thus initiated to compare the chemoselectivities, stereoselectivities, relative reactivities, and kinetic isotope effects in a radical-chain addition and a two-step, diradical-intermediate cycloaddition reaction with those obtained from similar studies of the cycloaddition of substituted allenes with NPMI.[5] As a model for the radical-chain addition process, the chemoselectivity,[6] relative reactivities,[7] and kinetic isotope effects[7] were determined for the radical-chain addition of benzenethiol to substituted allenes. (Unfortunately, the stereoselectivity aspects of this reaction could not be evaluated due to interfering thiyl radical catalyzed isomerizations of the initially formed products.)[6] In the present article the results of a similar study of the cycloaddition of substituted allenes with 1,1-dichloro-2,2-difluoroethene (1122) are presented and discussed. Cycloaddition reactions of 1122 have been adequately shown to proceed via two-step, diradical-intermediate pathways,[8] as has also the cycloaddition reactions of allene and 1,1-dimethylallene with tetrafluoro- and chlorotrifluoroethene.[9]

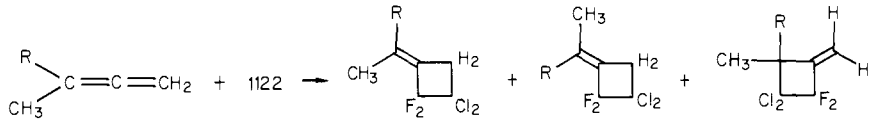
Results

Determination of the Structures of Adducts. The cycloaddition reactions of the substituted allenes with 1122 were carried out at 160 °C in sealed tubes in the presence of excess 1122 as solvent. After completion of the reaction (14–24 h), the excess 1122 was allowed to evaporate, and separation of the mixtures of adducts was attempted by GLC. Some of the isomeric adducts were obtained pure by preparative GLC; however, in some cases no, or only partial, separation could be achieved (see Experimental Section). Structural assignments could be made even on the partially or nonseparated fractions by 100- and 300-MHz NMR spectroscopy because of the substantially different chemical shifts of the ^1H and ^{19}F nuclei in the isomeric adducts.

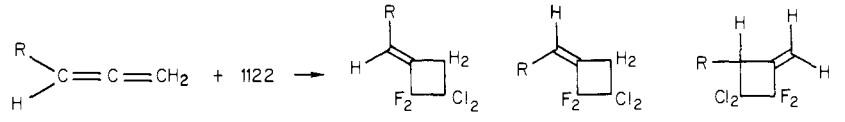
The reactions of the 1,1-di- and monosubstituted allenes with 1122 resulted in the formation of mixtures of the adducts **7–9** and **10–12**, shown in Scheme I. The stereochemical assignment for adducts **7** and **8** is based on the relative magnitude of long-range H–H and H–F coupling constants in which the transoid homoallylic coupling constants are greater than the cisoid homoallylic coupling constants.[10] In **7a** (R = CH_3) and **7c** [R = $C(CH_3)$],

(1) A review of the previously published results and the mechanistic conclusions derived therefrom appears in ref 2 and 5 and will not be presented here except as it directly relates to the present work.
(2) Pasto, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 37.
(3) Pasto, D. J. *Tetrahedron Lett.* **1980**, *21*, 4787.
(4) Pasto, D. J.; Heid, P. F. *J. Org. Chem.*, in press.
(5) Pasto, D. J.; Heid, P. F.; Warren, S. E. *J. Am. Chem. Soc.*, **1982**, *104*, following paper in this issue.
(6) Pasto, D. J.; Warren, S. E.; Morrison, M. A. *J. Org. Chem.* **1981**, *46*, 2837.
(7) Pasto, D. J.; Warren, S. E. *J. Org. Chem.* **1981**, *46*, 2842.
(8) (a) Montgomery, L. K.; Schueller, K.; Bartlett, P. D., *J. Am. Chem. Soc.* **1964**, *86*, 622; (b) Bartlett, P. D.; Dempster, C. J.; Montgomery, L. K.; Schueller, K. E.; Wallbillich, G. E. H. *Ibid.* **1969**, *91*, 405.
(9) (a) Taylor, D. R.; Warburton, M. R.; Wright, D. B. *J. Chem. Soc. C* **1971**, 385. (b) Taylor, D. R.; Wright, D. B. *Ibid.* **1971**, 391.
(10) Sternhall, S. *Rev. Pure Appl. Chem.* **1964**, *14*, 15.

Scheme I



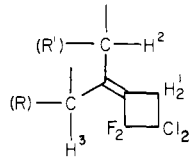
	7	8	9
a, R = CH_3	85.9		14.1
b, R = CH_3CH_2[a]	53.4	37.1	6.7
c, R = $(CH_3)_3C$	86.0	6.7	7.3



	10	11	12
a, R = CH_3CH_2[b]	50.5	27.3	15.4
b, R = $(CH_3)_2CHCH_2$	48.2	27.1	24.7
c, R = $(CH_3)_2CH$	55.0	20.0	25.0
d, R = $(CH_3)_3C$[c]	55.0		35.3

[a] Reaction mixture contains 2.7% of an unidentified adduct. [b] 6.8% unidentified product. [c] 10.7% unidentified product.

