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STEREOSELECTIVITY IN THE THERMAL REARRANGEMENT OF

OPTICALLY ACTIVE CYCLOBUTANES

A thesis presented

by

Antonietta Rose Mastrocola

to

The Department of Chemistry

in partial fulfillment of the requirements

for the degree of

Doctor of Philosophy

in the subject of

Chemistry

Harvard University

Cambridge, Massachusetts

September 1974

To my mother and the memory of my father
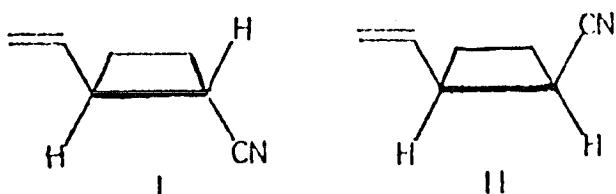
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ACKNOWLEDGEMENTS

STEREOSELECTIVITY IN THE THERMAL REARRANGEMENT OF
OPTICALLY ACTIVE CYCLOBUTANES

SUMMARY

Research Director

W. von E. Doering

Antonietta Mastrocola

September 1974

Optically active cis- and trans-1-cyano-2-vinylcyclobutane
(I and II) were found to undergo four independent reactions--diastere-
omerization, enantiomerization, decomposition to acrylonitrile and
butadiene, and ring expansion to 4-cyanocyclohexene.

Correlation of the optical purities and configurations of the
reactants and products showed that for both I and II diastereomeriza-
tion occurs with predominant inversion of configuration at the
cyano-bearing carbon. In the conversion of I to 4-cyanocyclohexene,
rearrangement with inversion of configuration at the cyano-bearing
carbon was favored by a factor of 1.40, while for II rearrangement
with retention of configuration at the cyano-bearing carbon was
favored by a factor of 2.14.

The results are discussed in terms of several theoretical
models for 1,4-diradicals.

TABLE OF CONTENTS

INTRODUCTION

Thermal unimolecular reactions provide unique advantages for the study of mechanisms of organic reactions. These reactions are characterized by the transformation of one molecule into another by the action of heat alone, without the requirement of a solvent or catalyst. The relative simplicity of these reactions allows certain fundamental questions to be investigated more readily; two such questions are how does a bond break and how do the geometry and energy of a molecule change in between the rupture of the bond in the reactant and formation of the bond in the product(s).
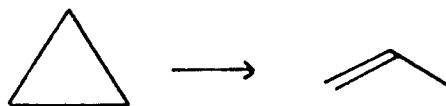
The question of how energy flows in a reacting molecule and becomes concentrated in the rupturing bonds is treated by the theories of unimolecular reactions.[1] The experimental testing of these theories has made heavy use of cyclopropanes and cyclobutanes[2] because of their simple structures and the homogeneous, first-order nature of their reactions.

The second question of how the geometry and energy of the molecule change during reaction can also be studied in these relatively simple molecules. The introduction of suitable labelling can provide

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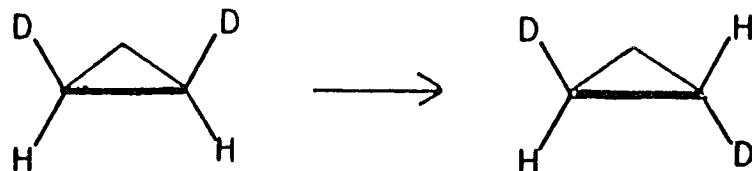
[1] (a) P. J. Robinson and K. A. Holbrook, "Unimolecular Reactions," Wiley-Interscience, London, 1972; (b) R. P. Wayne, "Comprehensive Chemical Kinetics," Volume 2, C. H. Bamford and C.F.H. Tipper, Ed., Elsevier, Amsterdam, 1972.

[2] (a) K. J. Laidler, "Comprehensive Chemical Kinetics," Volume 5, C. H. Bamford and C.F.H. Tipper, Ed., Elsevier, Amsterdam, 1972; (b) H. M. Frey, Advan. Phys. Org. Chem., 4, 147 (1966); (c) H. M. Frey and R. Walsh, Chem. Rev., 69, 103 (1969).

clues about changes in the geometry of the molecule during reaction and may also allow discovery of entirely new reactions. For example, even though the structural isomerization of cyclopropane[3] to propene was well known, its geometrical isomerization was not discovered until

the appropriately labelled cis-1,2-dideuteriocyclopropane[4] was investigated. Similarly, the introduction of optical activity into a
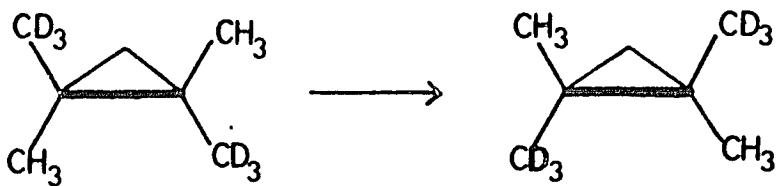
symmetrically disubstituted cyclopropane[5,6a] brought to light the previously unknown enantiomerization of cyclopropane, while its introduction into an unsymmetrically disubstituted cyclopropane[6]

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[3] T. S. Chambers and G. B. Kistiakowsky, J. Amer. Chem. Soc., 56, 399 (1934).
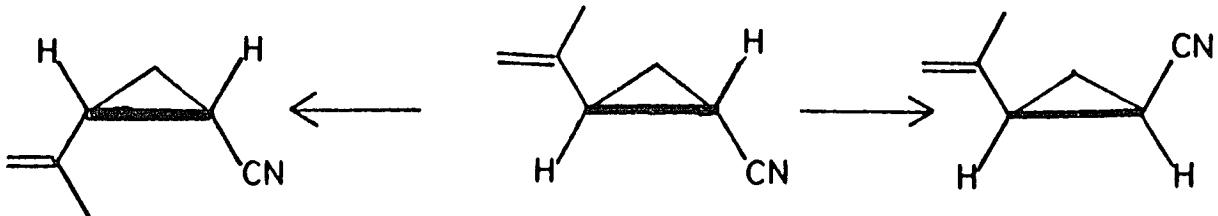
[4] B. S. Rabinovitch, E. W. Schlag and K. B. Wiberg, J. Chem. Phys., 28, 504 (1958).

[5] (a) J. A. Berson and J. M. Balquist, J. Amer. Chem. Soc., 90, 7343 (1968); (b) R. J. Crawford and T. R. Lynch, Can. J. Chem., 46, 1457 (1968).

[6] (a) W. L. Carter and R. G. Bergman, J. Amer. Chem. Soc., 90, 7344 (1968); R. G. Bergman and W. L. Carter, ibid., 91, 7411 (1969); (b) A. B. Chmurny and D. J. Cram, ibid., 95, 4237 (1973); (c) W. E. Doering and K. Sachdev, ibid., 96, 1168 (1974).
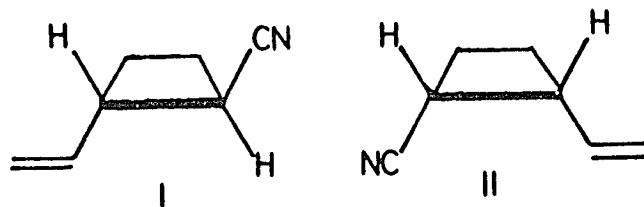
allowed the geometrical isomerization to be dissected into two

independent reactions:

Thus, a host of molecular motions can be uncovered with the introduc-

tion of labelling. Proposed mechanistic hypotheses then have to

account for a great variety of observed reactions. (In the case of

cyclopropane, some of these mechanistic alternatives have been

reviewed recently by Doering.[6c]) As usual, great caution must be

exercised lest changes in substituents lead to an unsuspected, deep-

seated change in mechanism.[6b,7]

Although reactions of cyclobutanes[2] have been studied

extensively, the nature of the labelling has not been sufficient to

allow all the potential reactions to be uncovered. The subjects of

this dissertation are the cyclobutanes I and II, more elaborately

labelled with optical   activity and two different substituents.

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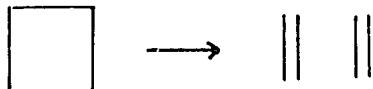
[7]N. E. Howe, E. W. Yankee, and D. J. Cram, ibid., 95, 4230 (1973).

Through the study of their reactions additional insight can be gained into the mechanism of their thermal rearrangement. Before the discussion of the present results, it may be useful to review the known thermally induced reactions of cyclobutanes and the mechanisms which have been proposed for them.

Reactions of Cyclobutanes

The thermal decomposition of cyclobutane[8] to two molecules of ethylene is a homogeneous, first-order, unimolecular reaction which is independent of surface effects and unaffected by the addition of ethylene, propene, and nitric oxide. The conclusion that the reaction

does not occur by a radical chain process[8c] is confirmed by the absence of d_2-ethylene in the pyrolysis of a 1:1 mixture of d_8- and

---

[8](a) C. T. Genaux and W. D. Walters, *ibid.*, 73, 4497 (1951);
(b) F. Kern and W. D. Walters, *Proc. Nat. Acad. Sci. U.S.*, 38, 937 (1952); (c) C. T. Genaux, F. Kern, and W. D. Walters, *J. Amer. Chem. Soc.*, 75, 6196 (1953); (d) H. O. Pritchard, R. G. Snowden, and A. F. Trotman Dickenson, *Proc. Roy. Soc. London A,* 218, 416 (1953);
(e) R. W. Carr and W. D. Walters, *J. Phys. Chem.*, 67, 1370 (1963).

$\underline{d}_0$-cyclobutane.[9a] The absence of an isotope effect in the

decomposition of $\underline{d}_4$- and $\underline{d}_8$-cyclobutanes,[9] allows the C-H distance as

a reaction coordinate to be ruled out.

The fall-off in rate constant as pressure is lowered, predicted

by theory for unimolecular reactions, has been studied extensively in

cyclobutane[10] and methylcyclobutane.[11] It is found that fall-off

occurs at pressures below 20 mm[8c] and that the high-pressure value of

rate constant is restored upon the addition of inert gases.[8d]

Despite extensive studies of the thermal decomposition of many

monosubstituted cyclobutanes (Table 1), no new reactions of

cyclobutanes were uncovered until investigation of cis- or trans-1,2-

dimethylcyclobutane[12i] revealed not only the expected cleavage to

olefins, but also a novel geometrical isomerization.

---

[9](a) J. Langrish and H. O. Pritchard, J. Phys. Chem., 62, 761 (1958); (b) R. Srinivasan and S.M.E. Kellner, J. Amer. Chem. Soc., 81, 5891 (1959); (c) R. W. Carr and W. D. Walters, ibid., 88, 884 (1966).

[10](a) J. N. Butler and R. B. Ogawa, ibid., 85, 3346 (1963); (b) R. W. Vreeland and D. F. Swinehart, ibid., 85, 3349 (1963); (c) P. C. Beadle, D. M. Golden, K. D. King and S. W. Benson, ibid., 94, 2943 (1972).

[11](a) A. F. Patarachia and W. D. Walters, J. Phys. Chem., 68, 3894 (1964); (b) T. F. Thomas, P. J. Conn, and D. F. Swinehart, J. Amer. Chem. Soc., 91, 7611 (1969).

Table 1. Activation Parameters for the Thermal Rearrangements of Cyclobutanes.

Reactant	Product(s)	Log A	E_a, kcal mol^{-1}	Ref.
Cyclobutane	Ethylene	15.62	62.5	8c,e
Methylcyclobutane	Ethylene + Propene	15.38	61.2	12a
Ethylcyclobutane	Butene-1 + Ethylene	15.56	62.0	12b
n-Propylcyclobutane	Pentene-1 + Ethylene	15.53	61.6	12c
Isopropylcyclobutane	3-Methylbutene-1 + Ethylene	15.63	62.6	12d
t-Butylcyclobutane	3,3-Dimethylbutene-1 + Ethylene	15.94	63.8	12e
1,1-Dimethylcyclobutane	Isobutylene + Ethylene	15.68	61.0	12f
1,1,3,3-Tetramethylcyclobutane	Isobutylene	16.24	64.8	12g
		16.31	65.1	12h

12(a) M. N. Das and W. D. Walters, Z. Physik. Chem., 15, 22 (1958).
   (b) R. E. Wellmann and W. D. Walters, J. Amer. Chem. Soc., 79, 1542 (1957).
   (c) S.M.E. Kellner and W. D. Walters, J. Phys. Chem., 65, 466 (1961).
   (d) M. Zupan and W. D. Walters, ibid., 67, 1845 (1963).
   (e) A. T. Cocks and H. M. Frey, J. Chem. Soc. A., 2566 (1970).
   (f) H. M. Frey and R. Walsh, Chem. Rev., 69, 103 (1969).
   (g) T. A. Babcock, J. Amer. Chem. Soc., 91, 7622 (1969).
   (h) A. T. Cocks and H. M. Frey, J. Chem. Soc. A., 1671 (1969).

Table 1, continued.

Reactant	Product(s)	E_a, kcal mol^{-1}	Log A	Ref.
cis-1,2-Dimethylcyclobutane	trans-1,2-Dimethylcyclobutane	60.1	14.80	12i
	2-Butene + Ethylene	63.0	15.56	12i
	Propene	60.4	15.47	12i
trans-1,2-Dimethylcyclobutane	cis-1,2-Dimethylcyclobutane	61.3	14.50	12j
	2-Butene + Ethylene	63.4	15.46	12j
	Propene	61.6	15.44	12j
cis-1,3-Dimethylcyclobutane	trans-1,3-Dimethylcyclobutane	63.3	15.07	12k
	Propene	63.7	15.96	12k
trans-1,3-Dimethylcyclobutane	cis-1,3-Dimethylcyclobutane	62.0	14.8	12k
	Propene	63.1	15.88	12k
Cyclobutanecarboxaldehyde	Ethylene + Propenal	53.3	14.43	12l

12 (i) H. R. Gerberich and W. D. Walters, J. Amer. Chem. Soc., 83, 8935 (1961).
(j) H. R. Gerberich and W. D. Walters, ibid., 83, 4884 (1961).
(k) A. R. Venkitaraman, Diss. Abst., (4) 1888 (1970).
(l) B. C. Rocquitte and W. D. Walters, J. Amer. Chem. Soc., 84, 4049 (1962).

Table 1, continued.

Reactant	Product(s)	Log A	E_a, kcal mol^{-1}	Ref.
Acetylcyclobutane	Methyl Vinyl Ketone + Ethylene	14.53	54.5	12m
Ethylcyclobutyl Ketone	Ethyl Vinyl Ketone + Ethylene	14.50	54.2	12n
Methyl Cyclobutanecarboxylate	Methyl Acrylate + Ethylene	14.84	57.3	12o
Cyclobutanecarbonitrile	Acrylonitrile + Ethylene	15.30	56.7	12p
trans-Cyclobutane-1,2-dicarbonitrile	Acrylonitrile	12.40	41.2	12p
Chlorocyclobutane	Ethylene + Chloroethylene	14.76	60.0	12q
	Butadiene + HCl	13.61	55.2	12q
cis-1,2-Dichloro-1,2,3,3,4,4-hexafluorocyclobutane	trans-1,2-Dichloro-1,2,3,3,4,4-hexafluorocyclobutane	15.10	60.3	12r
	1-Chloro-1,2,2-trifluoroethylene	15.39	65.3	12r

12
(m) L. G. Daignault and W. D. Walters, ibid., 80, 541 (1958).
(n) B. C. Rocquitte and W. D. Walters, J. Phys. Chem., 68, 1606 (1964).
(o) M. Zupan and W. D. Walters, J. Amer. Chem. Soc., 86, 173 (1964).
(p) S. F. Sarner, D. M. Gale, H. K. Hall and A. B. Richmond, J. Phys. Chem., 76, 2817 (1972).
(q) A. T. Cocks and H. M. Frey, J. Amer. Chem. Soc., 91, 7583 (1969).
(r) B. Atkinson and M. Stedman, J. Chem. Soc., 512 (1962).
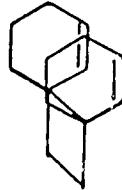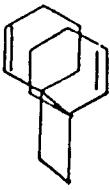
Table 1, continued.

Reactant	Product(s)	Log A	E_a, kcal mol^{-1}	Ref.
trans-1,2-Dichloro-1,2,3,3,4,4-hexafluorocyclobutane	cis-1,2-Dichloro-1,2,3,3,4,4-hexafluorocyclobutane	14.87	60.2	12r
	1-Chloro-1,2,2-trifluoroethylene	15.39	65.3	12r
cis-1,2-Diphenylcyclobutane	trans-1,2-Diphenylcyclobutane	12.9	35.6	12s
	Styrene	12.8	35.8	12s
Isopropenylcyclobutane	Ethylene and Isoprene	14.64	51.0	12t
	1-Methylcyclohexene	14.53	51.0	12t
trans-1,2-Divinylcyclobutane	1,5-Cyclooctadiene, Butadiene + 4-Vinylcyclohexene	-1.2 *	34.0 **	12u
cis-1,2-Divinylcyclobutane	1,5-Cyclooctadiene	-11.7 *	23.1 **	12u
trans-1,2-Divinyl-1,2-dimethylcyclobutane	1,6-Dimethyl-1,5-cyclooctadiene +	+2.9 *	30.9 **	12u
	1,4-Dimethyl-4-vinylcyclohexene	+11.0 *	32.2 **	12v
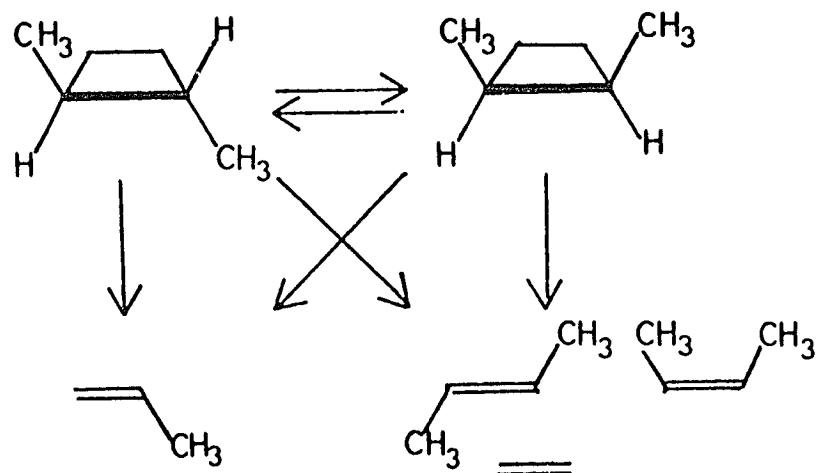
12 (s) G. Jones and Virginia Chow, J. Org. Chem., 39, 1447 (1974).
(t) R. J. Ellis and H. M. Frey, Trans. Faraday Soc., 59, 2076 (1963).
(u) G. S. Hammond and C. D. DeBoer, J. Amer. Chem. Soc., 86, 899 (1964).
(v) D. J. Trecker and J. P. Henry, ibid., 86, 902 (1964).
* $\Delta S^{\ddagger}$ ** $\Delta H^{\ddagger}$

Table 1, continued.
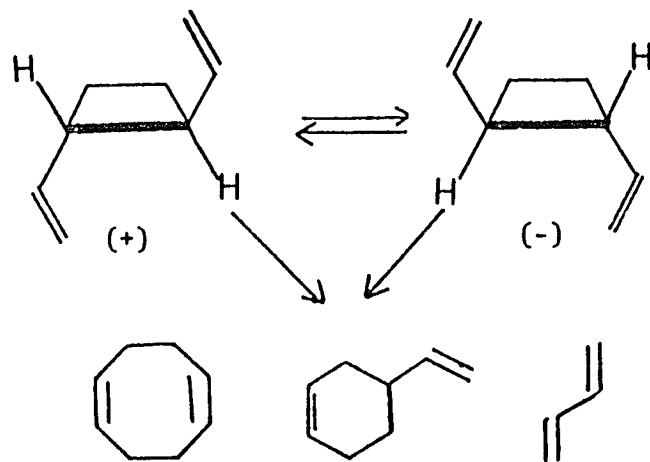
Reactant	Product(s)	Log A	E_a, kcal mol^{-1}	Ref.
trans-1-Methyl-1-vinyl-2-isopropenylcyclobutane	1,5-Dimethyl-1,5-cyclooctadiene, Methylisopropenylcyclohexene, and Isoprene	3.1*	34.2**	12u
Bicyclo[3,2,0]heptane	Cyclopentene + Ethylene	14.84	60.7	12w
	Hepta-1,6-diene	15.49	63.9	12w
	cis-Isomer	13.29	30.93	12x
	Methylenecyclohexene	14.29	32.08	12x
	trans-Isomer	13.52	30.96	12x

12(w) R. J. Ellis and H. M. Frey, J. Chem. Soc., 4184 (1964).
(x) J. Ekmanis, Ph.D. Thesis, Harvard University, 1974.
* $\Delta S^{\ddagger}$ ** $\Delta H^{\ddagger}$
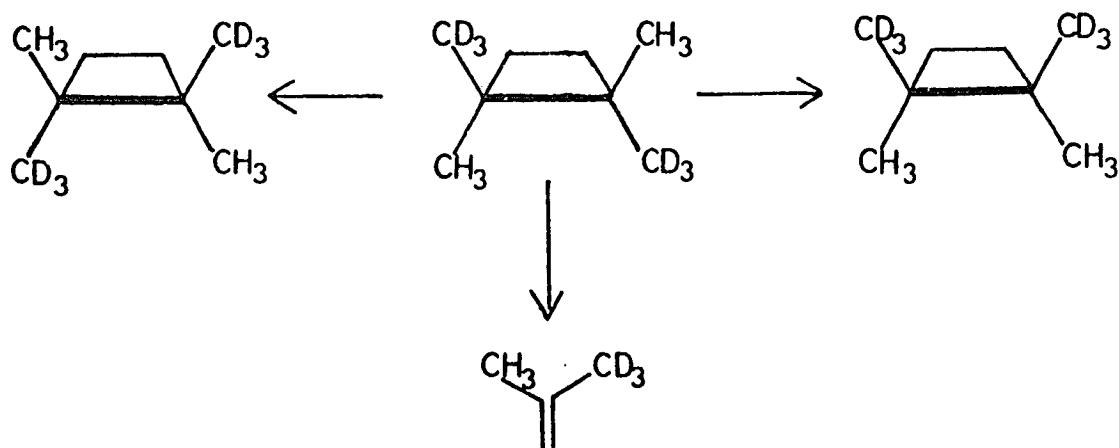
Labelling <u>trans</u>-1,2-divinylcyclobutane[12u] with optical activity

allowed still a third reaction to be uncovered. In addition to the

products of structural rearrangement and cleavage, the thermal

rearrangement of this molecule revealed the racemization of the start-

ing material as a new process. A subsequent related study by Berson[13]

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[13]J. A. Berson, D. C. Tompkins and G. Jones, <u>J. Amer. Chem. Soc.</u>, 9<u>2</u>, 5799 (1970).

of an optically active, deuterium labelled cyclobutane showed that cleavage was the most favorable reaction with neither geometrical isomerization nor racemization being observable within the limits of the analytical methods.

The mechanisms proposed for the thermal rearrangements of cyclobutanes have been of two types: one-step, concerted mechanisms and two-step diradical mechanisms. Knowledge of the general characteristics of concerted reactions and the evidence for the operation of this pathway is essential to a discussion of diradicals and their possible role.

Concerted Reactions

A reaction may be defined as concerted when the transition state partakes simultaneously of the formation of the bond in the product and the rupture of the bond in the reactant. Concerted reactions are envisioned as one-step processes with a single transition state

involving continuous overlap of the orbitals representing the starting material and the products.

Two major consequences of the coupling of bond-making and bond-breaking may be used as experimental criteria[14] for distinguishing concerted from non-concerted mechanisms. The first is stereospecificity. The continuous overlap of orbitals would be expected to control the geometry of the transition state so completely that no loss of stereochemical integrity could occur.

The detailed specification of the stereochemical courses to be followed is governed by theoretical considerations, the foremost among which is that of Woodward and Hoffmann.[15a] The controlling factor has been formulated in a number of ways,[15] but all have in common the control of the reaction path by the overlap of frontier orbitals, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). These formulations describe the appropriate geometry for the transition state of a concerted reaction.

If the geometrical constraints are too severe for the concerted transition state, the reaction may proceed by another, more favorable pathway, such as a step-wise, non-concerted process. Alternatively, another concerted transition state with a less strained geometry may

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[14]W. Doering, Symposium, XXIII IUPAC, Boston, Mass., 1971.

[15](a) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N.Y. 1970; (b) M.J.S. Dewar, Angew. Chem., 83, 859 (1971); Angew. Chem., Int. Ed. Engl., 10, 761 (1971); (c) E. Heilbronner, Tetrahedron Lett., 1923 (1964); (d) H. E. Zimmerman , Accounts Chem. Res., 4, 272 (1971).

become predominant. Such a proposal is to be found in the hypothesis of Berson and Salem,[16] control by the overlap of subjacent (i.e., not frontier) orbitals. In some cases the stabilization provided by the overlap of subjacent orbitals is predicted to be more favorable than that involving non-interacting radical centers.

A second phenomenological diagnostic of a concerted reaction is an enthalpy of activation which is lower than that predicted of a step-wise reaction involving two radicals.[17] As an example, the observed activation energy for the conversion of cis-1,2,3,4-tetramethylcyclobutene to 3,4-dimethylhexa-(2E,4Z)-diene is 35.8 kcal mol^{-1} [18] whereas an activation energy of 60 kcal mol^{-1} is predicted for path A [85 kcal mol^{-1} (C-C bond)[19] -25 kcal mol^{-1} (strain in 1,2-dimethylcyclobutene)[20]] and 47 - 48 kcal mol^{-1} for path B [60 kcal mol^{-1} (model A) -12 - 13 kcal mol^{-1} (stabilization of allyl group)[21]]. Compared to the enthalpies of activation predicted of

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[16]J. A. Berson and L. Salem, J. Amer. Chem. Soc., 94, 8917 (1972).
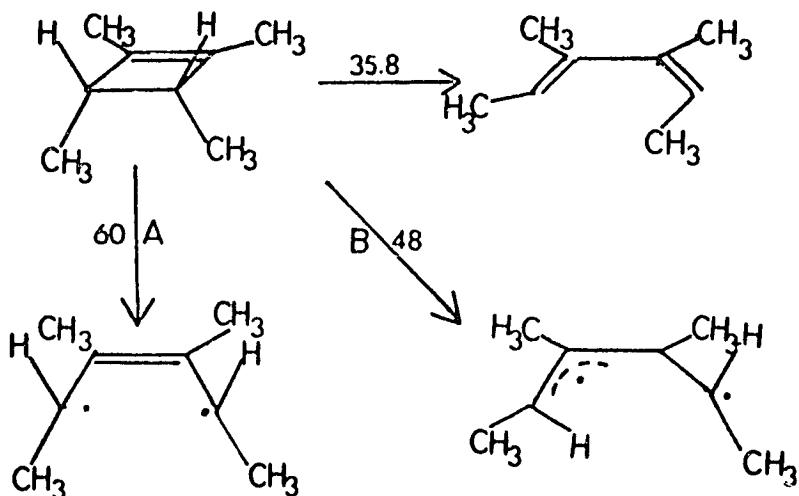
[17]S. W. Benson, "Thermochemical Kinetics," Wiley, New York, N.Y., 1968.

[18](a) H. M. Frey, G. R. Branton, and R. F. Skinner, Trans. Faraday Soc., 62, 1546 (1966); (b) R. Criegee, D. Seebach, R. E. Winter, B. Borretzen and H. A. Brune, Chem. Ber., 98, 2339 (1965).

[19]S. W. Benson, J. Chem. Ed., 42, 502 (1965).

[20]R. B. Turner, P. Goebel, B. J. Mallon, W. Doering, J. Coburn and M. Pomerantz, J. Amer. Chem. Soc., 90, 4315 (1968).

[21]W. E. Doering and G. H. Beasley, Tetrahedron, 29, 2231 (1973).

these two step-wise models, the experimental value is lower by at least 12 kcal mol^{-1}. In this example, both the stereochemical criterion and the energetic criterion are satisfied.

There are two problems associated with the application of the criterion of activation energy. One is the choice of a proper model for the non-concerted reaction and the calculation of its energy.[22] The second is the greater uncertainty in the determination of activation parameters relative to that in the determination of stereochemical ratios. For example, a stereochemical ratio of 60:40 for a reaction occurring at 200°C corresponds to $\Delta\Delta G^{\ddagger}$ of 0.37 kcal, whereas an optimistic limit for the error in an estimated activation energy is $\pm$5%. Thus, in an estimated activation energy of 45 kcal mol^{-1}, the error might amount to $\pm$2.3 kcal mol^{-1}.

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[22]This problem is discussed in detail by L. M. Stephenson and J. I. Brauman, Accts. Chem. Res.,7, 65 (1974).

Whenever a stereospecificity greater than 99:1 (corresponding to $\Delta\Delta G^{\ddagger}$ ~4.3 kcal mol^{-1} at 200°C) and a lowering in activation energy larger than 3 kcal mol^{-1} characterizes a reaction, it may safely be considered to be concerted. If both of these conditions are not satisfied, a number of situations may obtain. If the reaction is stereospecific and the activation energy is within 2 - 3 kcal of that calculated for a non-concerted "two-radical" model, the reaction may either proceed by a diradical (see below) which reacts stereospecifically or by a concerted path for which the stabilization due to continuous overlap of orbitals is small.
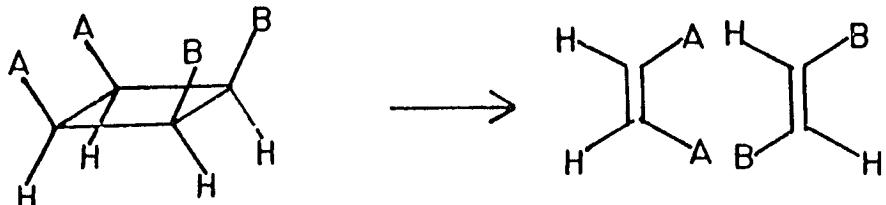
If the reaction is not stereospecific and the activation energy is comparable to that calculated for a non-concerted model, the reaction may proceed by way of a diradical mechanism, by the competition of two stereospecific concerted pathways, or by the competition of concerted and diradical mechanisms. It may be possible to determine if the last case obtains by applying the criterion of activation energy. Even when the rates of two reactions are comparable, differences in their activation energy might be larger than expected.[23] This situation may arise because concerted reactions often demand a transition state of highly restrictive geometry in order to facilitate the simultaneous making and breaking of bonds. This geometrically restrictive feature should express itself as a low A factor (more negative $\Delta S^{\ddagger}$) and consequently a rate of reaction relatively slower

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[23]D. A. Blackadder and C. Hinshelwood, _J. Chem. Soc._, 2728 (1958).

than a non-concerted reaction with a higher enthalpy of activation.

Thus, when the stabilization derived from concert is not large

enough to compensate for entropy factors, the competitive concerted

and non-concerted reactions might be observed side by side. Among a

series of competitive reactions, one with a lower $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ might

be concerted. If, however, $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ are all of comparable value,

no distinction among the three alternatives is possible, since it is

difficult to predict values of $\Delta S^{\ddagger}$ for any given reaction.[24]
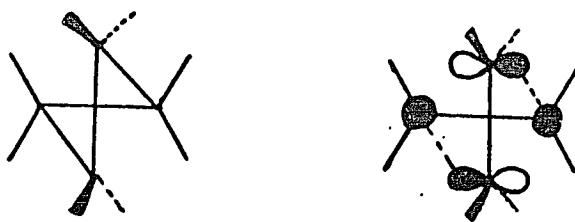
Concerted Mechanisms in Thermal Rearrangements of Cyclobutanes

The stereochemical course predicted by the Woodward-Hoffmann

rules[15a] for the decomposition of cyclobutane to two olefins requires

inversion of configuration at one center. This process is envisioned

as occurring through a transition state in which the cyclobutane ring

is highly distorted to allow the overlap of the highest occupied

molecular orbital of one olefinic moiety with the lowest unoccupied

orbital of the other.

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[24] T. L. Gilchrist and R. C. Storr, "Organic Reactions and Orbital Symmetry," Cambridge University Press, Cambridge, 1972, p. 21.

Several groups have attempted to determine the stereochemistry of the decomposition of cyclobutanes[25a-d] and its reverse, the cyclo-addition of two olefins.[25e] The results are summarized in Table 2. In two of the systems studied[25a,b] the stereochemistry of one of the olefinic parts is fixed by enclosure in a small ring (i.e., a trans-double bond would not be formed in a small ring). Paquette[25c] approaches the problem from a slightly different angle. The stereo-chemistry of the olefinic moiety was fixed by enclosing it in what would become tetrahydronaphthalene. The aim was to stabilize a potential 1,4 diradical by conjugation and to look at the stereochemistry of the olefinic product in a reaction that would presumably proceed by a non-concerted pathway. A range of stereochemical results was obtained for the rearrangement of the propellanes depending on the orientation and nature of the substitu-ents (Table 2).
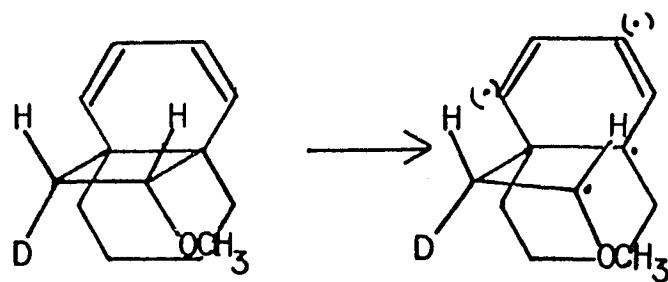
Table 2. Stereochemistry of Products of Thermal 2+2 Cycloreversions
and Cycloadditions.

Starting Material	Temperature,°C	Products*	%	Ref.
	414.3°		75.6	25a
			24.4	
	414.3°		52.6	25a
			47.4	
	450°		57	25b
			43	

25 (a) A. T. Cocks, H. M. Frey and I.D.R. Stevens, Chem. Comm., 458
(1969).
(b) J. E. Baldwin and P. W. Ford, J. Amer. Chem. Soc.,91, 7192
(1969).
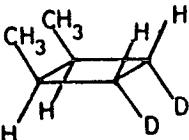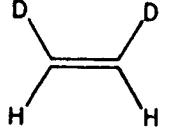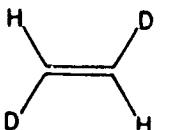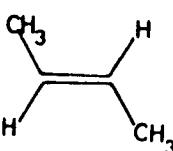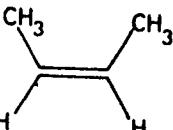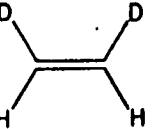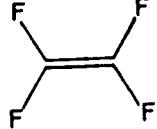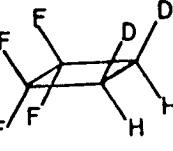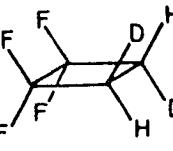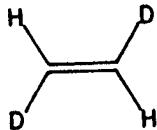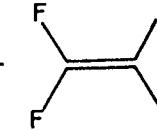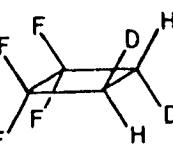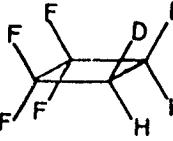
* "Products" represent those pertinent to the 2+2 thermal reaction.
In many cases there are side products. The percentages given
represent the relative proportions of cis-product and trans-product.

Table 2, continued.

