Multiplicity of Mechanisms in the Cope Rearrangement

BY GEORGE S. HAMMOND AND CHARLES D. DEBOER[1]
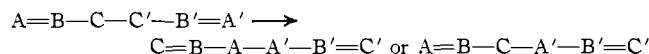
Thermal rearrangement of cis-1,2-divinylcyclobutane, trans-1,2-divinylcyclobutane, trans-1,2-dimethyl-1,2-divinylcyclobutane, and trans-1-isopropenyl-2-methyl-2-vinylcyclobutane have been studied in detail. The kinetic parameters show clearly that cis-1,2-divinylcyclobutane rearranges by a different mechanism from that which obtains with the compounds in which the two unsaturated functions are trans to each other. The latter are believed to go through biradical intermediates. Optically active trans-1,2-divinylcyclobutane undergoes racemization as well as rearrangement and produces 4-vinylcyclohexene having a trace of residual activity. Consequently, we infer that the rates of ring closure in the intermediate are of the same order of magnitude as the rates of rotation about single bonds.

Bisallylic hydrocarbons and their relatives undergo thermal rearrangements[2,3] illustrated by the rearrangement of 3,4-dimethyl-1,5-hexadiene. The process has

been known as the Cope rearrangement, although, to our knowledge, the name has only been applied to examples such as the above in which both of the allylic units undergo structural inversion. Other types are now known in which only one unit is inverted.[4] Furthermore, the fact that Cope rearrangements can be carried out in the vapor phase without extensive mixing of the units from unsymmetrical systems, and the elegant stereochemical studies of Doering and Roth,[5] show that the reactions can, under suitable circumstances, proceed by totally concerted mechanisms. This fact has led to reference to Cope rearrangements as a mechanistic type. As we will demonstrate, intramolecular rearrangements may also occur by stepwise mechanisms. Consequently, we advocate that the term "Cope rearrangement" be used to describe all processes of the following stoichiometric types, irrespective of the detailed mechanisms.

A=B—C—C'—B'=A' ⟶
       C=B—A—A'—B'=C' or A=B—C—A'—B'=C'

Several years ago Vogel[6] reported the relatively facile rearrangement of cis-1,2-divinylcyclobutane to cis,cis-1,5-cyclooctadiene. At the same time it was implied
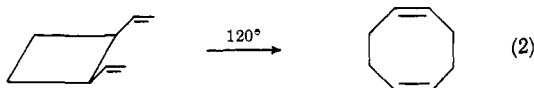

that the trans isomer rearranged only by cracking to butadiene followed by redimerization. We have found that the trans isomer rearranges by an intramolecular path. Because our studies of photodimerization of conjugated dienes[7] made available a number of appropriate materials, we have studied the kinetics of such rearrangements in detail.

Results and Discussion

The rearrangement of trans-1,2-divinylcyclobutane gives 4-vinylcyclohexene and cis,cis-1,5-cyclooctadiene. In some runs traces of cis-1,2-divinylcyclobutane were detected so it is entirely possible that the cis compound