Table II. Long-Range H-H and H-F Coupling Constants (Hz) in 7 and 8[a]



R	R'	1,2	1,3	2,F	3,F
CH_3	CH_3	1.9	2.3	3.3	2.3
CH_3	CH_3CH_2		2.5	3.61	2.5
CH_3CH_2	CH_3	1.93		3.73	
CH_3	$(CH_3)_3C$	1.72	2.41	3.37	2.41

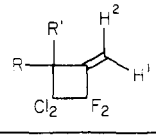
[a] H^1-F coupling constants were all <0.2 Hz.

the transoid H-H homoallylic coupling constants of 2.3 and 2.41 Hz ($J_{1,3}$ in Table II) are greater than the cisoid ($J_{1,2}$) coupling constants of 1.9 and 1.72 Hz in **8a** and **8c**, and the cisoid H-F homoallylic coupling constants ($J_{3,F}$) of 2.3 and 2.41 Hz in **7a** and **7c** are less than the transoid coupling constants ($J_{2,F}$) of 3.3 and 3.37 Hz in **8a** and **8c**. Not all of the long-range coupling constants in **7b** and **8b** (R = CH_3CH_2) could be determined because of the complexity of the multiplets for the methylene protons of the ethyl group in the NMR spectra. The stereochemistry of **7b** and **8b** (R = CH_3CH_2) could be assigned, however, on the basis of the long-range H-H and H-F coupling constants involving the methyl group, which are similar in magnitude with those observed in **7a** and **8b**, and **7c** and **8c**. The methyl and methylene groups in **7** and **8** that are cis to the ring difluoromethylene group all appear at *lower* field than their stereochemical counterparts (see Table I).

The assignments of the vinyl hydrogen resonances in **9** and **12** are based on the relative magnitudes of the long-range, allylic H-H and H-F coupling constants of which the cisoid coupling constants are greater than the transoid coupling constants.[10] In **9** the long-range H-F coupling constants to the lower-field vinyl hydrogen ($J_{1,F}$ of Table IV) are greater than those to the higher-field vinyl hydrogen ($J_{2,F}$). In **12** (R = CH_3CH_2 and $(CH_3)_2CH$), both the allylic H-H and H-F coupling constants are consistent with the lower-field vinyl hydrogen being cis to the ring difluoromethylene group. Thus, any group attached to the exocyclic double bond cis to the difluoromethylene group experiences a greater deshielding. This is a very useful correlation that can be applied to those systems in which not all of the long-range coupling constants can be determined because of the complexity of the resonance patterns.

The stereochemical assignments for **10** and **11** [R = CH_3CH_2, $(CH_3)_2CHCH_2$, and $(CH_3)_3C$] are based on the relative chemical shifts of the vinyl and alkyl hydrogens and the relative magnitudes of the long-range H-H and H-F coupling constants. In all cases the adducts possessing the lower-field vinyl hydrogen resonances possessed the higher-field alkyl resonances (see Table V), the larger allylic and homoallylic H-F coupling constants, and the smaller allylic H-H coupling constants (see Table VI). Conversely, the adducts possessing the higher-field vinyl hydrogen resonances also possessed the lower-field alkyl resonances, the smaller allylic and homoallylic H-f coupling constants, and the larger allylic H-H coupling constants. These chemical shift and coupling constant correlations are consistent with those discussed above for adducts **7-9** and **12**.

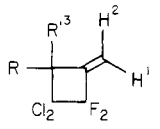
Table III. Chemical Shifts (δ) in Adducts 9 and 12



R	R'	H^1	H^2	R	R'	^{19}F[a]
H	CH_3CH_2	5.67	5.39	3.22	CH_2, 1.75; CH_3, 1.08 (7.2)	-36.2
H	$(CH_3)_2CHCH_2$	5.70	5.38	3.39	CH_2, CH, 1.67; CH_3, 0.99, 1.00[b] (6.3)	-23.7
H	$(CH_3)_2CH$	5.70	5.55	3.02	CH, 2.10; CH_3, 1.15, 1.11[b] (6.5)	-24.3, -25.0[b]
H	$(CH_3)_3C$	5.78	5.49	3.34	CH_3, 1.18	-23.3, -24.0[b]
CH_3	CH_3	5.71	5.42	1.43	CH_3, 1.43	
CH_3	CH_3CH_2	5.68	5.35	1.38	CH_2, 1.77, 1.79[b] (17.1); CH_3, 1.01 (7.3)	
CH_3	$(CH_3)_3C$	5.57	5.45	1.52	CH_3, 1.19	

[a] Relative to external trifluoroacetic acid. [b] Diastereotopic atoms.

