(retention time of 29 min) was identified as methyl *trans*-2-methylcyclopentanecarboxylate and the second component (retention time of 36 min) tentatively identified as a mixture of *cis*- and *trans*-3-methylcyclopentanecarboxylic acid methyl esters. This is in agreement with the published analysis given by Hill:[39] 300-MHz ^{1}H NMR ($CDCl_3$) δ 1.03 (d, J = 6.5, 3 H), 1.15 (m, 1 H), 1.63 (m, 2 H), 1.78–1.95 (2 overlapping m, 3 H), 2.10 (m, 1 H), 2.23 (m, 1 H), 3.65 (s, 3 H).

Reaction of *cis*-4-Methyl-3-phenylcyclopentene with MCPBA. To a solution of purified *cis*-4-methyl-3-phenylcyclopentene (ca. 25 mg obtained from prep GC) in 1 mL of CH_2Cl_2 was added excess *m*-chloroperoxybenzoic acid (MCPBA). Stirring was continued until TLC showed complete conversion to product. GC analysis showed the appearance of one new major peak, retention time of 7.8 min at 115 °C. The solution was washed with 1 M NaOH and water and dried over Na_2SO_4. Analytically pure material was obtained by chromatography (1:50:50 CH_3CN–hexanes–CH_2Cl_2). Chiral GC analysis showed only one peak at 115 °C, run time 28.4 min: 300-MHz ^{1}H NMR ($CDCl_3$) δ 0.55 (d, J = 6.8, 3 H), 1.43 (m, 1 H), 2.17 (m, 1 H), 2.25 (m, 1 H), 3.30 (d, J = 7.5, 1 H), 3.54 (d, J = 2.6, 1 H), 3.70 (d, J = 2.2, 1 H), 7.05 (d, 2 H), 7.30 (m, 3 H).

Reaction of *trans*-4-Methyl-3-phenylcyclopentene with MCPBA. The procedure was identical with that used to prepare the epoxide from the *cis*-cyclopentene. From *trans*-4-methyl-3-phenylcyclopentene, two new peaks were observed in the GC at 115 °C: retention times of 7.1 and 7.4 min in a ratio of 3:1. Chiral GC analysis at 115 °C gave three peaks, run times of 24.7, 25.0, and 25.5 min. The first two peaks were due to the enantiomers of the major epoxide. Underloaded column chromatography (1:50:50 CH_3CN–hexanes–CH_2Cl_2) gave separation of the two regioisomers for identification purposes: 300-MHz ^{1}H-NMR of the major product ($CDCl_3$) δ 0.93 (d, J = 6.7, 3 H), 1.36 (ddd, J = 1.1, 9.8, 14.1, 1 H), 1.75 (m, 1 H), 2.31 (dd, J = 7.0, 13.9, 1 H), 2.46 (d, J = 9.7, 1 H), 3.40 (br s, 1 H), 3.52 (br s, 1 H), 7.34 (m, 5 H).

Reaction of *trans*-4-Methyl-3-phenylcyclopentene with NBS followed by NaOH. *N*-Bromosuccinimide (NBS, 40 mg) was added to an ice-cooled solution of purified **25** (33 mg, 0.2 mmol) in 0.5 mL of water. This was warmed gently with a heat gun and then stirred at room temperature for 2 h at which time tLC indicated consumption of starting material. The aqueous solution was extracted with ether; the extracts were washed with brine and concentrated. The residue was then stirred with 30% aqueous NaOH (1 mL) for 1 day. The aqueous solution was extracted with pentane, the extracts were washed with 1 M HCl and brine, dried, and concentrated. GC analysis (115 °C) showed only one peak with retention time of 7.4 min. ^{1}H NMR analysis showed this to be identical with the minor isomer from the epoxidation of the same substrate with MCPBA: 300-MHz ^{1}H NMR ($CDCl_3$) δ 1.12 (d, J = 7.4, 3 H), 1.70 (m, 1 H), 2.14 (m, 2 H), 2.94 (br s, 1 H), 3.42 (br s, 1 H), 3.64 (br s, 1 H), 7.25 (m, 5 H).

General Techniques for Kinetic Determinations. Pyrolysis of the vinylcyclopropane **2** and 1-phenyl-2,5-hexadiene, **11**, were carried out in sealed tubes. Aliquots (10–20 mL) of a solution of the substrate and internal standard (tetralin or phenylcyclohexane) were injected into a thick-walled kinetics tube. This was subjected to three freeze–pump–thaw cycles at 10^{-6} Torr and sealed at the constriction. The tube was placed in a holder and immersed in a constant temperature bath.