is an intermediate in the formation of cyclooctadiene. In flow systems only traces of butadiene are dimerized under conditions such that trans-1,2-divinylcyclobutane is more than 50% rearranged. The ratios of products remain constant with time, arguing against a principal mechanism where butadiene is formed and then dimerized thermally to the products. Compounds 2
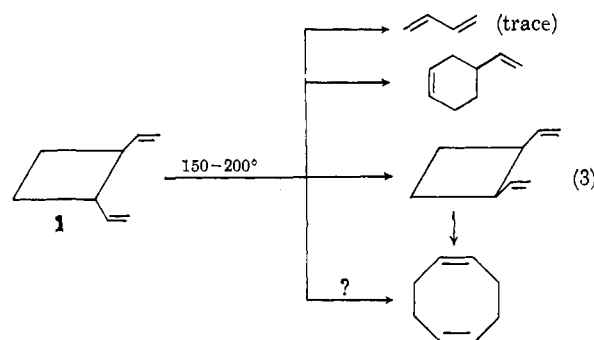
and 3, which are obtained by dimerization of isoprene, have been shown to undergo similar rearrangements.
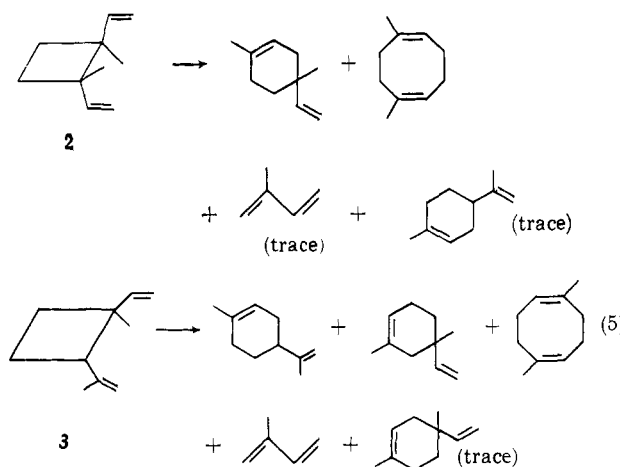
All of the reactions are cleanly first order with respect to starting materials as is illustrated in Fig. 1 and, as is shown in Fig. 2, data taken at different temperatures can be fitted to good Arrhenius plots. Table I summarizes the rate data and the activation parameters for the several reactions. Optically active 1, of unknown optical purity, was prepared by the method of Brown[8] by partial reduction of the divinyl compound with the product of addition of diborane to α-pinene. When the active material was subjected to the usual reaction conditions it lost optical activity at a rate faster than the rate of appearance of rearrangement products, and recovered starting material was found

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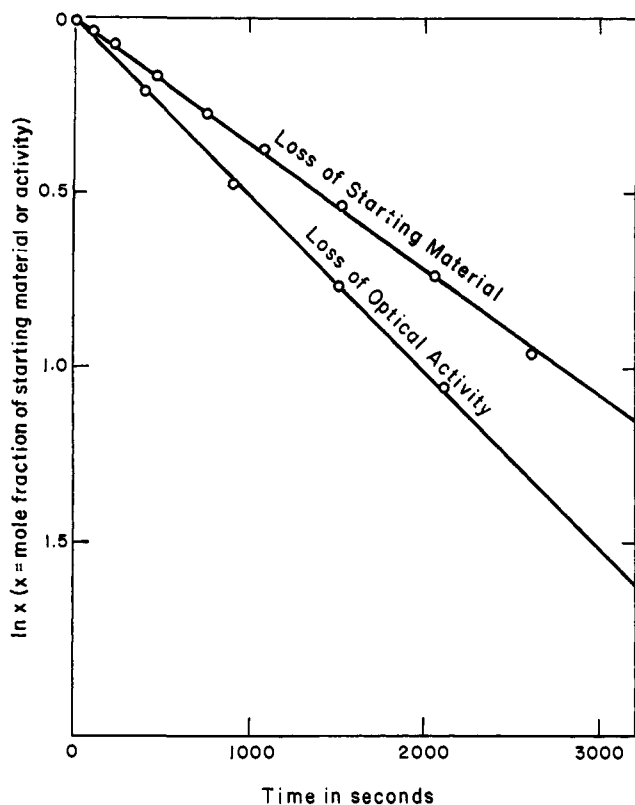
Fig. 1.—Rates of reactions of *trans*-1,2-divinylcyclobutane at 187.3°.

to be partially racemized. The rates of racemization were also measured and data are included in Table II.

TABLE I

RATES OF REARRANGEMENT

Compound	T, °C.	k, sec.$^{-1}$	$\Delta H^{\ddagger}$, kcal. mole^{-1}	$\Delta S^{\ddagger}$, e.u.
	139.3	$4.66 \pm 0.16 \times 10^{-6}$		
	153.9	$1.85 \pm .03 \times 10^{-5}$		
	175.2	$1.32 \pm .06 \times 10^{-4}$	34.0	-1.2
	187.3	$3.58 \pm .09 \times 10^{-4}$		
	210.3	$2.40 \pm .08 \times 10^{-3}$		
	65.4	$2.55 \pm .06 \times 10^{-5}$		
	79.8	$1.09 \pm .05 \times 10^{-4}$	23.1	-11.7
	96.8	$5.12 \pm .15 \times 10^{-4}$		
	108.5	$1.39 \pm .05 \times 10^{-3}$		
	92.4	$1.08 \pm .02 \times 10^{-5}$		
	109.2	$7.21 \pm .25 \times 10^{-5}$	30.9	$+2.9$
	121.9	$2.77 \pm .12 \times 10^{-4}$		
	135.7	$1.08 \pm .02 \times 10^{-3}$		
	135.7	$1.72 \pm .21 \times 10^{-5}$		
	149.2	$6.59 \pm .16 \times 10^{-5}$	34.2	$+3.1$
	161.3	$2.14 \pm .04 \times 10^{-4}$		
	176.8	$8.70 \pm .10 \times 10^{-4}$		