Table IV. Long-Range H-H and H-F Coupling Constants (Hz) in 9 and 12



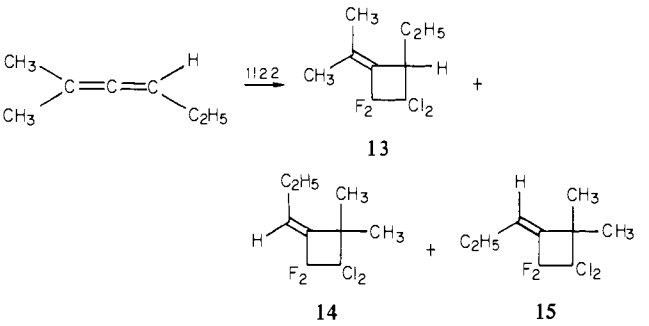
R	R′	1,2	1,3	2,3	1,F	2,F	3,F
CH_3CH_2	H	1.4	2.9	3.1	2.5	2.1	
$(CH_3)_2CH$	H		2.71	3.35	4.6	2.33	0.31, 1.03[a]
CH_3	CH_3	1.9			2.6	1.9	
CH_3	CH_3CH_2	1.82			2.55	1.91	
CH_3	$(CH_3)_3C$	2.6			1.7	0.8	

[a] The two fluorine atoms are diastereotopic, the lower-field F having a coupling constant of 1.03 Hz with H_3, the higher-field F having a coupling constant of 0.31 Hz with H_3.

In the reaction of *tert*-butylallene with 1122, only a single stereoisomer of structure **10** or **11** was formed, and a comparison of relative chemical shifts and coupling constants in the two stereoisomers was not possible. The stereochemistry of the adduct has been assigned on the basis of the similarity of the chemical shifts of the vinyl hydrogen and ring methylene and difluoromethylene groups and the similarity of the long-range H–H and H–F coupling constants with those for **10** [R = CH_3CH_2, $(CH_3)_2CHCH_2$, and $(CH_3)_2CH$], all of which fall within the ranges for those quantities possessed by the other substituted adducts of structure **10**.

The relative yields of the adducts derived in the reactions of the substituted allenes with 1122 were determined by integration of the ^1H and/or ^{19}F NMR spectra of the crude product mixtures and are given in Scheme I.

The trialkyl-substituted allene 3-ethyl-1,1-dimethylallene reacted with 1122 to form a mixture of the three adducts **13**, **14**, and **15** in relative yields of 85.1%, 10.4%, and 2.8%, respectively,



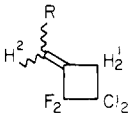
along with 1.7% of an unidentified product. The structures are assigned on the basis of NMR spectral data (see Experimental Section) by use of the correlations described earlier in this article.

Relative Reactivities of Substituted Allenes toward Cycloaddition with 1122. The relative reactivities of the various substituted allenes toward cycloaddition with 1122 were determined by competitive reaction techniques (see Experimental Section). The relative rate constants (k_{rel} = 1.00 for ethylallene) are given in Table VII.

Discussion

The formation of the cycloaddition products of the substituted allenes with 1122 can be rationalized in terms of the mechanism shown in Scheme II. The formation of the stereoisomeric adducts **7** and **8**, and **10** and **11**, requires the formation of the two stereoisomeric diradical intermediates **13** and **16**, the former undergoing ring closure to form only **14** and **15** and the latter to form only **15** and **17**.[11]

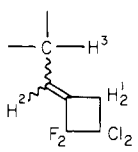
Table V. Chemcial Shifts (δ) in Adducts 10 and 11[a]



	H^1		H^2		R^a			$^{19}F^b$	
R	10	11	10	11	R	10	11	10	11
CH_3CH_2	3.31	3.27	6.21	5.85	CH_2	2.07 (7.2)	2.29 (7.9)	−18.7	−17.9
					CH_3	1.05 (7.6)	1.07 (7.4)		
$(CH_3)_2CHCH_2$	3.28	3.30	6.23	5.81	CH_2, CH	1.73	1.83	−18.4	−17.4
					CH_3	0.91 (7.1)	0.93 (7.1)		
$(CH_3)_2CH$	3.34	3.28	6.08	~5.6	CH	2.33 (8.8)	2.77 (8.8)	−18.7	−17.4
					CH_3	1.04 (6.6)	1.06 (6.6)		
$(CH_3)_3C$	3.47	[c]	6.12	[c]	CH_3	1.08	[c]	−18.1	[c]

[a] Numbers in parentheses are the J's between that set of hydrogens and the set nearer the double bond; i.e., in the case of 10 with R = CH_3CH_2, the coupling constant between the CH_2 and the vinyl hydrogen is 7.2 Hz, and that between the CH_3 and CH_2 is 7.6 Hz. [b] Relative to external trifluoroacetic acid. [c] 11 is not formed in a detectable quantity.