Constant Temperature Bath. The inside medium was sodium nitrite/potassium nitrate (50:50 w/w) fused salt. The temperature was maintained to ±0.1 °C by a precision temperature controller (Bayley Instrument Co., Model 124). The salt was heated by an MIS Chromalox heating cable (Niagara Electric Sales Co.) wound spirally against the inside wall of the stainless steel container. The stirrer assembly consisted of a three-blade, 2-in. diameter propeller attached to an 18 in. × $^5/_{16}$ in. stainless steel shaft. A ceramic coupling insulated the shaft in the bath from the shaft of the stirrer motor (Lightnin', Model L). The motor was supported by two 3.75 in. × 4.5 in. column clamps attached to a stainless steel frame constructed above the bath. Temperatures were measured with an uncalibrated single junction iron-constantan thermocouple connected to a millivolt potentiometer (Leeds and Northrup Co.) using an external ice water bath for reference.

Vapor Pressure Measurements. A 25-mL three-neck flask was charged with vinylcyclopropane **2** (70.2 mg, 0.44 mmol) and tetralin (6.321 g, 47.8 mmol). The flask was warmed to the appropriate temperature in an oil bath. When the flask had equilibrated, N_2 was blown over the solution with the effluent gas trapped in an acetone/CO_2 cooled bath. This was analyzed by GC for mole ratio of VCP:tetralin using cyclododecane for reference. Retention times, min (115 °C): tetralin, 2.5; cyclododecane, 5.6; vinylcyclopropane, 6.0. The calculated mole ratios are shown below.

temp, °C	mol **2**/mol tetralin
153 (3)	2.67 (2) × 10^{-3}
172 (3)	2.99 (3) × 10^{-3}
184 (4)	3.44 (2) × 10^{-3}

Calculations. All activation parameters were evaluated by direct nonlinear least-squares fit to the raw data on concentration vs time and temperature. These data are included in the supplementary material.

Acknowledgment. Support of this work by the NIH (Grant GM27022) and AFOSR (Grant 87-0165) is gratefully acknowledged.

Supplementary Material Available: Kinetic data for pyrolysis of compounds **2** and **11** (7 pages). Ordering information is given on any current masthead page.

(39) Hill, R. K.; Foley, P. J.; Gardella, L. A. *J. Org. Chem.* **1967**, *32*, 2330.

Effect of High Pressure on the [2 + 2] Cycloaddition of Difluoroallene and (*Z*)-β-Deuteriostyrene

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1,1-Difluoroallene and (*Z*)-β-deuteriostyrene undergo a [2 + 2] cycloaddition to form two regioisomeric products, (*Z*)- and (*E*)-4-deuterio-2,2-difluoro-3-phenyl-1-methylenecyclobutane, **1** (major), and (*Z*)- and (*E*)-2-deuterio-3-phenyl-1-(difluoromethylene)cyclobutane, **2** (minor), each with different degrees of stereochemical retention. The imposition of high pressure (2–13 kbar) on the reaction alters both the regioselectivity and the stereoselectivity of the reaction significantly, decreasing the former and increasing the latter. A mechanism involving two kinetically distinct diradical intermediates is proposed to rationalize the results.

The mechanism of the typical thermal [2 + 2] cycloaddition reaction is considered to be pretty well understood. No one disputes that such reactions are nonconcerted and involve diradical intermediates. Bartlett and

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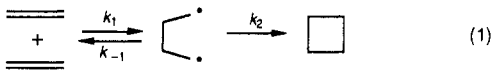
co-workers, in their elegant stereochemical studies more than 25 years ago, experimentally demonstrated the lack of stereospecificity inherent in a nonconcerted mechanism.[1]

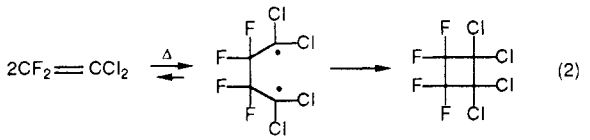
The mechanism, depicted generally in eq 1, is however not usually all that clearly defined. For example, while