All of the data point to a mechanistic discontinuity between the rearrangement of *cis*-1,2-divinylcyclo-butane (4) and the compounds in which the unsaturated groups are *trans* to each other. Compound 4 gives only a single major product, whereas the others give two or more principal products. Furthermore, rearrangement of 4 is characterized by a low activation
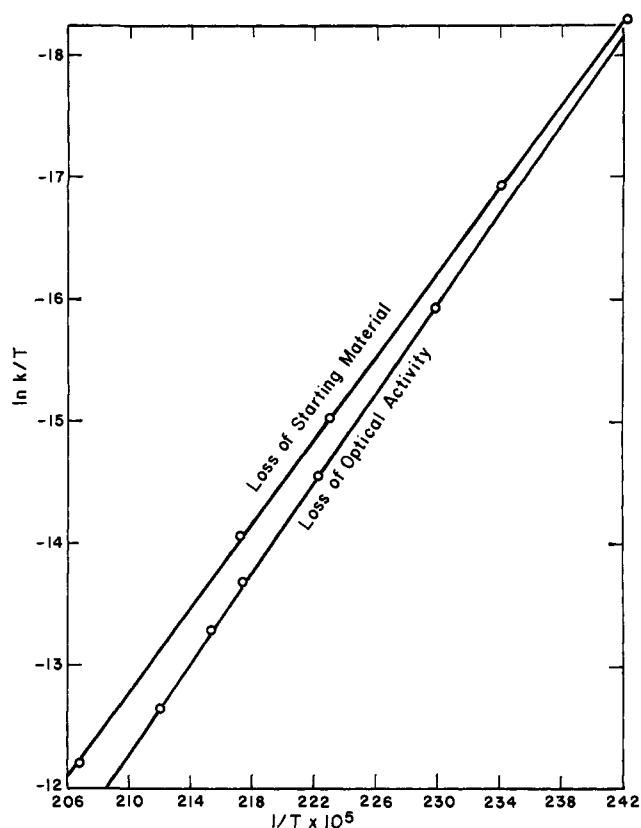

Fig. 2.—Variation of rates of reaction of *trans*-1,2-divinylcyclo-butane with temperature.

enthalpy and a substantial negative entropy of activation. The *trans* compounds all have larger activation enthalpies and near zero entropies of activation. Obviously the concerted mechanism proposed by Vogel is appropriate for the *cis* compound; the fact that the entropy of activation is large and negative indicates that the system becomes more constrained in the transition state.

TABLE II

RATE OF LOSS OF OPTICAL ACTIVITY OF
trans-1,2-DIVINYLCYCLOBUTANE

Temp., °C.	k, sec.$^{-1a}$
161.8	$5.23 \pm 0.10 \times 10^{-5}$
176.8	$2.16 \pm .05 \times 10^{-4}$
187.2	$5.21 \pm .06 \times 10^{-4}$
191.4	$7.79 \pm .09 \times 10^{-4}$
198.6	$1.50 \pm .05 \times 10^{-3}$

^{a} $\Delta H^{\ddagger} = 36.3$ kcal. mole^{-1}, $\Delta S^{\ddagger} = +4.6$ e.u.