Starting Material	Temperature, °C	Products*	%	Ref.
(CH₃O-substituted bicyclic structure, D, H)	314°	D–OCH₃ / H–H alkene	97	25c
		D–H / H–OCH₃ alkene	3	
(CH₃O-substituted bicyclic structure, H, D)	314°	D–OCH₃ / H–H alkene	77	25c
		D–H / H–OCH₃ alkene	23	
(CH₃O structure 74% + 26%)	314°	D–H / H–OCH₃ alkene	71	25c
		D–OCH₃ / H–H alkene	29	
(D structure 60% + 40%)	310°	H–D / D–H alkene	44	25c
		D–D / H–H alkene	66	

²⁵(c) L. A. Paquette and G. L. Thompson, ibid., 93, 4920 (1971); 94, 7127 (1972).

Table 2, continued.

Starting Material	Temperature,°C	Products*	%	Ref.
	425 ± 5°		52	25d
			48	
			44	
			56	
	150°		50	25e
			50	
	150°		50	25e
			50	

25(d) R. Srinivasan and J.N.C. Hsu, Chem. Comm., 1213 (1972).
(e) P. D. Bartlett, G. M. Cohen, S. P. Elliott, K. Hummel, R. A. Minns, C. M. Sharts and J. Y. Fukunaga, J. Amer. Chem. Soc., 94, 2899 (1972).
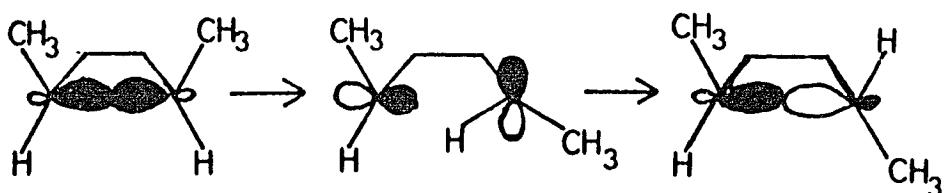
Thus, all attempts to establish a single concerted reaction as the pathway for the decomposition of cyclobutanes have failed. There are two possible rationalizations for the results of Table 2: the competition of a concerted and a non-concerted process, and an exclusively non-concerted pathway. These alternatives cannot be distinguished on the basis of these experiments which relate only to the criterion of stereospecificity.

In appropriately labelled systems (Table 1) the activation energy for the decomposition of a cyclobutane to olefins is about the same as that for its geometrical isomerization. For reasons discussed below, geometrical isomerization must be a non-concerted reaction and provides an ideal model for the comparison of activation energies. In all cases both the activation energies and A factors are higher for cleavage than for geometrical isomerization. Assuming that the only available concerted pathway for cleavage is the one predicted by the Woodward-Hoffmann rules, it seems unlikely that the highly constrained geometry described for this transition state would lead to a higher A factor (higher $\Delta S^{\ddagger}$) than for a geometrical isomerization proceeding by a step-wise mechanism. The higher enthalpy of activation for cleavage is consistent with non-concerted paths for these reactions.

The Geometrical Isomerization of Cyclobutanes

Both the Woodward-Hoffmann rules[15a] and the Berson-Salem[16] hypothesis can be used to determine which reactions are obliged to be
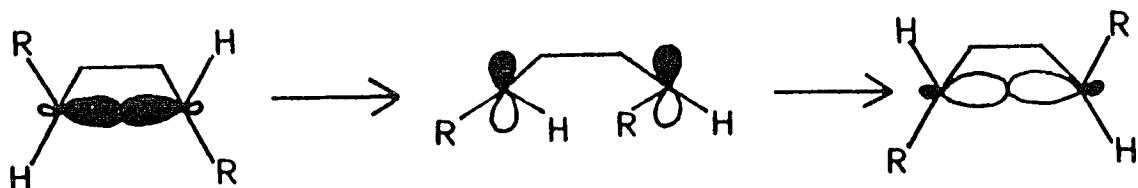
non-concerted. Both formulations require continuous bonding in the
transition state for a reaction to be concerted. A reaction which
cannot fill this requirement must then be non-concerted. Such a
reaction is the geometrical isomerization of cyclobutane. At some
point in the reaction path the orbitals are constrained to be

orthogonal to each other with the resultant cancellation of bonding
and anti-bonding interactions. Under these circumstances continuous
bonding throughout is impossible and the reaction is obliged to be
non-concerted. The activation energy for this necessarily
non-concerted reaction may then serve as an internal standard for the
application of the criterion of activation energy. This role as an
internal standard may be played by geometrical isomerizations in
systems in which other possibly concerted reactions are competitive
in rate.

Enantiomerization of Cyclobutanes
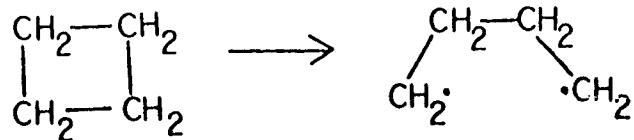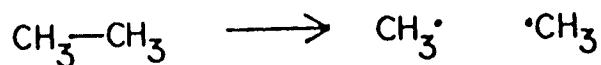
Continuous orbital overlap is allowed by Woodward-Hoffmann rules
in the enantiomerization of a cyclobutane:

Since only one stereochemical course is possible for this reaction, the criterion of stereospecificity is not applicable. The criterion of activation energy can be applied and, in the only example for which activation parameters have been determined, that of trans-1,2-divinylcyclobutane,[26] enantiomerization proceeds with slightly higher values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ than the competitive rearrangements.

Diradical Mechanisms

In thermal reactions of cyclobutanes, the alternative to the concerted mechanism has usually been formulated as a "diradical mechanism"[27] in analogy to the homolytic cleavage of ethane to two methyl radicals.

$$CH_3-CH_3 \longrightarrow CH_3\cdot \quad \cdot CH_3$$
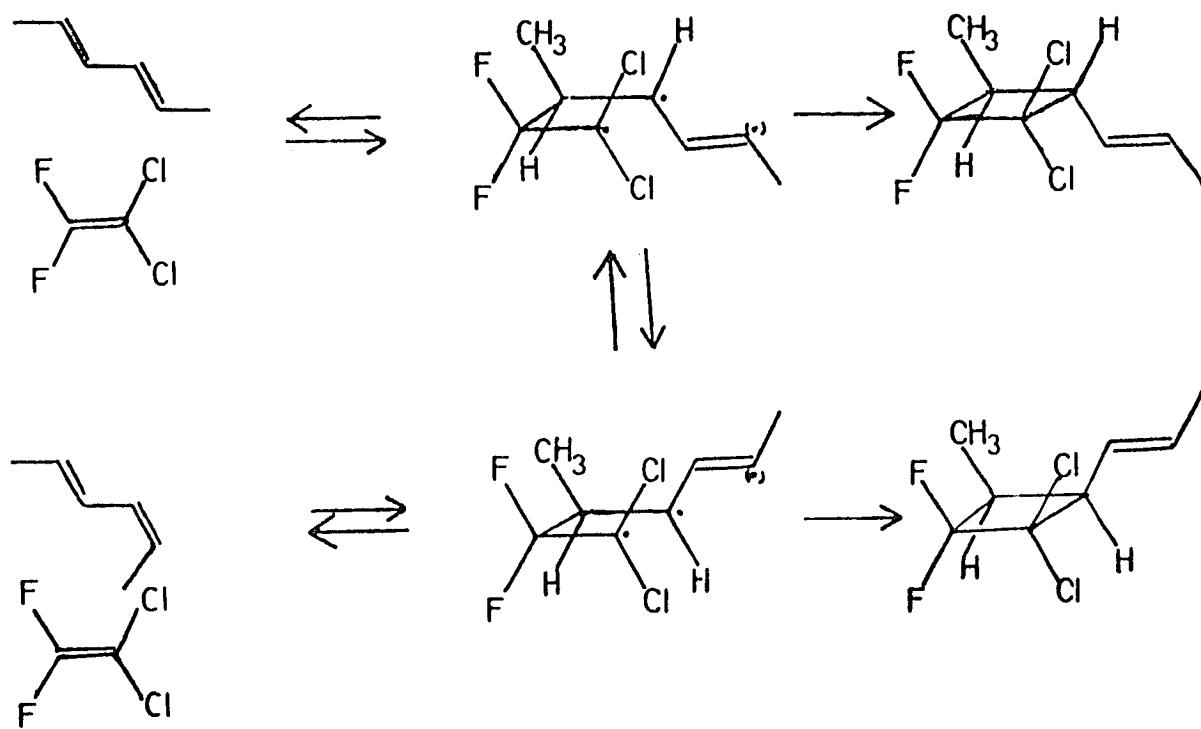
[26]G. S. Hammond and C. D. De Boer, J. Amer. Chem. Soc., 86, 899 (1964).

[27]For recent reviews, see the following references:
(a) R. G. Bergman, "Free Radicals," Volume 1, J. Kochi, Ed., Wiley-Interscience, New York, 1973; (b) L. Salem and C. Rowland, Angew. Chem. Int. Ed. Engl., 11, 92 (1972); (c) G. Jones, J. Chem. Ed., 51, 175 (1974).

The work of Bartlett[28] on the cycloaddition of olefins has led

to much of what is known about diradicals as intermediates. The

diradical has been defined as a species with no significant bonding

between the radical centers and with no force between them to limit

rotations. Thus, a diradical may or may not lead to a stereospecific

reaction depending on the magnitude of internal barriers to rotation

of the component radicals, whereas a concerted pathway must be

stereospecific.

Experimentally, such rotations have been observed in the cyclo-

addition of 2,4-hexadiene and 1,1-dichloro-2,2-difluoroethylene(1122).[29]

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[28]P. D. Bartlett, Quart. Rev. Chem. Soc. 24, 473 (1970); Science, 159, 833 (1968).

[29]L. K. Montgomery, K. Schueller and P. D. Bartlett, J. Amer. Chem. Soc., 86, 622 (1964).

Rotation in the hypothesized diradical results not only in the forma-
tion of non-stereospecific products but also in the isomerization of
the starting diene. This isomerization, which does not occur in the
absence of 1122, can best be rationalized by the formation of a
diradical within which bond rotation occurs prior to cleavage to the
starting diene. The regiospecificity of the reaction lends support
to the proposal that the diradical is an intermediate in the reaction.
Thus, addition occurs in the direction predicted from the assumption
that two chlorines should stabilize a radical center more efficiently
than two fluorines by $\sim$7 kcal mol^{-1}.[30] While the mark of a diradical
has generally been taken to be the generation of products in a
non-stereospecific manner, lack of stereospecificity can also be
rationalized as the competition of two concerted pathways.

The nature and energy of the tetramethylene diradical has been
the subject of theoretical investigations both by thermochemical[17,34]

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[30]An estimate of the stabilization of a radical by chlorine vs.
fluorine can be made by comparison of the activation energies of
cis-trans isomerization of 1,2-dideutereoethylene (65 kcal mol^{-1}),[31]
1,2-difluoroethylene (62.8 kcal mol^{-1})[32] and 1,2-dichloroethylene
(56.0 kcal mol^{-1}).[33] The stabilization of a chlorine vs. fluorine is
3.4 kcal mol^{-1}.

[31]J. E. Douglas, B. S. Rabinovitch, and F. S. Looney, J. Chem.
Phys.,23, 315 (1958).
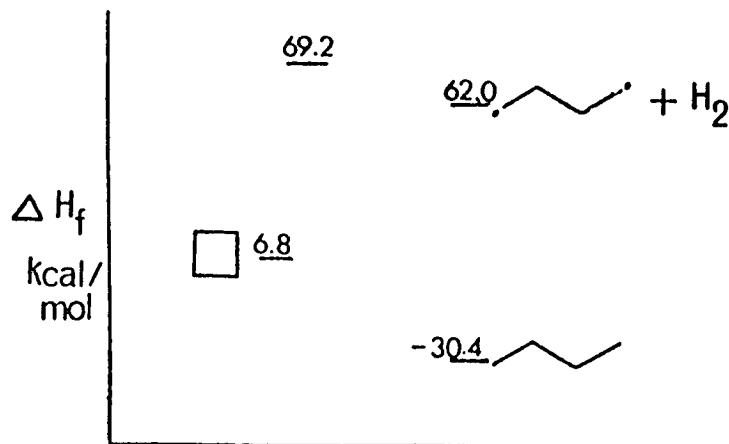
[32]P. M. Jeffers and W. Shaub, J. Amer. Chem. Soc.,91, 7706 (1969).

[33]L. D. Hawton and G. P. Semiluk, Can. J. Chem.,44, 2143 (1966).

[34]H. E. O'Neal and S. W. Benson, J. Phys. Chem.,72, 1866 (1968).

and quantum mechanical[35] methods.
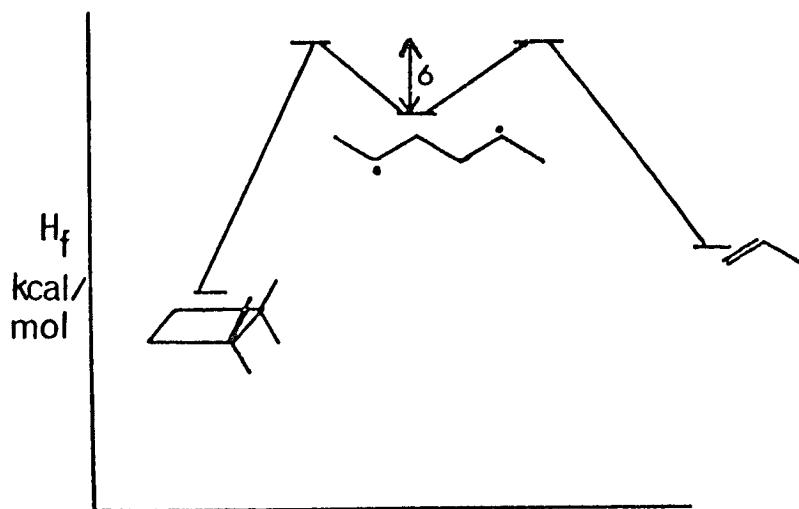
The thermochemical approach involves comparison of the calculated heat of formation of a diradical with the heat of formation of the transition state. To calculate the heat of formation of tetramethylene with non-interacting radical centers, Benson adds the dissociation energy of two C-H bonds (2×98 kcal/mol) to the heat of formation of n-butane (-30.3) and subtracts the dissociation energy of H_2 (104.2).[19] The resulting heat of formation of tetramethylene is

ΔH_f kcal/mol

69.2

62.0 $\diagup\diagdown\diagup^{\bullet}$ + H_2

☐ 6.8

-30.4 $\diagup\diagdown\diagup$

61.5 kcal mol^{-1}. Even though there is some doubt as to the validity of taking the second C-H dissociation energy as 98 kcal mol^{-1}, derivation of the heat of formation by two other reaction cycles--one by dissociation of the C-I and C-H bonds of n-iodobutane and the other by

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[35] (a) L. Salem and J. S. Wright, J. Amer. Chem. Soc., 94, 322 (1972); 91, 5947 (1969); Chem. Comm., 1370 (1969); (b) R. Hoffmann, S. Swaminathan, B. G. Odell and R. Gleiter, J. Amer. Chem. Soc., 92, 7091 (1970); (c) W. A. Goddard III, ibid., 94, 793 (1972); (d) M. D. Epiotis, ibid., 94, 1924, 1935 (1972); 95, 1191 (1973); (e) L. M. Stephenson, T. A. Gibson and J. I. Brauman , ibid., 95, 2849 (1973) and references cited therein.

taking the dissociation of a general alkane $-(CH_2)_n-(CH_2)_4-(CH_2)_n-$
give good agreement and an average value of 62 kcal mol^{-1}. It follows
that the heat of formation of the diradical is about 55 kcal mol^{-1}
above the heat of formation of cyclobutane $(\Delta H_F = 6.8$ kcal mol$^{-1})$.
Since the experimental activation energy of cleaving cyclobutane to
two molecules of ethylene [$Ea = 62$ kcal mol^{-1}] is higher than this
difference by ~6 kcal mol^{-1}, it is concluded that the cleavage of
tetramethylene involves an activation energy of 6 kcal mol^{-1} (see
diagram). For the reactions of 1,2-dimethylcyclobutanes,[34] the heat
of formation of the (in this case disubstituted) tetramethylene
diradical can be compared to the heat of formation of the transition

state for geometrical isomerization and cleavage to propene. In both
reactions, the diradical is 6 kcal mol^{-1} lower in energy than the
transition state. Since there is reason to believe that the barrier
to rotation in _monoradicals_ is small[34,36] (≤ 1 kcal mol^{-1}) this picture

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[36]P. Krusic, P. Meakin and J. P. Jesson, _J. Phys. Chem._,75, 3438
(1971).
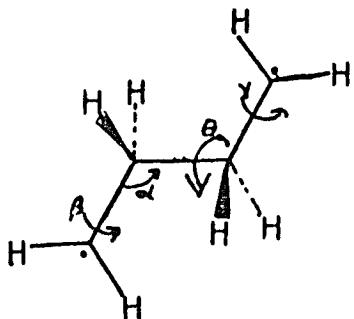
is consistent with the view that a 1,4-diradical is capable of stereo-equilibration before either reclosure to cyclobutanes or cleavage to olefin. One cannot rule out the possibility that in diradicals there are through bond interactions[35e] that may make the rotational barriers high. A diradical model of this sort is capable of accommodating a wide variety of stereochemical results depending on the relative heights of the barriers to rotation, reclosure, and cleavage.

This calculated barrier to reclosure of the diradical to cyclo-butane conflicts with the experimental observations that single radicals recombine with little or no activation energy.[37] How the calculated barrier is to be rationalized is still unresolved, but it may be viewed as the energy required for closing a strain-free, transoid tetramethylene diradical to a transition state which incor-porates some of the strain of cyclobutane.

Quantum mechanical calculations[35a,b] predict a different energy profile for the tetramethylene diradical. In contrast to the charac-terization of tetramethylene as a diradical which is protected by energy barriers of 6 kcal mol^{-1}, the calculations show no local minima for tetramethylene. This is not to say that tetramethylene is a

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[37](a) R. Gomer and G. B. Kistiakowsky, J. Chem. Phys., 19, 85 (1951); (b) G. B. Kistiakowsky and E. K. Roberts, J. Chem. Phys., 21, 1637 (1953); (c) M.H.J. Wiznen, J. Chem. Phys., 28, 271 (1958); (d) P. Ausloos and E.W.R. Steacie, Can. J. Chem., 33, 1062 (1955); (e) C. A. Heller, J. Chem. Phys., 28, 1225 (1958); (f) J. A. Kerr and A. F. Trottman-Dickenson, Trans. Farad. Soc., 55, 572, 921 (1959); (g) E. I. Metcalfe and A. F. Trottman—Dickenson, J. Chem. Soc., 4620 (1962); (h) E. I. Metcalfe, ibid., 3560 (1963); (i) J. J. Throssel, Int. J. Chem. Kinet., 4, 273 (1972).
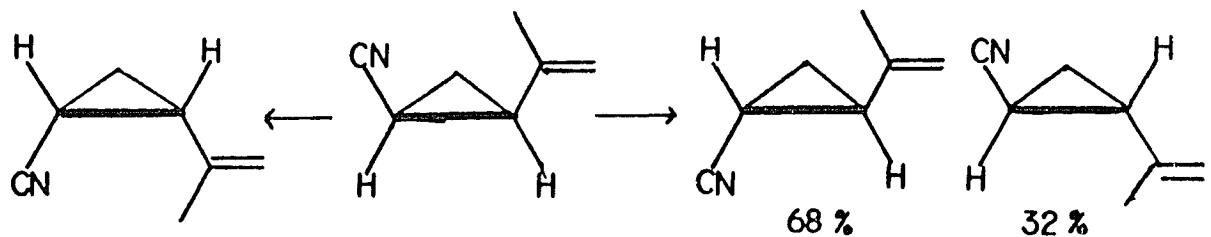
transition state existing for only one vibrational lifetime. Rather,

the energy for this model of tetramethylene does not vary with changes

in angles α, β, γ and θ. Hoffmann[35b] concludes that tetramethylene

will spend relatively long times ($> 10^{-12}$ sec) exploring this more or

less equienergetic surface making it "operationally indistinguishable"

from a diradical intermediate protected by energy barriers. Since

over a large portion of the energy surface, the energy of tilting a

methylene from its equilibrium position costs little energy, the

authors believe that this picture can account very well for the

cis-trans isomerization observed in cyclobutanes as well as the

cleavage to olefins. Thus, stereoequilibration of the diradical would

be predicted by this model.

A third characterization of a 1,4-diradical is analogous to that

proposed by Doering[6c] for a 1,3-diradical to explain the results of

the thermal rearrangement of some cyclopropanes.[6] In this picture, a

1,3-diradical is not an intermediate, but a transition state with the

lifetime of one vibration. In the thermal rearrangement of optically

active 1-cyano-2-isopropenylcyclopropanes, three independent processes

were observed: enantiomerization of the starting material and

diasteriomerization to a pair of optical antipodes. Since the results

could not be rationalized by a scheme consisting of a set of interme-

diate diradicals which can interconvert by the rotation of one bond

68 %   32 %

at a time with ring closure competitive with bond rotation, Doering

offered a new hypothesis based on the RRKM theory of unimolecular

reactions.

Ring opening is pictured in its initial stages as following a

Morse type of curve for the dissociation of a diatomic molecule. As

the distance of separation increases, the energy of the system

approaches that of two radicals separated by an infinite distance

(i.e., bonding between the radical centers is zero). However, since

the two radicals are connected by a (one carbon) bridge, further

separation encounters the bending vibration of the methylene bridge.

The complete description of the diradical then becomes the superposi-

tion of two potential energy curves: that for C-C stretch and that

for $-CH_2-$ bend. Superposition of the torsional modes of cyclopropane
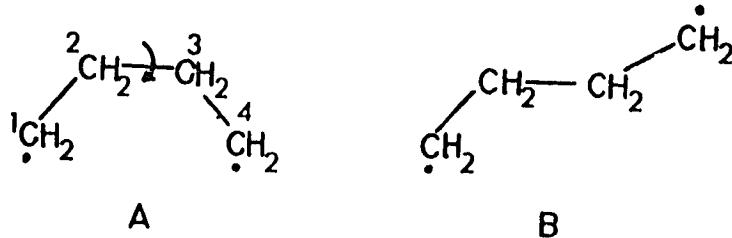
(which are treated as separable modes, in much the same way as is done for infrared frequencies) on this combination stretching - bending mode is required to transform the stretching - bending motion into an observable reaction.

The different amounts of products arising from rotation about the bonds bearing the isopropenyl and cyano groups are described as resulting from different "rotational propensities" for substituents and it is suggested that these propensities may be an intrinsic property of the juxtaposition of two groups in a particular ring system. For example, in the cyclopropane ring the rotational propensity of cyano-hydrogen vs. isopropenyl-hydrogen is 2.20,[6c] of methyl-hydrogen vs. ethyl-hydrogen, 1.17[6a] and phenyl-hydrogen vs. phenyl-carbethoxy, 13.3.[6b]

Stretching with rotation is a continuous process in the same way that a vibration is a continuous process. Any displacement from the maximum separation of the radical centers results in a positive bonding interaction. In this sense a diradical can be described as a transition state with the lifetime of one vibration. The energy of the two separated radical centers is closer to that of two radicals at infinite distance, since at the outer reaches of the vibration, bonding between the centers has fallen to zero.[6c]
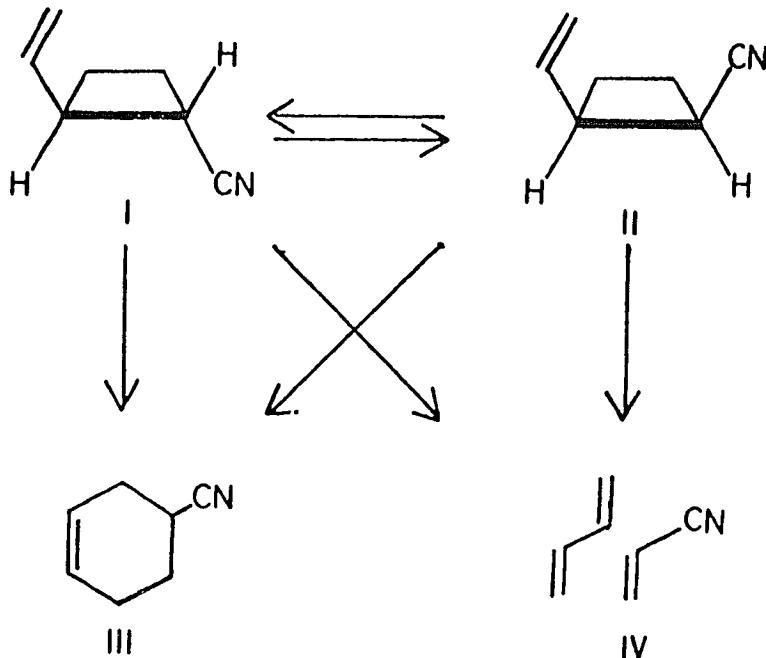
Critical to the statement that any displacement from the maximum radical separation distance leads to positive bonding is that the diradical closes with no enthalpy of activation. As cited previously,

this observation is made for the combination of a wide range of

radicals--even of two such bulky groups as t-butyl[37h] or of a highly

stabilized radical such as allyl with simple radicals.[37i] In the case

of cyclopropanes it was concluded that "the best trap for a diradical

is its own reclosure to a covalent bond." The application of this

statement to larger rings than cyclopropane is not straightforward.

The diradical derived from cyclopropane differs from its higher

homologues in the flexibility of the carbon chain connecting the two

radical centers and in the number of conformationally distinct options

in the latter. In cyclopropane the restoring force of the methylene

bending mode brings the two radical centers to within bonding distance.

A   B

The escape to other products (e.g. migration to form olefin or :CH_2

extrusion) is relatively unfavorable. Adding one more methylene to

the bridge connecting the radical centers alters the situation drasti-

cally. Rotation around the C2-C3 bond provides an escape route of low

activation energy ($\sim$3 kcal mol^{-1}) for the radical centers while

increasing the entropy of the system. A rotation of this sort can

convert a diradical of structure A, which might be described as a

diradical-as-transition-state into a diradical B, which could be more

accurately described by the definition of a diradical as a conforma-

tionally equilibrated, barrier-protected intermediate.[34]

It is the purpose of this dissertation to determine the effect
of the larger ring system on the mechanism of thermal rearrangement.
The actual molecules studied are optically active trans-1-cyano-2-
vinylcyclobutane (I) and cis-1-cyano-2-vinylcyclobutane (II). The
rearrangement produces four products: butadiene, acrylonitrile, the
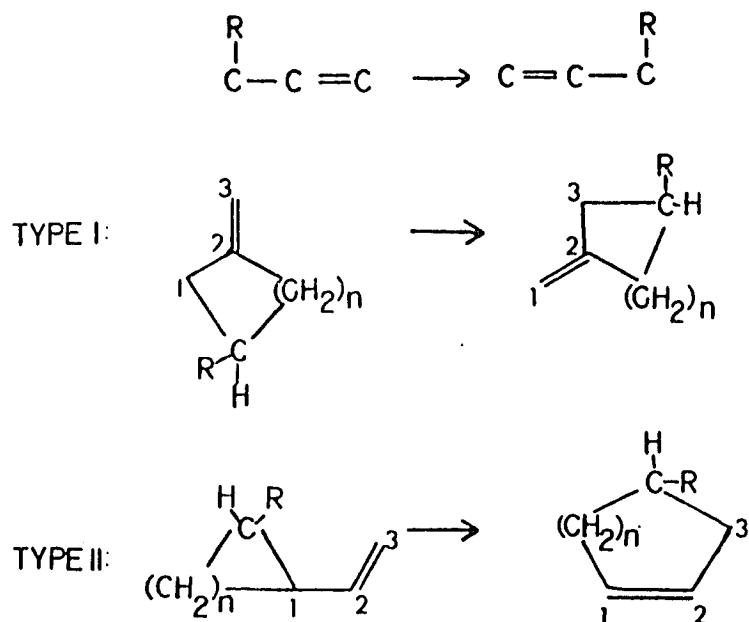
geometrical isomer of the starting material and the product of a [1,3]
sigmatropic shift, 4-cyanocyclohexene. By examination of the extent
of retention of optical activity in the products and the configurational
relationships between starting material and products, it can be deter-
mined if the model of a continuous diradical as a transition state can
be extended to a 1,4 diradical.

In contrast to the previously studied cyclopropane system in
which only very small amounts of cyanocyclopentene are produced, ring
enlargement constitutes a substantial portion of the reaction of I and

II.   In the rearrangement to 4-cyanocyclohexene, it is possible to study the stereochemistry of a [1,3] sigmatropic rearrangement in addition to the rearrangements in which the cyclobutane ring is regenerated.
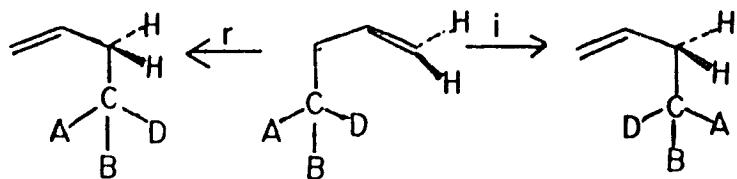
[1,3] Sigmatropic Rearrangements

A sigmatropic rearrangement of order [i,j] has been defined by Woodward and Hoffmann[15a] as "the migration of a σ bond, flanked by one or more π electron systems to a new position whose termini are i-1 and j-1 atoms removed from the original bonded loci in an uncatalyzed, intramolecular reaction." Existing studies of [1,3] sigmatropic rearrangements are limited to migrations of carbon and fall into two categories:
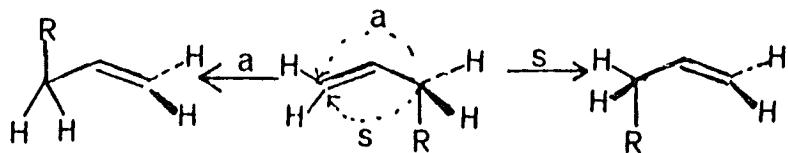
In type I, the migrating center is linked to carbon 2 of the allyl framework by a carbon chain. Where n = 0 and n = 1 the examples correspond to the degenerate methylenecyclopropane and methylenecyclobutane rearrangements, respectively. In type II the migrating center is linked to carbon 1 of the allyl framework through a carbon ring. Here, n = 0 and n = 1 correspond to the ring expansion of vinylcyclopropane and vinylcyclobutane to cyclopentene and cyclohexene, respectively.

There are four distinct stereochemical results which arise from the combination of the two possible modes of reaction of the migrating center and the two possible modes of reaction of the allyl moiety. The migrating center may react with either retention of configuration (r) or inversion of configuration (i) and the migration may occur across
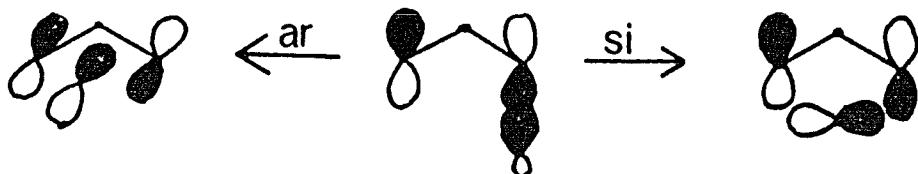
the same side of the π framework (suprafacial, s) or across the nodal plane of the π framework (antarafacial, a).
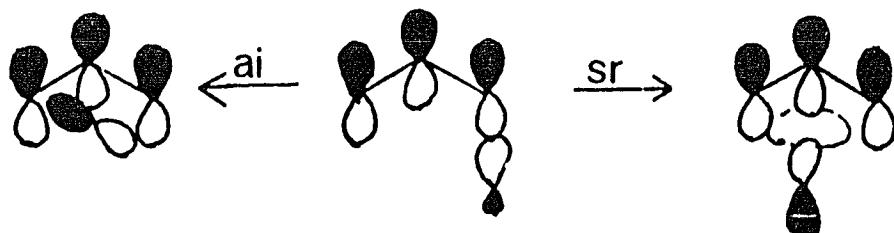
Much of the study of [1,3] sigmatropic shifts has been directed to determining if the reactions proceed by one-step, concerted

processes or two-step, diradical processes. The two criteria outlined previously (stereospecificity and activation energy) may be used to determine if the reactions follow a concerted path. For the first criterion the theoretical treatments of concerted reactions may be used to predict the stereochemical course followed by a concerted reaction. The frontier orbital approach of Woodward and Hoffmann[15a] predicts of a concerted reaction that migration will occur suprafacially with inversion of configuration and/or antarafacially with retention of configuration. These two stereochemical outcomes are the result of continuous overlap of frontier orbitals in the transition state (in the allylic system, the ψ_2 orbital with a nodal plane at the middle atom):

Continuous overlap of subjacent orbitals (the ψ_1 orbital of the allylic system) according to Berson and Salem involves migration in a suprafacial manner with retention of configuration and/or in an antarafacial manner with inversion of configuration:

Berson and Salem[16] have calculated the relative favorability of three possible pathways for a [1,3] sigmatropic rearrangement: concerted through the overlap of frontier orbitals, concerted through the overlap of subjacent orbitals, and diradical. For a system consisting of an allyl group and a p orbital, the ordering of energies is calculated to be: "frontier orbital" concerted < "subjacent orbital" concerted < diradical. The energy difference between any two of these paths is small (1.3 to 3.2 kcal mol^{-1}), however, and other factors (e.g. steric) may determine which of the three paths will predominate.
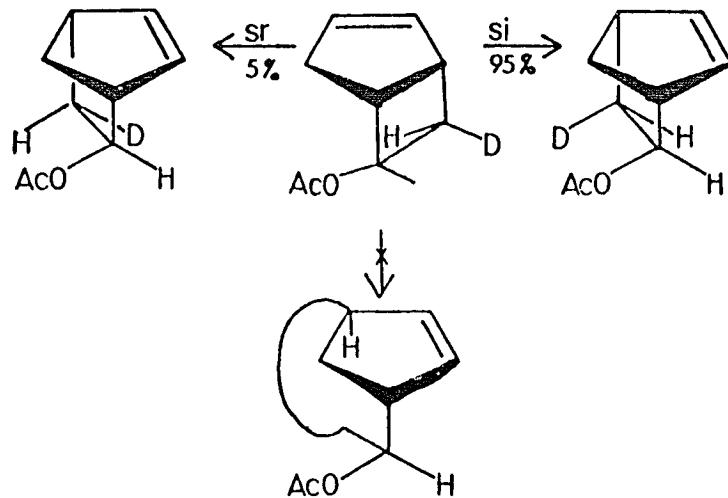
Studies of the methylenecyclopropane rearrangement,[38] the methylenecyclobutane rearrangement[39] and the vinylcyclopropane rearrangement[40] have shown that none of these reactions follows exclusively one stereochemical course. Several studies of vinylcyclobutanes in which the stereochemistry of the [1,3] sigmatropic rearrangement has been elucidated will be described in greater detail since they are so directly related to the subject of this dissertation, the ring expansion of trans- and cis-1-cyano-2-vinylcyclobutane.

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[38] W. Doering and L. Birladeanu, Tetrahedron, 29, 499 (1973).

[39] (a) E. T. Fossel, Ph.D. Thesis, Harvard University, 1970. (b) J. E. Baldwin and R. H. Fleming, J. Amer. Chem. Soc. 95, 5249, 5256, 5261 (1973).

[40] (a) P. H. Mazzocchi and J. J. Tamburin, ibid. 92, 7220 (1970); (b) W. E. Doering and E.K.G. Schmidt, Tetrahedron, 27, 2005 (1971).