(1)

the key to the efficacy of a particular [2 + 2] reaction is obviously the "goodness" of the initial carbon–carbon bond-formation step (and this step is generally considered to be rate-determining), just as critical is the relative efficiency of k_{-1} and k_2. The general reversibility of the initial step has been amply demonstrated, although it is an invisible process for most [2 + 2]'s that have been studied. Therefore it is likely that k_2 might often have some rate-determining character, especially in reactions of less reactive alkenes. Indeed, as one imposes increasingly high temperatures to accomplish the overall reaction, one will because of entropy factors be inevitably increasing the relative importance of k_{-1} with respect to k_2. On the other hand, imposition of ultrahigh pressures would be expected to enhance the efficacy of the overall process, both increasing the rate of k_1 and enhancing the relative competitiveness of k_2 versus k_{-1}.[2]

Included in our understanding of this reaction is the fact that the reaction is not all that common, with only reasonably activated alkenes readily undergoing the reaction in decent yields.[3] Fluorinated alkenes exhibit unusual reativity in [2 + 2] reactions, probably because of the significant thermodynamic advantage derived from conversion of an sp^2-hybridized CF_2 group into an sp^3-hybridized CF_2 group (eq 2). This thermodynamic benefit



(2)

would serve to lower the activation energy for the first carbon–carbon bond-forming step (k_1) of the cycloaddition, and it would reduce the reversibility of this step as well since the newly formed CF_2–CF_2 σ bond is known to have a higher bond dissociation energy than its hydrocarbon counterpart.[4] In many cases fluorine-containing addends would also give rise to a greater thermodynamic driving force for k_2, since it is known that the apparent ring strain of fluorinated cyclobutanes can be considerably less than for the comparable hydrocarbon systems.[5]

Details of the nature and behavior of those diradicals formed as intermediates in [2 + 2] cycloadditions are very difficult to obtain. The regiochemistry of [2 + 2] reactions is generally determined by the initial carbon–carbon bond-forming step, but the stereochemistry of the overall reaction is obviously the result of complex, dynamic interconversions of conformationally related diradical intermediates. Thus the initially formed diradical undergoes interconversion with other, conformationally related diradicals in competition with cyclization to product and dissociation to starting materials.

The details of the diradical interconversions are very difficult to probe mechanistically. Kinetic studies, stereochemical studies, and isotope effect studies all can and have provided insight, but generally, by their nature, they give information about the overall reaction and/or the rate-determining step. All that occurs between formation of the first intermediate and formation of the products has for the most part proved to be inscrutable.

There have been attempts to scrutinize the behavior of various 1,4-diradicals as generated by means other than the [2 + 2] cycloaddition in the hope that insight would be provided on the cycloaddition mechanism. Such studies have involved deazetation reactions wherein loss of nitrogen gives rise to 1,4-diradical intermediates[6] and thermal isomerizations wherein a carbon–carbon bond homolysis leads to a 1,4-diradical.[7] Unfortunately, in spite of the observation of some very interesting chemistry in and of itself, including learning a lot about how dynamically interconverting diradicals do behave,[8] the results of such studies cannot be related to the observed behavior of those 1,4-diradicals formed in [2 + 2] cycloadditions. This conclusion recognizes the fact that the conformational, thermodynamic, and dynamic profile of that diradical intermediate immediately formed in the initial carbon–carbon bond-forming step of a [2 + 2] cycloaddition is very different from those formed from nitrogen extrusion or C–C bond homolysis processes. The 1,4-diradicals formed from each of these different processes enter the energy surface at entirely different points with entirely different energies and dynamic momenta.

Thus, if one wants to learn about the details of the mechanism of the [2 + 2] cycloaddition reaction, which means trying to understand the nature, both structural and dynamic, of the intermediate 1,4-diradical system, one must do it by studying [2 + 2] reactions!

Allene [2 + 2] Cycloadditions

Allenes have been demonstrated to be advantageous addends for use in [2 + 2] mechanistic studies.[9,10] First, they are relatively reactive in [2 + 2] cycloadditions, with the result that extreme conditions are not necessary for their study. In such reactions, while there are exceptions, initial bond formation is generally at C_2, likely because a stabilized allyl radical is formed by rotation of the methylene group of the attacked bond into planarity with the other, orthogonal π bond. Substitution on the allene molecule by virtually any substituent serves to enhance its reactivity. However, there is an aspect of allene [2 + 2] cycloadditions that provides a unique opportunity for probing mechanism. This derives from the fact that allene [2 + 2] cycloadditions have an additional branching point in the mechanism, the competition between which has the potential to provide considerable mechanistic insight (eq 3). That is, the intermediate diradical can cyclize to form either of two products, depending on which end of the allyl radical is to become incorporated into the cyclobutane ring.