In the rearrangement of the isoprene dimers, trace amounts of products are formed which cannot come from the diradical intermediate postulated. These trace products correspond to the major products observed in thermal dimerization of isoprene. Thus it seems there is a small amount of a competing mechanism from the thermal dimerization of the isoprene produced. This does not affect our rate measurements since we follow loss of cyclobutanes which are not produced in significant amount by the thermal dimerization of isoprene under our conditions.


$$4 \longrightarrow \begin{bmatrix} \text{transition} \\ \text{state} \end{bmatrix} \longrightarrow \qquad (6)$$
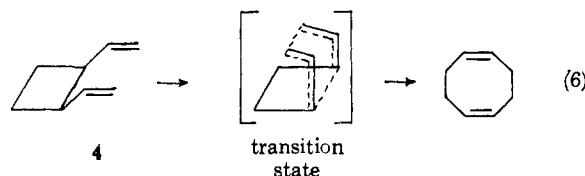
The results show, incidentally, that a transition state having all six allylic centers opposed, although not preferred,[5] is not really a high energy configuration.

The *trans* compounds undoubtedly undergo reaction by a biradical mechanism. Benson[9] has shown that such a mechanism is almost certainly involved in the isomerization of cyclopropane.[10] The activation enthalpies are just about as would be expected for a biradical mechanism. The bond dissociation energy in ethane is about 85 kcal. per mole.[11] The enthalpy required to break the bond between the allylic units in 1 should be $85 - (2 \times$ *allylic resonance energy*) $-$ (*relief of ring strain*). The appropriate numbers are a little difficult to guess, but the resonance energy of an allylic unit is probably close to 12 kcal. per mole.[12] The strain in a cyclobutane ring is estimated as ~ 23 kcal. per mole.[13] Not all of the strain is relieved by breaking the bond but not allowing rotation, since strain arising from bond opposition[14] will remain largely unrelieved in the transition state. Since the observed activation enthalpies are of the right order of magnitude, it is probably proper to recycle the reasoning and take the results as a measure of the energy required to break the bond.

Consideration of the details of the reaction reveals a complication. Since allylic units are known to be stereochemically stable,[15] the ultimate consequences of a bond-breaking reaction depend upon the conformation of the system at the time the bond is broken. Rearrangement of divinylcyclobutane to vinylcyclo-

(enantiomer of starting material)

(7)

hexene requires an intermediate biradical having one *cis*-allylic unit, whereas racemization or formation of *cis*-divinylcyclobutane may involve two *trans*-allylic units.

Since conformation 1a should be slightly less strained than 1b, one might expect rearrangement to vinylcyclohexene to have a higher activation energy than racemization, in contrast to our observations. However, the measured activation energies are not exactly the activation energies for bond breaking since the intermediates must undergo rotations and close new rings before net reaction is consummated. Something can be learned concerning competition between rotation and ring closure by consideration of intermediate 5. This species must undergo two rotations before it arrives at a configuration, 6, that is enantiomeric with the original biradical. Along the way it passes through a conformation which can undergo ring closure to form *cis*-divinylcyclobutane.

5   6   (8)
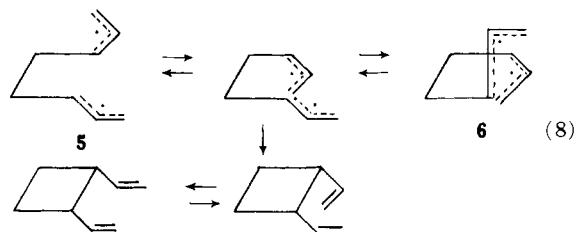
Careful examination of the vinylcyclohexene formed from optically active 1 showed that the former had a small rotation. Since we do not know the absolute rotation of either starting material or product, we do not know the extent of the stereospecificity of the reaction. We would *guess*, however, that it is small. The data are given in Table III. The most economical

TABLE III

OPTICAL ROTATION OF 4-VINYLCYCLOHEXENE FORMED AT VARIOUS TEMPERATURES

T, °C.	Rotation of product[a]
176.3	0.124°
192.9	.076
204.5	.054

[a] Starting material had a rotation of 2.0°

explanation of the data is found in the postulate that the rates of ring closure are only modestly smaller than the rates of internal rotation and that the activation energy for ring closure is about 1 kcal. higher than the barriers to rotation. The fact that the optical rotation of the vinylcyclohexene decreases as the temperature is raised is, of course, partially due to the fact the activation energy for racemization of 1 is higher than that for rearrangement.

Experimental

Materials.—The cyclobutane derivatives were prepared by photosensitized dimerization of isoprene and butadiene, as previously reported,[7] and were purified by preparative gas chromatography followed by bulb-to-bulb distillation. Identification of products was done by retention times in vapor chromatographs.