In bicyclo[3.2.0]hept-2-ene-endo-6-yl acetate-exo-7-d[41] which

rearranges to 5-norbornen-exo-2-yl acetate-exo-3-d and -endo-3-d, the

allyl framework is fixed in a five membered ring. The effect of this

stereochemical limitation is to restrict migration across the allyl
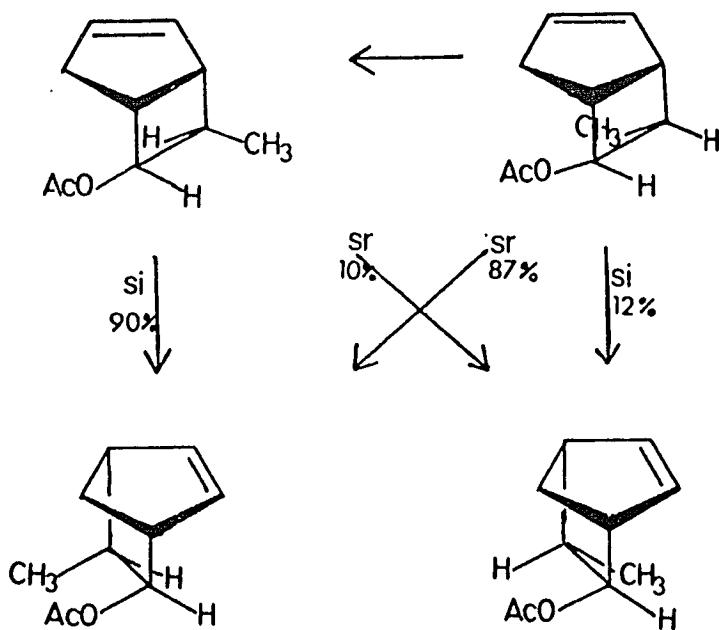
frame to the suprafacial mode since migration in the antarafacial mode

would lead to a highly strained trans-bridged bicyclo[2.2.1]heptyl

ring system. In addition to side products, thermal rearrangement of

bicyclo[3.2.0]hept-2-ene-endo-6-yl acetate-exo-7-d gives the product

of [1,3] sigmatropic rearrangement, 95% of which is 5-norbornen-exo-

2-yl acetate-exo-3-d and 5% of which is 5-norbornen-exo-2-yl acetate-

endo-3-d.

Substitution of a methyl group[42] for deuterium results in a less

stereoselective reaction with 3-exo-methyl-5-norbornen-exo-2-yl

[41]J. A. Berson and G. L. Nelson, J. Amer. Chem. Soc., 89, 5503
(1970).

[42](a) J. A. Berson and G. L. Nelson, ibid., 92, 1096 (1970);
(b) G. L. Nelson, Ph.D. Thesis, University of Wisconsin, 1969.

acetate consisting of 90% of the [1,3] rearrangement product. In these two examples, the predominant pathway has the stereochemistry predicted by the Woodward-Hoffmann rules: suprafacial with inversion. In 7-endo-methylbicyclo[3.2.0]hept-2-ene-6-endo-yl acetate the direction of the stereoselectivity is altered with 87% of the [1,3]
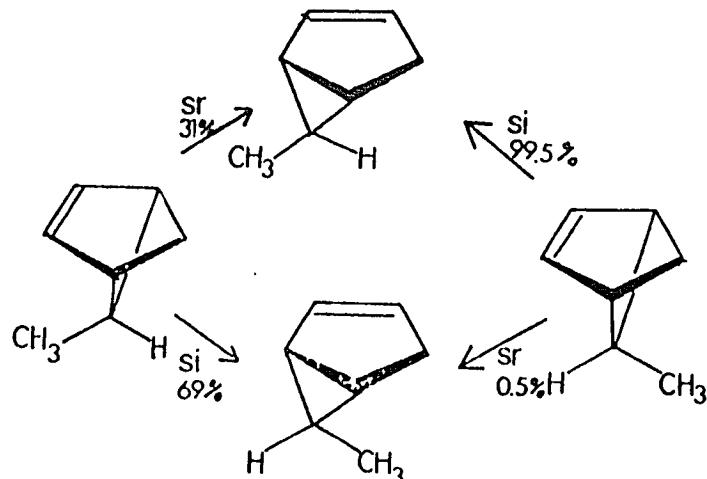
rearrangement product (3-exo-methyl-5-norbornen-exo-2-yl acetate) having the stereochemistry which is the same as that predicted by the overlap of subjacent orbitals in the transition state. The rearrangement also produces 7-exo-methylbicyclo[3.2.0]hept-2-ene-6-endo-yl acetate, in a reaction which must proceed without continuous overlap in the transition state.
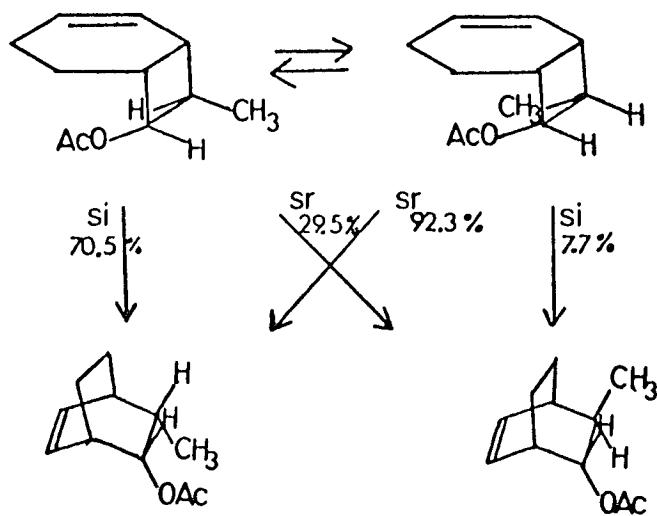
Roth[43] observed similar results in the rearrangement of methyl substituted bicyclo[2.1.1]hexenes. 5-Endo-methylbicyclo[2.1.1]hex-2-ene

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[43]W. R. Roth and A. Friedrich, Tetrahedron Letters, 2607 (1969).

rearranges with predominant inversion of configuration while the corresponding 5-exo-methyl compound, although still rearranging with predominant inversion of configuration, reacts less stereoselectively by a factor of 100.
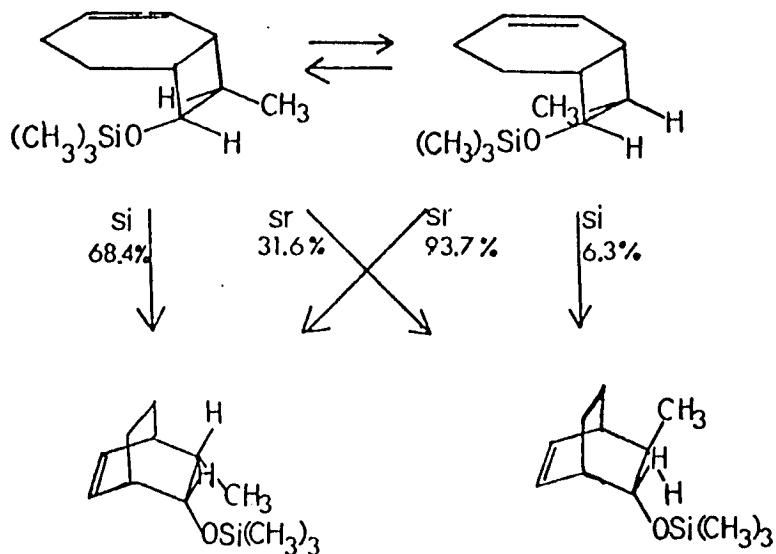
In the thermal rearrangement of methyl substituted bicyclo[4.2.0]octenes,[44] the endo compounds rearrange with predominant

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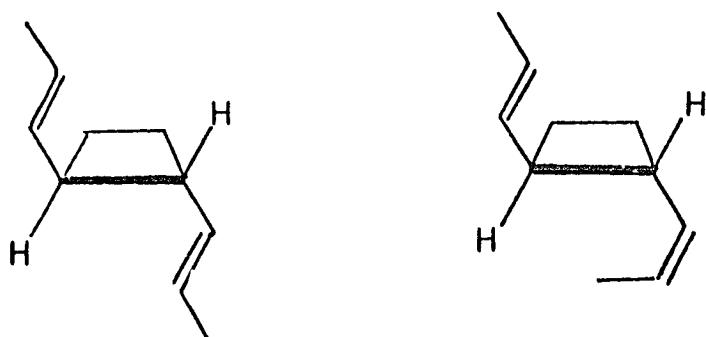
[44] (a) J. A. Berson and R. W. Holder, J. Amer. Chem. Soc. 95, 2037 (1973); (b) R. W. Holder, Ph.D. Thesis, Yale University, 1972.

retention of configuration, while the _exo_ compounds rearrange with predominant inversion of configuration at the migrating center. Among the other reactions observed in these systems is the epimerization of the starting material.
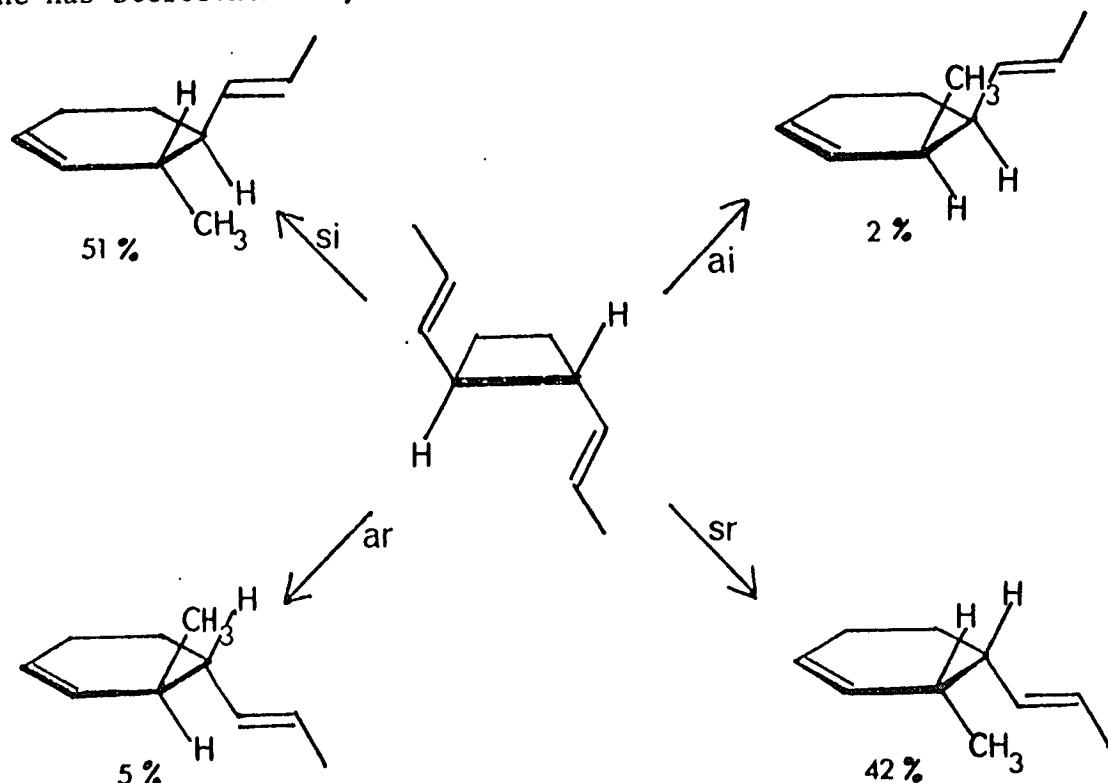
The last example is that of optically active dipropenylcyclo-butanes.[45] Since the allyl system is no longer constrained to

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[45](a) J. A. Berson and P. B. Dervan, _J. Amer. Chem. Soc._ 95, 269 (1973); (b) P. B. Dervan, Ph.D. Thesis, Yale University, 1972.

reaction in the suprafacial mode, an appropriate label (a methyl group) was placed on the allyl system. Examination of the ratio of the diastereomeric [1,3] shifted products and the enantiomeric composition of each of the diastereomers allows the products to be partitioned into the four possible stereoisomers. Of the two diastereomers formed, one has stereochemistry consistent with that resulting from the two
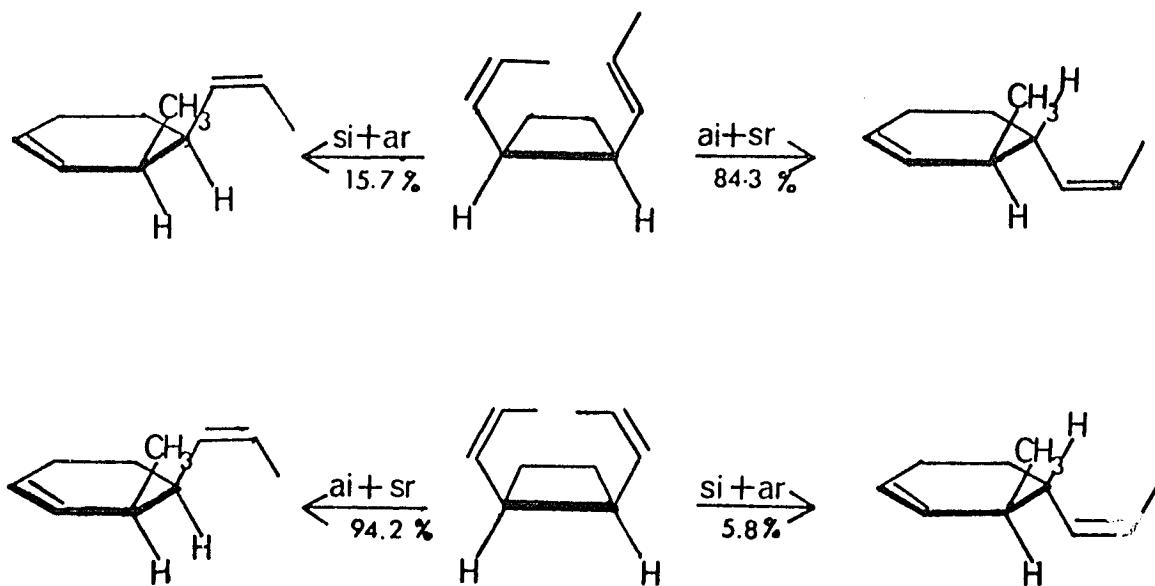
Woodward-Hoffmann allowed processes (ar + si), while the other has the same stereochemistry as that resulting from the two subjacent orbital stabilized processes (ai + sr). The enantiomeric purity of each diastereomer allows the ratio of antarafacial to suprafacial processes to be determined. Dissection of the reaction of (1R:2R)-trans-1E,2Z-dipropenylcyclobutane gives si, 50%; ar, 2%; sr, 48%; ai, 0% and that

of (1R:2R)-trans-1E,2E-dipropenylcyclobutane gives si, 51%; ar, 5%; sr, 42%; ai, 2%. In these trans-disubstituted cyclobutanes, the predominant pathway is still the suprafacial mode, and the reactions are even less stereoselective than in the bicyclic cases.

Thermal rearrangement of cis-1Z,2Z- and cis-1E,2Z-dipropenyl-cyclobutanes did not allow dissection of the reaction into the four

possible pathways because the former compound is achiral and the latter, although chiral, was not synthesized in optically active form. Examination of the relative proportions of the two diasteriomeric products did allow the reaction of these cis-dipropenylcyclobutanes to be divided into the relative amounts of (ar + si) and (sr + ai) products.

The predominant pathways in both cases are sr and ai which are forbidden products by the Woodward-Hoffmann rules. Partitioning of each diastereomer is impossible because of the lack of optical activity in the starting material. If it is true that the suprafacial processes overwhelmingly predominate, then, in these cases, the proportion of products which react with retention of configuration is greater in the cis-disubstituted compounds than in the corresponding trans-disubstituted compounds. This finding parallels the results in the previous bicyclic examples where the endo-substituted compounds (where the substituent on the migrating terminus is cis to the allyl system) show greater proportions of retention of configuration in the product than the corresponding exo-substituted compounds (where the substituent on the migrating terminus is trans to the allyl system). The stereochemical data are summarized in Table 3.

Thus, none of these vinylcyclobutane rearrangements follows one stereochemical pathway exclusively. On the basis of stereochemistry alone, one cannot differentiate three mechanistic alternatives: the competition of two stereospecific, concerted pathways; the competition of a concerted path with a diradical; or a process proceeding completely by a diradical.

Activation energies have been determined for several vinylcyclobutane rearrangements. Isopropenylcyclobutane rearranges to methylcyclohexene with an activation energy of 51 kcal mol^{-1}.[12t] The

Table 3. Stereochemical Distribution of the Products of [1,3]
Sigmatropic Rearrangements.

Reactant	sr	si	Ref.
exo series			
5-exo-Methylbicyclo[2.1.1]hex-2-ene	0.5%	99.5%	43
Bicyclo[3.2.0]hept-2-ene-endo-6-yl acetate-exo-7-d	5%	95%	41
7-exo-Methylbicyclo[3.2.0]hept-2-ene-endo-6-yl acetate	9%	90%	42
8-exo-Methylbicyclo[4.2.0]oct-2-ene-endo-7-yl acetate	29%	71%	44
8-exo-Methyl-endo-7-O-trimethylsilylbicyclo[4.2.0] oct-2-ene	31%	68%	44
trans-1Z,2Z-Dipropenylcyclobutane	45%	55%	45
trans-1Z,2E-Dipropenylcyclobutane	49%	51%	45
endo series			
5-endo-Methylbicyclo[2.1.1]hex-2-ene	31%	69%	43
4-endo-Methylbicyclo[3.2.0]hept-2-ene-endo-6-yl acetate	88%	12%	42
8-endo-Methylbicyclo[4.2.0]oct-2-ene-endo-7-yl acetate	92%	8%	44
8-endo-Methyl-endo-7-O-trimethylsilylbicyclo[4.2.0] oct-2-ene	94%	6%	44

activation energies for the overall rates of disappearance of several

bicyclic compounds have been determined; bicyclo[3.2.0]heptene,

49.6 kcal mol^{-1}:[46] bicyclo[3.2.0]hept-2-ene-endo-6-yl acetate-exo-7-d,

47.1 kcal mol^{-1};[42b] 7-exo-methylbicyclo[3.2.0]hept-2-ene-endo-6-yl

acetate, 47.1 kcal mol^{-1};[42b] and 8-exo-methyl-endo-7-O-trimethylsilyl-

bicyclo[4.2.0]oct-2-ene, 47.6 kcal mol^{-1}.[44b] One can calculate an

activation energy for a "two radical" reaction of 48.6 - 49.6 kcal

mol^{-1} [E_a n-propylcyclobutane (61.6 kcal mol^{-1})[12c] - 1 allyl stabili-

zation (12 - 13 kcal mol^{-1})].[22] The small difference between the

observed and calculated activation energies suggests that if any of

the reactions is concerted the stabilization due to continuous overlap

of orbitals in the transition state is small (2 - 3 kcal mol^{-1}). In

several of these examples a reaction which is constrained to be

non-concerted (epimerization) is in effective competition with the

[1,3] sigmatropic rearrangements. This fact also suggests that the

stabilization due to the continuous overlap of orbitals, if present,

must be small.

Even this second criterion for a concerted reaction does not

allow a clear distinction to be made among the three mechanisms con-

sistent with the stereochemical results. Indeed, if the calculations

of Berson and Salem[16] are correct, these alternatives cannot be dif-

ferentiated since the difference in energy between them is small.

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[46]A. T. Cocks and H. M. Frey, J. Chem. Soc. A, 2564 (1971).

Berson and Holder[44] and Berson and Dervan[45] suggest that the concerted reaction brought about by subjacent orbital stabilization must be at least one of the pathways for the reaction. This proposal is based on the fact that as the frame holding the allyl group becomes more flexible in going from bicyclohexene to bicycloheptene to bicyclooctene and finally to a completely free allyl moiety in the cyclobutanes (Table 3) the proportion of "sr" product increases steadily. The increased flexibility of the allyl frame allows the overlap of the migrating p-orbital with the central carbon of the allyl group to occur more readily. This overlap stabilizes the path relative to a diradical path or the path predicted by the Woodward-Hoffmann rules.
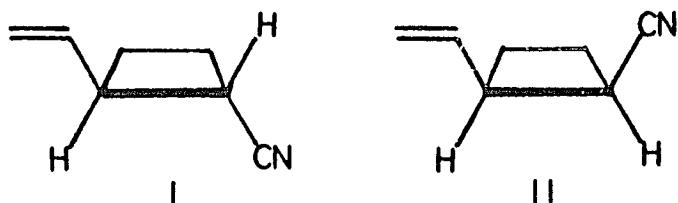
Diradical mechanisms cannot be ruled out for these examples of [1,3] sigmatropic shifts. A difficulty is to be found in the unpredictability of the relative rates of bond rotations in diradicals. In the previously cited examples of the propellanes (Table 2), the stereochemistry of the ethylenes formed on thermolysis depended not only on the nature of the substituent but also on its orientation in the starting material. Not even the dideuteriopropellane gives a statistical distribution of cis- and trans-dideuterioethylenes, the ratio being 57:43. In the discussion of the results of the rearrangement of optically active trans-1E,2E-dipropenylcyclobutane, Berson and Dervan[45] propose that if the reactions proceed exclusively by a diradical mechanism the distribution of products should be governed by

statistical considerations; the relative proportions of the paths should be sr > si > ar > ai, with sr being the most favored process since it involves the smallest number of bond rotations. Arguments of this type are of doubtful value when one considers that trans-1-cyano-2-isopropenylcyclopropane[6c] is converted to its enantiomer (a process requiring two bond rotations) faster than it is converted to either diastereomer (processes requiring one bond rotation).
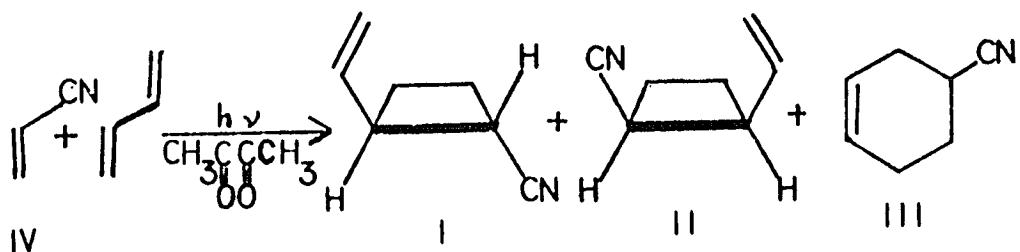
Thus, even though the stereochemistry of these rearrangements has been well studied and the activation parameters for some of them have been determined, a number of mechanistic alternatives remain for these reactions.

RESULTS AND DISCUSSION

The molecules chosen for this study of the stereochemical course of the thermal rearrangements of cyclobutanes are trans- and cis-1-cyano-2-vinylcyclobutane (I and II). The synthesis and elucidation of

structure of I and II had been reported by Dilling and Kroening.[47] Their method, the photosensitized cycloaddition of butadiene and acrylonitrile, was used to prepare small amounts of racemic I and II.

Heating of racemic I or II at 217.8° in the gas phase gives mixtures of I, II, III, and IV (Figure 1). All thermal rearrangements proceed with >98% mass balance. Changing the surface by carrying out the reactions in tubes made of lead potash-glass instead of Pyrex, a procedure which is known to modify the course of some thermal reactions,[48] gives identical results. No 3-cyanocyclohexene is observed within the limits of detection by gas chromatography (0.2%).

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[47]W. L. Dilling and R. D. Kroening, Tetrahedron Lett., 695 (1970).

[48]W. Doering and G. H. Beasley, Tetrahedron, 29, 2231 (1973).
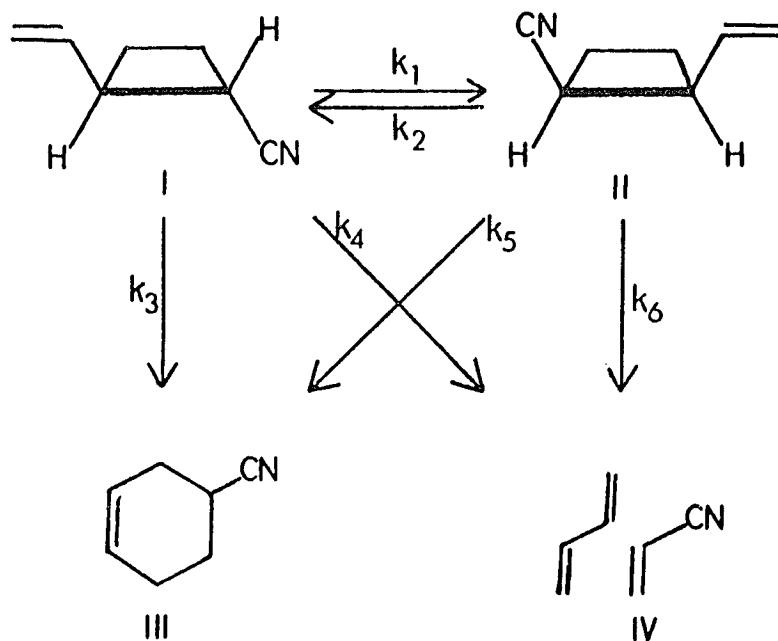
Figure 1. Kinetic Scheme for Interconversions of I, II, III and IV.

That butadiene and acrylonitrile (IV) are not formed by the retro-Diels-Alder reaction of 4-cyanocyclohexene (III) is confirmed by the following experiment. Heating of III for twelve hours at 217.8° in the gas phase results in quantitative recovery of III. Similarly, that I, II and III are formed by cleavage of I or II to butadiene and acrylonitrile and subsequent cycloaddition of acrylonitrile and butadiene is ruled out on the basis of two considerations. Since cycloaddition of acrylonitrile and butadiene gives III, I and II in the proportions 200:1:1,[47] the observed product distribution (see Tables 12 and 13 in Experimental Section) cannot be accounted for by this mechanism. Further, the rate of cycloaddition of acrylonitrile and butadiene is too small to account for the formation

of III. The rate of cycloaddition[49a] of butadiene and acrylonitrile to

form III is about the same as that of butadiene and acrolein to form

cyclohexenecarboxaldehyde. The gas phase rate of the latter reaction

is $k = 10^{6.2} e^{\frac{-19,700}{RT}}$ $\ell \, mol^{-1} \, sec^{-1}$.[49b] The maximum concentration of

butadiene and acrylonitrile present (calculated from the amount of

acrylonitrile present at the last kinetic point at the highest tempera-

ture in a tube of 8 ml capacity) (see Tables 12 and 13 in Experimental

Section) is $7.18 \times 10^{-4} mol \, \ell^{-1}$. From these two quantities the maximum

number of moles of III formed from butadiene and acrylonitrile after

four hours is calculated to be 0.38% of the total reaction mixture or

3% of the III observed (see Tables 12 and 13 of Experimental Section).

The actual amount of III formed by this route is less than 3% because

the concentration of acrylonitrile begins at zero and gradually

increases as the reaction progresses.

As can be seen from the preliminary results of the thermal

rearrangement of I and II, the kinetic scheme, although simplified by

the irreversible formation of III and IV, is complicated by the fact

that I and II interconvert and that I and II form III and IV at

comparable rates (i.e., within a factor of three). The specific rate

constants for the kinetic scheme of Figure 1 can be obtained by the

solution of the following set of differential equations with the help

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[49](a) G. J. Janz and N. E. Duncan, J. Amer. Chem. Soc., 75, 5389
(1953); (b) G. B. Kistiakowsky and J. R. Lacher, ibid., 58, 123 (1936).

of a computer program (described in the Experimental Section and
listed in Appendix I), which calculates the concentration of each

$$\frac{d[I]}{dt} = -(k_1 + k_3 + k_4) [I] + k_2 [II]$$

$$\frac{d[II]}{dt} = -(k_2 + k_5 + k_6) [II] + k_1 [I]$$

$$\frac{d[III]}{dt} = k_3 [I] + k_5 [II]$$

$$\frac{d[IV]}{dt} = k_4 [I] + k_6 [II]$$

component at the experimental times for a given set of trial rate
constants, and also calculates $\bar{\sigma}$, a measure of the closeness of the
fit of the calculated and the experimental concentrations. The first
set of trial rate constants is obtained by considering the reactions
of I (and II) to be essentially irreversible at the beginning of the
reaction. The rate constants obtained in this manner are systemati-
cally varied, one at a time (by a method outlined in detail in the
Experimental Section), until the best fit of calculated and experimen-
tal concentrations is obtained.

The criterion used for the determination of the best fit is
similar to that used in the standard least squares regression in
which a set of points is fitted to a straight line. The quantity $\bar{\sigma}$ is
minimized for each component of the reaction mixture by variation of
the corresponding k's, where

$$\bar{\sigma}_I = \sqrt{\frac{\sum_n ([I]_{expt'l} - [I]_{calcd})^2}{(n-1)}}$$

n = the number of experimental points

$[I]_n$ = the concentration of I at kinetic point n

Thus, in principle, best values for a particular k are obtained from four sets of experimental data resulting from the fitting of the concentrations of I, II, III and IV, respectively. By way of example, in the determination of k_1, the specific rate constant for the conversion of I to II, the values of $\bar{\sigma}_I$ at each value of k_1 were plotted as were the values of $\bar{\sigma}_{II}$, $\bar{\sigma}_{III}$ and $\bar{\sigma}_{IV}$ vs. k_1 (k_2 through k_6 being held constant) (see Figure 2). In this instance as well as all the others, two of the resulting four curves are essentially flat; that is, the concentrations of two of the products are essentially insensitive to value of the specific rate constant being varied. In the case of k_1, $\bar{\sigma}_{III}$ and $\bar{\sigma}_{IV}$ are nearly constant for all values of k_1. Understandably, the two $\bar{\sigma}$'s most sensitive to the value of k_1 are those of the two components directly affected by k_1, I and II. When the best values for all of the rate constants have been obtained, the values of k_1 corresponding to the minimum value of $\bar{\sigma}_I$ and the minimum value of $\bar{\sigma}_{II}$ are nearly identical. In this way a best value for k_1 is obtained. The best values of the specific rate constants at 217.8° are shown in Figure 3 and Table 4. In Tables 4, 5, 6 and 7, the values of the
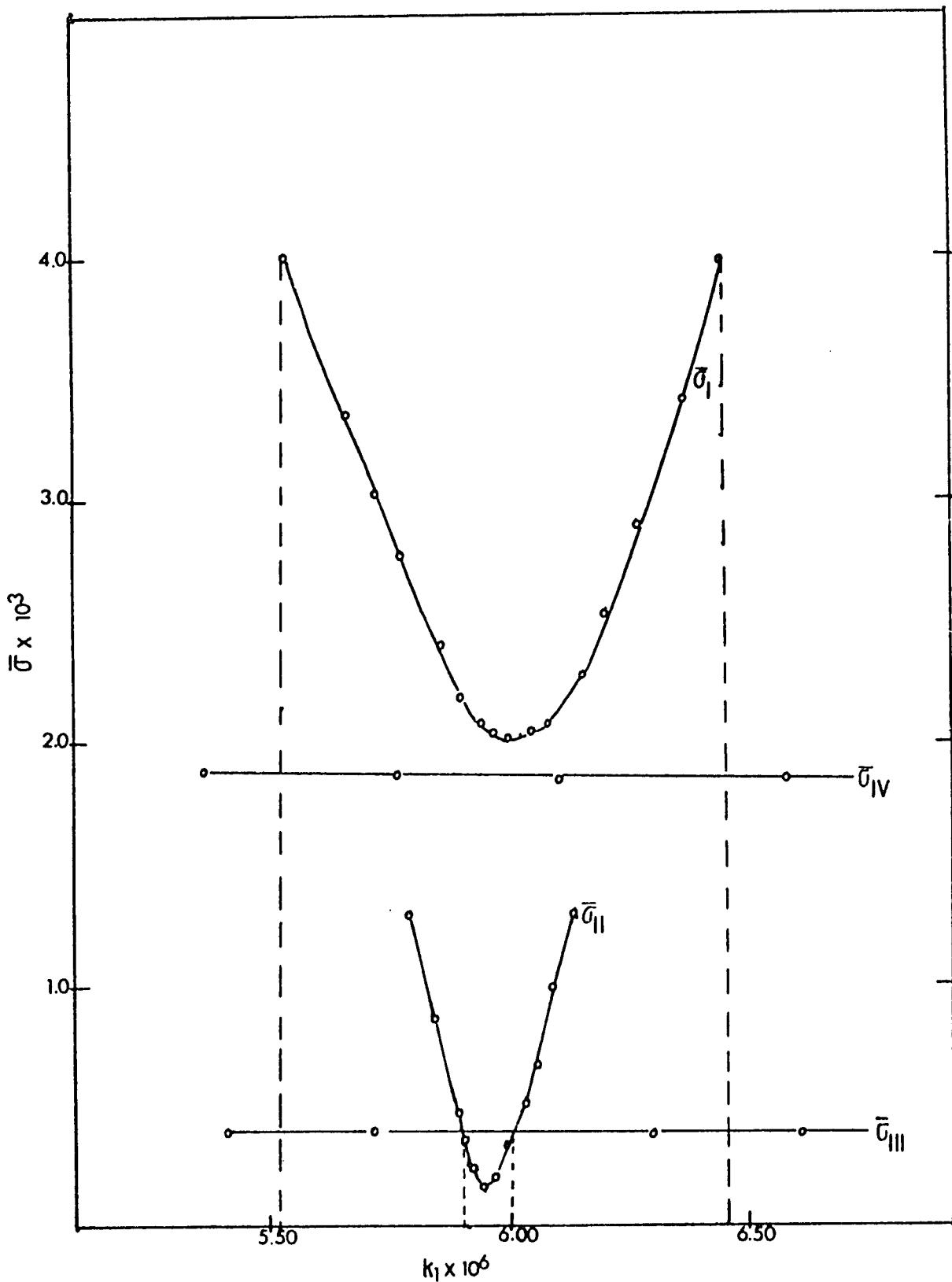
Figure 2. Plot of $\bar{\sigma}$ vs. k_1 at 217.8°. The error in k_1 is determined by the x- intercepts of $2\bar{\sigma}_I$ minimum and $2\bar{\sigma}_{II}$ minimum.

Table 4. Rate Constants and Their Probable Errors at 217.8°C as Determined from Plots of $\bar{\sigma}$ vs. k.

Rate Constant	I[c]		II		III		IV	
	k^a	$\bar{\sigma}_I^b$	k	$\bar{\sigma}_{II}$	k	$\bar{\sigma}_{III}$	k	$\bar{\sigma}_{IV}$
$k_1 = k_{I \to II}$	5.99±0.45 (±7.5%)	0.002009	5.96±0.04 (±0.6%)	0.000170		0.00345		0.001818
$k_2 = k_{II \to I}$	15.29±0.15 (±1.0%)	0.000646	15.29±1.50 (±9.8%)	0.005734		0.000330		0.005219
$k_3 = k_{I \to III}$	4.97±0.39 (±7.8%)	0.002001		0.000159	4.95±0.04 (±0.8%)	0.000244		0.001881
$k_4 = k_{I \to IV}$	4.16±0.40 (±9.6%)	0.002030		0.000160		0.000398	4.16±0.40 (±9.6%)	0.000818
$k_5 = k_{II \to III}$		0.000843	6.60±1.22 (±18.4%)	0.005717	6.60±0.05 (±0.8%)	0.000247		0.005480
$k_6 = k_{II \to IV}$		0.000843	8.66±1.3 (±15.0%)	0.005751		0.000247	8.64±0.54 (±6.2%)	0.005305

a) All k in units of $10^{-6} sec^{-1}$; error limit is range of k corresponding to $2\bar{\sigma}$; where no k is given $\bar{\sigma}$ is constant for all values of k.

b) Value of $\bar{\sigma}$ at its minimum.

c) Component from which k is determined.

Table 5. Rate Constants and Their Probable Errors at 207.1°C as Determined from Plots of $\bar{\sigma}$ vs. k.