Table VI. Long-Range H-H and H-F Coupling Constants (Hz) in 10 and 11[a]



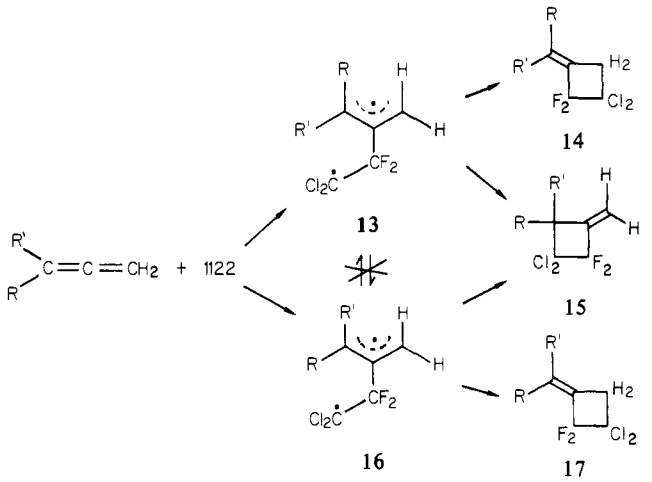
	1,2		1,3		1,F		2,F		3,F	
R	10	11	10	11	10	11	10	11	10	11
CH_3CH_2	2.9	---	---	---	~0.7	~0.5	2.89	2.2	2.9	1.5
$(CH_3)_2CHCH_2$	2.9	---	---	---	~0.6	~0.4	2.91	2.2	2.91	1.5
$(CH_3)_2CH$	2.93	---	0.74	---	~0.5	~0.6	2.93	2.1	1.52	1.4
$(CH_3)_3C$	2.86	---	---	---	~0.7	---	2.86	---	---	---

[a] The number of significant figures represents the degree of certainty in determining the magnitude of the coupling constant. Entries indicated by --- could not be determined due either to overlapping patterns in the spectra of inseparable mixtures or to the inability to analyze very complex resonances having no characteristic patterns.

Table VII. Relative Reactivities of Substituted Allenes toward Attack by 1122 and Benzenethiyl

substituted allene	relative reactivities 1122	relative reactivities $C_6H_5S\cdot$
ethyl	1.00	1.00
isobutyl	0.97	0.95
isopropyl	0.72	0.69
tert-butyl	0.53	0.54
1,1-dimethyl	11.6	12.5
1-ethyl-1-methyl	8.9	11.6
1-*tert*-butyl-1-methyl	1.6	6.4
3-ethyl-1,1-dimethyl	24.0	19.8

Scheme II



An understanding of the intimate details of the formation of the diradical intermediates **13** and **16** is available from an analysis of kinetic isotope effect (KIE) and the stereoselectivity data. Critical to the understanding of the mechanism of formation of **13** and **16** is the knowledge of which double bond of the allene is undergoing attack and bond formation. A priori, radical formation should be favored at the most highly substituted terminal carbon atom of the allene chromophore. This requires attack on the 2p AO on C_2 of the most highly substituted double bond with rotation of the developing radical center to form the planar allyl radical portion of the intermediate, as is illustrated in Scheme III. The KIE's measured for the addition to 1,1-dimethylallene confirm this prediction. The origin of the KIE's arising from deuterium substitution at C_3 and the methyl groups of 1,1-dimethylallene has been discussed in conjunction with the radical-chain addition of benzenethiol;[7] deuterium substitution at C_3 results in a $k_{H_2}/k_{D_2} < 1.0$ due to an increase in the stretching and bending force constants of the C_3–H bonds, while deuterium substitution at the methyl groups results in a mass effect on the rotation of the $(CH_3)_2C$ group for which the maximum value of k_{H_6}/k_{D_6} should be 1.20.[12] The observed value for k_{H_2}/k_{D_2} is 0.88 ± 0.02, while that for the rotational isotope effect k_{H_6}/k_{D_6} is 1.15 ± 0.01. Both values are consistent with attack at the 2p AO on C_2 of the most highly substituted double bond of the allene.

During the formation of **13** and **16**, the rotational and translational motions illustrated in **18** and **19** in Figure 2 must occur. In **18** the largest group R′ attached to C_1 rotates away from the approaching reagent X. This mode of rotation generates no adverse steric effects between R′ and the approaching reagent X but does result ultimately in the formation of the less thermodynamically endo orientation of R′ in the allyl radical. Rotation of the R′ group toward the approaching reagent X as in **19** generates an adverse steric interaction between R′ and X, which will increase as the size of R′ increases. This mode of rotation, however, results in the formation of the most thermodynamically stable allyl radical. The experimental results definitely indicate that the steric effects between R (or R′) and the approaching