Flow Tube Experiments.—The rearrangements in the vapor phase at 1 atm. pressure were run in a Pyrex flow tube 8 mm. in diameter and 2 ft. long. The tube was equipped with a thermocouple well, an inlet for nitrogen, a septum for admitting the starting material, and a Dry Ice condenser to capture products. About 1 ft. of the tube was wrapped with nichrome wire and asbestos. The flow rate of nitrogen was such that the average residence time was about 1 sec. The distribution of products at various temperatures is shown in Table IV.

Kinetic Procedures.—The rates of formation of products were measured in small sealed tubes 2 mm. in diameter and 40 to 50 mm. in length containing from 10 to 50 μl. of neat starting material. In preliminary experiments the volume of free space in the tube and thus the pressure in the tube was varied systematically to check for pressure effects. None was found. The material
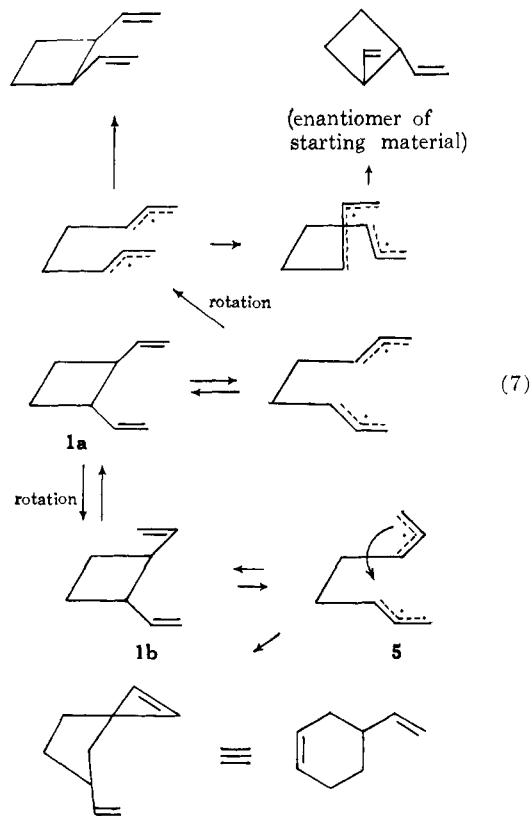
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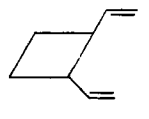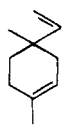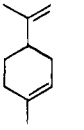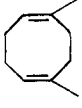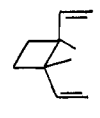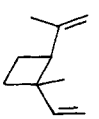
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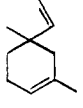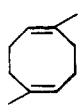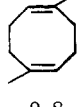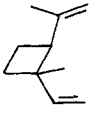
TABLE IV

PRODUCT DISTRIBUTIONS

———————Products, %———————

Starting material	Temp., °C.	[2]	[cyclohexene]	[cyclooctadiene]
	210.3	7.0	67.5	26.3
	187.3	6.1	68.2	25.6
	175.2	4.8	69.3	25.8
	153.9	3.8	70.4	25.7
	139.3	3.5	71.3	25.2
				[X] (probably cis-,trans-1,5-cyclooctadiene)
	65.4	1.5		98.5
	79.8	2.0		98.0
	96.8	2.5		97.5
	108.5	3.0		97.0

	Temp., °C.	[2]			
	92.4	14.5	72.9	5.4	7.2
	109.2	16.0	71.9	5.0	7.1
	121.9	17.1	70.0	4.3	8.6
	135.7	18.0	69.5	3.9	8.6
	135.7	11.1	1.3	45.7	32.1	9.8
	149.2	12.2	0.7	41.0	33.8	12.3
	161.3	12.5	1.2	39.1	31.4	15.8
	176.8	14.0	1.05	35.4	30.7	18.8

of the tube was changed from Pyrex to soft glass to investigate possible wall effects. None was found. Another test for wall effects involved addition of cyclohexane to the early runs. The cyclohexane was also used as an internal standard to check the possibility that material was destroyed in side reactions such as polymerization since nonvolatile materials would not be detected. No loss of material was indicated. The material in the tubes was frozen in liquid nitrogen, a vacuum was applied, and the tubes were sealed while frozen. All tubes were stored in the cold before use.