Rate Constant	I[c]		II		III		IV	
	k^a	$\bar{\sigma}_I{}^b$	k	$\bar{\sigma}_{II}$	k	$\bar{\sigma}_{III}$	k	$\bar{\sigma}_{IV}$
$k_1 = k_{I \to II}$	2.29±0.10 (±4.4%)	0.000894	2.27±0.07 (±3.1%)	0.000692		0.000285		0.000483
$k_2 = k_{II \to I}$	6.29±0.13 (±2.1%)	0.001005	6.28±0.28 (±4.4%)	0.002493		0.000518		0.002689
$k_3 = k_{I \to III}$	1.92±0.08 (±4.2%)	0.000735		0.000698	1.88±0.02 (±1.3%)	0.000279		0.000484
$k_4 = k_{I \to IV}$	1.60±0.07 (±4.4%)	0.000725		0.000697		0.000144	1.56±0.05 (±3.0%)	0.000584
$k_5 = k_{II \to III}$		0.000960	2.63±0.14 (±5.3%)	0.002479	2.67±0.05 (±1.9%)	0.000494		0.002690
$k_6 = k_{II \to IV}$		0.000969	3.45±0.21 (±6.0%)	0.002498		0.000519	3.44±0.30 (±8.7%)	0.002706

a) All k in units of 10^{-6}sec^{-1}; error limit is range of k corresponding to $2\bar{\sigma}$; where no k is given $\bar{\sigma}$ is constant for all values of k.

b) Value of $\bar{\sigma}$ at its minimum.

c) Component from which k is determined.

Table 6. Rate Constants and Their Probable Errors at 191.7°C as Determined from Plots of $\bar{\sigma}$ vs. k.

Rate Constant	I[c]		II		III		IV	
	k^a	$\bar{\sigma}_I{}^b$	k	$\bar{\sigma}_{II}$	k	$\bar{\sigma}_{III}$	k	$\bar{\sigma}_{IV}$
$k_1 = k_{I \to II}$	4.57±0.67 (±14.6%)	0.002380	4.53±0.25 (±5.5%)	0.000950		0.000999		0.00045
$k_2 = k_{II \to I}$	12.86±0.62 (±4.8%)	0.002447	12.86±1.66 (±12.9%)	0.006098		0.001258		0.00255
$k_3 = k_{I \to III}$	4.52±1.06 (±23%)	0.002378		0.000950	4.52±0.61 (±13.5%)	0.001001		0.00045
$k_4 = k_{I \to IV}$	3.05±0.57 (±18.7%)	0.002378		0.000950		0.000999	2.99±0.14 (±4.7%)	0.000455
$k_5 = k_{II \to III}$		0.002448	5.36±1.7 (±31.7%)	0.006092	5.31±0.31 (±5.8%)	0.001256		0.002552
$k_6 = k_{II \to IV}$		0.002448	6.54±2.4 (±36.7%)	0.006094		0.001258	6.47±0.71 (±10.9%)	0.002553

a) All k in units of $10^{-7} sec^{-1}$; error limit is range of k corresponding to $2\bar{\sigma}$; where no k is given $\bar{\sigma}$ is constant for all values of k.

b) Value of $\bar{\sigma}$ at its minimum.

c) Component from which k is determined.

Table 7. Rate Constants and Their Probable Errors at 178.4°C as Determined from Plots of $\bar{\sigma}$ vs. k.

Rate Constant	I[c]		II		III		IV	
	k^a	$\bar{\sigma}_I^b$	k	$\bar{\sigma}_{II}$	k	$\bar{\sigma}_{III}$	k	$\bar{\sigma}_{IV}$
$k_1 = k_{I \rightarrow II}$	11.96±0.6 (±5.0%)	0.001362	11.90±0.2 (±1.7%)	0.000460		0.000445		0.001420
$k_2 = k_{II \rightarrow I}$	34.4±0.2 (±5.8%)	0.000322	34.5±0.4 (±1.2%)	0.000631		0.000208		0.000795
$k_3 = k_{I \rightarrow III}$	10.31±0.50 (±4.8%)	0.001366		0.000464	10.31±0.2 (±1.9%)	0.000442		0.001420
$k_4 = k_{I \rightarrow IV}$	7.39±0.54 (±7.3%)	0.001364		0.000164		0.000445	7.313±0.54 (±7.4%)	0.001422
$k_5 = k_{II \rightarrow III}$		0.000836	14.09±0.48 (±3.4%)	0.000639	14.22±0.13 (±0.9%)	0.000215		0.000791
$k_6 = k_{II \rightarrow IV}$		0.000838	15.63±0.46 (±2.9%)	0.000636		0.000208	15.76±0.46 (±2.9%)	0.000791

a) All k in units of $10^{-8} sec^{-1}$; error limit is range of k corresponding to $2\bar{\sigma}$; where no k is given $\bar{\sigma}$ is constant for all values of k.

b) Value of $\bar{\sigma}$ at its minimum.

c) Component from which k is determined.

the specific rate constants and their probable errors (at four
temperatures, 217.8°, 207.1°, 191.7° and 178.4°) are given along with
the minimum value of $\bar{\sigma}$ for each component.

The probable error in the specific rate constants is arbitrarily
defined as the range of k described by the values of k corresponding
to $2\bar{\sigma}$ for each component (see Figure 2). The quantity, $\bar{\sigma}$, is a
measure of the closeness of fit of the computer generated curve of
concentration against time to the experimental curve of concentration
against time. The absolute value of $\bar{\sigma}$ is a measure of the error in
the determination of k, but it presumably does not have the same
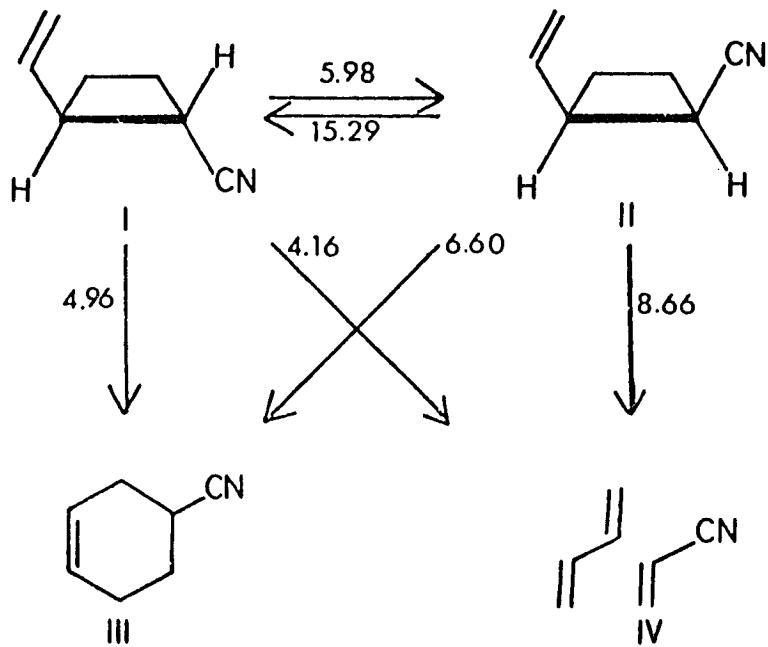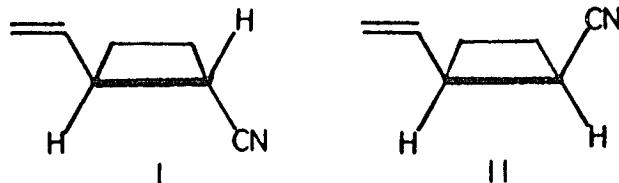
Figure 3. Specific rate constants for interconversion of I and II
and their rearrangements to III and IV at 217.8° in the
gas-phase in units of $10^{-6} \sec^{-1}$.

statistical significance as σ owing to the fact that a curve and not a straight line is being fitted. Thus, in a general way, $\overline{\sigma}$ is associated with the error in a given k by the statement that the smaller the minimum value of $\overline{\sigma}$, the narrower the range of k associated with $2\overline{\sigma}$ and the smaller the error in k.

To complete the study of the thermal rearrangements of racemic I and II the activation parameters for the reactions were determined from the least squares fit of log k vs. 1/T for k_1 through k_6 where T is the temperature in degrees Kelvin, the intercept is log A, and the slope is $-E_a/2.303R$ (see Figures 4 and 5).

As can be seen from inspection of Table 8, the activation energies and A factors for all the reactions observed are about the same and, within experimental error, agree with the value expected for a diradical mechanism. The study of the rearrangements of I and II is

simplified by the assumption that the breaking of the C1-C2 bond is expected to be facilitated by the stabilizing contribution of both the cyano group (8 kcal mol^{-1})[50] and the allyl group (12-13 kcal mol^{-1}).[48] The estimated activation energy for the rearrangements proceeding by

[50](a) W. Doering and K. Sachdev, in preparation;
(b) S. F. Sarner, D. M. Gale, H. K. Hall and A. B. Richmond, _J. Phys. Chem._, 76, 2817 (1972).

Table 8. Activation Parameters[a] for the Thermal Rearrangements of I and II.

Reaction	$\log A$[b]	E_a[c]	$\Delta H^{\ddagger}$[d]	$\Delta S^{\ddagger}$[e]
I →	$14.88 \pm 1.8\%$	$44.27 \pm 1.3\%$	43.3	6.6
I $\xrightarrow{k_1}$ II (k_1)	$14.41 \pm 2.1\%$	$44.10 \pm 1.5\%$	43.2	4.5
I $\xrightarrow{k_3}$ III (k_3)	$13.86 \pm 2.7\%$	$43.08 \pm 1.9\%$	42.1	2.0
I $\xrightarrow{k_4}$ IV (k_4)	$14.89 \pm 1.9\%$	$45.53 \pm 1.3\%$	44.6	6.7
II →	$14.88 \pm 2.6\%$	$43.55 \pm 1.9\%$	42.6	6.6
II $\xrightarrow{k_2}$ I (k_2)	$14.24 \pm 2.7\%$	$42.77 \pm 1.9\%$	41.8	3.7
II $\xrightarrow{k_5}$ III (k_5)	$14.13 \pm 2.6\%$	$43.37 \pm 1.9\%$	42.4	3.2
II $\xrightarrow{k_6}$ IV (k_6)	$15.09 \pm 2.8\%$	$45.25 \pm 2.0\%$	44.3	7.6

a) Determined by least squares fit of log k vs. 1/T, where k is the specific rate constant and T is the temperature in degrees Kelvin.

b) A in $\sec^{-1}$; error is the standard deviation of the intercept of log k vs. 1/T.

c) E_a in kcal mol^{-1}; error is the standard deviation of the slope of log k vs. 1/T.

d) in kcal mol^{-1} at 200°C.

e) in cal mol^{-1} $°K^{-1}$ at 200°C.
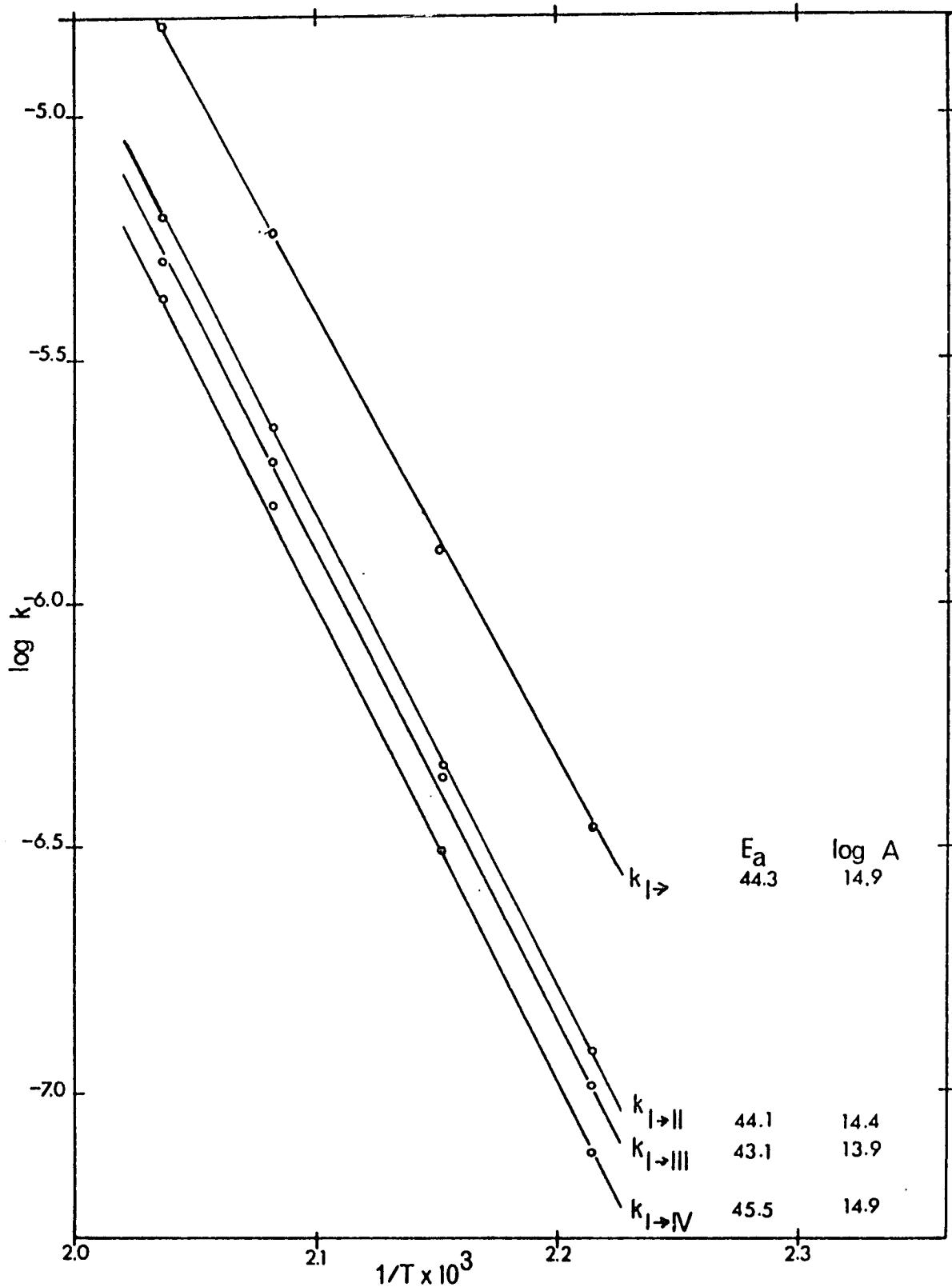
Figure 4. Plots of log k vs. 1/T for the reactions of I.
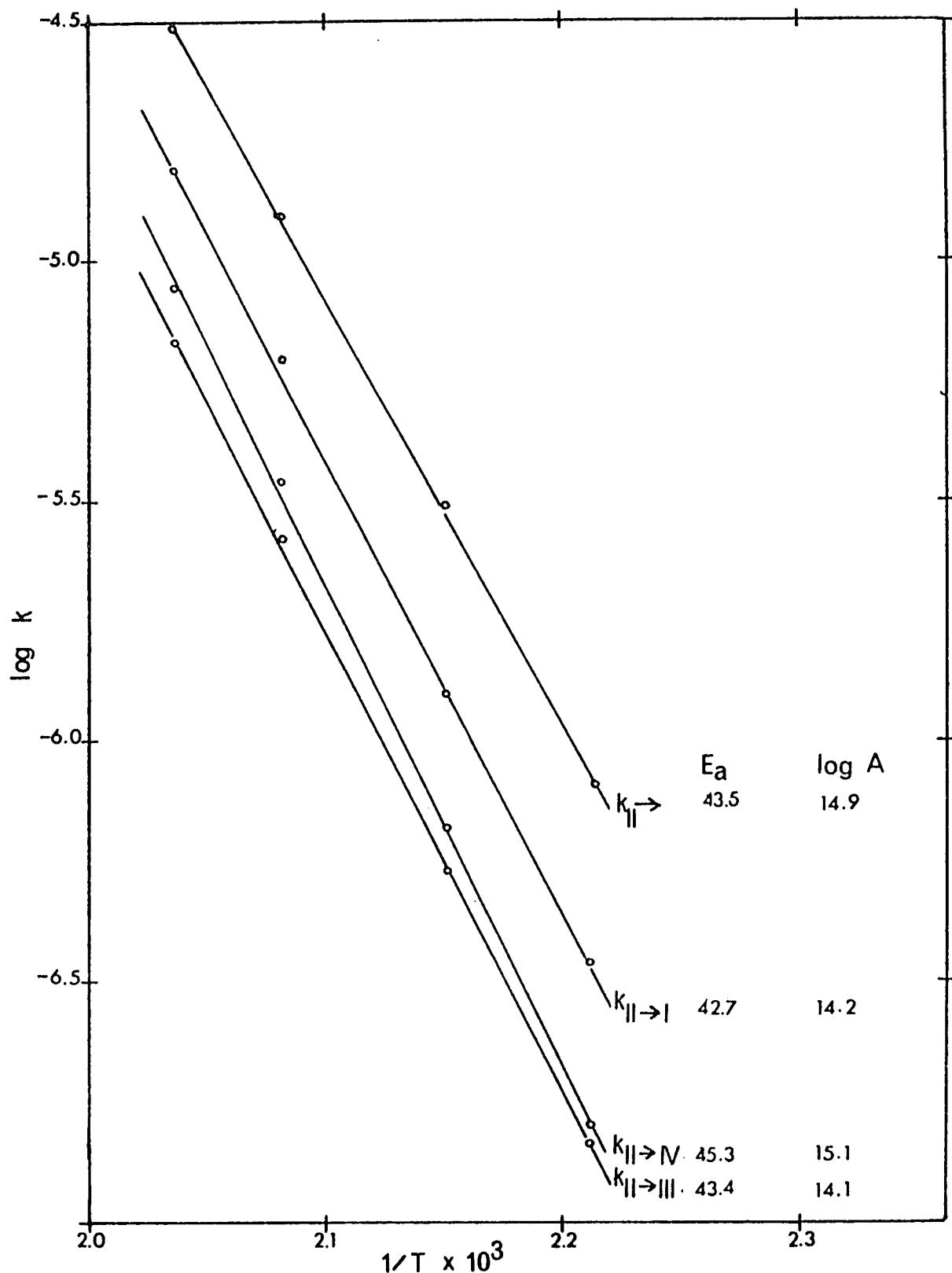
Figure 5. Plots of log k vs. 1/T for the reactions of II.

the cleavage of the C1-C2 bond is thus 42 kcal mol^{-1} [62 kcal mol^{-1} (E_a of cyclobutane decomposition)[51] - 12-13 kcal mol^{-1} (allyl stabilization)[48] -8 kcal mol^{-1} (cyano stabilization)[50]]. None of the rate constants shows a cancelling of a comparatively lower E_a by a small value of A in the expression $k = Ae^{-E_a/RT}$, which would result from negative values of $\Delta S^{\ddagger}$. Both low A factors (negative $\Delta S^{\ddagger}$) and low activation energies are characteristic of concerted, one-step mechanisms. In theory, this cancellation could make the rates of non-concerted reactions comparable to those of concerted reactions.

Application of the criterion of activation energy for concerted vs. non-concerted mechanisms leads to the conclusion that none of the thermally induced reactions of these cyclobutanes is a concerted, one-step process, neither the necessarily non-concerted geometrical isomerizations nor the reactions which are capable of being concerted, the [1,3] sigmatropic shift and the decomposition to olefins. If these reactions are not concerted, then the presumed alternative is a diradical mechanism.

Synthesis and Thermal Rearrangement of Optically Active I and II

In order to shed some light on the properties of the presumed diradical--whether it is an intermediate or a transition state, stereoequilibrated or not--the fate of chirality in the thermal

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[51](a) C. T. Genaux, F. Kern, and W. D. Walters, J. Amer. Chem. Soc., 75, 6196 (1953); (b) R. W. Carr and W. D. Walters, J. Phys. Chem., 67, 1370 (1963).

rearrangements of optically active I and II was studied. Introduction of optical activity into the unsymmetrically disubstituted cyclobutanes, I and II, allows two separate diastereomerizations to be uncovered; one relates (1S:2R)-I to (1S:2S)-II and the other relates (1S:2R)-I to (1R:2R)-II. The enantiomerization of (1S:2R)-I to (1R:2S)-I can also be revealed (Figures 6 and 7).
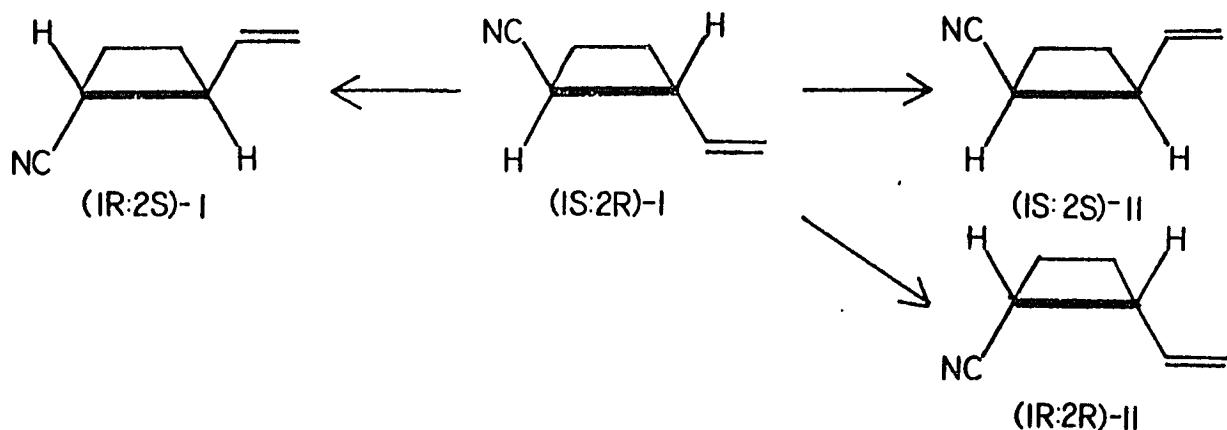
Figure 6. Diastereomerization and Enantiomerization of Optically Active I.
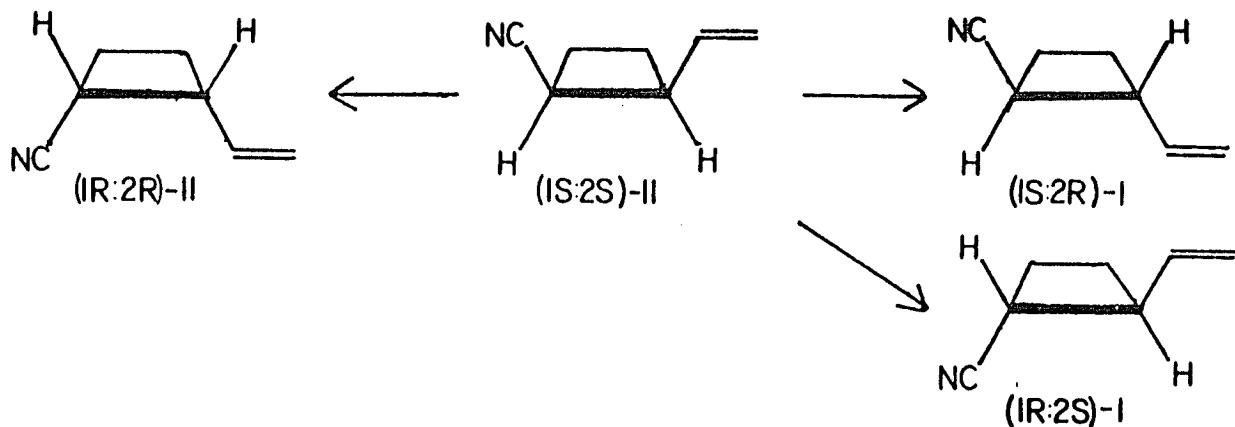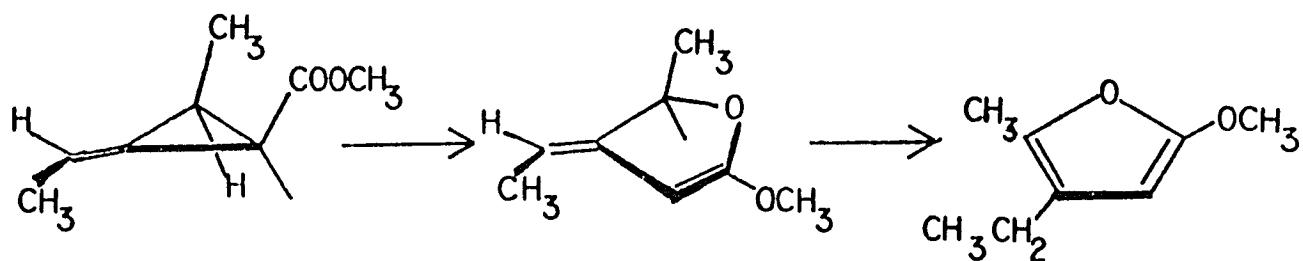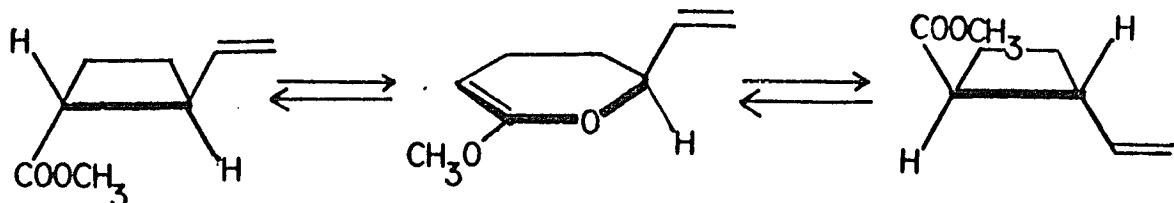
Figure 7. Diastereomerization and Enantiomerization of Optically Active II.

Diastereomerization of I or II requires rotation around at least one bond, C1-C4 or C2-C3, while enantiomerization requires rotation about both the C1-C4 and C2-C3 bonds. Use of a cyano group rather than an ester group eliminates at least one possible mechanism for the racemization of I and II. Previously, it had been discovered in the thermal rearrangement of a methylene cyclopropane[52] that the ester group could become involved in the formation of a furan.

Analogously, a possible mechanism for the racemization of V would involve the reversible intermediacy of a dihydropyran:

With a cyano group in place of an ester group, the intervention of an excessively strained intermediate with an allenic moiety in a six-membered ring would be required.

Because the vinyl group is insufficiently labelled, the four possible modes of the [1,3] sigmatropic rearrangement of optically

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[52]W. Doering and L. Birladeanu, Tetrahedron, 29, 499 (1973).

active I and II to III can only be separated into two pairs: (ar + sr) and (ai + si); that is, the stereochemistry of the migrating center can be revealed but not that of the allyl group about which the rearrangement occurs (see Figure 8).
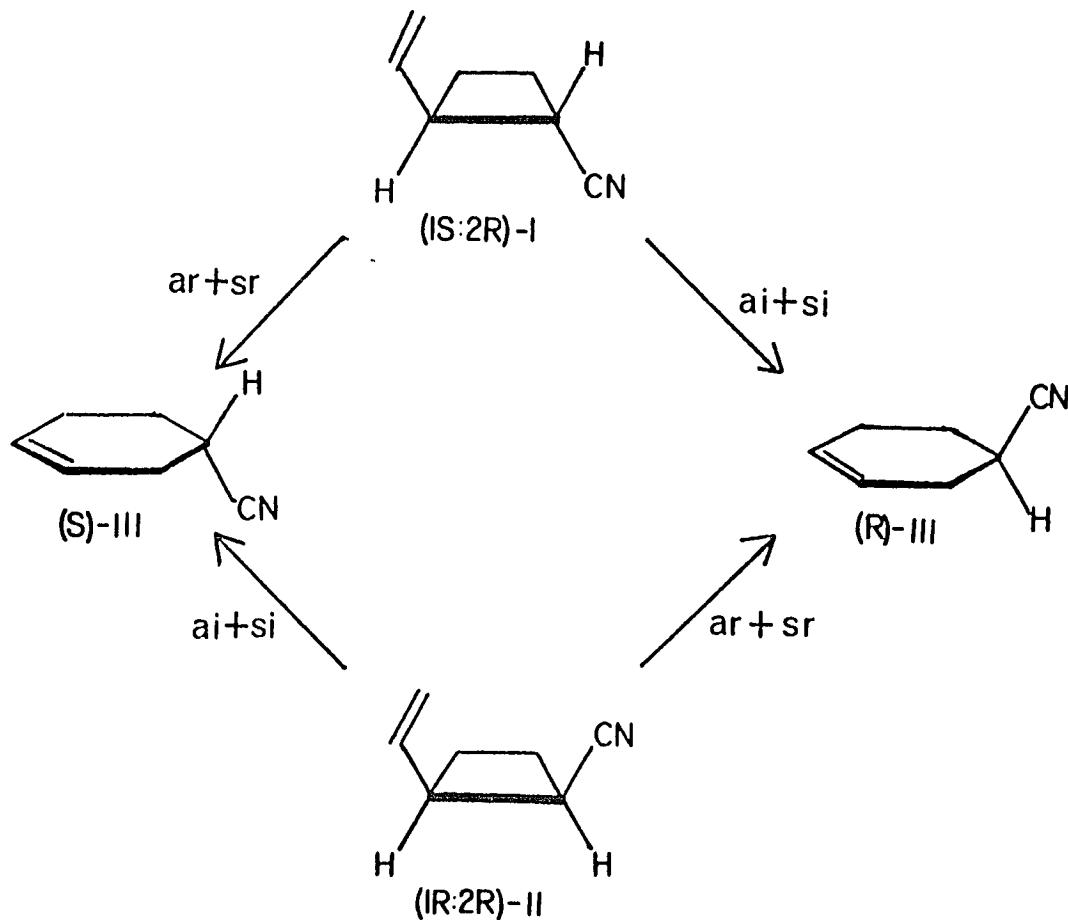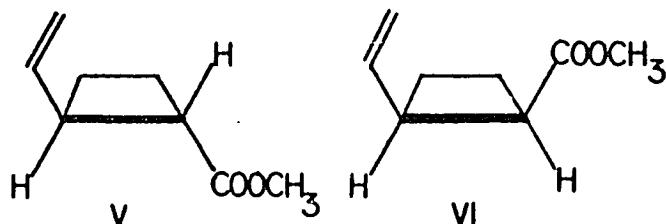
Figure 8. [1,3] Sigmatropic Rearrangement of (1S:2R)-I.

Since the cleavage of I and II proceeds in a regiospecific manner to give only butadiene and acrylonitrile, I and II are not adequately labelled to reveal the stereochemistry of the cyclo-reversion to olefins.

Quantitative dissection of the stereochemistry of the rearrange-
ment of I and II requires knowledge of the optical purities and
relative configurations of I, II and III.
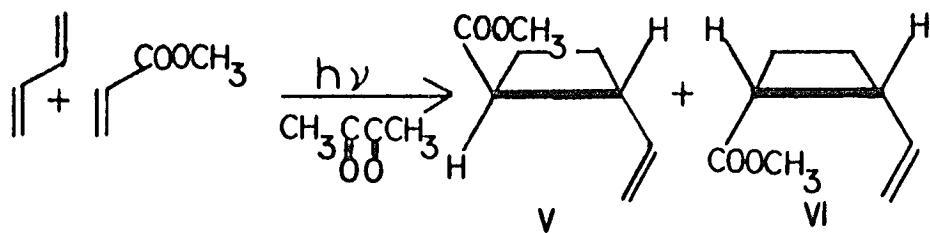
Synthesis of Optically Active I and II

The esters V and VI are attractive precursors for the synthesis
of the optically active nitriles I and II. The corresponding

carboxylic acids can be resolved by recrystallization of their
alkaloid salts, and the carboxylic acid function can be easily
converted to the nitrile group.

The methyl esters V and VI can be synthesized by the photo-
sensitized cycloaddition of butadiene and methyl acrylate. Their
structures are consistent with the ir and nmr spectra and exact mass

determination. The stereochemical assignments of V and VI were made
on the basis of the chemical shifts of the allylic and vinylic protons.
As is the case in the corresponding nitriles, these protons appear at

lower field in the cis-compound than in the trans-compound. But

this synthesis is impractical since the mixture of isomers has to be

separated by gas chromatography.

An alternative synthesis of ester V involves unexceptional steps

from the readily available trans-1,2-cyclobutanedicarboxylic acid

VIII.[53] Partial hydrolysis of the dimethyl ester IX leads to methyl

hydrogen trans-cyclobutanedicarboxylate (X),[55] which, in turn, is

selectively reduced to the alcohol-ester XI by the action of

diborane.[55,56] Oxidation of XI with DMSO-SO_3 and triethylamine gives

the aldehyde-ester XII.[57] The reaction of XII with methylene

triphenylphosphorane[58] gives a 9:1 mixture of V and VI, which is then

hydrolyzed to a mixture of trans-XIII and cis-XIII. Since diester IX

contains only 5% of the corresponding cis-diester, some of the VI

formed in the Wittig reaction of XII could arise through the base-

catalyzed epimerization of XII.

[53]E. R. Buchman, A. O. Reims, T. Shei, and M. J. Schlatter,
J. Amer. Chem. Soc., 64, 2696 (1942).

[54]R. Kuhn and A. Wasserman, Helv. Chim. Acta, 11, 600 (1928);
H. Bode, Ber., 332 (1934).

[55]C. C. Schroff, W. S. Stewart, S. J. Uhm and J. W. Wheeler,
J. Org. Chem., 36, 3356 (1971).

[56]H. C. Brown and B. C. Subba Rao, J. Amer. Chem. Soc., 82, 681
(1960).

[57]J. R. Parikh and W. E. Doering, ibid., 89, 5505 (1967).

[58]R. Greenwald, M. Chaykovsky, and E. J. Corey, J. Org. Chem.,
28, 1128 (1963).
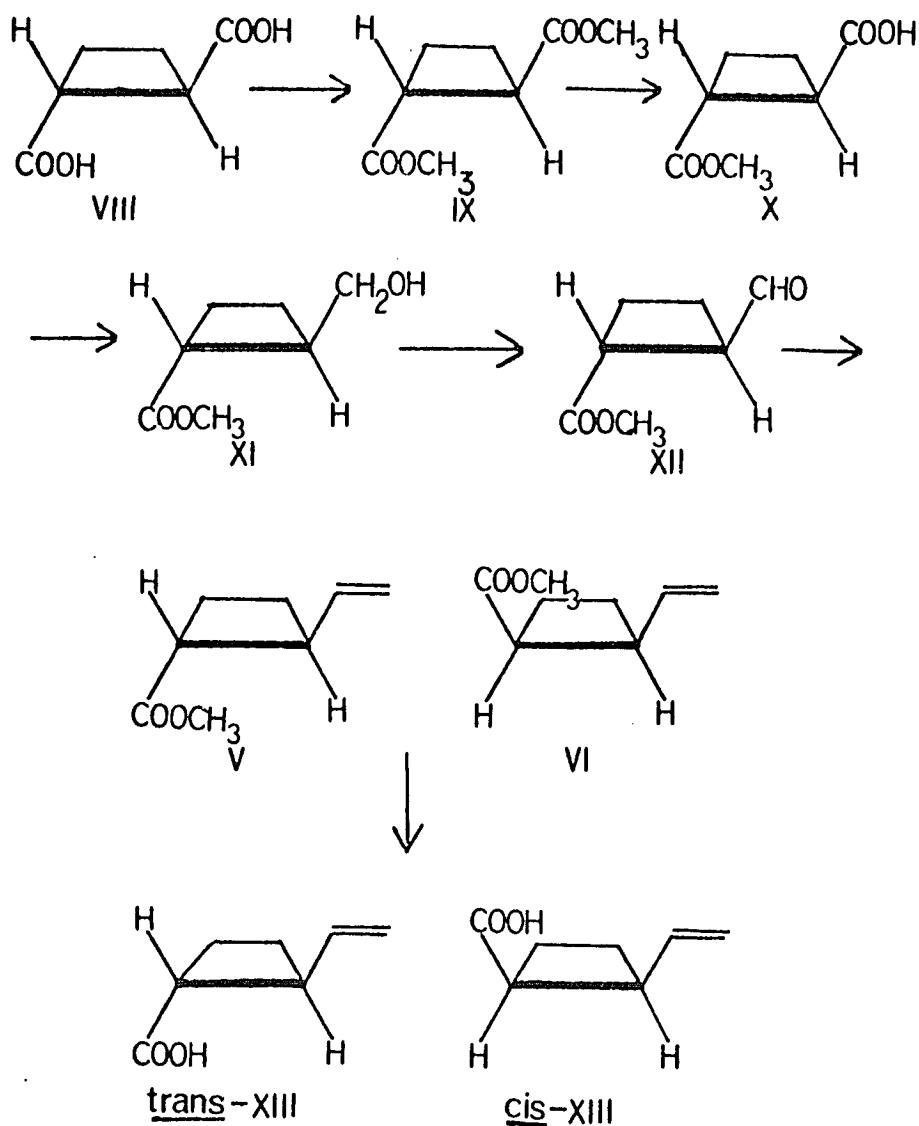
Figure 9. Synthesis of 2-vinylcyclobutanecarboxylic acid.