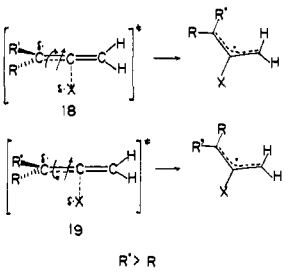
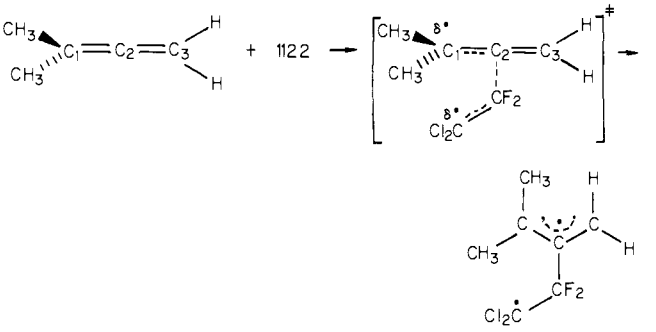


Figure 2.

Scheme III



reagent, generated on rotation of the RCR′ portion of the allene, dominates and that the extent of rotation is greater than that of translation in the transition state, suggestive of a rather early transition state.

The relative reactivities of the substituted allenes with 1122 parallel those observed in the radical addition of benzenethiyl[7] (see Table VII). The decrease in reactivity in the monoalkylallene and 1,1-dialkylallene series as the size of the R group increases is essentially totally due to a decrease in the rate of formation of diradical intermediate **16** (also see following discussion). The increase in reactivity in the sequence monoalkyl- < 1,1-dialkyl- < 1,1,3-trialkylallenes is due to incremental raising in the energies of the π MO's in the sequence, which results in an increase in the rate of reaction.[7]

Ring Closure of the Diradical Intermediates. The inspection of models suggests that **16** (R = H) should be able to close to **17** or **15** with equal facility in an early transition state regardless of the conformation in which **16** may be formed or in which it exists. In a late transition state formation of **17** should be favored for steric reasons, the formation of **17** being increasingly favored as the size of R′ increases. In contrast, the ring closure of **13** to form **14** should be more facile than the closure to form **15**. The diradical intermediate should be formed, or exist, in predominantly the conformation in which the dichloromethylene radical group is oriented toward the $\dot{C}H_2^{\delta\cdot}$ end of the allyl radical portion, and ring closure to form **14** is substantially less sterically encumbered than is closure to form **15**. The lack of formation of **17** (R = $C(CH_3)_3$, R′ = H) in the reaction of *tert*-butylallene with 1122 suggests that diradical intermediate **16** is not formed to any significant extent; any that is formed undergoes the less favored ring closure to form **15**.

The direction of ring closure of the diradical intermediates is dependent on the degree of substitution at the termini of the allyl radical portion of the diradical intermediate and on the size of the alkyl group(s) attached to the allyl radical (see data in Table VII). The diradical intermediates derived from the 1,1-dialkylallenes show a significantly greater tendency to ring close to the *least* substituted end of the allyl radical. This is undoubtedly

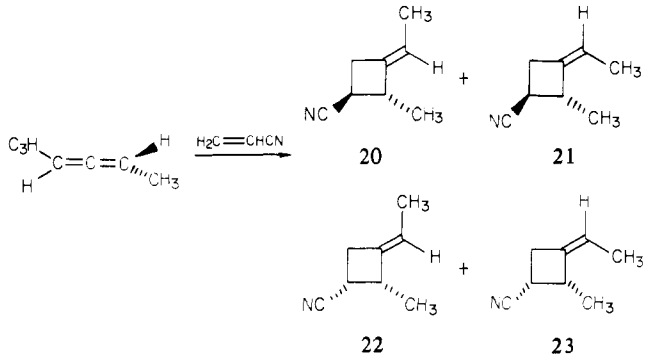
(11) Ring closure must occur much more rapidly than stereoisomerization of the allyl radical portion of the diradical intermediate (see ref 8a and 9b).

(12) In the attack by benzenethiyl there is an electron polarization contribution due to δ+ formation as well as δ• to k_{H_6}/k_{D_6}.[7] In attack by the carbon-based radicals $F_3C\cdot$[13] and c-$C_3H_5\cdot$,[14] the charge polarization contribution to the isotope effect is very small (<2%).