(1) Wheland, R.; Bartlett, P. D. *J. Am. Chem. Soc.* **1970**, *92*, 3822, and references therein.
(2) (a) Matsumoto, K.; Sera, A.; Uchida, T. *Synthesis* **1985**, 1. (b) Stewart, C. A., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 635; (c) Rimmelin, J.; Jenner, G. *Tetrahedron* **1974**, *30*, 3081.
(3) Roberts, J. D.; Sharts, C. M. *Org. React.* **1962**, *12*, 1.
(4) (a) Rodgers, A. S.; Ford, W. G. F. *Int. J. Chem. Kinet.* **1973**, *5*, 965. (b) Chen, S. S.; Rodgers, A. S.; Chao, J.; Wilhoit, R. C.; Zwolinski, B. J. *J. Phys. Chem., Ref. Data* **1975**, *4*, 441. (c) Wagner, P. J.; Thomas, M. J. *J. Am. Chem. Soc.* **1976**, *98*, 241.
(5) Smart, B. E. *Molecular Structure* and *Energetics*; VCH Publishers: New York, 1986; Vol. 3, pp 180–183.
(6) (a) Dervan, P. B.; Uyehara, T.; Aantilli, D. S. *J. Am. Chem. Soc.* **1979**, *101*, 2069. (b) Dervan, P. B.; Santilli, D. S. *J. Am. Chem. Soc.* **1980**, *102*, 3863.
(7) Gajewski, J. J. *Hydrocarbon Thermal Rearrangements*; Academic Press: New York, 1981.
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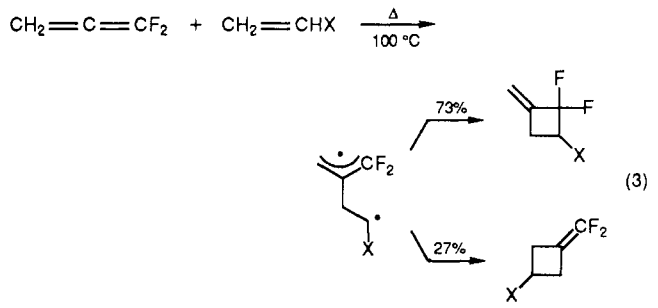
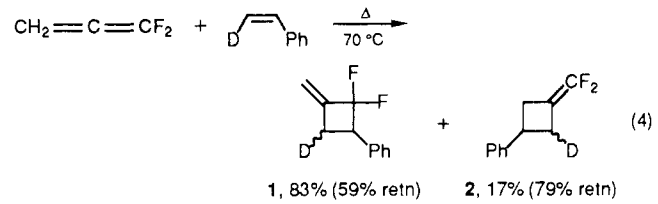
(9) Dolbier, W. R., Jr.; Burkholder, C. R. *J. Org. Chem.* **1984**, *49*, 2381.
(10) Pasto, D. J.; Kong, W. *J. Org. Chem.* **1988**, *53*, 4807, and references therein.



There is an additional advantage in the use of allenes for [2 + 2] mechanistic studies in that reversal of the first step is usually not competitive with product formation.[11] In simplifying the mechanism and ensuring that k_1 is totally rate-determining, both kinetic and stereochemical studies become more straightforward. The relative lack of competitiveness of k_{-1} is, of course, due to the fact that the allylic resonance gained by initial bond formation at C_2 of the allene must be lost in reversing the reaction. That is to say, the potential energy well in which the intermediate resides is much deeper in allene cycloadditions that it is for other [2 + 2] cycloadditions. The observed diminished reversibility indicates that the barrier to product formation is not increased as much as that for reversal to starting materials.

In our [2 + 2] studies[9,12] we have used 1,1-difluoroallene (DFA) as the allene addend of choice for two reasons. First, the fluorine substituent is *small* and would be expected to exert little if any steric effect upon the path of the reaction. While having little steric influence, the fluorine substituent nevertheless provides one with a remarkable structural label, being NMR-active. Second, the kinetic and thermodynamic factors that result from use of DFA as a [2 + 2] addend have been demonstrated to virtually assure both irreversibility of initial bond formation and kinetic control in formation of adducts. Therefore, product ratios are capable of providing intrinsic kinetic information.

Our examination of the stereochemistry of the [2 + 2] reaction between DFA and (*Z*)-β-deuteriostyrene provided us with the first indication that such studies had the potential to provide new and important mechanistic insight[13] (eq 4).