A thermostated oil bath with ±0.1° temperature control was used for the rate studies. Because small, thin-walled tubes were used, the error due to equilibration time was less than 1% of the total time of the shortest run. The tubes were all quenched by swirling in a water bath at room temperature.

Analyses were carried out with a Loenco Model 15-B-2 gas chromatograph with a 6-ft. column of 10% Carbowax 20M on firebrick at a temperature of 75° with 10 p.s.i. of helium pressure. Integrations were done with an automatic disk integrater.

Optically Active trans-1,2-Divinylcyclobutane.—Brown's method of partial asymmetric hydroboration of divinylcyclobutane was used.[8] α-Pinene (43.7 g., [α]^{27}D −23.0°, distilled from balsam fir oil) was placed in a 500-ml., round-bottomed flask with 120 ml. of diglyme which had been distilled from lithium aluminum hydride. Sodium borohydride (4.35 g.) was added and the mixture was cooled in ice water and stirred with a magnetic stirrer. When cool, 22 g. of freshly distilled boron trifluoride etherate was added and the reaction mixture stirred in ice water for 4 hr. trans-1,2-Divinylcyclobutane (35 g.) was added and the mixture stirred in an ice bath for 4 more hours. Then 10 ml. of water was added to destroy the excess sodium borohydride and the mixture was distilled under vacuum into a Dry Ice condenser until the volume of the pot was reduced by one half. The distillate was dried and redistilled through a spinning-band column. This distillate was purified further by preparative gas chromatography on a Carbowax column and finally a bulb-to-bulb distillation gave 9.7 g. of trans-1,2-divinylcyclobutane having [α]^{27}D 2.0°. This material was diluted with pure racemic divinylcyclobutane to give material with a full-scale deflection on the 0.1° scale of a Bendix Ericsson Type 143 A automatic polarimeter with a 4 cm. path length in the polarimeter cell.

Racemization Kinetics.—The optically active divinylcyclobutane was then sealed in 1-ml. portions into 13 × 125 mm. test tubes. These were heated in the oil bath to effect racemization. Since large tubes were used, time zero was taken at 200 sec. After quenching, the activity of the contents of the tube was measured with the same polarimeter.

Since the 4-vinylcyclohexene produced was only slightly active, a new batch of undiluted active divinylcyclobutane was prepared and rearranged. The 4-vinylcyclohexene was separated from the other products by preparative gas chromatography and the activity measured to give a nearly full-scale deflection on the polarimeter. The rotation of the recovered starting material was also measured and found to have decreased from 2.0 to 1.2°.

Since the amount of activity of the 4-vinylcyclohexene depended on the temperature of the rearrangement, active 4-vinylcyclohexene was sealed in a tube and left for 11 hr. at 200°. At the end of this time its activity was found to be unchanged. The racemization rates are all corrected for the activity of the product.

[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT DEPARTMENT, UNION CARBIDE CORP., CHEMICALS DIVISION, SOUTH CHARLESTON 3, W. VA.]

Cumulative Effects in Small Ring Cleavage Reactions. A Novel Cyclobutane Rearrangement

BY DAVID J. TRECKER AND JOSEPH P. HENRY

trans-1,2-Divinyl-1,2-dimethylcyclobutane (I) undergoes a novel rearrangement at moderately elevated temperatures to 1,4-dimethyl-4-vinyl-1-cyclohexene (II) and 1,6-dimethyl-1,5-cyclooctadiene (III). The activation energy (32.2 kcal./mole) suggests that the driving force for the rearrangement stems from cumulative diallylic stabilization of the biradical intermediate IV. Cleanly first order over the temperature range 101–128°, the reaction is represented by the Arrhenius expression $k = 2.3 \times 10^{14} \exp(-32,200/RT)$.

Facility of small ring cleavage reactions has been attributed to (a) relief of ring strain[1,2] and (b) stabilization of the reaction intermediate—generally considered to be a short-lived biradical.[2,3] Thus, where

ethane requires 84 kcal./mole for homolysis of the carbon–carbon band,[4] a similar cleavage is accomplished in cyclopropane[5] with the expenditure of 64.2 kcal./mole. Addition of a vinyl group to the cyclopropane ring further facilitates bond breaking, presumably be-

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