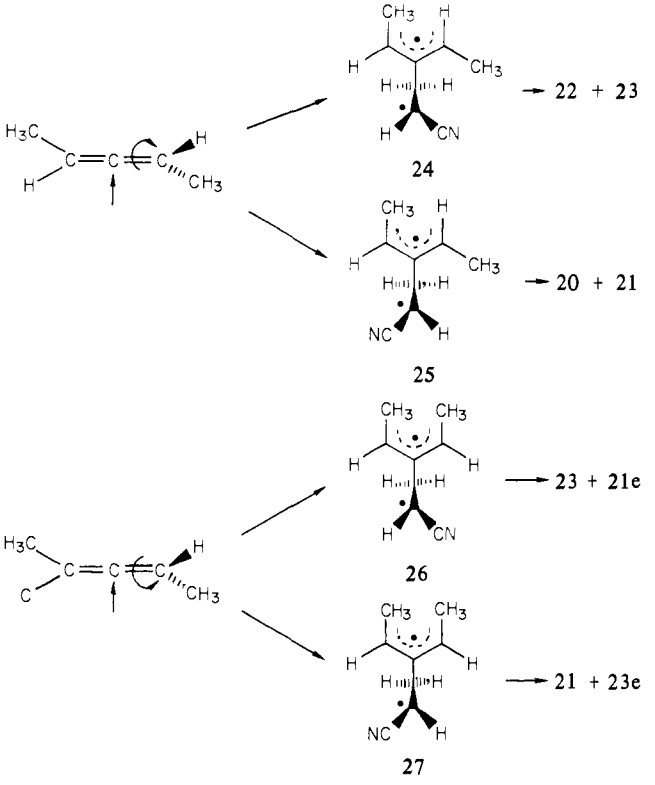
(13) Feld, M.; Stefani, A. P.; Szwarc, M. *J. Am. Chem. Soc.* **1962**, *84*, 4451.

(14) Stefani, A. P.; Chuang, L.-Y. Y.; Todd, H. E. *J. Am. Chem. Soc.* **1978**, *92*, 4168.

Scheme IV



Scheme V



due to the greater steric conjestion encountered in the transition state for ring closure to the most highly substituted end and is consistent with the results of gas-phase studies.[15] The data derived with the monoalkylallenes, however, show that as the size of the R group increases, ring closure to the *most* highly substituted end of the allyl radical increases. This steric effect seems to be in opposition to that causing the difference between the relative importance of the two modes of ring closure of the mono- and disubstituted systems. This effect appears to be due to the desire to form the least sterically crowded product; i.e., the longer C—CR bond in **12** relative to the C=CR bond in **10** and **11** allows the R group to be more distant from the other atoms in the adducts. A similar trend in product distributions was observed in the radical-chain addition of benzenethiol to substituted allenes.[6]

Comparison with the Diradical-Intermediate Cycloaddition Mechanism Proposed for Cycloaddition with Acrylonitrile. The foregoing description for the formation and ring closure of the diradical intermediates differs substantially from that suggested by Baldwin and Roy[16] to account for the stereospecificity reported for the cycloaddition of 1,3-dimethylallene with acrylonitrile, which has been proposed to proceed via a two-step, diradical-intermediate mechanism. The reaction of optically active 1,3-dimethylallene with acrylonitrile produces a mixture of the four adducts **20–23** shown in Scheme IV, all of which were optically active. Baldwin and Roy proposed[16] that "a new model for the interaction in allene–olefin (2 + 2) cycloadditions may be developed by assuming the olefin takes the least hindered approach to the allene, and the methylene group of the allene rotates to overlap with the adjacent double bond does so only in the sense specified by orbital symmetry requirements"[16,17] to form the diradical intermediates **24** and **25**, as illustrated in Scheme V. It should be noted that only a single stereoisomeric form of the allyl radical portion is present in **24** and **25**. The present results indicate that if this reaction proceeds via a diradical intermediate, **26** and **27** should also be formed. Intermediate **26** will undergo ring closure to form **23** and the enantiomer of **21**, **21e**, while **27** will result in the formation of **21** and the enantiomer of **23**, **23e**. Thus **21** and **23** should be of lower optical purity than **20** and **22**. Finally, should the acrylonitrile approach the 1,3-dimethylallene with the =CHCN portion oriented downward (the more sterically hindered process), enantiomers of all of the adducts **20–23** will be formed. Unfortunately, the optical purity of the adducts was not determined, and thus, it is impossible to assess the relative importance of the processes other than those proposed by Baldwin and Roy. It is obvious that further studies of this reaction are called for in order to clarify the details of the mechanism of this cycloaddition process.

Table VIII. High-Resolution *m/e* Values for Allene–1122 Cycloadducts

adduct	allene[b]	*m/e* calcd ($C_7H_8{}^{35}Cl_2F_2$)	obsd
10	ethyl	199.997	199.993
11		199.997	199.991
12		199.997	199.995

adduct	allene[b]	*m/e* calcd ($C_9H_{12}{}^{35}Cl_2F_2$)	obsd
10	isobutyl	228.028	228.024
11		228.028	228.033
12		228.028	228.028

adduct	allene[b]	*m/e* calcd ($C_8H_{10}{}^{35}Cl_2F_2CH_3$)	obsd
10]	isopropyl	198.989	198.986
11 and 12[c]		198.989	198.985

adduct	allene[b]	*m/e* calcd ($C_9H_{12}{}^{35}Cl_2F_2$)	obsd
10	*tert*-butyl	228.028	228.024
12		228.028	228.026

adduct	allene[b]	*m/e* calcd ($C_7H_8{}^{35}Cl_2F_2$)	obsd
7	1,1-dimethyl	199.997	199.998
9		199.997	199.998

adduct	allene[d]	*m/e* calcd ($C_8H_{10}{}^{35}Cl_2F_2$–^{35}Cl)	obsd
7 and 8[d]	1-ethyl-1-methyl	179.044	179.041
9		179.044	179.046

adduct	allene[b]	*m/e* calcd ($C_{10}H_{14}{}^{35}Cl_2F_2$–$CH_3$)	obsd
7 and 8	1-*tert*-butyl-1-methyl	227.021	227.019
9		227.021	227.019

adduct[a]	allene[b]	*m/e* calcd ($C_9H_{12}{}^{35}Cl_2F_2$)	obsd
13	3-ethyl-1,1-dimethyl	228.028	228.027