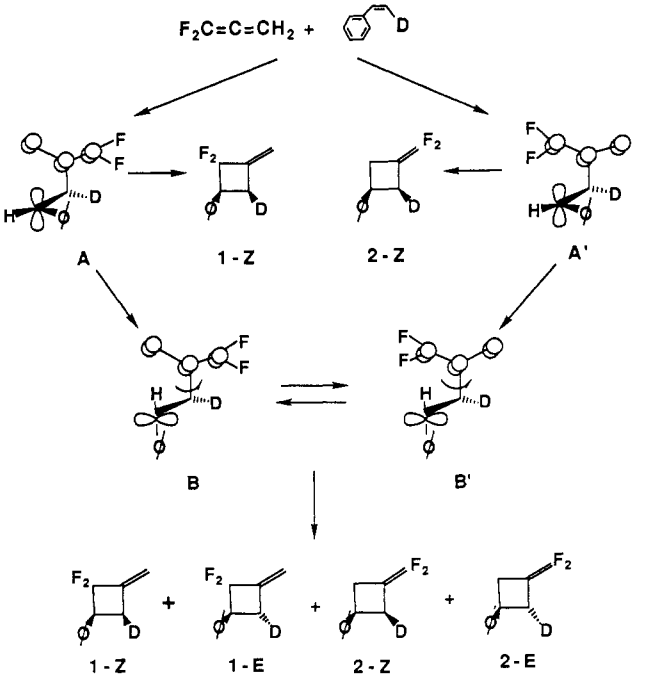


1, 83% (59% retn) 2, 17% (79% retn)

In reaction 4, two products, **1** and **2**, were obtained with different degrees of retention of stereochemistry. Such results could be rationalized only by a mechanism involving *two* kinetically distinct diradical intermediates. Scheme I depicts the proposed mechanism.

It was assumed that these two diradical "intermediates" were actually two conformationally related *systems* of diradicals, A–A′ and B–B′, which exhibit different kinetic

Scheme I



behavior.[14] In Scheme I, A and A′ are depicted as initially formed diradicals with structures consistent with minimal conformational change. Such diradicals are projected to be highly reactive and as such should exhibit relatively low regiochemical selectivity in cyclization, which should, upon cyclization, be expected to lead to products with high if not total retention of the cis configuration of the deuterium substituent relative to the phenyl substituent. Competitive with such cyclization would be a highly favorable conformational conversion to a more stable pair of intermediates. Intermediates B and B′, in contrast, are depicted as having structures within which the phenyl substituent has rotated so as to minimize nonbonded interactions, thus creating diradical intermediates that should be thermodynamically more stable and have less kinetic reactivity. While B and B′ would probably not be formed in equal amounts, they should cyclize with virtually identical regiochemistries (but clearly different from the regiochemistry exhibited by A and A′), with the result that from this mixture of B and B′, products **1** and **2** should be formed in different amounts (i.e., **1** observed to be favored), but with identical stereochemistries. Therefore if the products had derived only from intermediates A and A′ or only from intermediates B and B′, they should have been formed with identical stereochemistries. The contrary observed results are, however, consistent with the mechanistic scenario depicted in Scheme I, wherein both of the diradical intermediate systems (A, A′) and (B, B′), each expected to exhibit different regiochemical and stereochemical behavior, are involved in the formation of products.

In our mechanistic scheme we have imposed certain reasonable, but arbitrary, kinetic characteristics upon these kinetically distinct systems of diradicals in order to explain the results. Diradicals A and A′ are characterized as being highly reactive species that cyclize with high stereoselectivity, to products **1** and **2**, but which mostly are projected as converting to a more stable, less reactive system of diradicals, B, B′, which themselves cyclize to **1** and **2**, but with less stereoselectivity. If fact, if one simply assumes

(11) Lack of the reversibility has been demonstrated by (a) no observed isomerization in recovered *cis*-β-deuteriostyrene from its [2 + 2] cycloaddition reaction with DFA[13] and (b) the lack of competitive cleavage in thermal methylenecyclobutane rearrangements.[7]

(12) Dolbier, W. R., Jr.; Piedrahita, C. A.; Houk, K. N.; Strozier, R. W.; Gandour, R. W. *Tetrahedron Lett.* **1978**, 2231.

(13) Dolbier, W. R., Jr.; Wicks, G. E. *J. Am. Chem. Soc.* **1985**, *107*, 3626.