Resolution of trans-XIII (as a 90:10 mixture of trans-XIII and cis-XIII) is accomplished by the recrystallization of its quinine salt from ethanol and water. Progress of the resolution is followed by recovery of the mixture of acids from the quinine salt after each recrystallization, treatment of the recovered acid with diazomethane, separation of V and VI by gas chromatography and measurement of the rotation of the purified V. Six recrystallizations of the quinine salt brings the recovered ester V to constant rotation. This (unreliable) criterion for optical purity leads to material of 97% optical purity (see below). A more reliable determination of the maximum rotation of V and a determination of its absolute configuration is made through its chemical correlation to dimethyl cyclobutane-1,2-dicarboxylate. Treatment of (-)-V successively with $KMnO_4$-$NaIO_4$[59] and diazomethane leads to (1R:2R)-(-)-IX, the configuration and maximum rotation of which are known.[60] From the maximum rotation of optically pure IX ($[\alpha]_D$ -148.7°) the maximum rotation of V is calculated to be $[\alpha]_D$ -132.2° (Figure 10).

Synthesis of I from resolved-XIII is accomplished by the treatment of the triethylamine salt of the acid with ethyl chloroformate

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[59]J. W. ApSimon , A.S.Y. Chau, W. G. Craig, and H. Krehm, Can. J. Chem.,45, 1439 (1967).

[60]The absolute configuration and maximum rotation of IX is known by the chemical correlation[61] of IX to α-pinene.

[61](a) J. A. Berson and P. B. Dervan, J. Amer. Chem. Soc., 95, 267 (1973); (b) P. B. Dervan, Ph.D. Thesis, Yale University, 1972 and references cited therein.
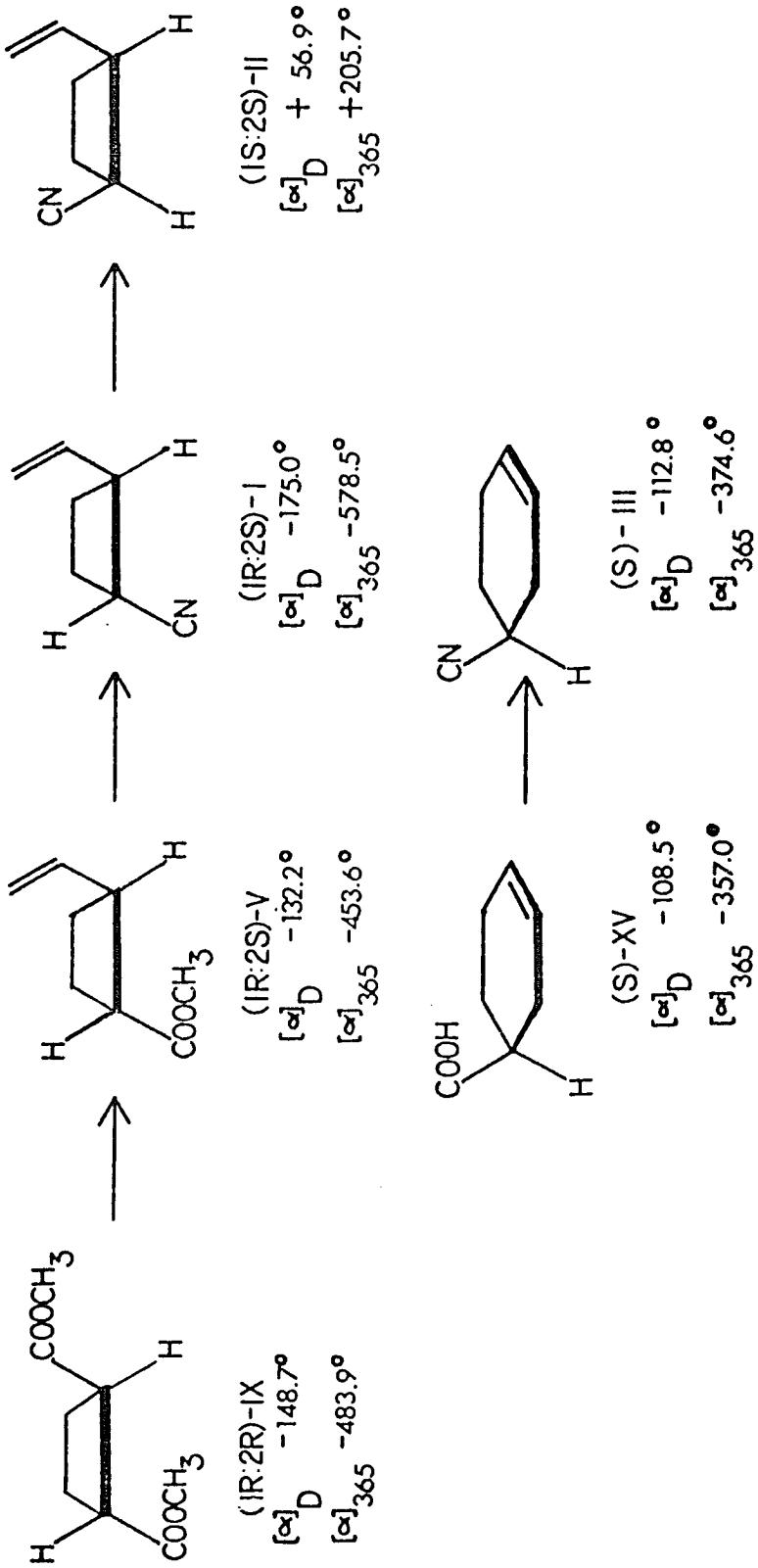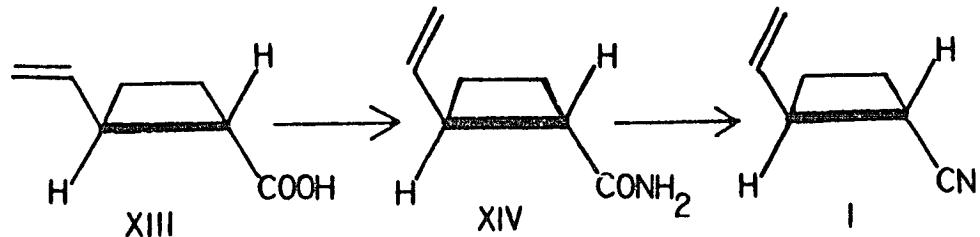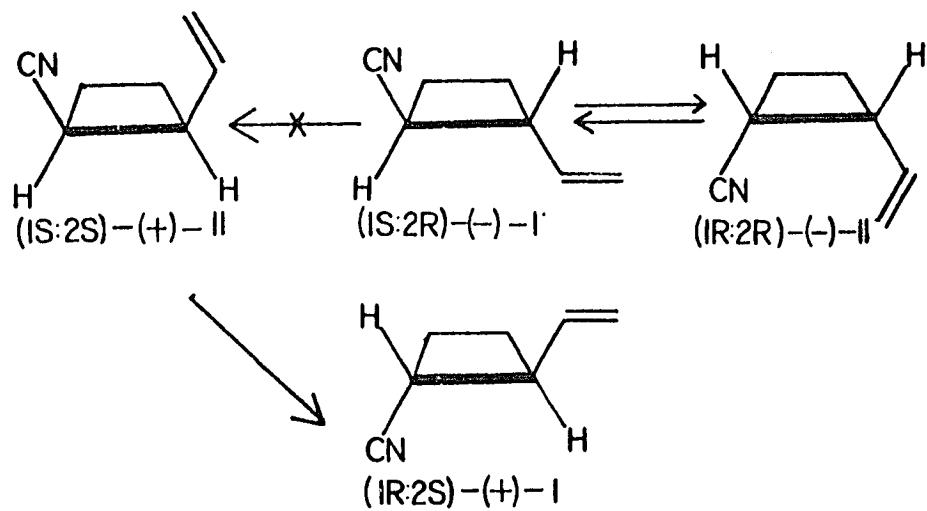
Figure 10. Maximum Rotations and Absolute Configurations of I, II and III.

to form the mixed anhydride, followed by reaction with gaseous NH_3 to give the amide, XIV.[6c] Dehydration of the amide proceeds smoothly

with p-toluenesulfonylchloride in pyridine to give nitrile I.[6c] Since no racemization is likely to occur in the synthesis of I from XIII, the nitrile is assumed to be formed with the same level of optical purity and the same absolute configuration as the starting XIII. Both the synthesis and the determination of the maximum rotation and absolute configuration of optically active II are accomplished by the epimerization of optically active I with potassium t-butylate in

dimethyl sulfoxide. The reaction leads to an equilibrium mixture of I and II. Recovery of I without racemization leads to the conclusion that only one of the two hydrogens α to the substituents is being

removed. The more likely candidate is the hydrogen α to the cyano group rather than the hydrogen α to the vinyl group. Because of this selective hydrogen removal, only one of the two possible enantiomers of II is being generated from a given enantiomer of I. The optically active II isolated from the epimerization mixture has the same level of optical purity as the starting material and the absolute configuration of I by an inversion of configuration about the cyano-bearing carbon. Optically pure (1S:2R)-(-)-V of $[\alpha]_{365}$ -578.5° would lead to optically pure (1R:2R)-(+)-II of $[\alpha]_{365}$ +205.7°.

The absolute configuration and maximum rotation of 4-cyanocyclo-hexene (III) is needed to complete the picture. (S)-III is synthesized from (S)-cyclohexene-4-carboxylic acid (XV) of known optical purity[62] by the same method used to synthesize I from V. Thus, optically pure (S)-(-)-XV $[\alpha]_{365}^{25}$ -357.0° gives (S)-(-)-(III) $[\alpha]_{365}$ -374.6°.

Thermal Rearrangement of Optically Active I and II

Heating of (1S:2R)-I $[\alpha]_{365}$ +529.9° for three hours in the gas phase gives 85.4% (1S:2R)-I, $[\alpha]_{365}$ +505.7°; 5.04% (1R:2R)-II, $[\alpha]_{365}$ -32.2°; 5.15% (R)-III, $[\alpha]_{365}$ +54.8°; and 4.41% of IV. Thus, I suffers 4.5% racemization and II and III are formed with 17.0% and

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[62]The absolute configuration and maximum rotation of (S)-cyclohexene-4-carboxylic acid is known by its chemical correlation to 4-vinylcyclohexene[63] and the correlation of 4-vinylcyclohexene to 3-methylcyclohexanone.[61]

[63]W. E. Doering, M. Frank-Neumann, D. Hasselmann and R. L. Kaye, J. Amer. Chem. Soc., 94, 3833 (1972).

16.0% retention of optical activity, respectively. Heating of

(1S:2S)-II $[\alpha]_{365}$ +175.2°, under the same conditions gives 72.06%

(1S:2S)-II, $[\alpha]_{365}$ +133.2°; 13.0% (1R:2S)-I, $[\alpha]_{365}$ -81.4°; 6.40%

(S)-III, $[\alpha]_{365}$ -98.4°; and 8.5% IV. Recovered II suffers 23.9%

racemization and I and III are formed with 16.5% and 30.8% retention

of optical activity, respectively. Heating of optically active III

for 12 hours at 217.8°C results in recovery of III with undiminished

rotation.

Several conclusions can be drawn from these preliminary experi-

ments. The preferred pathway for diastereomerization connects the

geometrical isomers I and II which are related by an inversion of

configuration at the cyano-bearing carbon (Figure 11). In the [1,3]

sigmatropic rearrangements of I and II to III, the predominant pathway

corresponds to inversion of configuration at the migrating center in

the rearrangement of I to III, and retention of configuration of the

migrating center in the rearrangement of II to III (Figure 12).

The next objective was to determine the specific rate constants

in the kinetic scheme of Figure 13. This determination allows the

quantitative dissection of the rates of the geometrical isomerizations

and of the [1,3] sigmatropic rearrangements; it can also establish

whether enantiomerization is a direct and independent process. The

rate constants are determined by solution of the following differential

equations which describe the kinetic scheme of Figure 13.
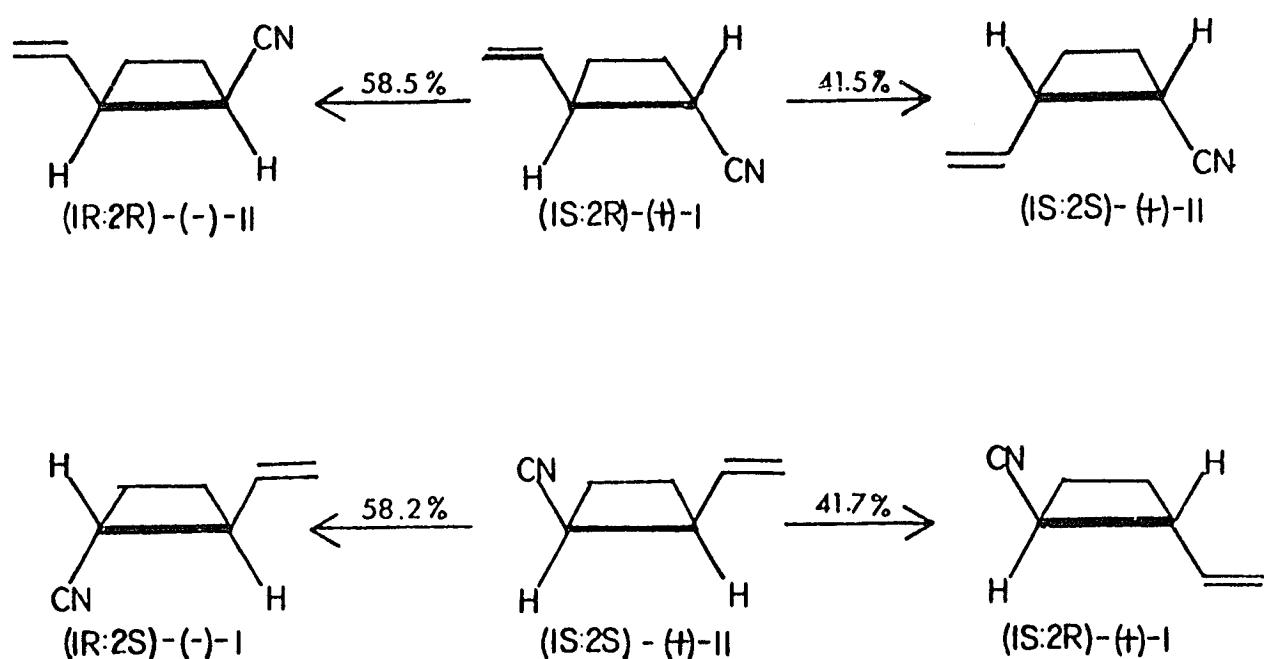
Figure 11. Enantiomeric Distribution of the Diastereomeric Products of I and II at 3 hr at 217.8°.
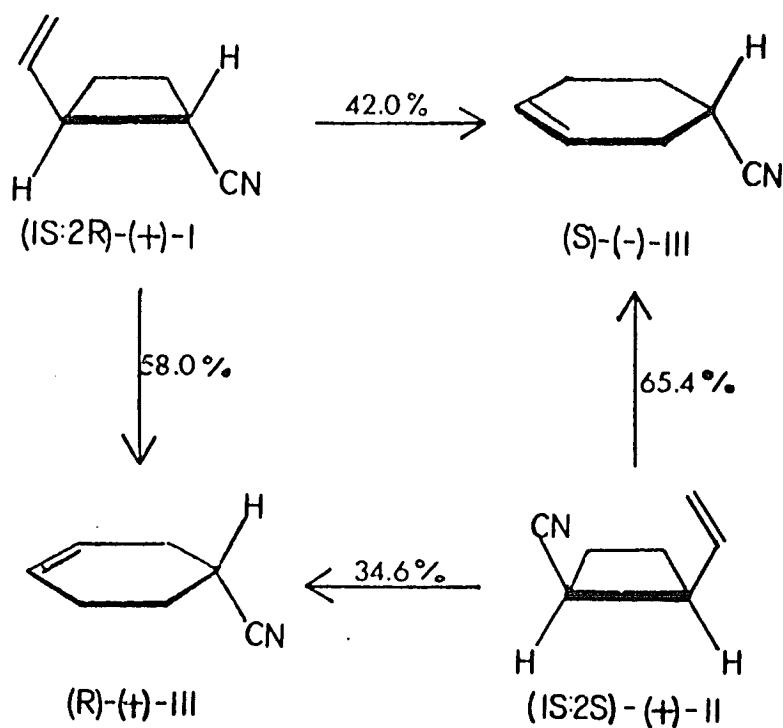
Figure 12. Enantiomeric Distribution of III from the Thermal Rearrangement of I and II for 3 hr at 217.8°.
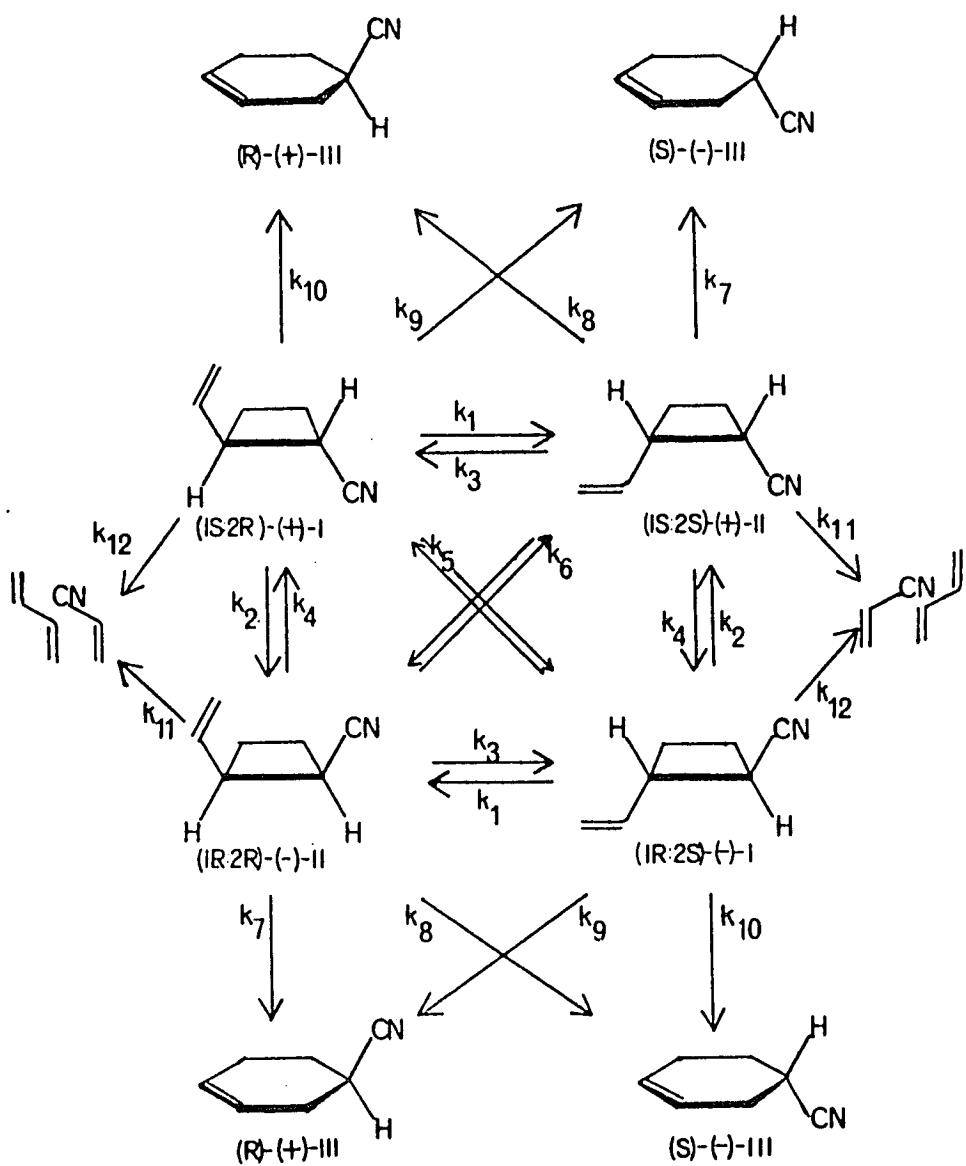
Figure 13. Kinetic Scheme for Interconversions of Optically Active I and II.

$$\frac{d[(+)-I]}{dt} = -(k_1+k_2+k_5+k_9+k_{10}+k_{12})[(+)-I] + k_3[(+)-II] + k_4[(-)-II] + k_5[(-)-I]$$

$$\frac{d[(-)-I]}{dt} = -(k_1+k_2+k_5+k_9+k_{10}+k_{12})[(-)-I] + k_3[(-)-II] + k_4[(+)-II] + k_5[(+)-I]$$

$$\frac{d[(-)-II]}{dt} = -(k_3+k_4+k_6+k_7+k_8+k_{11})[(-)-II] + k_1[(-)-I] + k_2[(+)-I] + k_6[(-)-II]$$

$$\frac{d[(+)-III]}{dt} = -k_{10}[(+)-I] + k_9[(-)-I] + k_7[(+)-II] + k_8[(-)-II]$$

$$\frac{d[(-)-III]}{dt} = k_9[(+)-I] + k_{10}[(-)-I] + k_8[(+)-II] + k_9[(-)-II]$$

$$\frac{d[IV]}{dt} = k_{12}[(+)-I] + k_{12}[(-)-I] + k_{11}[(+)-II] + k_{11}[(-)-II].$$

Initial guesses for the rate constants of the isomerization reactions are obtained by partitioning the specific rate constants obtained for racemic material. This partitioning is accomplished by measuring the rotation of the recovered products at five kinetic points of low conversion (maximum total conversion of the starting material = 30%), plotting the rotation of each product vs. time and extrapolation of the resulting line back to zero time. The rotation at zero time can then be used to calculate the ratio of enantiomers in a given product corrected for racemization of the starting material (and also of the product itself for I and II). The specific rate constants found by solution of the differential equations with the help of the computer program are given in Figure 14 and Table 9.

Approximate rates of enantiomerization were obtained by plotting $\ln \alpha$ vs. time for the recovered starting material. The slope of the lines for I and II gave their rates of racemization which become rates of enantiomerization upon division by two. These initial values for k_5 $(k_{(+)-I \to (-)-I})$ and k_6 $(k_{(+)-II \to (-)-II})$ were lowered somewhat by computer refinement but remained far greater than zero (see Figure 14 and Table 9). In order to emphasize the fact that the interconversion of enantiomers is a direct process, two curves of the concentration of (-)-I against time resulting from the rearrangement of (+)-I are shown in Figure 15. One curve is generated by plotting the concentrations calculated by this computer program with the best fit of rate constants; performing the same calculation with $k_5 = k_6 = 0$ (see Figure 15)
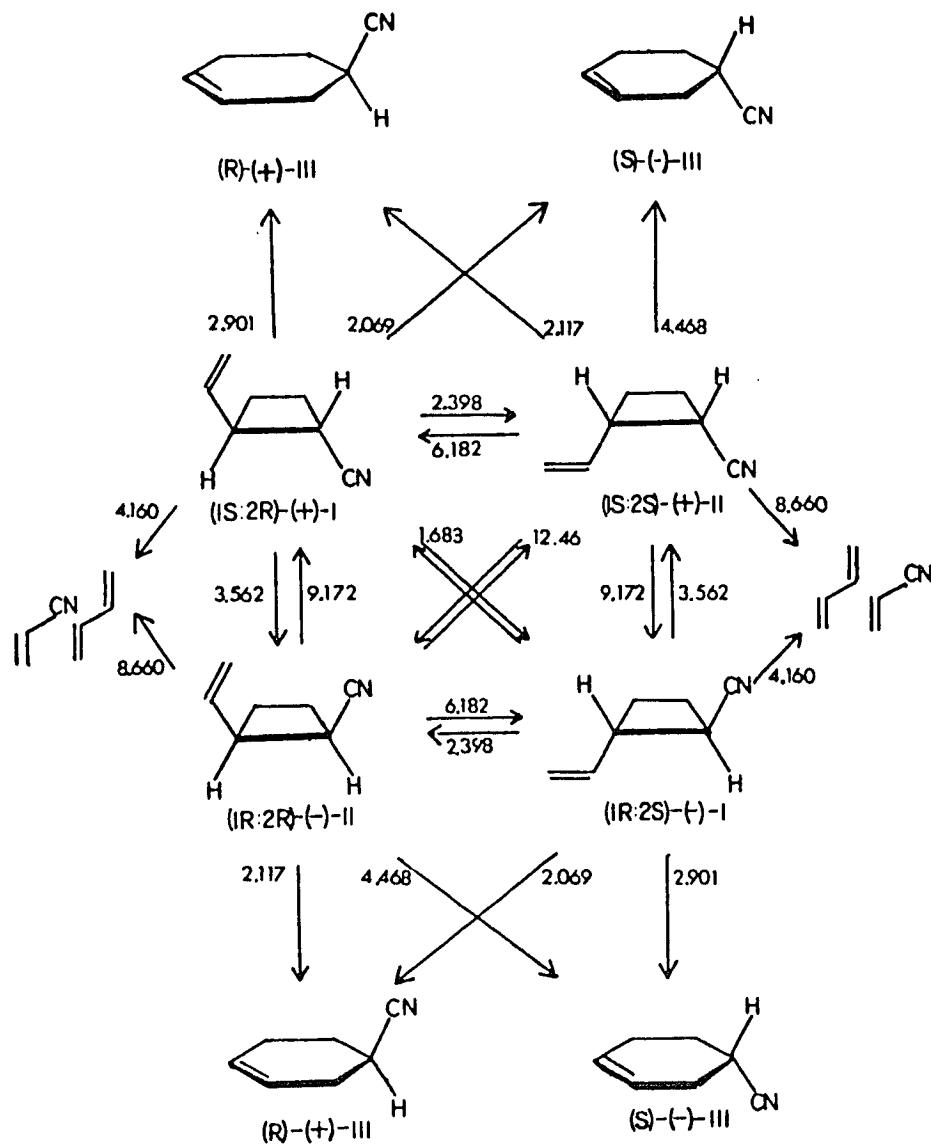
Figure 14. Kinetic Scheme for Interconversions of Optically Active I and II. All rate constants are in units of $10^{-6}\,\mathrm{sec}^{-1}$.

Table 9. Rate Constants and Their Probable Errors for the Reactions of Optically Active I and II, as Determined from Plots of $\bar{\sigma}$ vs. k.

Specific Rate Constant[a]	(+)-I[c]	(-)-I	(+)-II	(-)-II	(+)-III	(-)-III	IV
k_1 $^a k_2$ (+)-I-(-)-II $\frac{1}{b}$	2.552±2.57 (33%) / 0.03115	— / 0.001698	2.398±0.02 (0.8%) / 0.00277	— / 0.000181	— / 0.000176	— / 0.000096	— / 0.001674
k_2 $^a k_2$ (+)-I-(-)-II $\frac{1}{\sigma}$	3.562±0.614 (17.2%) / 0.003155	— / 0.001700	— / 0.000082	3.562±0.045 (1.3%) / 0.000181	— / 0.000176	— / 0.000096	— / 0.001671
k_3 $^a k_3$ (+)-II-(+)-I $\frac{1}{\sigma}$	6.182±0.061 (1%) / 0.000224	— / 0.000465	6.182±0.197 (3%) / 0.004846	— / 0.01066	— / 0.000255	— / 0.000309	— / 0.005222
k_4 $^a k_4$ (+)-II-(-)-I $\frac{1}{\sigma}$	— / 0.000224	9.172±0.39 (4%) / 0.000463	9.170±1.338 (14.6%) / 0.004846	— / 0.001066	— / 0.000255	— / 0.000209	— / 0.005229
k_5 $^a k_5$ (+)-I-(-)-I $\frac{1}{\sigma}$	1.699±0.7 (41.2%) / 0.001195	1.683±0.28 (16%) / 0.001685	— / 0.000081	— / 0.000181	— / 0.000177	— / 0.000096	— / 0.001674
k_6 $^a k_6$ (+)-II-(-)-II $\frac{1}{\sigma}$	— / 0.000224	— / 0.000465	12.46±1.8 (14.1%) / 0.004844	12.46±0.18 (1.4%) / 0.001073	— / 0.000255	— / 0.000209	— / 0.005222
k_7 $^a k_7$ (+)-II-(-)-III $\frac{2}{\sigma}$	— / 0.000224	— / 0.000465	2.096±1.27 (60%) / 0.004846	— / 0.001066	2.117±0.063 (2.9%) / 0.000255	— / 0.000209	— / 0.005222
k_8 $^a k_8$ (+)-II-(-)-III $\frac{2}{\sigma}$	— / 0.000224	— / 0.000465	4.424±1.342 (30%) / 0.004844	— / 0.001066	— / 0.000255	4.468±0.055 (1.2%) / 0.000209	— / 0.005222
k_9 $^a k_9$ (+)-I-(-)-III $\frac{2}{\sigma}$	2.069±0.56 (27.4%) / 0.003155	— / 0.001700	— / 0.000082	— / 0.001810	— / 0.001760	2.069±0.02 (1%) / 0.000096	— / 0.001674
k_{10} $^a k_{10}$ (+)-I-(-)-III $\frac{2}{\sigma}$	2.901±0.61 (20.5%) / 0.003155	— / 0.001700	— / 0.000082	— / 0.000181	2.901±0.03 (1%) / 0.000176	— / 0.000096	0.001674
k_{11} $^a k_{11}$ -IV	—	—	—	—	—	—	8.644±0.539 (6%)[d] / 0.005335
k_{12} $^a k_{12}$ -IV	—	—	—	—	—	—	4.165±0.41 (9%)[c] / 0.001697

[a] All k in units of 10^{-6} sec^{-1}; error limit is range of k corresponding to $2\bar{\sigma}$; where no k is given $\bar{\sigma}$ is constant for all values of k.

[b] Value of $\bar{\sigma}$ at its minimum.

[c] Component for which $\bar{\sigma}$ is determined.

[d] Repeated from Table 4.
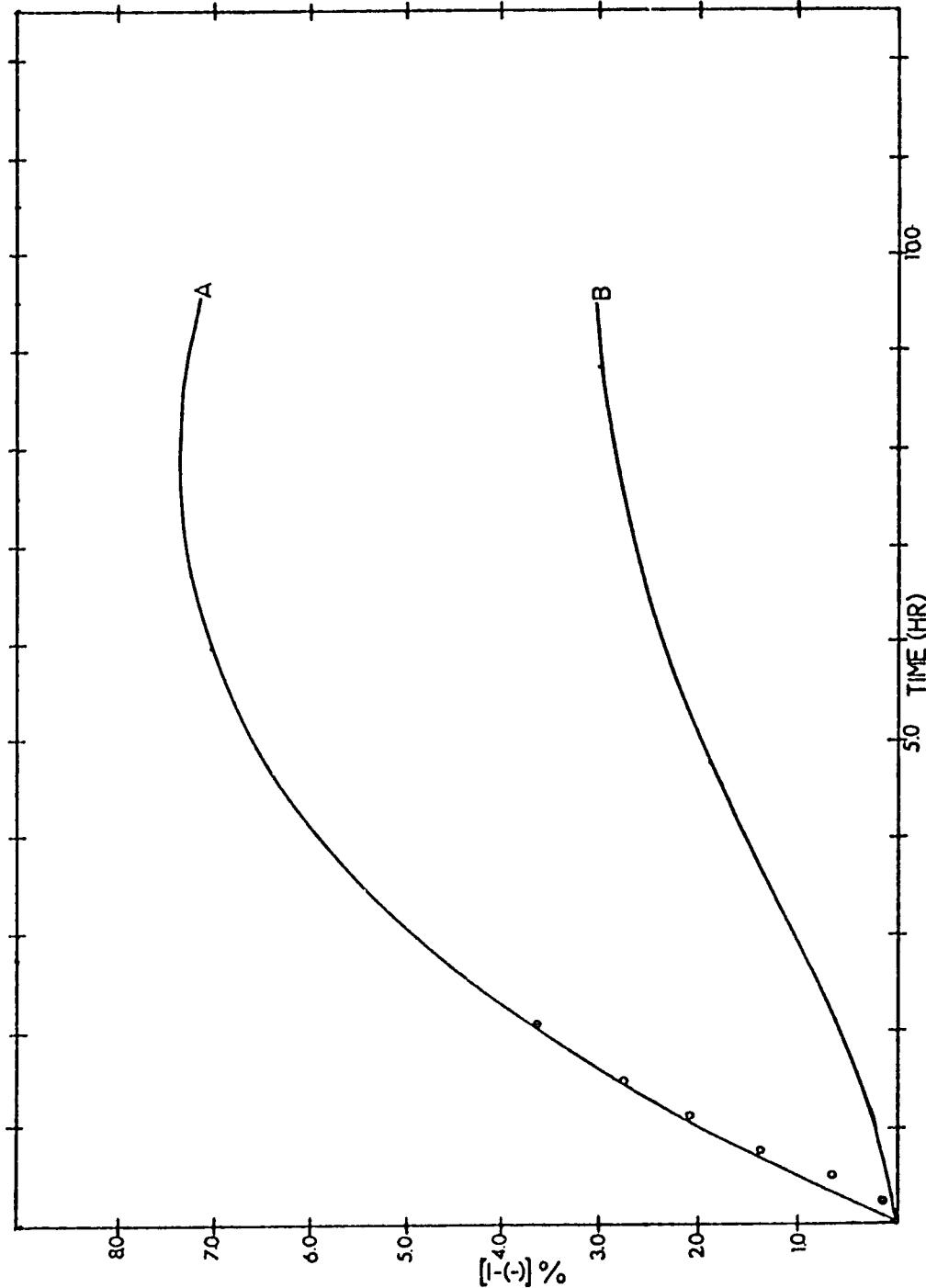
Figure 15. Plot of [(-)-I] vs. time. Line A gives the curve generated by computer with the best fit of specific rate constants k_1 through k_{12}. Line B gives the curve generated by computer with the best fit of specific rate constants, but with $k_5 = k_6 = 0$. The symbol, $\triangle$, gives the experimental concentrations.

generates a second curve. The experimentally determined concentrations of (-)-I can then be compared with these two curves. It can be seen that the experimental concentrations of (-)-I are best fit by a non-zero rate constant for the conversion of (+)-I directly to (-)-I and cannot be accounted for exclusively by the intermediacy of optically degraded II. Similar results are obtained for the conversion of (+)-II to (-)-II.

Effect of Pressure and Solvent on the Thermal Rearrangement of I and II.

Thermal rearrangement of I was carried out in 10% solutions of benzene and acetonitrile, and of II in acetonitrile and at 1 mm pressure. In Table 10, the results are listed along with the results of the gas-phase rearrangements at higher pressures. The results are not qualitatively changed in these solvents, but the overall rate of the reaction is increased slightly. This fact manifests itself in the formation of proportionately more III. The products are formed with less retention of optical activity. Changing to a different glass or carrying out the reaction at lower pressures (1 mm) changed the results neither quantitatively nor qualitatively.