[a] Adducts 14 and 15 were identified by their NMR spectra only. [b] The R group in the allene. [c] Mixture. [d] Inseparable mixture.

(15) Montague, D. C. *Int. J. Chem. Kinet.* **1973**, *5*, 513.

(16) Baldwin, J. E.; Roy, U. V. *J. Chem. Soc. D* **1969**, 1225.

(17) Baldwin and Roy reference Hoffmann and Woodward (Hoffmann, R.; Woodward, R. B. *Acc. Chem. Res.* **1968**, *1*, 17) and unpublished observations. However, it is not obvious how orbital symmetry requirements apply to this process.

Summary

The stereochemical, relative reactivity, and kinetic isotope effect data derived from the study of the cycloaddition of substituted allenes with 1,1-dichloro-1,2-difluoroethene provides a detailed understanding of the processes involved in the formation of the diradical intermediates and their ring closure. The present reaction provides an excellent model for comparison with other cycloaddition reactions of allenes whose mechanisms are still in question.

Experimental Section

Cycloaddition Reactions of Substituted Allenes with 1,1-Dichloro-2,2-difluoroethene (1122). General Procedure. A solution of 50 mL of the allene in 1.5 mL of 1122 in an NMR tube was triply freeze degassed and sealed under vacuum. The tube was placed in a sand bath at 160 °C for 1–2 days, at which time most of the allene had reacted. The tube was chilled and cracked open, and the excess 1122 was allowed to slowly evaporate. The 300-MHz NMR spectrum of the crude reaction mixture was recorded and integrated to determine the relative yields of the adducts. All of the peaks in the 300-MHz spectra could be identified with those in the spectra of the separated adducts. No detectable cyclodimerization or polymerization of any allene was indicated to have occurred, although GC/MS indicated some cyclodimerization of the 1122 had occurred. Portions of crude reaction mixtures were separated (except as noted in Table VIII) by preparative GLC on a 24 ft × $^1/_8$ in. 20% Carbowax 20M on Chromosorb P column at 165 °C. In the few cases where complete separation could not be achieved, the NMR and MS data were recorded on the mixtures. The NMR spectra of the isolated adducts were recorded at 100 or 300 MHz by FT techniques. The data are recorded in Tables I–VI, and in the following paragraphs for adducts **13–15**. Adduct compositions were determined by high-resolution MS m/e measurements on the parent ion or the highest mass fragment when the intensity of the parent ion was very low. The high-resolution m/e's are recorded in Table VIII.

NMR data for adducts **13–15**: **13** ($CDCl_3$) δ 1.10 (t, J = 7.2 Hz, 3 H), 1.76 (br s, 3 H), 1.85 (m, 2 H), 1.92 (br s, 3 H), and 3.24 (br t, J = 7.0 Hz, 1 H); **14** δ 1.06 (t, J = 7.8 Hz, 3 H), 1.47 (s, 6 H), 2.15 (m, 2 H), and 6.05 (t, J = 7.0 Hz, 1 H); **15** δ 1.03 (t, J = 7.3 Hz, 3 H), 1.46 (s, 6 H), 2.16 (m, 2 H), and 5.63 (t, J = 7.1 Hz, 1 H).

Determination of Relative Reactivities. A 100-μL quantity of a mixture of 100 μL of heptane, 200 μL of ethylallene or 1-ethyl-1-methylallene (as the standard reference allene), and 200 μL of a substituted allene was added to approximately 3.3 mmol of 1122 that had been condensed in a 5-mm heavy-walled Pyrex tube. The mixture was triply freeze degassed and was sealed under a vacuum. The sealed tube was placed in a sand bath at 160 °C and was periodically removed, and the NMR spectrum of the reaction mixture was recorded. When the reaction had proceeded to approximately 50% consumption of the allenes (the exact extent of conversion being determined by integration of the NMR spectrum of the reaction mixture), the tube was chilled and cracked open, and the contents were quickly transferred to a micro vial equipped with a syringe cap. The micro vial was kept at dry ice temperature, and aliquots were removed by a dry ice chilled micro syringe for injection into a gas chromatograph. Reference allene- and substituted allene-to-heptane areas were measured for the before-reaction and after-reaction mixtures, which were converted to relative moles of reference and substituted allene before and after reaction by predetermined densities. The relative rates of reaction were calculated by an iterative computer program for competing second-order reactions. The GC and GC/MS chromatograms indicated that some oligomerization of 1122 had occurred; however, since all reactions were carried out to approximately the same extent in a substantial excess of 1122, no correction was made in the calculations on the time-dependent concentration of 1122.