(14) An enantiomeric scheme, with enantiomeric intermediates, would result from attack from above the DFA.

total retention of stereochemistry for cyclization from A and total loss of stereochemistry for cyclization from B, one can calculate a mechanistic scenario within which the observed results would be obtained if 25% of the products were formed from intermediates A and A′ (15% of product **1** and 10% of product **2**), while 75% of the products came from diradicals B, B′ (68% of product **1** and 7% of product **2**). One can see that, consistent with the mechanistic model, the more reactive intermediates (A, A′) are seen to cyclize less regioselectively (i.e., 3:2) than are the less reactive intermediates (B, B′) (9.7:1).

One could have imposed less extreme arbitrary stereochemical requirements upon the intermediates, in which case one would have obtained qualitatively similar but quantitatively different results. The qualitative nature of Scheme I is required, however, if one is to explain the results satisfactorily.

Various probes of such a mechanism as that proposed above can be envisoned including those wherein either the allene or the styrene component would be structurally modified. Indeed, we have recently reported a study of the effect of α-substitution on the styrene component,[15] while Pasto and co-workers have examined the stereochemistry of dimethylallene–dimethyl maleate/fumarate cycloadditions,[16] with the results of such studies being generally consistent with our mechanistic scheme.

On the other hand, it was considered that a more subtle perturbation of the dynamics of this mechanism, wherein structural change along with its concomitant complications regarding steric and electronic effects on the kinetic and thermodynamic picture would not be required, might be able to provide unique insight. The probability of significant effects of very high pressure upon the regio- and stereochemical outcome of the reaction was considered to be such a potentially subtle and thus potent probe. Given $d \ln k/dP = -\Delta V^{\ddagger}/RT$,[17] it was predicted, in view of the expected $-\Delta V^{\ddagger}$ for the cyclization of the diradicals in system A as compared to little expected ΔV for any rotational conversion of A to B, that under increasingly high pressure the reaction could be induced to derive increasingly from diradicals A and A′, and thus product formation should become less regioselective and more stereoselective. In an earlier communication we reported on the effect of pressure on the regioselectivity of this reaction, results totally consistent with the model-derived predictions discussed above.[18] In this paper, we present a complete study of the effect of high pressure (1.8–13 kbar) on the regio- and stereochemistry of the [2 + 2] cycloaddition between 1,1-difluoroallene and (*Z*)-β-deuteriostyrene, the results of which, we believe, convincingly demonstrate the overall validity of our earlier proposed mechanism.

Results and Discussion

Individual polyethylene reaction vessels containing appropriate amounts of 1,1-difluoroallene, (*Z*)-β-deuteriostyrene, and hydroquinone (free-radical inhibitor) were pressurized to pressures from 1.8 to 13.0 kbar. After a period of time the vessels were opened and products analyzed by GC to obtain ratios of regioisomers. **1** and **2** were the only products formed other than the inevitable oligimers of DFA. After separation by preparative GC, the product stereochemistries for the individual regioisomers were determined by proton NMR.

Table I. Pressure Dependence of Product Ratios for the DFA/(*Z*)-β-Deuteriostyrene Reaction

P, kbar	1,[a] %	*Z*:*E* ratio[b]	2,[a] %	*Z*:*E* ratio[b]
1.8	86.1 ± 0.13	66.3:33.7	13.9	88.0:12.0
4.1	84.1 ± 0.06	71.6:28.4	15.9	89.9:10.1
5.9	82.1 ± 0.27	73.2:26.8	17.9	91.2:8.8
8.0	77.7 ± 0.26	74.5:25.5	22.3	92.3:7.7
11.0	70.6 ± 0.50	83.2:16.8	29.4	94.6:5.4
13.0	69.6 ± 0.09	85.5:14.5	30.4	95.2:4.8

[a] As determined by GLPC. [b] Standard deviations in the *Z*:*E* ratios for **1** were no more than ±0.16%, and for **2**, ±0.67%, by ^{1}H NMR.