Table 10. Effect of Pressure, Phase and Glass on Rearrangement of I and II at 217.8° ±0.3°.

Starting Material	Phase[a]	Starting Material %	Rac. in Rec. St. Mat., %	Product	%	$[\alpha]_{365}$ [b]	Product	%	$[\alpha]_{365}$	IV, %
(+)-II	gas, 700mm[e]	64.7	30.7	(-)-I	15.93	-79.04°	(-)-III	8.32	-88.2°	11.05
(+)-II	gas, 1mm	69.1	31.9	(-)-I	16.31	-77.30°[e]	(-)-III	8.28	-89.6°[c]	6.31
(+)-II	CH_3CN (10%)	60.7	18.9	(-)-I	10.11	-54.14°[c]	(-)-III	12.70	-49.30[c]	16.43
II	gas, 700mm[f]	64.6	--	I	14.87		III	8.03		12.46
(+)-I	gas, 700mm[e]	81.16	5.6	(-)-II	6.17	-30.12°	(+)-III	6.74	+53.85	5.90
(+)-I	CH_3CN (10%)	78.18	4.1	(-)-II	5.24	-20.75°[d]	(+)-III	10.01	+7.89[d]	6.90
(+)-I	φH (10%)	77.5	6.4	(-)-II	5.37	-18.82°[d]	(+)-III	10.9	+25.6°[d]	5.12
I	gas, 700mm[f]	81.2	--	II	5.93		III	6.62	--	6.20

a) All thermal rearrangements were carried out for four hours.

b) All rotations were determined in cyclohexane.

c) Corrected to 85.2% optical purity of the starting material.

d) Corrected to 91.6% optical purity of the starting material.

e) These experiments are repeated from Tables 12 and 13 to facilitate comparison.
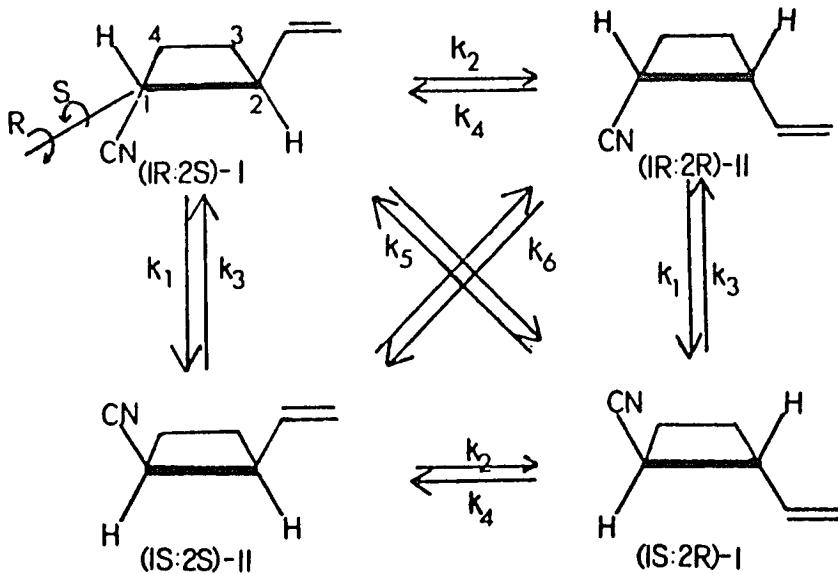
f) Corning 0120 glass (lead potash).

Mechanisms for Thermal Rearrangement of Cyclobutanes

Before discussing some of the possible mechanisms for the thermal rearrangement of these cyclobutanes, it is useful to describe the experimental results in terms of the minimum number of 180° rotations of carbon-carbon bonds required to carry the starting material into each of the products. In particular, the numerical relationships that exist among the specific rate constants for the observed reactions can describe the relative preference for rotation of bonds in the reacting molecule. This discussion parallels that of Doering and Sachdev[6c] and uses the terminology introduced by them to describe the reactions of 1-cyano-2-isopropenylcyclopropanes.

In addition to cleavage to butadiene and acrylonitrile, both I and II undergo five independent isomerizations. These five reactions can be divided into two categories: the reactions involving the degenerate rearrangement of the cyclobutane ring, and the reactions involving ring expansion of the vinylcyclobutane to a cyclohexene. The first category consists of enantiomerization and geometrical isomerization to a pair of optical antipodes. In terms of 180° rotations of carbon-carbon bonds, I and II undergo two geometrical isomerizations: one requiring rotation about the C1-C4 bond (with specific rate constants of k_2 and k_4), and the other requiring rotation about the C2-C3 bond (with specific rate constants of k_1 and k_3). The ratio of the specific rate constants for the reactions of I and II requiring rotation about the same bond is just the equilibrium constant:

$$\frac{k_3}{k_1} = \frac{k_4}{k_2} = K = 2.575$$

The ratio, R_{CN}, defines a "rotational propensity"[6c] as the relative preference of a bond bearing a cyano group to rotate over that of a bond bearing a vinyl group. Because of microscopic reversibility, the measurement of R_{CN} from either I or II must give the same value. These relationships allow four of the rate constants of Figure 14 to be written in the following manner:

$$k_1 = k_{(+)-I \rightarrow (+)-II} = \quad k_1 \quad = 2.398 \times 10^{-6} \text{sec}^{-1}$$

$$k_2 = k_{(+)-I \rightarrow (-)-II} = R_{CN} k_1 = (1.484)(2.398 \times 10^{-6})$$

$$k_3 = k_{(+)-II \rightarrow (+)-I} = \quad K k_1 \quad = (2.577)(2.398 \times 10^{-6})$$
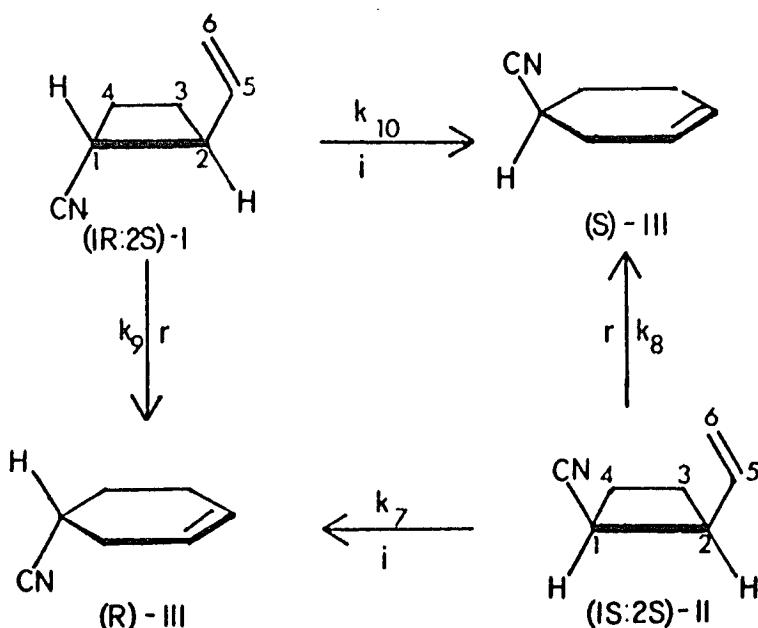
$$k_4 = k_{(+)-II \rightarrow (-)-I} = K R_{CN} k_1 = (1.484)(2.577)(2.398 \times 10^{-6})$$

Enantiomerization requires a rotation of 180° about both the

C1-C4 bond and the C2-C3 bond. The relative preference of these biro-

tational processes in comparison to the slowest of the mono-rotational

processes may be defined by the two factors, R_{CC} and R_{TT}.

$$k_5 = k_{(+)-I \to (-)-I} = R_{TT} \, k_1 = (0.7018)(2.398 \times 10^{-6}) = 1.653 \times 10^{-6} \text{sec}^{-1}$$

$$k_6 = k_{(+)-II \to (-)-II} = R_{CC} \, k_1 = (5.195)(2.398 \times 10^{-6}) = 12.46 \times 10^{-6} \text{sec}^{-1}$$

The second category of reactions, which consists of a ring

expansion to the enantiomers of III, requires a rotation of 120° about

the C3-C4 bond in order to bring C1 to within bonding distance of C6.

If optical activity is introduced into I and II, any rotation about

the C1-C4 bond can be detected. Rearrangement with retention of

configuration at C1 is associated with no rotation about C1-C4 while

rearrangement with inversion of configuration requires at least one rotation of 180° about C1-C4. The rearrangement of I to III proceeds readily with rotation about C1-C4 bond (k_{10}/k_9 = 1.40) whereas the rearrangement of II to III proceeds preferentially without rotation about C1-C4 (k_7/k_8 = 2.14). Rearrangement of either I or II in the suprafacial mode involves no rotation (or an even number) about the C2-C3 bond, whereas rearrangement in the antarafacial mode requires one rotation (or an odd number) about the C2-C3 bond. Because the present system is insufficiently labelled, this distinction cannot be made. Neither is it possible to determine the sense (R or S) of any rotation.

Even though these reactions can be described in terms of a small set of 180° bond rotations, the actual reaction may involve a larger number of bond rotations. By way of example, a 180° rotation is indistinguishable from rotations of 180° + n 360°. Similarly, simultaneous 180° rotations about the C1-C4 and C2-C3 bonds are indistinguishable from simultaneous rotations of (180° + n_1 360°) and (180° + n_2 360°) about the C1-C4 and C2-C3 bonds, respectively. Thus, the number of detailed mechanistic possibilities is large and is further increased by the fact that the sense of rotation about each bond may be R or S.

Thus, in theory, a wide variety of mechanisms consisting of different combinations of rotations about the carbon-carbon bonds of the rearranging cyclobutane exist. In practice, the number of mechanistic possibilities is reduced by the observation that significant amounts

of optical activity are retained in the chiral products. Since large
numbers of bond rotations occurring between fission of a bond and its
reclosure would lead to racemic products, the number of rotations must
be limited.

There are two sets of mechanistic alternatives for the thermal
rearrangements of I and II. The concerted set involves the simultane-
ous making and breaking of bonds. The set of the stepwise mechanisms
involves independent bond breaking and bond making steps.

Concerted Mechanisms

In the previous analysis, it was seen that four of the six reac-
tions of I and II may in theory be concerted reactions. Only the geo-
metrical isomerizations are incapable of being concerted. Application
of the criterion of activation energy to the reactions of racemic I
and II leads to the conclusion that neither the cleavage to olefins
nor the ring-expansion to cyclohexene must proceed by a concerted
mechanism. Activation parameters have not been determined for the
enantiomerization of I and II, so that direct application of this
criterion is not possible. However, two considerations make it seem
unlikely that this reaction is concerted. First, the rates of enanti-
omerization are comparable to those of the other reactions of I and
II. Of the reactions of I enantiomerization is the slowest (9% of the
total) while, of the reactions of II, it is the fastest (22% of the
total). The relative slowness of these reactions acquires an energetic
significance provided that there is no fortuitous cancellation of the

$e^{-Ea/RT}$ term and the A factor. In the only racemization of a cyclobutane for which activation parameters have been obtained, the racemization of $\underline{trans}$-1,2-divinylcyclobutane,[12u] $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are both higher than the corresponding parameters for the other rearrangements. In this instance the specific rate constant for racemization is larger than that for rearrangement. On the basis of the criterion of activation energy the enantiomerizations of I and II are not concerted reactions.

The criterion of stereospecificity can be applied only to the ring enlargement to 4-cyanocyclohexene (III). Lack of sufficient labelling of I and II allows the application of this criterion neither to the cleavage to olefins, nor to enantiomerization where only one stereochemical outcome is possible. On the basis of the criterion of stereospecificity the rearrangements of I and II to III are not concerted. However, the experimental results may be rationalized as a competition of two concerted processes. If one assumes that the [1,3] sigmatropic rearrangements of I and II occur by suprafacial pathways ($\underline{i.e.}$, no rotation about the C2-C3 bond) as was the case for the rearrangement of $\underline{trans}$-1,2-dipropenylcyclobutanes, then the rearrangement of I to III can be described as the competition of two concerted pathways, the one allowed by the Woodward-Hoffmann rules (58.4%) and the other by the Berson-Salem formulation (41.6%), while the rearrangement of II to III may be described as 67.8% Berson-Salem and 32.1% Woodward-Hoffmann.

On the basis of both criteria, it appears highly unlikely that any of the observed reactions is proceeding by a concerted mechanism. However, the possibility that the isomerization of I and II to III may be proceeding by two competing concerted pathways cannot be ruled out.
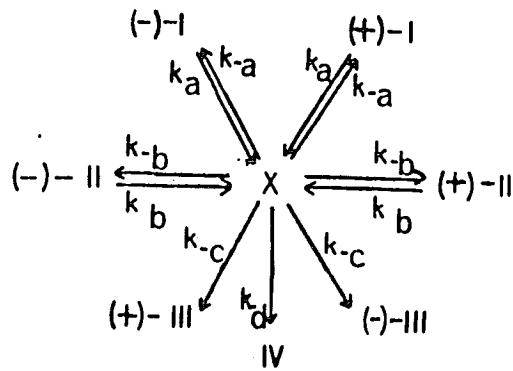
Mechanisms Proceeding via Diradicals

Diradical mechanisms for the rearrangements of cyclobutanes all require the involvement of tetramethylene:

The various proposals for the nature of tetramethylene have been reviewed in the introduction, and it remains to determine if any of these proposals can provide a rationalization for these experimental results.

Mechanisms with diradical intermediates may take several forms. In one the diradical is viewed as a rotationally equilibrated common intermediate from which all of the observed products are formed in secondary reactions. Such a mechanism cannot account for the total reaction of I or II, since the chiral products are formed with an excess of one enantiomorph over the other. An upper limit to the contribution of this mechanism may be estimated from the following kinetic scheme:

By the steady state approximation the concentration of [X] is given by the following equation,

$$[X] = \frac{k_a}{f}[(+)-I] + \frac{k_a}{f}[(-)-I] + \frac{k_b}{f}[(+)-II] + \frac{k_b}{f}[(-)-II]$$

where $f = 2k_{-a} + 2k_{-b} + 2k_{-c} + k_{-d}$ (i.e., f = the total reaction of the common intermediate). The rate of formation of each product can be written from this scheme and compared with the expressions on page 80. For example, if the rate of formation of (+)-I is

$$\frac{d[(+)-I]}{dt} = k_{-a}[X] - k_a[(+)-I] = -(k_1 + k_2 + k_5 + k_9 + k_{10} + k_{11})[(+)-I]$$

$$+ k_3[(+)-II] + k_4[(-)-II] + k_5[(+)-I]$$

then $k_{-a}\frac{k_a}{f} = k_5$ and $k_b\frac{k_{-a}}{f} = k_3 = k_4$. Performing the same operation for $\frac{d[(+)-II]}{dt}$, $\frac{d[(+)-III]}{dt}$ and $\frac{d[IV]}{dt}$ leads to the following relationships:

$$k_1 = k_2 = k_a \frac{k_{-b}}{f} \qquad\qquad k_7 = k_8 = k_b \frac{k_{-c}}{f}$$

$$k_3 = k_4 = k_b \frac{k_{-a}}{f} \qquad\qquad k_9 = k_{10} = k_a \frac{k_{-c}}{f}$$

$$k_5 = k_a \frac{k_{-a}}{f} \qquad\qquad k_{11} = k_b \frac{k_{-d}}{f}$$

$$k_6 = k_b \frac{k_{-b}}{f} \qquad\qquad k_{12} = k_a \frac{k_{-d}}{f}$$

The specific rate constant for forming each product from a given starting material is the rate constant for forming X from I or II (k_a or k_b, respectively), times the fraction of X that goes to a particular product. (e.g., for (+)-III or (-)-III this fraction is $\frac{k_{-c}}{f}$). From the above relationships:

$$k_a = 2\frac{k_{-a}k_a}{f} + 2\frac{k_{-b}k_a}{f} + 2\frac{k_{-c}k_a}{f} + \frac{k_{-d}k_a}{f}$$

$$= 2k_5 + k_1 + k_2 + k_9 + k_{10} + k_{12}$$

$$= 1.85 \times 10^{-5} \text{sec}^{-1}$$

$$k_b = 2k_{-b}\frac{k_b}{f} + 2\frac{k_{-a}k_b}{f} + 2\frac{k_{-c}k_b}{f} + \frac{k_{-d}k_b}{f}$$

$$= 2k_6 + k_3 + k_4 + k_7 + k_8 + k_{11}$$

$$= 5.50 \times 10^{-5} \text{sec}^{-1}$$

If the whole reaction goes by way of a common intermediate the fraction of the reaction of the common intermediate going to a given product must be the same regardless of whether the starting material is I or II. The following relationships should then hold:

Product Formed

(1) I $$\frac{k_3}{k_b} = \frac{k_4}{k_b} = \frac{k_5}{k_a}$$

(0.1114) (0.1667) (0.0919)

(2) II $$\frac{k_1}{k_a} = \frac{k_2}{k_a} = \frac{k_6}{k_b}$$

(0.1297) (0.1925) (0.2245)

(3) III $$\frac{k_9}{k_a} = \frac{k_{10}}{k_a} = \frac{k_7}{k_b} = \frac{k_8}{k_b}$$

(0.1120) (0.1568) (0.0381) (0.0805)

(4) IV $$\frac{k_{11}}{k_b} = \frac{k_{12}}{k_a}$$

(0.2246) (0.1557)
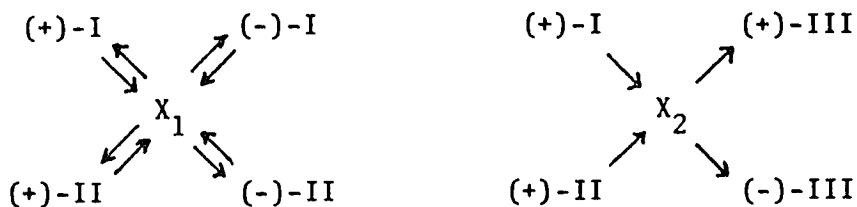
The actual values of these ratios are written in parentheses below them. If it is assumed that in each group of equations (1), (2), (3) and (4), the smallest fraction gives the maximum contribution of the common intermediate to the formation of that product, then the maximum contribution to the reaction of I by the common intermediate is:

$$k_1 + k_2 + 2k_5 + k_9 + k_{10} + k_{12}$$

$$= 0.1297\,k_a + 0.1297\,k_a + 2(0.0919)\,k_a + 0.0381\,k_a + 0.1551\,k_a$$

$$= 0.675\,k_a$$

A maximum of 67.5% of the reaction of I can be proceeding by way of a common intermediate. Performing a similar computation for II leads to the conclusion that a maximum of 67.5% of its reaction may
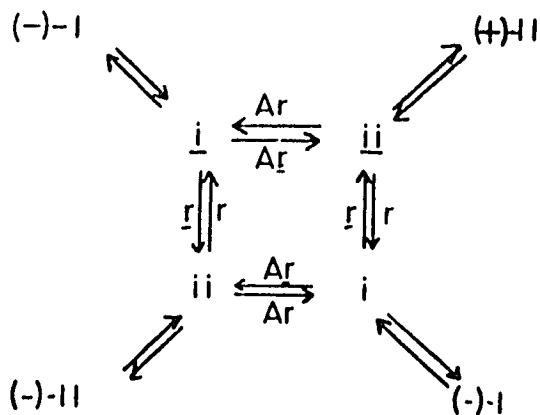
proceed by way of a common intermediate.

Another possible mechanism with common intermediates is the one described by the following schemes:

This scheme proposes the involvement of two common intermediates--one (X_1) for the automerizations of the cyclobutanes and the other (X_2) for the ring expansion to cyclohexene. Performing the same type of analysis for these schemes as for the previous one leads to the conclusion that there is a maximum of 81.9% involvement of a common intermediate in the automerizations of I and II. With respect to formation of cyclohexenes, 81.2% involvement of a common intermediate was calculated for I and 64.3% for II.

A third scheme may be proposed for account for the automerizations of the cyclobutanes. (This discussion is taken from the paper of Doering and Sachdev[6c] and applied to this system.) This scheme involves four diradicals which may be interconverted by 180° rotations

of only one bond at a time. Since there is some retention of optical activity in the products, the rates of these rotations (r, $\underline{r}$, Ar and A$\underline{r}$) are not permitted to be faster than getting on and off the array (k_2, k_{-2}, k_1, k_{-1}). Similarly, getting on and off the array may not be very fast as compared to rate of moving around the array in order to permit the direct formation of (+)-I from (-)-I and (+)-II from (-)-II.

When (+)-I is the starting material, the concentrations of $\underline{i}$, i, ii and $\underline{ii}$ at the beginning of the reaction ($\underline{i}.\underline{e}.$, when $k_2[(-)-II]$, $k_1[(+)-II]$ and $k_1[(-)-II]$ are zero) are

$$\underline{i} = \frac{k_2[(+)-I] + r(ii + A\underline{ii})}{P}$$

$$i = \frac{\underline{r}\,(ii + A\underline{ii})}{P}$$

$$\underline{ii} = \frac{\underline{r}\,(\underline{i} + Ai)}{Q}$$

$$ii = \frac{\underline{r}\,(i + A\underline{i})}{Q}$$

where $P = \underline{r}\,(\beta+1+A)$

$Q = r\,(\alpha+1+A)$

and $\alpha = \dfrac{k_{-1}}{r}$ $\beta = \dfrac{k_{-2}}{\underline{r}}$

With (+)-I as the starting material, the solution for $\underline{i}$, i, $\underline{ii}$ and ii is:

$$\underline{i} = \frac{MQZ}{\underline{r}Y} \qquad \underline{ii} = \frac{M(Z + 2A^2)}{Y}$$

$$i = \frac{2AMQ}{\underline{r}Y} \qquad ii = \frac{MA(Z + 2)}{Y}$$

where $M = \dfrac{k_2[(+)-I]}{r}$

$$Y = Z^2 - 4A^2$$

$$Z = (PQ/r\underline{r}) - 1 - A^2$$

Similarly, another set of equations may be derived if (+)-II is the starting material:

$$\underline{i} = \frac{N(Z + 2A^2)}{Y} \qquad \underline{ii} = \frac{NPZ}{\underline{r}Y}$$

$$i = \frac{NA(Z + 2)}{Y} \qquad ii = \frac{2NAP}{\underline{r}Y}$$

where $N = \dfrac{k_1[(+)-II]}{\underline{r}}$

Using these equations, expressions for any of the experimentally determined rate constants may be derived. One may write three of these ratios:

$X = \dfrac{k_5}{k_6}$, the ratio of the rate constants for enantiomerization;

$Y = R_{CN} = \dfrac{k_2}{k_1} = \dfrac{k_4}{k_3} = 1.48$, the rotational propensity;

and $\quad Z = \dfrac{k_3}{k_6}$, the ratio of the rates of diasteriomerization and enantiomerization of II.

The ratios X, Y and Z in terms of α β and A are:

$$X = \frac{k_5}{k_6} = K(\frac{\alpha}{\beta})^2 \frac{\beta+1+A}{\alpha+1+A}$$

$$Y = R_{CN} = \frac{k_4}{k_3} = A \frac{\alpha\beta + (\alpha+\beta+2)(1+A)}{\alpha\beta + (\alpha+\beta+2A)(1+A)}$$

$$Z = \frac{k_3}{k_6} = \frac{\beta}{\alpha} \frac{\alpha\beta + (\alpha+\beta+2A)(1+A)}{2A(\beta+1+A)}$$

An exact solution of these three equations X, Y and Z for α, β and A would give the relationship between the rates of getting off the array (k_{-1}, k_{-2}) to travelling around the array which would generate the observed ratio of rate constants. The solutions of X, Y and Z for various values of A were sketched in Figures 16 and 17. The three lines come closest to intersection for $A = \infty$ where k_6/k_5 takes the value 10.470. If k_6 is $12.46 \times 10^{-6}\text{sec}^{-1}$ then k_5 must be $1.189 \times 10^{-6}\text{sec}^{-1}$ instead of 1.68×10^{-6} to account for the results; or, if k_5 is fixed at 1.68×10^{-6} then k_6 must be $17.59 \times 10^{-6}\text{sec}^{-1}$. Thus 29% of the automerizations cannot be accounted for by this scheme with $A = \infty$.
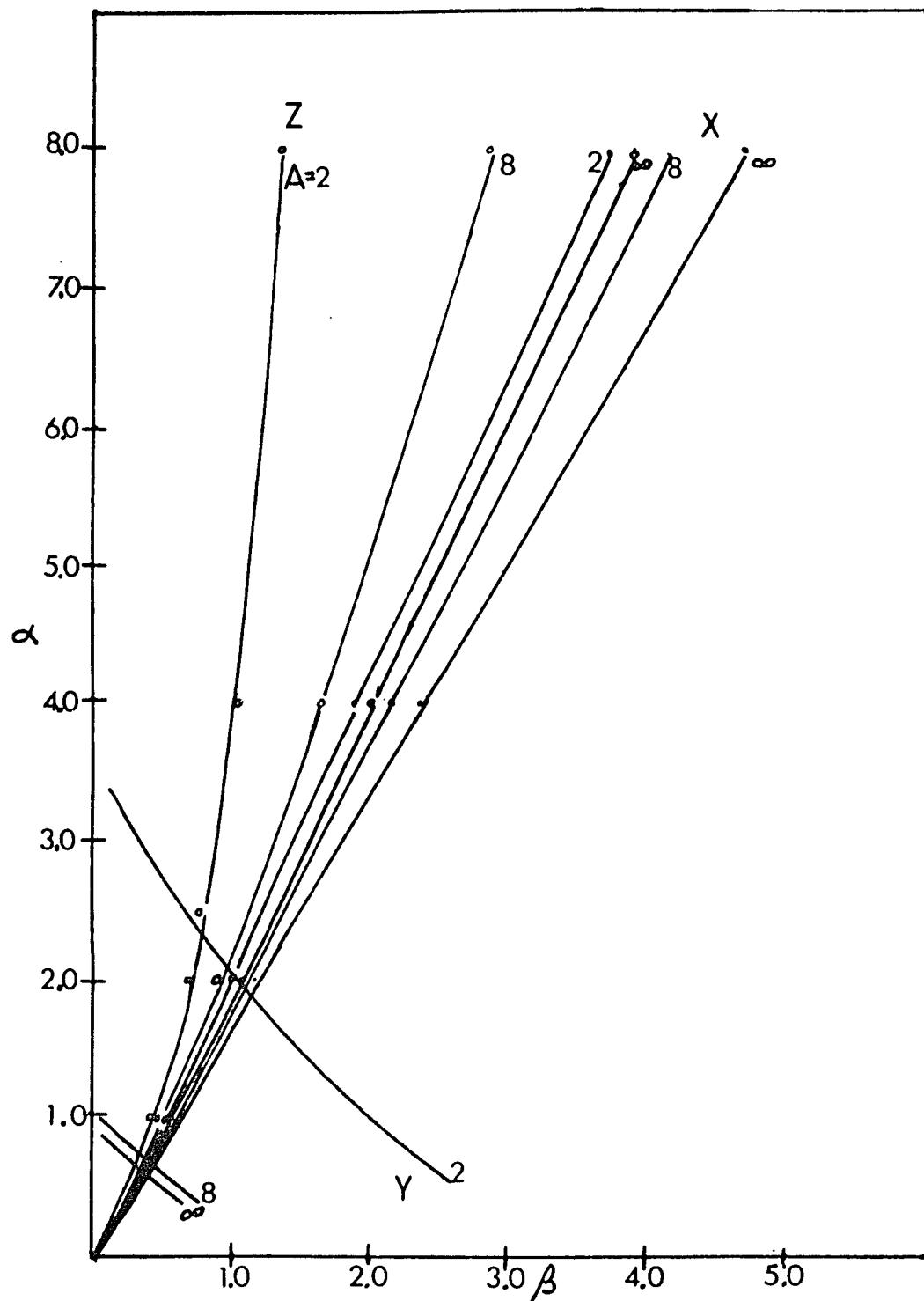
Figure 16. X, Y and Z as a function of α, β and A.
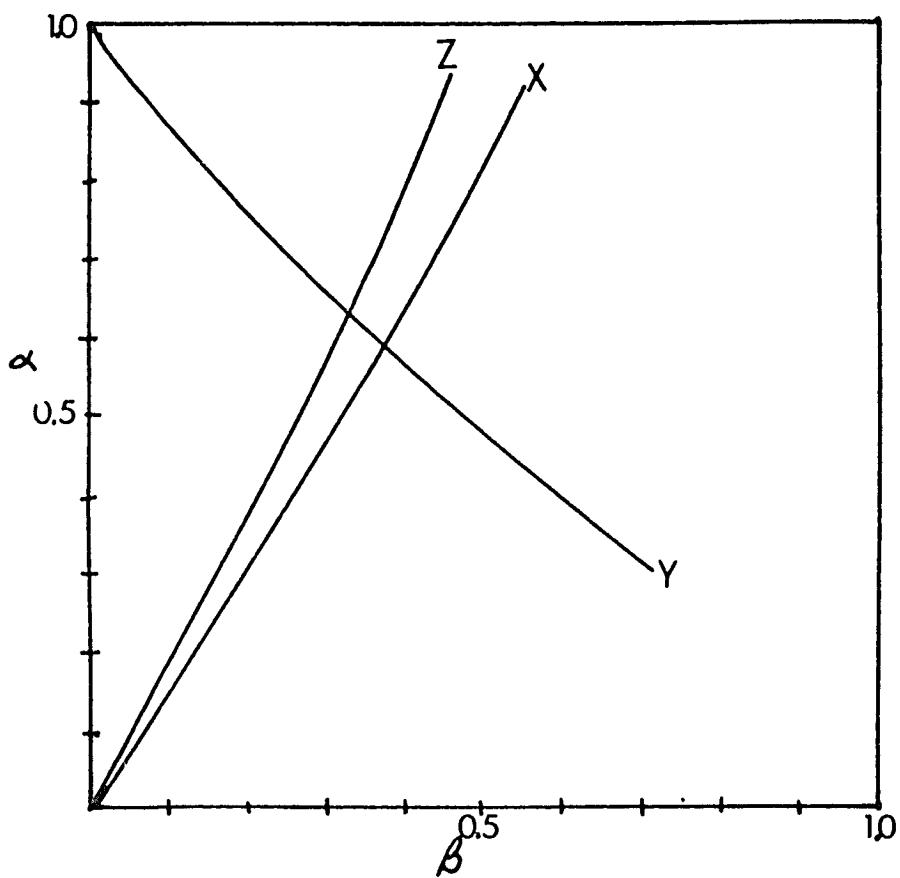
Figure 17. X, Y and Z as a function of α and β for A = ∞.

Choosing a lower and more reasonable value of A = 4.0 gives the result that 34.8% of the reaction cannot be accounted for by this scheme. Thus, even a mechanism involving a series of diradicals which interconvert and collapse to products at comparable rates cannot account for the ratios of the experimentally determined rate constants.

The Nature of Tetramethylene in the Rearrangements of I and II
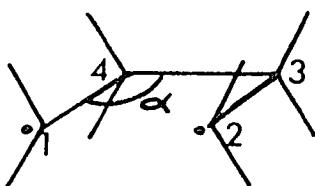
In the introduction, three models for the behavior of tetramethylene were presented. The experimental results can be examined in terms of these models.

One of the models for tetramethylene was suggested by the results of quantum mechanical calculations.[35b] Recall that in this model of the tetramethylene, the diradical is long-lived species, resting on a plateau of constant energy and can make many conformational changes before collapsing to products. This diradical would lead to the formation of chiral products in racemic form. Although it may provide an adequate model for a "common intermediate" (in this case tetramethylene is not an intermediate in the sense of being protected by barriers to cleavage or reclosure, but is operationally indistinguishable from such an intermediate), it cannot account for the total reaction of I or II.

A second model, one arising from the thermochemical calculations,[34] describes tetramethylene as an intermediate protected by energy barrier to cleavage and reclosure. Two alternatives can be

considered for the relative rates of bond rotation, reclosure, and cleavage. One alternative is that the rate of rotation in radical bearing bonds is less than 1 kcal mole^{-1}.[34,36] Since the barriers to cleavage and reclosure are calculated to be 7 kcal mole^{-1} [34], this alternative would lead to the formation of the chiral products in racemic form. The second alternative is that the rate of bond rotation in the radical and bond reclosure are comparable. As was shown previously, even a scheme of this type fails to rationalize all of the experimental results.
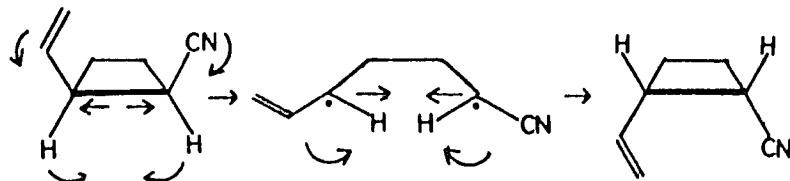
A third model for tetramethylene is that of the continuous diradical.[6c] The reactions of these cyclobutanes can be described as resulting from the superposition of the stretching mode of the C1-C2 bond and of a mode which involves twisting about one of the other cyclobutane bonds. As the C1-C2 bond is stretched, the bonding between the carbon centers falls to zero.[35b] Hoffmann[35b] has calculated for cyclobutane that at $\alpha = 116°$ and C1-C2 $= 2.9 \text{Å}$ the overlap
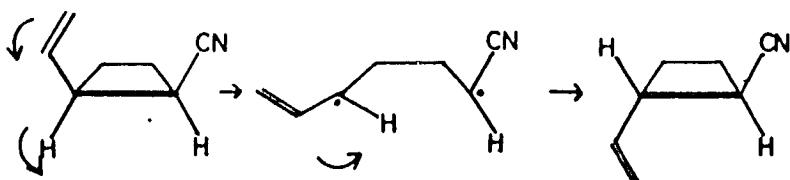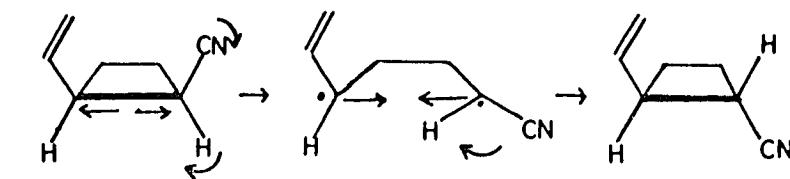
between C1 and C2 is zero. Since the bonding between the two centers is zero, one may describe the system as a diradical. Thus, a thermally activated cyclobutane is envisioned as having a large amplitude of stretching for C1-C2, at the outer reaches of which there is effectively

no bonding between C1-C2. One of the things that makes a bond disso-
ciation of this type different from the dissociation of a diatomic
molecule is that the "radical" endo are connected by a two-carbon
bridge. The result is that at its outer reaches the C1-C2 stretching
vibration merges with the bending modes of the methylene groups of the
two-carbon bridge. The restoring force of this bending mode inevitably
brings the two radical centers back to within bonding distance of each
other. Thus any displacement from the maximum extension of the C1-C2
bond can only lead to bonding.
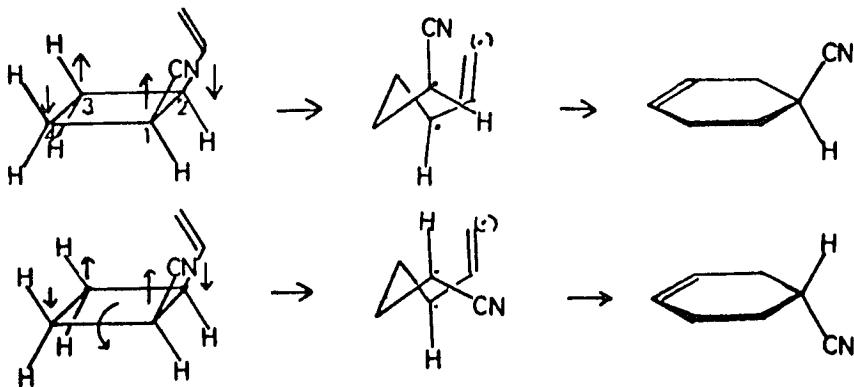
The streching mode becomes a reacting mode when certain other
vibrational modes of cyclobutane are superimposed. The superposition
of the rotations about both the C1-C4 and C2-C3 bonds as the stretch-
ing of the C1-C2 bond can lead to enantiomerization:

The superposition of only one of these bond rotations on the stretching
of C1-C2 can lead to the geometrical isomer of the starting material.
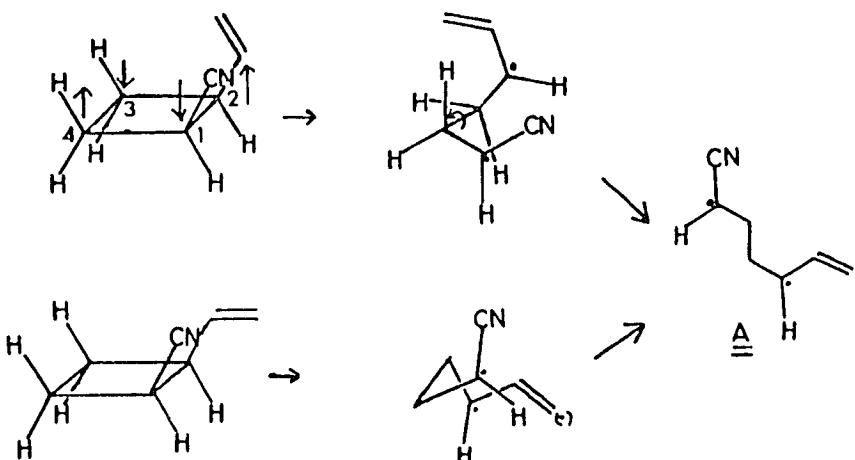
The isomerization of I or II to III can be viewed as an extension of

the ring puckering[35a] mode of cyclobutane, with or without an addi-

tional rotation about C1-C4.