Determination of the Kinetic Isotope Effects in the Reaction of 1,1-Dimethylallene with 1122. k_{H_2}/k_{D_2}. A 90-μL quantity of a mixture of 1,1-dimethylallene and its 3,3-d_2 analogue (32.56 ± 0.21% 3,3-d_2 determined by mass spectrometric techniques) was placed in an NMR tube with approximately 3.3 mmol of 1122. The contents of the tube were triply freeze degassed, and the tube was sealed under vacuum. The tube was heated in a sand bath at 160 °C. The tube was periodically removed and the NMR spectrum was recorded. When the reaction was 47% complete, the contents of the tube were chilled, the tube was opened, and the unreacted 1,1-dimethylallene and 1122 was removed on a vacuum line. The recovered 1,1-dimethylallene was analyzed by mass spectrometry, showing the presence of 32.23 ± 0.43% 3,3-d_2. The mixture of adducts was separated by preparative GLC and the individual adducts were analyzed by mass spectrometry, showing adduct **7** (R = CH_3) (86.5% of the mixture) to contain 34.28 ± 0.36% d_2 and adduct **9** (R = CH_3) to contain 31.20 ± 0.46% d_2. (All peak intensities were corrected for P + 2 and P − 2 contributions.)

k_{H_6}/k_{D_6}. A 60-μL quantity of a mixture of 1,1-dimethylallene and its 1,1-bis(trideuteriomethyl) analogue (33.59 ± 0.25% d_6) in 3.3 mmol of 1122 was reacted as described above to 58.4% consumption of the allene mixture. The recovered unreacted dimethylallene contained 35.98 ± 0.19% d_6, adduct **7** (88.6% of the adduct mixture) contained 33.43 ± 0.08% d_6, and adduct **9** contained 38.41 ± 0.27% d_6.

Acknowledgment. Partial support of this research was provided by the National Science Foundation (Grant No. CHE77-06827). We thank Donald Schifferl of our department for assistance in obtaining the 300-MHz NMR spectra.

Registry No. 7a, 30758-33-9; **7b**, 81583-62-2; **7c**, 81583-63-3; **8b**, 81583-64-4; **8c**, 81583-65-5; **9a**, 30908-56-6; **9b**, 81583-66-6; **9c**, 81583-67-7; **10a**, 81583-68-8; **10b**, 81583-69-9; **10c**, 81583-70-2; **10d**, 81583-71-3; **11a**, 81583-72-4; **11b**, 81583-73-5; **11c**, 81583-74-6; **12a**, 81583-75-7; **12b**, 81583-76-8; **12c**, 81583-77-9; **12d**, 81583-78-0; **13**, 81583-79-1; **14**, 81583-80-4; **15**, 81583-81-5; (1122), 79-35-6; $C_6H_5S\cdot$, 4985-62-0; ethylallene, 591-95-7; isobutylallene, 13865-36-6; isopropylallene, 13643-05-5; *tert*-butylallene, 26981-77-1; 1,1-dimethylallene, 598-25-4; 1-ethyl-1-methylallene, 7417-48-3; 1-*tert*-butyl-1-methylallene, 7417-50-7; 3-ethyl-1,1-dimethylallene, 29212-09-7.

Cycloaddition Reactions of Allenes with *N*-Phenylmaleimide. A Two-Step, Diradical-Intermediate Process

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Contribution from the Department of Chemistry, University of Notre Dame, Notre Dame, Indiana 46556. *Received October 5, 1981*

Abstract: The stereoselectivities, chemoselectivities, relative reactivities, and kinetic isotope effects have been determined in the cycloaddition reactions of substituted allenes with *N*-phenylmaleimide. The comparison of these results with those derived from the studies of the cycloaddition of 1,1-dichloro-2,2-difluoroethene and the radical-chain addition of benzenethiol to allenes strongly indicates that the cycloadditions with *N*-phenylmaleimide occur via a two-step, diradical-intermediate process. The stereochemical features controlling the formation of the stereoisomeric diradical intermediates and their ring closures are discussed. In addition to the cycloaddition processes, competitive ene reactions occur to produce intermediate dienes, which react further to produce 1:2 adducts or nonreactive alkyne-containing 1:1 adducts. These ene reactions also appear to proceed via diradical intermediates.

Considerable attention has been devoted to the study of cycloaddition reactions of allenes. Stereochemical studies have revealed that the stereochemistry about both the alkene and allene portions is retained. The cycloaddition of 1,1-dimethylallene with dimethyl fumarate has been reported to produce two adducts in which >99% stereoselectivity is retained,[1]

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