Table II. Calculated Fractions of Products Deriving from Intermediates A and B (Assuming Mechanistic Model)

	% total product		% product 1		% product 2	
P, kbar	from A	from B	from A	from B	from A	from B
1.8	38.7	61.3	28.1	58.0	10.6	3.3
4.1	49.1	50.9	36.4	47.7	12.7	3.2
5.9	52.8	47.2	38.0	44.1	15.0	3.2
8.0	56.9	43.1	38.1	39.6	18.9	3.4
11.0	73.1	26.9	46.8	23.8	26.3	3.2
13.0	76.9	23.1	49.5	20.2	27.4	2.9

The results of these experiments are given in Table I, from which it can be seen that there is a very noticeable effect of pressure upon both the regiochemistry and the stereochemistry of product formation, with the regioselectivity of the reaction diminishing significantly as one increases the pressure, while the stereoselectivity increases for both products. Indeed, at 13 kbar the minor product, **2**, exhibits 95% retention of the cis configuration. As indicated in Table II, again assuming the proposed quantitative mechanistic model, such a degree of stereochemical retention translates into an increase to about 77% of product formation deriving from intermediate A (as opposed to 25% at ambient pressure).[13] This comprises a very significant perturbation upon the outcome of this reaction, and it speaks very clearly in terms of the mechanistic insight that it provides. The results indicate that the imposition of high pressure upon the cycloaddition reaction gives rise to a pathway that is both less regioselective and more stereoselective. This is consistent with our hypothesis of a highly reactive initially formed intermediate that cyclizes nonregioselectively and highly stereoselectively via a process that at ambient pressure is unfavorably competitive with conformational conversion to a less highly reactive diradical intermediate. With cyclization of A having a negative volume of activation and its conformational conversion expected to have little ΔV, the imposition of high pressure would be expected to lead to results such as those observed. Recognizing that $(d \ln k_A/k_B)/dP = -\Delta\Delta V^{\ddagger}_{A-B}/RT$,[17] one can calculate the apparent difference in activation volumes for the two competitive paths to be −3.6 cm^3/mol.

In terms of the details of our hypothesized mechanism, one cannot be certain, of course, as to the *structures* of intermediates A and B. Those depicted merely represent reasonable conjectures as to what might be occurring on the energy surface. The present work does, however, give clear insight into the *dynamic* nature of these intermediates. Again, while our choice of extreme stereochemical behavior for the intermediates (i.e., total stereospecificity for cyclization from A and total *lack* of stereoselectivity for cyclization from B) is quantitatively arbitrary, it indeed cannot be far from the fact in view of our observation that the minor product, **2**, exhibits such high stereoselectivity

(15) Dolbier, W. R., Jr.; Seabury, M. J. *Tetrahedron Lett.* **1987**, *28*, 1491.
(16) Pasto, D. J.; Yang, S. H. *J. Am. Chem. Soc.* **1984**, *106*, 152.
(17) Klotz, I. M.; Rosenberg, R. M. *Chemical Thermodynamics*, 4th ed.; Bemjamin/Cummings: Reading, MA, 1986; p 277.
(18) Dolbier, W. R., Jr.; Seabury, M. J. *J. Am. Chem. Soc.* **1987**, *109*, 4393.

(95%) for its formation at 13.0 kbar.

In our earlier communication on the response of the regiochemistry of this reaction to high pressure, the effect of viscosity changes was also probed and discussed.[18] Indeed, it was observed that an increase in viscosity also led to the observation of a decrease in regiochemistry for the reaction. Some time ago, Firestone proposed that observed effects on rate, which were attributed to negative volumes of activation, could just as well be rationalized as deriving from viscosity effects.[19] However, extrapolations of our measured viscosity effects at ambient pressure to the utilized high pressures led us to conclude that viscosity effects could not be used to explain *all* of the observed effects on regiochemistry and that differences in volumes of activation were probably the major source of the observed effects.

While we have not carried out extensive new experiments on the effects of viscosity, one experiment made it quite clear that viscosity effects do play an important role in the effects we have observed. In the earlier reported high-pressure regiochemical study all experiments were carried out using pentane as a solvent. However, in the present study, all experiments were carried out without solvent. In a comparison of the regiochemical data from the two studies, one finds that all of the runs done in pentane solvent resulted in significantly greater observed regioselectivity than those done at analogous pressures but without solvent, that is, effectively with styrene as solvent. Thus in a plot of regiochemistry versus pressure, the two sets of data gave parallel straight lines. To be certain that these disparate results, achieved by using different apparatuses and run by different workers, were indeed simply the result of the presence of pentane solvent in the earlier work, an additional experiment was carried out at the end of our current study, using non-deuterium-labeled styrene and pentane as solvent (pentane:styrene = 13:1).

Indeed, the reaction, which was carried out at 4.1 kbar, was significantly more regioselective, giving a product ratio of 6.25 (86.2% **1**) versus the 5.3 (84.1% **1**) observed in the solventless experiment. In fact this value of 6.25 was totally consistent with the Seabury data reported earlier.[18] The only logical explanation for the difference in results with and without solvent is the effect of diminished viscosity in the experiments run in pentane. Thus the viscosity of the medium does apparently exert a significant effect upon the regiochemical and probably also the stereochemical outcome of this reaction, although we did not examine the latter.