The relative favorability of the observed reactions is then

governed by the probability that these vibrational modes will combine

with the C1-C2 stretching mode. In this model, as long as the vibra-

tional mode in question moves one radical center to within bonding

distance of another, bonding will occur; that is $\Delta H^{\ddagger}$ for bond formation

is essentially zero.

However, the molecular vibrations need not always operate in the

direction of bringing the two radical centers to within bonding

distance. The same puckering mode which can rationalize the formation

of ring expanded products, can lead to quite different results if the

vinyl group is not in the cisoid conformation or if puckering occurs

in the "wrong" sense:

Whether $\underline{A}$ has a discrete existence as an intermediate depends on $\Delta H^{\ddagger}$ for cleaving the C3-C4 bond. If $\Delta H^{\ddagger}$ is zero the cleavage of the tetramethylene in any of its conformations including $\underline{A}$ will be competitive with trapping of the radical centers to form isomerized products. A second possibility is that $\underline{A}$ has an energy barrier to cleavage. The species $\underline{A}$ would then be best described by the Benson[34] model for a diradical, as an intermediate protected by energy barriers. As an intermediate diradical $\underline{A}$ could account for up to 80% of the automerizations or 67% of the total reaction of I and II.

Thus, a mechanism with a continuous 1,4 diradical is capable of rationalizing all of the results--including the intervention of a common intermediate diradical. However, the results may also be rationalized as some combination of concerted and diradical mechanisms, and these two alternatives cannot be distinguished.

Although the model of a continuous diradical is capable of rationalizing these results after the fact, the predictive power of this model will be small until more is known about relative rotational

propensities in this and other systems and about what factors determine these propensities. For the present case, it seems reasonable that a cyano-bearing bond should be able to rotate more readily than a bond bearing a vinyl group because of the smaller bulk of the cyano group. It is not at all clear, however, why a bi-rotational process enantiomerization (of II) should be more favorable than any of the mono-rotational processes, nor why the even greater changes in structure required for isomerization of I and II to III still allow these processes to compete favorably with the simplest of the observed reactions.

EXPERIMENTAL

Optical rotations were determined on a Perkin-Elmer 141 digital readout polarimeter. The observed rotations, α, are precise to $\pm 0.002°$. Optical rotations are reported as $[\alpha]_D^{25}$ -ABC°, $[\alpha]_{365}^{25}$ -DEF° (abc°, def°, c xxx, solvent) where abc° and def° are the observed rotations, α, at 589 nm and 365 nm, respectively, for concentration equal to xxx grams/100 ml of solvent. If the rotation of the sample was determined more than once, the specific rotations reported are the average of those obtained from the data in the parentheses that follow. Volumetric errors are estimated to be $\pm 1.0\%$. The ethanol used as solvent in obtaining rotations is absolute ethanol. The CCl_4 and cyclohexane used for rotations are spectrograde.

Nmr spectra were recorded on a Varian T-60 spectrometer and the chemical shifts were reported in ppm downfield from tetramethysilane. Infrared spectra were determined on a Perkin-Elmer 337 grating spectrophotometer. (Spectra of all new compounds are shown in Appendix II.) Mass spectral analyses were made with an AEI Model MS-9 double focussing mass spectrometer. All melting points and boiling points are uncorrected. Microanalyses were carried out by Scandinavian Microanalytical Lab., Herlev, Denmark.

Quantitative analyses of mixtures were effected on a Perkin-Elmer 990 gas chromatograph with a flame ionization detector. Relative areas were determined with an Autolab 6300 digital integrator. Purification and separation of larger quantities were accomplished by preparative glpc on Aerograph A90-P and A90-P3 gas chromatographs. The following columns were used:

Column A: 6 ft x 0.25 in. o.d.: 20% Carbowax 20M on 60/80 mesh non-acid-washed Chromosorb P.

Column B: 5 m x 0.25 in.: 20% General Electric methyl silicone gum rubber (SE-30) on 60/80 mesh Chromosorb P washed with NaOH in methanol.

Column C: 5 m x 0.25 in.: 20% 1,2,3-Tris-(2-cyanoethoxy)-propane (TCEP) on 60/80 mesh non-acid-washed Chromosorb P.

Column D: 3 m x 0.25 in.: 20% Carbowax 20M on 50/60 mesh Anakrom - acid and base washed and silanized (ABS).

Column E: 300 ft x 0.01 in.: Carbowax 20M Capillary Column.

Racemic <u>trans</u>-(I) and <u>cis</u>-(II)-1-Cyano-2 vinylcyclobutane.[47]

Into a 420-ml immersion-well, photolysis flask with two side-arms were placed 171 ml (2.6 mol) freshly distilled acrylonitrile (IV) and 44.4 ml (0.26 mol) 2,3-butanedione. One of the side-arms was fitted with a calcium sulfate drying tube and the other with a gas inlet tube. The flask was placed into a one-gallon Dewar flask containing Dry-Ice and acetone. The lamp housing was then cooled with methanol which had been circulated through a Dry Ice - acetone bath. Butadiene-1,3 (Matheson Instrument Grade) (226 ml, 2.6 mol) was distilled into the cooled flask. The mixture was irradiated with light from a 450 w high pressure Hanovia lamp filtered through Pyrex. The progress of the photolysis was followed by glpc (Column A: 125°, He 60 ml/min). Three new peaks appeared. The mixture was irradiated for 16 hr in two eight-hour periods until the new peaks stopped growing relative to the butanedione. This point represented 2% conversion. Excess butadiene was allowed to evaporate at room temperature and atmospheric pressure. Excess acrylonitrile and butanedione were removed by evaporation at room temperature and reduced pressure (10 mm). The distilled residue (bp 42° / 2 mm) was separated into its components by preparative glpc under the same conditions used for analysis of the photolysis mixture.

Fraction 1. (I) (8.5 min, 880 mg): nmr $(CCl_4)\delta$ 2.2 (m, 4H), 2.8 (m, 1H), 3.2 (m, 1H), 5.0 and 5.2 (m, 2H), 5.9 (m, 1H); ir (CCl_4) 2240 cm^{-1} (C≡N), 3100 cm^{-1} (=CH).

Fraction 2. (II) (12 min, 800 mg): nmr $(CCl_4)\delta$ 2.3 (m, 4H), 3.3 (m, 2H), 5.0, 5.1 and 5.3 (m, 2H), 6.0 (m, 1H); ir (CCl_4) 2235 cm^{-1} $(C\equiv N)$, 3075 cm^{-1} (=CH).

Fraction 3. (III) (15.5 min, 400 mg): nmr $(CCl_4)\delta$ 2.2 (m, 5H), 2.8 (m, 2H), 5.7 (d, 2H); ir (CCl_4) 2240 cm^{-1} $(C\equiv N)$.

The spectra agree with those reported.[47] Fraction 1 was assigned the structure trans-1-cyano-2-vinylcyclobutane (I); fraction 2, cis-1-cyano-2 vinylcyclobutane (II); and fraction 3, 4-cyanocyclohexene (III).

Racemic Methyl trans- and cis-2-Vinylcyclobutane-1-carboxylate

(V and VI). These compounds were prepared by the same general procedure used for the preparation of the corresponding nitriles. Freshly distilled methyl acrylate (194 ml, 2.26 mol), 19.2 ml (0.226 mol) 2,3-butanedione, and 2.26 mol of butadiene were irradiated for 40 hr in 10-hr periods. The progress of the photolysis was followed by analysis of aliquots by glpc (Column B: 140°, He 60 ml/min). Photolysis was discontinued when the product peaks (retention times 26, 28 and 45 min) stopped growing relative to the methyl acrylate peak. After excess butadiene, methyl acrylate, and butanedione had been removed, a small amount of the distilled (bp 32°/0.8 mm) residue was separated by preparative glpc under the same conditions used for analysis.

Fraction 1 (26 min): nmr $(CCl_4)\delta$ 2.0 (m, 4H), 3.0 (m, 2H) 3.6 (s, 3H), 5.1, 5.2, 4.9 (m, 2H), 5.9 (m, 1H); ir (CCl_4) 1740 cm^{-1} (C=O); mass spectrum m/e Calcd for $C_8H_{12}O_2$: 140.083724. Found: 140.0844274.

Fraction 2 (28 min): nmr $(CCl_4)\delta$ 2.1 (m, 4H), 3.2 (m, 2H), 3.6

(s, 3H), 4.9 and 5.1 (m, 2H), 5.9 (m, 1H); ir (CCl_4) 1740 cm^{-1} (C=O);

mass spectrum $\underline{m/e}$ Calcd for $C_8H_{12}O_2$: 140.083724. Found: 140.0840344.

'Fraction 3 (45 min): nmr $(CCl_4)\delta$ 2.2 (m, 7H), 3.7 (s, 3H), 5.7

(s, 2H); ir (CCl_4) 1740 cm^{-1}.

Fraction 1 was assigned the structure methyl

trans-2-vinylcyclobutane-1-carboxylate (V); fraction 2, methyl

cis-2-vinylcyclobutane-1-carboxylate (VI); and fraction 3, methyl

3-cyclohexene-1-carboxylate (VII).

The rest of the material was separated on column C (130°, He

60 ml/min). The cyclobutanes obtained by preparative glpc were

contaminated by 5% of the other epimer.

Dimethyl trans-1,2-Cyclobutanedicarboxylate (IX). Cyclobutane-

1,2-dicarboxylic acid (VIII)(100 g, 0.68 mol, Aldrich) 100 g of methanol

and 100 mg of p-toluenesulfonic acid were treated in 600 ml refluxing

benzene in a 1-ℓ flask fitted with a reflux condenser and Dean-Stark

trap. Heating was continued until water no longer separated (6 hr).

Distillation of the residue remaining after evaporation of benzene gave

104 g (90%) of a colorless liquid: bp 56°/0.5 mm (lit.[55] 105-107°/

13 mm); ir (neat) 1740 cm^{-1} (-C=O); nmr $(CCl_4)\delta$ 2.2 (m, 4H), 3.35

(m, 2H), 3.7 (s, 6H).

Methyl Hydrogen trans-Cyclobutane-1,2-dicarboxylate (X). A 204-g

sample (1.19 mol) of IX was heated in 500 ml of refluxing methanol

containing 56 g (1.0 mol) of KOH. After the methanol had been removed

under reduced pressure, the residue was diluted with 100 ml of water and extracted with ether. The aqueous layer was acidified with concentrated HCl and continuously extracted with ether for three days. Distillation of the residue of the dried (MgSO$_4$) ether extract gave 63.34 g (40%) of X: bp 110-112°/0.1 mm. (lit.[55] 106-108°/1 mm); ir (CCl$_4$) 1745 cm^{-1} (C=O ester), 1705 cm^{-1} (C=O acid); nmr (CCl$_4$)δ 2.2 (m, 4H), 3.4 (m, 2H), 3.65 (s, 3H), 12.2 (s, 1H).

Methyl <u>trans</u>-2-Hydroxymethylcyclobutane-1-carboxylate (XI). To a flame-dried, 500-ml, three-necked flask fitted with a nitrogen inlet, a reflux condenser protected by a calcium sulfate drying tube, and an addition funnel were added 8.5 g (0.224 mol) of sodium borohydride and 225 ml of dry (distilled from LiAlH$_4$) tetrahydrofuran.[56] With the aid of the addition funnel, 39.6 g (0.25 mol) of X was added cautiously to the magnetically stirred sodium borohydride suspension. A solution of boron trifluoride ethyl ether (freshly distilled from CaH$_2$, 42.6 g, 0.3 mol) in 50 ml of dry tetrahydrofuran, was added to the mixture over a period of one hour. The mixture was allowed to stir overnight under nitrogen. The mixture was poured into 300 ml of water and extracted with five 200-ml portions of ether. The ethereal extracts were washed with 100 ml of saturated sodium bicarbonate solution and 100 ml of brine and dried over MgSO$_4$. The residue remaining after removal of ether and tetrahydrofuran was distilled to give 22.1 g (61%) of XI: bp 70°/0.3 mm (lit.[55] 81-82°/1 mm); ir (CCl$_4$) 3425 cm^{-1} (-OH), 1740 (C=O); nmr (CCl$_4$)δ 2.0 (m, 4H), 2.85 (m, 2H), 3.5 (d, 2H, J = 5Hz), 3.6 (s, 3H), 3.9 (s, 1H).

trans-2-Carbomethoxycyclobutanecarboxaldehyde (XII). Into a

flame-dried 1-ℓ three-necked flask fitted with a nitrogen inlet,

drying tube, magnetic stirrer and a 250-ml flask connected by a

90°-bend glass connector were placed 166 ml of dry triethylamine,

23.8 g (0.165 mol) of XI, and 166 ml of dry dimethyl sulfoxide.

Trimethylamine-sulfur trioxide[57] (69.5 g, 0.495 mol) in 50 ml of

dimethyl sulfoxide, was added as a slurry to the mixture by way of

the 250-ml flask. After the mixture had been stirred overnight, it

was acidified with 3N HCl and extracted with four 200-ml portions

of methylene chloride. The extracts were washed with six, 150-ml

portions of water, 150 ml of saturated sodium bicarbonate solution,

and dried over $MgSO_4$. Distillation of the residue of the methylene

chloride extracts gave 10.97 g (47%) of XII: bp 63°/3 mm; ir (CCl_4)

1745 cm^{-1} (ester C=O), 1735 (shoulder, aldehyde C=O); nmr $(CCl_4)\delta$ 2.2

(m, 4H), 3.35 (m, 2H), 3.75 (s, 3H), 10.0 (s, 1H). The aldehyde

formed a 2,4-dinitrophenylhydrazone, mp 139°.

Anal. Calcd for $C_{13}H_{14}N_4O_6$: C, 48.45; H, 4.38; N, 17.38.

Found: C, 48.34; N, 17.45; H, 4.49.

Methyl trans-2-Vinylcyclobutane-1-carboxylate (V). Sodium

hydride (1.83 g of a 57% mineral oil dispersion, 0.039 mol) was placed

in a 250-ml, three-necked flask and washed with pentane. The flask

was equipped with a rubber serum cap, a reflux condenser fitted with a

three-way stopcock and a magnetic stirrer. The system was evacuated

filled with N_2. Twenty ml of dimethyl sulfoxide was introduced by

means of a syringe, and the mixture was heated at 75-80° until hydrogen evolution stopped (45 min). The resulting solution of methyl sulfinyl carbanion [58] was cooled in an ice water bath and to it was added 14.28 g (0.04 mol) of methyltriphenylphosphonium bromide in 40 ml of warm dimethyl sulfoxide. The mixture was allowed to stir for 15 min at room temperature before the addition of 2.89 g (0.026 mol) of XII. After the mixture had been stirred at room temperature overnight, it was poured into 250 ml of water and extracted with three 100-ml portions of pentane. The pentane was washed with 100 ml of 50% dimethyl sulfoxide-water and 100 ml of water. Evaporation of the dried ($MgSO_4$) pentane extracts gave 2.39 g of residue (62.5%). Analysis of the mixture by glpc (Column C: 110°, He 60 ml/min) shows a 9:1 mixture of two compounds with retention times (29.5 and 33 min) identical with those of V and VI, respectively, synthesized by photolysis of butadiene and methyl acrylate. The nmr (CCl_4) [δ 2.1 (m, 4H), 3.0 (m, 2H), 3.6 (s, 3H), 4.9, 5.1 (m, 2H), 5.9 (m, 1H)] is consistent with this conclusion.

trans-2-Vinylcyclobutane-1-carboxylic Acid (XIII). Crude V (14.36 g, 0.102 mol) was heated for 12 hr in 80 ml of refluxing 80% methanol containing 8 g (0.14 mol) of KOH. Methanol was removed under reduced pressure and the residue was dissolved in 20 ml of water. The aqueous solution was washed with 20 ml of pentane and 20 ml of ether. The aqueous layer was cooled in ice and acidified with 5% HCl. The acidic solution was extracted with three 20-ml portions of ether and the ether dried over $MgSO_4$. The residue (9.5 g, 78%) remaining after

distillation of the ether was used without further purification for the resolution.

Distillation of another sample of acid showed bp $55°/0.05$ mm; nmr $(CCl_4)\delta$ 2.1 (m, 4H), 3.1 (m, 2H), 5.1 (m, 2H), 6.0 (m, 1H), 12.5 (s, 1H); ir (CCl_4) 1700 cm^{-1} (C=O); mass spectrum $\underline{m/e}$ Calcd for $C_7H_{10}O_2$: 126.068075. Found: 126.06875.

Resolution of trans-2-Vinylcyclobutane-1-carboxylic Acid.

Crude XIII (14.5 g, 0.115 mol) and quinine (37.26 g, 0.115 mol) were dissolved in 50 ml of absolute ethanol. After 400 ml of water had been added to the solution, it was heated to boiling. Absolute ethanol was added at the boiling point until all of the solid dissolved. The solution deposited colorless needles on standing at room temperature overnight. Since crude XIII contained 5-10% of the cis-acid, the progress of the resolution was followed by recovering samples of acid from salt, treating the acid with ethereal diazomethane,[64] and separating the pure trans ester (V) by glpc (Column C: 120°, He 60 ml/min).

After one recrystallization of the salt, the corresponding pure V had $[\alpha]_{578}^{27}$ +59.9°, $[\alpha]_{365}^{27}$ +196.4° (0.961°, 3.147°; c 1.6033, ethanol). The second recrystallization afforded V of $[\alpha]_{578}^{25}$ +107.8°, $[\alpha]_{365}^{25}$ +352.5° (1.222°, 3.996°; c 1.1337, ethanol). The third recrystallization afforded 16.73 g of salt with V of $[\alpha]_{578}^{27}$ +127.5°, $[\alpha]_{365}^{27}$ +417.0° (0.942°, 3.080°; c 0.7386, ethanol). A sample of the salt was

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[64] F. Arndt, Org. Syn., Coll. Vol. II, p. 165, p. 461.

recrystallized three more times without isolating the ester. Ester V from salt recrystallized six times had $[\alpha]_{578}^{27}$ +135.2°, $[\alpha]_{365}^{27}$ +441.8° (1.240°, 4.051°; c 0.9134, ethanol), (1.512°, 4.942°; c 1.1233, ethanol). One more recrystallization of the salt gave V with $[\alpha]_{578}^{27}$ +132.3°, $[\alpha]_{365}^{27}$ +434.6° (0.385°, 1.270°; c 0.2901, ethanol), 1.733°, 5.668°; c 1.3140, ethanol). Trans-ester V from the sixth and seventh recrystallizations of the salt were free of cis-ester VI by glpc.

Acid recovered from the mother liquor of the first recrystallization was treated with diazomethane. The resulting pure V had $[\alpha]_{578}^{27}$ -118.7°, $[\alpha]_{365}^{27}$ -387.4° (-1.129°, -3.684°; c 0.9510, ethanol). The acid had about 10% of the cis isomer, as determined by glpc of the corresponding ester.

(+)-trans-2-Vinylcyclobutane-1-carboxamide (XIV). A solution of 4.26 g (0.034 mol) of (+)-trans-XIII [with trans-V of $[\alpha]_{578}^{27}$ +127.5°, $[\alpha]_{365}^{27}$ +417.0° (0.942°, 3.080°; c 0.7386, ethanol)] and 3.42 g of triethylamine (0.034 mol) in 30 ml of methylene chloride was added dropwise with stirring to a solution of 4.5 ml of ethyl chloroformate[6c] in 30 ml of methylene chloride cooled to -30°. Over the period of addition (1.5 hr), the temperature was maintained at -30° to -25°. After the mixture had been stirred at -20° to -5° for 1.5 hr, NH_3 was bubbled through the mixture for 20 min. Stirring was continued at room temperature for 3 hr. The white solid was filtered and washed with methylene chloride. The methylene chloride solution was washed with 10% NaOH, 3N HCl, saturated $NaHCO_3$, and water. The dried ($MgSO_4$)

methylene chloride was removed under reduced pressure to give 2.93 g
(72%) of a white solid: mp after recrystallization from methylene
chloride - petroleum ether, 85°; nmr $(CDCl_3)$ δ 2.2 (m, 4H), 3.2 (m, 2H),
5.0 (m, 1H), 5.3 (m, 1H), 6.2 (m, 1H); ir $(CDCl_3)$ 3530 cm^{-1} (NH),
3400 (N-H), 1675 (C=O); $[\alpha]_{578}$ +107.5°, $[\alpha]_{365}$ +393.9° (0.291°, 1.066°;
c 2.706, $CHCl_3$).

A recrystallized sample of racemic XIV had mp 102-103°; mass
spectrum _m/e_: Calcd for $C_7H_{11}NO$: 125.084059. Found: 125.084044.

(-)-trans-1-Cyano-2 vinylcyclobutane (I). The starting material
was crude XIV originating from XIII with corresponding (-) trans-V of
$[\alpha]_{578}^{27}$ -118.7°, $[\alpha]_{365}^{27}$ -387.4° (-1.129°, -3.684°; c 0.9510, ethanol).
The crude amide contained 10% cis-isomer (as determined by glpc
analysis of the corresponding ester).

To a flame-dried 25-ml flask, which had been flushed with
nitrogen, there was added 1.44 g (11.5 mmol) of (-)-XIV. The flask
was stoppered with a rubber serum cap, through which 2 ml of dry
pyridine was added by means of a syringe. To the solution cooled to
0°, 2.2 g (11.5 mmol) of p-toluenesulfonyl chloride[6c] in 2 ml dry
pyridine was added. The mixture was stirred at 27° for 10 hr, diluted
with ether and filtered from the resulting precipitate. The ether was
washed with water, 5% HCl, saturated $NaHCO_3$ and dried with $MgSO_4$. The
crude nitrile was separated into two components by preparative glpc
(Column D: 120°, He 60 ml/min).

Fraction 1 (16 min, 592 mg): nmr (CCl_4) δ 2.16 (m, 4H), 2.8 (m, 1H), 3.2 (m, 1H), 4.9 (m, 1H), 5.2 (m, 1H), 5.8 (m, 1H); ir (CCl_4) 2240 cm^{-1} $(C\equiv N)$, 1630 $(C=C)$.

Fraction 2 (24 min, 68 mg): nmr (CCl_4) δ 2.2 (m, 4H), 3.3 (m, 2H), 5.0, 5.1, and 5.3 (m, 2H), 6.0 (m, 1H); ir (CCl_4) 2240 cm^{-1} $(C\equiv N)$, 1650 $(C=C)$.

The nmr and ir spectra of fractions 1 and 2 are identical to those of I and II obtained from the photolysis of butadiene and acrylonitrile.

The trans-nitrile, I, had $[\alpha]_{578}^{27}$ +157.0°, $[\alpha]_{365}^{27}$ -497.0° (-0.508°, -1.608°; c 0.3235, cyclohexane). The cis-nitrile, II, was rechromatographed: $[\alpha]_{578}^{27}$ -9.3°, $[\alpha]_{365}^{27}$ -30.8° (-0.098°, -0.326°, c 1.0578, cyclohexane).

In a separate experiment, I ($[\alpha]_{578}^{25}$ +156.2°, $[\alpha]_{365}^{25}$ +493.0° (+1.981°, +6.251°; c 1.2681, cyclohexane)) was rechromatographed and its rotation remeasured: $[\alpha]_{578}^{25}$ +155.8°, $[\alpha]_{365}^{25}$ +490.9° (+1.531°, +4.823°; c 0.9825, cyclohexane). This procedure caused no racemization within the error of the measurement. The same was true for II: $[\alpha]_{578}^{25}$ +50.8°, $[\alpha]_{365}^{25}$ + 174.8° (0.439°, 1.511°; c 0.8643, cyclohexane); rechromatographed: $[\alpha]_{578}^{25}$ +50.5°, $[\alpha]_{365}^{25}$ +174.7° (0.378°, 1.307°; c 0.7480, cyclohexane).

Epimerization of I and II. The procedure used is that of Doering and Sachdev.[6c] To a N_2-flushed, flame-dried, 5-ml pear-shaped flask fitted with a magnetic stirrer was added 22 mg I and 0.2 ml of dry

dimethyl sulfoxide at 30°. About 10 mg of potassium t-butylate was added to the solution. The reaction was quenched by the addition of 1 ml of water at the end of 10 min. The pentane extract was analyzed by glpc (Column E: 130°, He 35 psi) and the relative areas of I and II determined: I = 76.31%, II = 23.68%, K = 0.310. The experiment was repeated with II: I = 75.64%, II = 24.36%, K = 0.322.

In a separate experiment starting with I, the product was separated by glpc (Column D: 120°, He 60 ml/min), and shown to be identical to II: nmr (CCl_4) δ 2.3 (m, 4H), 3.3 (m, 2H), 5.0, 5.2, 5.4 (m, 2H), 6.0 (m, 1H); ir (CCl_4) 2240 cm^{-1} $(C{\equiv}N)$.

(+)-cis-1-Cyano-2-vinylcyclobutane [(+)-II].

An 881-mg sample of (-)-I $([\alpha]_{578}^{27}$ -157.0°, $[\alpha]_{365}^{27}$ -497.0° (-0.508°, -1.608°; c 0.3235, cyclohexane)) was treated with potassium t-butylate and dimethyl sulfoxide according to the previous procedure. The mixture was separated by preparative glpc (Column D: 120°, He 60 ml/min). The cis nitrile, II, was rechromatographed: $[\alpha]_{578}^{22}$ +51.0°, $[\alpha]_{365}^{22}$ +175.2° (0.542°, 1.861°; c 1.0623, cyclohexane). The recovered trans-nitrile, I, had $[\alpha]_{578}^{22}$ -156.6°, $[\alpha]_{365}^{22}$ -493.7° (-1.151°,-3.623°; c 0.7318, cyclohexane).

(S)-(-)-3-Cyclohexene-1-carboxamide (XVI).

A 1.26-g (10 mmol) sample of (S)-(-)-3-cyclohexene-1-carboxylic acid (XV) $([\alpha]_{578}^{25}$ -88.99°, $[\alpha]_{365}^{25}$ -279.6° (-0.648°, -2.026°; c 0.7192, CCl_4), (-0.441°, -1.393°; c 0.5018, CCl_4); 78.4% optically pure[62]) was treated with 1.01 g (10 mmol) triethylamine and 1.35 ml ethyl chloroformate according to

the procedure used for the preparation of XIV. The white solid

obtained was used without further purification to synthesize III.

<u>(S)-(-)-4-Cyanocyclohexene [(S)-(-)-III]</u>. A 239-mg (1.9 mmol)

sample of the above (S)-(-)-XVI was treated with 363 mg (1.9 mmol) of

$\underline{p}$-toluenesulfonyl chloride according to the procedure used for the

preparation of I. The resulting nitrile had $[\alpha]_{578}^{25}$ -90.9°, $[\alpha]_{365}^{25}$ -293.2°

(-0.735°, -2.391°; c 0.8117, cyclohexane), (-0.827°, -2.672°; c 0.9061,

cyclohexane). The maximum rotation of III (obtained by correction for

the 78.4% optical purity of XVI) is then $[\alpha]_{578}^{25}$ -115.9°, $[\alpha]_{365}^{25}$ -374.6°.

<u>Conversion of (1R:2R)-(-)-VIII to (1R:2R)-(-)-IX.</u> Treatment of

0.0432 g (0.3 mmol) of (1R,2R)-(-)-VIII ($[\alpha]_D^{25}$ -155.0°, $[\alpha]_{578}^{25}$ -162.1°,

$[\alpha]_{365}^{25}$ -512.4°(-1.836°, -1.925°, -6.080°; c 1.1847, H$_2$O), (-1.408°,

-1.471°, -4.651°; c 0.9076, H$_2$O), 98.10% optically pure) with

ethereal diazomethane, followed by washing with saturated NaHCO$_3$ and

water led to 0.04128 g (80%) of (-)-IX: $[\alpha]_D^{25}$ -146.0°, $[\alpha]_{578}^{25}$ -151.4°,

$[\alpha]_{365}^{25}$ -474.9° (-1.043°, -1.091°, -3.422° ; c 0.7200, CCl$_4$) (-0.764°,

-0.786°, -2.465°; c 0.5195, CCl$_4$). The maximum rotation of IX[61] at

only one wavelength has been reported ($[\alpha]_D^{25}$ 147°) and agrees with

our value of $[\alpha]_D^{25}$ -148.7°, $[\alpha]_{578}^{25}$ -154.3°, $[\alpha]_{365}^{25}$ -483.9°.

<u>Conversion of (1R:2S)-(-)-V to (1R:2R)-(-)-IX.</u> To 0.07784 g of V

(0.556 mol) ($[\alpha]_D^{25}$ -114.0°, $[\alpha]_{578}^{25}$ -118.7°, $[\alpha]_{365}^{25}$ -391.3° (-0.350°,

-0.364°, -1.202°; c 0.3065, ethanol), (-0.449°, -0.520°, -1.711°;

c 0.4392, ethanol)) in 20 ml of 80% aqueous $\underline{t}$-butyl alcohol kept at

pH 8 by the addition of solid K_2CO_3, 0.984 g (4.60 mmol) of sodium metaperiodate and 10 mg potassium permanganate in 27.8 ml water was added with stirring. After the mixture had been stirred for 10 min, the t-butyl alcohol was removed under reduced pressure. The residue was taken up in 10 ml of water and acidified with 10% HCl. The dried ($MgSO_4$) ether extract was treated with diazomethane and was washed with saturated $NaHCO_3$ solution and water. Preparative glpc (Column D: 150°, He 100 ml/min) of the residue of the dried ($MgSO_4$) ether extract gave 0.05114 g (53.5%) of IX ($[\alpha]_D^{25}$ -128.3°, $[\alpha]_{578}^{25}$ -133.1°, $[\alpha]_{365}^{25}$ -417.9° (-0.718°, -0.736°, -2.314°; c 0.5545, CCl_4), (0.560°, -0.588°, -1.842°; c 0.4402, CCl_4); 86.3% optically pure). Based on the maximum rotation of diester IX, the maximum rotation of V is $[\alpha]_D^{25}$ -132.2°, $[\alpha]_{578}^{25}$ -137.6°, $[\alpha]_{365}^{25}$ -453.6°.

Figure 10 and Table 11 summarize the configurational relationships and maximum rotations of I, II, III, V, VIII, IX and XV.

General Procedure for Thermal Rearrangements. All thermal rearrangements were performed in Pyrex ampoules which had been soaked in NH_4OH overnight, rinsed with distilled water until the washings were neutral, rinsed with acetone and dried. Immediately before use, the ampoules were flame dried with nitrogen purging. Two sizes were used: A: 15cm x 1cm o.d. with 10cm x 0.6cm o.d. stem (~8 ml volume when sealed) and B: 20.5cm x 1.2cm o.d. with 11cm x 0.7cm o.d. stem (~16 ml volume when sealed). The nitriles were introduced with microsyringe and the ampoules sealed under 10^{-4} mm pressure. The

Table 11. The Maximum Specific Rotations and Absolute Configurations of I, II, III, V, IX, and XV.

	$[\alpha]_D$	$[\alpha]_{578}$	$[\alpha]_{546}$	$[\alpha]_{436}$	$[\alpha]_{365}$
(1R:2R)-(-)-trans-1,2-Cyclobutane-dicarboxylic Acid (VIII)	-158°[a]	-165.4°	-188.4°	-325.8°	-522.7°
(1R:2R)-(-)-Dimethyl-trans-1,2-Cyclobutanedicarboxylate (IX)	-148.7°[b]	-154.3°	-176.3°	-303.5°	-483.9°
(1R:2S)-(-)-Methyl-trans-2-Vinyl-Cyclobutanecarboxylate (V)	-132.2°[c]	-137.6°	-157.4°	-277.1°	-453.6°
(1R:2S)-(-)-trans-1-Cyano-2-Vinylcyclobutane (I)	-175.0°[d]	-181.4°	-206.9°	-361.0°	-578.5°
(1S:2S)-(+)-cis-1-Cyano-2-Vinylcyclobutane (II)	+56.9°[d]	+59.0°	+67.8°	+122.9°	+205.7°
(S)-(-)-Cyclohexene-4-Carboxylic Acid (XV)	-108.5°[b]	-113.5°	-129.9°	--	-357°
(S)-(-)-4-Cyanocyclohexene (III)	-112.8°[d]	-115.9°	-132.6°	-232.1°	-374.6°

All [α] measured at 25° ±3.0° in the following solvents:

a) H_2O b) CCl_4 c) CH_3CH_2OH d) Cyclohexane

ampoules were suspended in the vapors of a boiling solvent bath by a copper wire fastened to a hook at the end of the ampoule. The temperature of the vapors was measured with an iron-constantan thermocouple and a Leeds and Northrup No. 8686 millivolt potentiometer.

Thermal Rearrangement of II. Two ampoules, size B, were filled with 50 $\mu\ell$ each of II. The ampoules were heated 12 hr at 217.8° $\pm 0.3°$ (bp of naphthalene). The products were separated on Column D (115°, He 60 ml/min): (1 min) butadiene and (2 min) acrylonitrile were identified by retention times; (16 min) I: nmr (CCl_4) δ 2.2 (m, 4H), 2.8 (m, 1H), 3.2 (m, 1H), 5.0 and 5.2 (m, 3H) and ir (CCl_4) 2240 cm^{-1} $(C\equiv N)$ are identical to those of an authentic sample; (22 min) recovered II; (40 min) III: nmr (CCl_4) δ 2.2 (m, 4H), 2.8 (m, 2H), 5.8 (s, 2H) and ir (CCl_4) 2240 cm^{-1} are identical to those of an authentic sample.

Kinetics of the Thermal Rearrangement of Racemic I and II. The rates of reaction of I and II were determined at the boiling points of four solvents: naphthalene (217.8°), tetrahydronaphthalene (207.1°), a constant boiling mixture of cis- and trans-decalin (191.7°), and p-cymene (178.4°).