It is difficult to evaluate the relative importance of the viscosity effects versus the effects that are due to differences in volume of activation. In our earlier communication, wherein we attempted to distinguish viscosity and volume effects, we did not distinguish shear viscosity, which we measured for the solvents that we used, from microviscosity, which is actually what one needs to know to evaluate the effect of solvent viscosity on microscopic molecular events. It has indeed been suggested before that the macroscopic parameter η_s is not a good measure of the effective viscosity experienced by the twisting molecule.[20] Potentially it should be possible to evaluate experimentally such factors, but such is outside the scope of this work. Therefore it is not possible to determine unambiguously the relative importance of viscosity effects and $\Delta V^{\ddagger}$ effects within the context of the present study.

In the end, for the purpose of this mechanistic study, it is immaterial whether the observed effects are the results of the relative effects of viscosity on the partitioning of intermediate A between cyclization to products **1** or **2** versus conformational conversion to B or the whether they are the result of differences in the volumes of activation for the two competitive processes. The *conclusions* that derive from the results are the same regardless of the cause.

Experimental Section

Preparation of Reactants. (Z)-β-Deuteriostyrene[13] and difluoroallene[21] were prepared following previous reported procedures.

Reaction Vessel Preparation. The reaction containers were constructed of flexible low-density polyethylene tubing (0.17-in. i.d., 0.25-in. o.d.). One end of tubing is flame sealed, and (Z)-β-deuteriostyrene (0.3 mL) is introduced along with bit of hydroquinone inhibitor. The open end of this tubing is heated until it is transparent; then the tapered end of Pyrex tubing ($^3/_8$ in.) bearing a ground-glass joint is inserted approximately 3 cm into this end of the warm polyethylene tube. A seal between the Pyrex and the polyethylene forms upon cooling. Having the ground glass joint fitted onto the polyethylene tube allows standard vacuum line techniques to be employed. Difluoroallene can then be vacuum transferred into the reaction tube (7:1 (Z)-β-deuteriostyrene to difluoroallene). The polyethylene tube is then sealed by using a cool flame. To prevent rupture of the vessel, the bottom of the reaction tube must remain in liquid N_2 while the new top seal cools to ambient temperature. The sample tube is removed from the liquid N_2 and allowed to reach room temperature before it is introduced into the high-pressure apparatus.

High-Pressure Apparatus. All high-pressure experiments were performed at ambient temperature using a double-walled piston-and-cylinder designed apparatus[22] with an inner liner of $^3/_4$-in.-diameter cylinder bore having a maximum working pressure of 13.6 kbar. The sample tubes were pressurized from 1.8 to 13.0 kbar over 142–0.5 h. The longer reaction times were necessary at lower pressures to ensure acceptable yields. Combined yields of products **1** and **2** varied from 66% to 98% Product ratios were found to be independent of reaction times.

Isomer Ratio Analyses. Ratios of products **1** and **2** were determined from an average of three or more injections, using a Hewlett-Packard 5709 gas chromatograph (FID) with a 10-ft 20% QF-1 column. 2,2-Difluoro-3-phenyl-1-methylenecyclobutane (**1**) and 3-phenyl-1-(difluoromethylene)cyclobutane (**2**) have been previously characterized.[13]

1 and **2** were separated preparatively for NMR analysis using a Varian-Aerograph 90-P gas chromatograph (TCD, $^1/_4$ in. × 10 ft, 20% QF-1 column), and individual stereoisomer ratios were determined by using a Varian VXR-300 300-MHz NMR as previously described.[13] T_1 population inversion experiments showed the longest T_1 of compounds **1** and **2** were found to be <5.7 and <3.8 s, respectively; thus respective pulse delays of 28 and 18 s were used.

Solvent Effect Experiment. Pentane was added to (Z)-β-deuteriostyrene (19:1 ratio) in a reaction vessel. The reaction vessel was fitted with a Pyrex tube and charged with difluoroallene, and the reaction run as described above.

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Registry No. (Z)-**1**, 124200-33-5; (E)-**1**, 124200-34-6; (Z)-**2**, 96245-40-8; (E)-**2**, 96245-39-5; DFA, 430-64-8; (Z)-PhCH=CHD, 21370-59-2.

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