Each of I and II was mixed with about an equal volume of benzonitrile (purified on Column D: 150°, He 60 ml/min). About 12 $\mu\ell$ of the nitrile-benzonitrile mixture was introduced into each of six ampoules size A. Five of the ampoules were suspended in the vapor bath, and an ampoule removed at the end of each specified time

interval. Prior to analysis, the stems of the ampoules were cooled in liquid nitrogen and were broken off; the contents were immediately diluted with 100 µℓ of m-xylene.

The products were analyzed by glpc (Column E: 130°, He 35 psi) on the Perkin-Elmer 990. Relative areas were determined with the aid of an Autolab 6300 digital integrator. Response factors[65] for I, II, III and IV were determined relative to benzonitrile (XVII) (the standard). A standard solution by weight of the nitriles was analyzed by glpc under the conditions used for analysis of the kinetic points. The area of each component in counts was divided by its weight in the standard solution: A/W. The A/W ratios for I-IV were divided by A/W for benzonitrile to give F, the response factors. For the 217.8° run the response factors were: benzonitrile (47.5 min) ≡ 1.000; I (25.5 min), 0.957; II (34.0 min), 0.928; III (41.5 min), 0.949; and IV (10.2 min), 0.722. Because the detector in the Perkin-Elmer 990 was replaced in between the 217.8° run and the runs at the lower temperatures, the response factors were redetermined: I, 0.965; II, 0.958; III, 0.939; IV, 0.793. In the analysis of the reaction products, the formation of butadiene (8.5 min) was not followed because it evaporated too rapidly from the solution to give reproducible results.

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[65] H. M. McNair and E. A. Bonelli, "Basic Gas Chromatograph," Varian Aerograph, 1968, p. 141-142.

The relative weights of the products were determined from the relative areas by the formula:

$$W_x = (W_s/A_s) \cdot (A_x/F_x)$$

where W = weight, A = area in counts, F = response factor and x and s are the component and standard, respectively. In these runs, the relative weight of the standard was taken arbitrarily as 100 ($W_s = 100$). The relative weight of each component (W_x) was divided by its molecular weight and the mol % of each component was computed. Recovery at each point was determined by comparison to the unheated ampoule:

Unheated II:
$$W_{II} = (W_s/A_s) \cdot (A_{II}/F_{II})$$

$$= (100/1013899) \cdot (1264931/0.928)$$

$$W_{II} = 134.43$$

$$\text{Mol II} = \frac{134.43}{107} = 1.256 \times 10^{-x}$$

II after 45 min @ 217.8°:
Mol II = 1.142 = 92.99%
Mol I = 0.046 = 3.77%
Mol III = 0.0204 = 1.66%
Mol IV = 0.019 = 1.57%
_____
1.228

$$\text{Recovery} = \frac{1.228}{1.256} \times 100 = 97.7\%$$

The data are summarized in Tables 12 and 13.

The uncorrected overall rates of disappearance of I and II were determined by a plot of ℓn (Co/C) vs. time. The slopes, which give the rate constants, and the intercepts were determined by the method of least squares. The results are summarzied in Table 14.

Rate constants for the conversion of I and II to individual products were determined by solution of the simultaneous differential equations (given on page 53) derived from the kinetic scheme of Figure 1. Solution of the equations was carried out by using trial values of k_1 through k_6, comparing the calculated concentrations with the experimental ones, and systematic variation of the rate constants until the best agreement of calculated and experimental concentrations was obtained. This procedure was accomplished with the aid of a computer program for numerical integration written by Professor M. Saunders for the PDP-10. Mr. David Dixon, who modified the program for use on the PDP 11/45, added an iterative variation of rate constants and the error computation described below. The modified program is contained in Appendix I.

Input into the program includes the maximum time (t), an inter-val of integration (Δt), the experimental concentrations and times, and a set of trial rate constants. The solution of the differential equations, which are contained in a subroutine, is performed by the Runge-Kutta method of numerical integration at each Δt up to the maximum time. The program prints the calculated concentrations at the experimental times in addition to the difference between the

Table 12   Thermal Rearrangement of I.   Per Cent Composition vs. Time and Temperature.

Temperature	Time (sec)	% I[a]	% II	% III	% IV	Recovery[b] %
217.8°	2700.	96.37 ± 0.23	1.49 ± 0.00	1.28 ± 0.01	0.86 ± 0.06	99.0
217.8°	5400.	92.62 ± 0.48	2.83 ± 0.00	2.57 ± 0.02	1.96 ± 0.13	99.3
217.8°	8100.	88.67 ± 0.19	4.01 ± 0.02	3.87 ± 0.02	3.43 ± 0.23	100.0
217.8°	10800.	85.39 ± 0.24	5.04 ± 0.01	5.15 ± 0.02	4.41 ± 0.41	99.4
217.8°	14400.	81.19 ± 0.24	6.17 ± 0.01	6.74 ± 0.02	5.90 ± 0.34	99.0
207.1°	5400.	96.96 ± 0.04	1.20 ± 0.01	0.97 ± 0.00	0.85 ± 0.05	100.0
207.1°	10800.	93.98 ± 0.04	2.31 ± 0.02	1.95 ± 0.02	1.74 ± 0.04	99.0
207.1°	16200.	91.37 ± 0.09	3.09 ± 0.01	2.95 ± 0.01	2.56 ± 0.10	99.9
207.1°	23400.	87.80 ± 0.11	4.31 ± 0.02	4.27 ± 0.01	3.60 ± 0.12	100.0
207.1°	27000.	86.12 ± 0.10	4.82 ± 0.02	4.90 ± 0.03	4.13 ± 0.10	99.9
191.7°	21600.	97.59 ± 0.03	0.91 ± 0.01	0.82 ± 0.01	0.66 ± 0.02	99.1
191.7°	43200.	95.45 ± 0.06	1.71 ± 0.01	1.57 ± 0.01	1.25 ± 0.07	99.3
191.7°	64800.	93.35 ± 0.06	2.45 ± 0.01	2.32 ± 0.01	1.86 ± 0.06	100.0
191.7°	86400.	90.63 ± 0.19	3.37 ± 0.02	3.33 ± 0.02	2.61 ± 0.14	100.0
191.7°	108000.	88.49 ± 0.11	4.09 ± 0.01	4.17 ± 0.00	3.20 ± 0.13	99.7
178.4°	129600.	96.36 ± 0.04	1.43 ± 0.00	1.30 ± 0.00	0.95 ± 0.04	99.5
178.4°	259200.	92.82 ± 0.08	2.69 ± 0.02	2.57 ± 0.00	1.91 ± 0.10	99.7
178.4°	388800.	89.56 ± 0.13	3.92 ± 0.02	3.94 ± 0.02	2.57 ± 0.17	99.4
178.4°	518400.	86.44 ± 0.32	4.79 ± 0.06	5.09 ± 0.05	3.66 ± 0.37	100.0
178.4°	648000.	83.08 ± 0.15	5.71 ± 0.02	6.40 ± 0.02	4.78 ± 0.19	99.5

a)   Per cent of each isomer is the average of three determinations ± the standard deviation.

b)   Total recovery based on benzonitrile as the internal standard.

Table 13. Thermal Rearrangement of II. Per Cent Composition vs. Time and Temperature.

Temperature	Time (sec)	% I[a]	% II	% III	% IV	Recovery[b] %
217.8°	2700.	3.77 ± 0.01	92.99 ± 0.19	1.66 ± 0.01	1.57 ± 0.08	99.7
217.8°	5400.	7.25 ± 0.01	85.57 ± 0.08	3.34 ± 0.02	3.85 ± 0.38	99.7
217.8°	8100.	10.30 ± 0.02	78.82 ± 0.16	4.92 ± 0.04	5.95 ± 0.58	97.0
217.8°	10800.	13.06 ± 0.20	72.06 ± 0.18	6.40 ± 0.03	8.46 ± 0.79	98.0
217.8°	14400.	15.93 ± 0.03	64.70 ± 0.13	8.32 ± 0.00	11.05 ± 0.64	98.1
207.1°	5400.	3.05 ± 0.01	93.89 ± 0.03	1.31 ± 0.01	1.73 ± 0.03	99.7
207.1°	10800.	6.17 ± 0.07	88.08 ± 0.33	2.74 ± 0.02	2.98 ± 0.43	99.5
207.1°	16200.	8.70 ± 0.04	82.02 ± 0.33	4.01 ± 0.01	5.25 ± 0.36	100.0
207.1°	21600.	11.19 ± 0.02	76.74 ± 0.41	5.32 ± 0.01	6.73 ± 0.44	100.0
207.1°	27000.	13.18 ± 0.05	72.10 ± 0.16	6.46 ± 0.00	8.24 ± 0.15	99.8
191.7°	21600.	2.63 ± 0.00	95.02 ± 0.04	1.09 ± 0.01	1.25 ± 0.04	99.0
191.7°	43200.	5.12 ± 0.01	90.22 ± 0.08	2.09 ± 0.01	2.54 ± 0.09	100.0
191.7°	64800.	6.94 ± 0.03	86.45 ± 0.16	3.08 ± 0.03	3.51 ± 0.20	100.0
191.7°	86400.	9.64 ± 0.02	80.63 ± 0.06	4.38 ± 0.02	5.33 ± 0.08	100.0
191.7°	108000.	11.57 ± 0.03	76.52 ± 0.11	5.38 ± 0.05	6.49 ± 0.17	100.0
178.4°	86400.	2.81 ± 0.02	94.70 ± 0.15	1.17 ± 0.02	1.32 ± 0.11	100.0
178.4°	172800.	5.43 ± 0.00	89.15 ± 0.05	2.33 ± 0.02	2.72 ± 0.06	100.0
178.4°	259200.	7.85 ± 0.01	84.89 ± 0.22	3.46 ± 0.01	3.76 ± 0.23	100.0
178.4°	352800.	10.31 ± 0.02	79.94 ± 0.23	4.69 ± 0.01	5.03 ± 0.20	100.0
178.4°	439200.	12.25 ± 0.03	75.74 ± 0.39	5.72 ± 0.02	6.21 ± 0.45	100.0

a) Per cent of each isomer is the average of three determinations ± the standard deviation.

b) Total recovery based on benzonitrile as the internal standard.

Table 14. Least Squares Fit of $\ln c_o/c$ vs. Time for the Thermal
Rearrangement of I and II.

T(°C)   I $\xrightarrow{\Delta}$

217.8° $\ln c_o/c = (0.1470 \times 10^{-4} \pm 0.234 \times 10^{-6})t + (-0.1722 \times 10^{-2} \pm 0.2160 \times 10^{-2})$

207.1° $\ln c_o/c = (0.5189 \times 10^{-5} \pm 0.1129 \times 10^{-6})t + (+0.8616 \times 10^{-2} \pm 0.2074 \times 10^{-2})$

191.7° $\ln c_o/c = (0.1146 \times 10^{-5} \pm 0.3530 \times 10^{-7})t + (-0.2188 \times 10^{-2} \pm 0.2529 \times 10^{-2})$

178.4° $\ln c_o/c = (0.2831 \times 10^{-6} \pm 0.3122 \times 10^{-7})t + (+0.5832 \times 10^{-3} \pm 0.1341 \times 10^{-2})$

                               II $\xrightarrow{\Delta}$

217.8° $\ln c_o/c = (0.3114 \times 10^{-4} \pm 0.2662 \times 10^{-6})t + (-0.1195 \times 10^{-1} \pm 0.2457 \times 10^{-2})$

207.1° $\ln c_o/c = (0.1233 \times 10^{-4} \pm 0.1512 \times 10^{-6})t + (-0.3780 \times 10^{-2} \pm 0.2708 \times 10^{-2})$

191.7° $\ln c_o/c = (0.2525 \times 10^{-5} \pm 0.1053 \times 10^{-6})t + (-0.7130 \times 10^{-2} \pm 0.7547 \times 10^{-2})$

178.4° $\ln c_o/c = (0.6322 \times 10^{-6} \pm 0.3000 \times 10^{-8})t + (+0.4766 \times 10^{-3} \pm 0.8715 \times 10^{-3})$

Table 15. Corrected Specific Rate Constants for the Disappearance
of I and II.

T(°C)	k_I
217.8	$1.51 \times 10^{-5} \text{sec}^{-1}$
207.1	$5.73 \times 10^{-6} \text{sec}^{-1}$
191.7	$1.20 \times 10^{-6} \text{sec}^{-1}$
178.4	$2.95 \times 10^{-7} \text{sec}^{-1}$

T(°C)	k_{II}
217.8	$3.05 \times 10^{-5} \text{sec}^{-1}$
207.1	$1.24 \times 10^{-5} \text{sec}^{-1}$
191.7	$2.46 \times 10^{-6} \text{sec}^{-1}$
178.4	$6.39 \times 10^{-7} \text{sec}^{-1}$

experimental and calculated concentrations. For each of I through

IV, the agreement of the experimental and observed concentrations

over time is expressed as

$$I = \sqrt{\frac{\sum_n ([I]_n calc - [I]_n exptl)^2}{n - 1}}$$

where $[I]$ = the concentration of I at kinetic point n.

n = the number of experimental points.

The program then varies a specified rate constant by a given fraction

(e.g., converts k_1 to $k_1 + 0.1 \, k_1$) and re-performs the calculation.

This procedure continues for the number of iterations requested. A

sample print-out is shown in Figure .

In general, a set of trial rate constants is taken and each one

is varied successively while the others are kept constant. The

values of $\bar{\sigma}_I$ through $\bar{\sigma}_{IV}$ are plotted vs. the variation in a given k

as shown in Figure 2. For any given rate constant, two of the $\bar{\sigma}$'s

are sensitive and two, insensitive to a change in a particular k.

For k_1 (the rate of conversion of I → II) $\bar{\sigma}_I$ and $\bar{\sigma}_{II}$ are sensitive,

while $\bar{\sigma}_{III}$ and $\bar{\sigma}_{IV}$ are insensitive to changes in k_1; that is, $\bar{\sigma}$ for

the starting material and product are most sensitive to changes in k.

From the value of k at a minimum in $\bar{\sigma}$, a new value of k can then be

obtained. Since, for values of k_1 through k_6 far away from the best

fit, the minima in the plots of $\bar{\sigma}$ against k did not in general

coincide, a new value of k was taken at the minimum value of $\bar{\sigma}$. for

the product formed. From a given set of trial rate constants, new

k_1	k_2	k_3	k_4	k_5	k_6
.2033E-05	0.6315E-05	0.1907E-05	0.1528E-05	0.2716E-05	0.3621E-05

Experimental Concentrations

Time(sec)	[I]	[II]	[III]	[IV]
5400.0	0.96960	0.01200	0.00970	0.00850
10800.0	0.93990	0.02310	0.01950	0.01740
16200.0	0.91370	0.03090	0.02950	0.02560
23400.0	0.87800	0.04310	0.04280	0.03600
27000.0	0.86120	0.04820	0.04900	0.04130

Calculated Concentrations

Time(sec)	[I]	[II]	[III]	[IV]
5400.0	0.97161	0.01027	0.01004	0.00808
10800.0	0.94385	0.01975	0.02012	0.01628
16200.0	0.91720	0.02832	0.03006	0.02443
23400.0	0.88328	0.03844	0.04307	0.03520
27000.0	0.86698	0.04299	0.04948	0.04055

(Experimental-Calculated) Concentrations

Time(sec)	[I]	[II]	[III]	[IV]
5400.0	-0.002008	0.001729	-0.000338	0.000417
10800.0	-0.003947	0.003347	-0.000621	0.001120
16200.0	-0.003497	0.002580	-0.000556	0.001172
23400.0	-0.005284	0.004656	-0.000269	0.000796
27000.0	-0.005785	0.005207	-0.000475	0.000751

$\bar{\sigma}_I$	$\bar{\sigma}_{II}$	$\bar{\sigma}_{III}$	$\bar{\sigma}_{IV}$
0.001500	0.001437	0.000147	0.000307

Figure 18. Sample Computer Output of the Program Lists in Appendix I. The Rate Constants k_1 through k_6 are Given Along with the Calculated and Experimental Concentrations and the Values of $\bar{\sigma}$.

values of k_1 through k_6 were thus obtained. This variation procedure was repeated until each new k changed by less than 1% from one round to the next. At this point the minimum in $\bar{\sigma}$ for the starting material and the product appeared at the same value of k.

Tables 4 - 7 give the rate constants at each temperature with an error range. The range of rate constants was taken as the values of k corresponding to $2\bar{\sigma}$. (See figure 2) The tables also give the % error that this range represents and the minimum value of $\bar{\sigma}$ for each component. Where the function of $\bar{\sigma}$ vs. k is essentially a straight line, no range of k's is given. Table 15 gives the corrected overall rates of decomposition of I and II.

The activation parameters were determined by plotting log k vs. 1/T and fitting the data by the method of least squares. The results are summarized in Table 8 where the errors are the standard deviations obtained from a least squares fit.

Thermal Rearrangement of (+)-I and (+)-II. Thermal rearrangements were carried out by following the general procedure given previously. (+)-II had $[\alpha]_{578}^{23}$ +50.90°, $[\alpha]_{365}^{23}$ +175.2° (+0.439°, 1.511°; c 0.8643, cyclohexane), (0.378°, 1.307°; c 0.7480, cyclohexane), (0.542°, 1.861°; c 1.0623, cyclohexane), (0.513°, 1.764°; c 1.0086, cyclohexane), (0.430°, 1.480°; c 0.8400, cyclohexane) and was 85.2% optically pure. For each point a number of ampoules size B were filled with 50 uℓ (~700 mm final pressure) of (+)-II and heated at 217.8° ±0.3°. The contents of the ampoules were separated by glpc

(Column D: 120°, He 60 ml/min). Each component was rechromatographed and its rotation measured. The rotation solutions were checked (Column E: 130°, He 35 psi) for contamination by the other isomers. The rotation of recovered (+)-II was measured twice. The rotation of I was measured, the nitrile recovered from the cyclohexane solution, and the rotation remeasured. The III formed was chromatographed three times and its rotation measured only once (never enough nitrile to recover from the solution).

Five points at 45, 90, 135, 180 and 240 min were taken. For the 90 min point, the starting material was (+)-II recovered from the 45 min point (79.5% optically pure). Corrections were made on the rotations of I and III from the 90 min point by multiplying the observed specific rotation by (+175.2/163.6), the ratio of the rotation of starting (+)-II used at the other points to rotation of the starting (+)-II used at the 90 min point. The data are summarized in Tables 16 - 18.

The sample of (+)-I used as starting material for 90, 180 and 240 min had $[\alpha]_{578}^{25}$ +167.7°, $[\alpha]_{365}^{25}$ +529.9° (1.139°, 3.601°; c 0.6805, cyclohexane), (0.805°, 2.542°; c 0.4780, cyclohexane), (1.140°, 3.600°; c 0.6809, cyclohexane) and was of 91.6% optical purities. The sample of (+)-I used for the 135 minute point had $[\alpha]_{578}^{25}$ +163.4°, $[\alpha]_{365}^{25}$ +516.8° (0.982°, 3.109°; c 0.6016, cyclohexane), (0.820°, 2.590°; c 0.5012, cyclohexane) and was 89.3% optically pure. The procedures used for the thermal rearrangement and separation of products were the same as for (+)-II except that the rotation of III

Table 16. Specific Rotation of (+)-II Recovered from the Thermal Rearrangement of (+)-II at 217.8°C.

Time (min)	c (mg/ml)	α_{578} [a,c]	$[\alpha]_{578}$ [b,c]	α_{546}	$[\alpha]_{546}$	α_{436}	$[\alpha]_{436}$	α_{365}	$[\alpha]_{365}$
45	7.690	0.367°	47.7°	0.421°	54.7°	0.751°	97.7°	1.259°	163.7°
	5.835	0.278°	47.6°	0.319°	54.7°	0.569°	97.5°	0.954°	163.5°
			47.6°e		54.7°		97.6°		163.6°
90[d]	10.505	0.437°	41.6°	0.500°	47.6°	0.896°	85.3°	1.499°	142.7°
	9.234	0.384°	41.6°	0.441°	47.3°	0.7910°	85.7°	1.323°	143.3°
			41.6°		47.4°		85.5°		143.0°
135	11.170	0.459°	41.1°	0.529°	47.1°	0.944°	84.5°	1.578°	141.2°
	9.504	0.392°	41.5°	0.449°	48.0°	0.810°	85.9°	1.362°	143.5°
			41.4°		47.5°		85.2°		142.4°
180	9.626	0.373°	38.7°	0.428°	44.5°	0.764°	79.4°	1.276°	132.5°
	10.584	0.415°	39.2°	0.475°	44.9°	0.850°	80.3°	1.417°	133.9°
			39.0°		44.7°		79.8°		133.2°
240	9.768	0.346°	35.4°	0.397°	40.6°	0.709°	72.5°	1.186°	121.4°
	9.389	0.331°	35.2°	0.380°	40.5°	0.679°	72.3°	1.139°	121.3°
			35.3°		40.5°		72.4°		121.4°

a) The observed rotation

b) The specific rotation

c) All rotations were determined at 25°C $\pm$3.0° in spectrograde cyclohexane.

d) Starting material was (+)-II recovered from the 45 minute point.

e) Average value of the specific rotation.

Table 17. Specific Rotation of (-)-I Recovered from the Thermal Rearrangement of (+)-II at 217.8°C.

Time (min)	c (mg/ml)	α_{578} [a,c]	$[\alpha]_{578}$ [b,c]	α_{546}	$[\alpha]_{546}$	α_{436}	$[\alpha]_{436}$	α_{365}	$[\alpha]_{365}$
45	4.172	-0.123°	-29.5°	-0.140°	-33.5°	-0.243°	-58.2°	-0.389°	-93.2°
	6.500	-0.194°	-29.8°	-0.221°	-34.0°	-0.381°	-58.6°	-0.613°	-94.3°
			-29.6°[d]		-33.8°		-58.4°		-93.7°
90	4.436	-0.119°	-28.6°[e]	-0.134°	-32.2°	-0.231°	-55.8°	-0.370°	-89.3°
	3.131	-0.085°	-29.0°	-0.094°	-32.0°	-0.161°	-55.1°	-0.259°	-88.6°
			-28.8°		-32.1°		-55.5°		-88.9°
135	5.310	-0.144°	-27.1°	-0.164°	-30.9°	-0.283°	-53.3°	-0.455°	-85.7°
	2.106	-0.059°	-28.0°	-0.066°	-31.3°	-0.115°	-54.6°	-0.184°	-85.4°
			-27.5°		-31.1°		-53.9°		-86.5°
180	5.098	-0.135°	-26.5°	-0.155°	-30.4°	-0.268°	-52.6°	-0.428°	-83.9°
	3.040	-0.081°	-26.6°	-0.092°	-30.3°	-0.162°	-53.3°	-0.256°	-84.2°
			-26.6°		-30.3°		-52.9°		-84.1°
240	4.059	-0.104°	-25.6°	-0.118°	-29.1°	-0.203°	-50.0°	-0.324°	-79.8°
	2.785	-0.069°	-24.8°	-0.080°	-28.7°	-0.137°	-49.2°	-0.218°	-79.3°
			-25.2°				-49.6°		-79.0°

a) The observed rotation

b) The specific rotation

c) All rotations were determined at 25°C $\pm$ 3.0° in cyclohexane.

d) Average value of the specific rotation.

e) Starting Material was (+)-II recovered from the 45 minute point; rotations are corrected for the optical purity of the starting material.

Table 18. Specific Rotation of (-)-III Recovered from the Thermal Rearrangement of (+)-II at 217.8°C.

Time (min)	c (mg/ml)	α_{578} [a,b]	$[\alpha]_{578}$ [b,c]	α_{546}	$[\alpha]_{546}$	α_{436}	$[\alpha]_{436}$	α_{365}	$[\alpha]_{365}$
45	2.719	-0.094°	-34.6°	-0.102°	-39.4°	-0.185°	-68.0°	-0.300°	-110.3°
90	2.126	-0.054°[d]	-27.1°	-0.066°	-33.1°	-0.129°	-65.1°	-0.201°	-101.22
135	1.616	-0.050°	-30.9°	-0.056°	-34.6°	-0.099°	-61.3°	-0.159°	-98.4°
180	2.220	-0.069°	-31.0°	-0.078°	-35.0°	-0.136°	-61.1°	-0.219°	-98.4°
360	2.374	-0.065°	-27.4°	-0.075°	-31.6°	-0.131°	-55.2°	-0.210°	-88.5°

a) the observed rotation

b) the specific rotation

c) All rotations were determined at 25°C $\pm$ 3.0° in cyclohexane.

d) The Starting material was (+)-II recovered from the 45 minute point; rotations are corrected for the optical purity of the starting material.

was measured twice. The results are summarized in Tables 19 - 21.

The rate of racemization of (+)-I ($[\alpha]_{578}^{25}$ -154.8°, $[\alpha]_{365}^{25}$ -489.6°

(-0.561°, -1.775°; c 0.3636, cyclohexane), (-0.504°, -1.599°;

c 0.3255, cyclohexane), (-1.057°, -3.331°; c 0.6804, cyclohexane);

84.6% optically pure) was measured independently by heating 10

in each of six tubes size A, and with drawing a tube at the end of

45, 91.5, 135, 180, 240, and 360 minutes. The results are summarized

in Table 22.

Approximate rates for the conversions of optically active

compounds were obtained by graphical methods. The rate of

racemization of (+)-II was obtained by a least squares fit of the

plot of $\ln(\alpha_o/\alpha)$ vs. time. The slope of

$$y = (2.556 \times 10^{-5} \pm 1.6818 \times 10^{-7} sec^{-1})t + (-1.54 \times 10^{-3} \pm 1.55 \times 10^{-3})$$

divided by 2 gives the rate of enantiomerization of II uncorrected

for back reaction of product I:

$$k_{(+)-II \to (-)-II} = 1.278 \times 10^{-5} sec^{-1}.$$

The rate of racemization of I was obtained by a least squares

fit of a plot of $\ln[\alpha]_{365}$ vs. time. The slope of

$$y = (-5.044 \times 10^{-6} \pm 1.377 \times 10^{-7})t + (6.2059 \pm 1.6807 \times 10^{-3})$$

gives the uncorrected rate of racemization of I with $k_{(-)-I \to (+)-I}$ =

$2.522 \times 10^{-6} sec^{-1}$. The intercept corresponds to $[\alpha_o]_{365}$ 495.7 $\pm 1.0°$

(the specific rotation of the starting material at zero time).

Table 19. Specific Rotation of (+)-I Recovered from the Thermal Rearrangement of (+)-I at 217.8°.

Time (min)	c (mg/ml)	α_{578} [a,c]	$[\alpha]_{578}$ [b,c]	α_{546}	$[\alpha]_{546}$	α_{436}	$[\alpha]_{436}$	α_{365}	$[\alpha]_{365}$
90	7.116	+1.170°	+164.4°	+1.3 2	+187.2°	+2.299	+323.0°	+3.690°	+518.2°
	6.845	+1.124	+164.2°	+1.282	+187.3°	+2.211	+323.0°	+3.545	+517.9°
			+164.3°d		+187.2°		+323.0°		+518.0°
135	7.447	+1.197	+164.8°	+1.366	+188.1°	+2.356	+324.4°	+3.777	+520.0°
	9.555	+1.563	+167.7°	+1.785	+191.5°	+3.066	+329.0°	+4.867	+522.3°
			+166.3°e		+189.8°		+326.7°		+521.2°
180	6.504	1.032	+159.90°	1.177	+182.3°	2.041	+315.0°	3.280	+504.9°
	8.191	1.246	+160.5°	1.490	+183.1°	2.578	+315.7°	4.144	+506.4°
			+160.2°		+182.7°		+315.4°		+505.7°
240	9.965	1.577	+158.2°	1.796	+180.2°	3.101	+311.2°	4.970	+498.7°
	7.454	1.185	+159.0°	1.352	+181.4°	2.336	+313.4°	3.746	+502.5°
			+158.6°		+180.8°		+312.3°		+500.6°

a) The observed rotation

b) The specific rotation

c) All rotations were determined at 25° ± 3° in cyclohexane.

d) Average value of the specific rotation.

e) Corrected to account for the different optical purity of the starting material.

Table 20. Specific Rotation of (-)-II Recovered from the Thermal Rearrangement of (+)-I at 217.8°C.

Time (min)	c (mg/ml)	α_{578} [a,c]	$[\alpha]_{578}$ [b,c]	α_{546}	$[\alpha]_{546}$	α_{436}	$[\alpha]_{436}$	α_{365}	$[\alpha]_{365}$
90	4.124	-0.041°	-9.94°	-0.048°	-11.63°	-0.089°	-21.58°	-0.146°	-35.39°
	7.875	-0.080°	-10.18°	-0.091°	-11.57°	-0.163°	-20.73°	-0.274°	-34.86°
			-10.06°d		-11.60°		-21.15°		-35.12°
135	7.556	-0.080°	-10.84°	-0.089°	-11.93°	-0.156°	-21.16°	-0.255°	-34.59°
	4.866	-0.046°	-9.68°	-0.054°	-11.37°	-0.096°	-20.22°	-0.160°	-33.71°
			-10.26°e		-11.65°		-20.67°		-34.15°
180	4.213	-0.040°	-9.49°	-0.046°	-10.92°	-0.082°	-19.46°	-0.136°	-32.28°
240	10.533	-0.093°	-8.82°	-0.107°	-10.15°	-0.192°	-18.22°	-0.320°	-30.38°
	6.529	-0.054°	-8.24°	-0.067°	-10.26°	-0.117°	-17.92°	-0.195°	-29.86°
			-8.53°		-10.20°		-18.02°		-30.12°

a) The observed rotation

b) The specific rotation

c) All rotations were determined at 25° $\pm$ 3° in cyclohexane.

d) Average value of the specific rotation.

e) Corrected to account for the different optical purity of the starting material.

Table 21. Specific Rotation of (+)-III Recovered from the Thermal Rearrangement of (+)-I at 217.8°C.

Time (min)	c (mg/ml)	α_{578} [a,c]	$[\alpha]_{578}$ [b,c]	α_{546}	$[\alpha]_{546}$	α_{436}	$[\alpha]_{436}$	α_{365}	$[\alpha]_{365}$
90	4.442	0.076°	+17.1°	0.085°	+19.1°	0.150°	+33.8°	0.247°	+55.6°
135	6.320	0.100°	+16.22°	0.119°	+19.29°	0.206°	+33.41°	0.339°	+55.0°
	3.948	0.065°	+16.87°	0.077°	+19.99°	0.130°	+33.75°	0.215°	+55.8°
			+16.54° [d,e]		+19.65°		+33.58°		+55.4°
180	11.146	0.188°	+16.86°	0.217°	+19.47°	0.378°	+33.91°	0.613°	+55.00°
	7.950	0.134°	+16.85°	0.153°	+19.24°	0.267°	+33.58°	0.434°	+54.59°
			+16.85°		+19.35°		+33.74°		+54.80°
240	8.523	+0.140°	+16.43°	+0.164°	+19.24°	+0.279°	+32.73°	+0.453°	+53.15°
	3.611	+0.060°	+16.61°	+0.068°	+18.83°	+0.121°	+33.50°	+0.197°	+54.55°
			+16.52°		+19.04°		+33.11°		+53.85°

a) The observed rotation

b) The specific rotation

c) All rotations were determined at 25° ±3° in cyclohexane.

d) Average value of the specific rotation.

e) Corrected to account for the different optical purity of the starting material.

Table 22. Racemization of (+)-I at 217.8°. The Specific Rotation of Recovered (+)-I.

Time (min)	c (mg/ml)	α_{578} [a,c]	$[\alpha]_{578}$ [b,c]	α_{546}	$[\alpha]_{546}$	α_{436}	$[\alpha]_{436}$	α_{365}	$[\alpha]_{365}$
45	6.448	-1.004°	-155.7°	-1.145°	-177.6°	-1.973°	-306.0°	-3.159°	-489.9°
	5.800	-0.873°	-154.0°	-1.019°	-175.7°	-1.765°	-304.3°	-2.821°	-486.4°
			-154.8°d		-176.6°		-305.1°		-488.2°
91.5	5.825	-0.893°	-153.3°	-1.020°	-175.1°	-1.761°	-302.3°	-2.816°	-483.4°
	6.257	-0.957°	-152.9°	-1.093°	-174.7°	-1.887°	-301.6°	-3.019°	-482.5°
			-153.1°		-174.9°		-301.9°		-483.0°
135	4.198	-0.630°	-150.0°	-0.720°	-171.5°	-1.247°	-297.0°	-1.992°	-474.5°
	4.335	-0.655°	-151.1°	-0.747°	-172.3°	-1.296°	-298.2°	-2.070°	-477.5°
			-150.6°		-171.9°		-297.6°		-476.0°
180	4.486	-0.661	-147.3°	-0.756	-168.5°	-1.310	-292.0°	-2.096	-467.2°
	6.960	-1.039	-149.3°	-1.186	-170.4°	-2.044	-293.7°	-3.273	-470.3°
			-148.3°		-169.5°		-292.8°		-468.7°
240	4.801	-0.706	-147.0°	-0.804	-167.5°	-1.390	-289.5°	-2.222	-462.8°
	5.410	-0.790	-146.0°	-0.902	-166.7°	-1.561	-288.5°	-2.494	-460.9°
			-146.5°		-167.1°		-289.0°		-461.9°
360	4.465	-0.630	-141.1°	-0.717	-160.6°	-1.243	-278.4°	-1.987	-445.0
	3.611	-0.506	-140.1°	-0.576	-159.5°	-0.997	-276.1°	-1.600	-443.1
			-140.6°		-160.0°		-277.2°		-444.0

a) The observed rotation

b) The specific rotation

c) All rotations were determined at 25° ±3° in cyclohexane.

d) The average value of the specific rotation.

The approximate rates of conversion of (+)-II to (-)-I and (+)-II to (+)-I were obtained by plotting $[\alpha]_{365}$ of I formed from (+)-II vs. time. A least squares fit of the data gave

$$y = (0.11924 \times 10^{-2} \pm 0.85022 \times 10^{-4})t + (-96.34 \pm 0.7848).$$

The intercept is the rotation of I at zero time: $[\alpha]_{365}^{25}$ -96.34°, which corresponds to 19.58% retention of optical purity. R_A becomes

$$\frac{k_{(+)-II \to (-)-I}}{k_{(+)-II \to (+)-I}} = 1.48 \quad \text{and} \quad k_{(+)-II \to (+)-I} = 6.147 \times 10^{-6} \text{sec}^{-1} \quad \text{and}$$

$$k_{(+)-II \to (-)-I} = 9.142 \times 10^{-6} \text{sec}^{-1}.$$

A plot of $[\alpha]_{365}$ of III formed from (+)-II vs. time gives

$$y = (0.162935 \times 10^{-2} \pm 0.3069 \times 10^{-3})t + (-112.84 \pm 2.83).$$

Its rotation ($[\alpha]_{365}$ -112.8°) at zero time corresponds to an optical purity of 35.4% and an inversion/retention ratio of 0.5223, which gives $k_{(+)-II \to (-)-III} = 4.335 \times 10^{-6} \text{sec}^{-1}$ and

$$k_{(+)-II \to (+)-III} = 2.264 \times 10^{-6} \text{sec}^{-1}.$$

The rates of conversion of (+)-I to (-)-II and (+)-I to (+)-II were determined in a similar fashion to give

$$y = (0.570319 \times 10^{-3} \pm 0.44774 \times 10^{-4})t - 38.4353 \pm 0.458.$$

20.4% optical purity at zero time

$$R_A = 1.51$$

$$k_{(+)-I \to (-)-II} = 3.605 \times 10^{-6} \text{sec}^{-1}$$

$$k_{(+)-I \to (+)-II} = 2.384 \times 10^{-6} \text{sec}^{-1}$$

A plot of $[\alpha]_{365}$ of III formed from (+)-I gives:

$$y = (-0.200 \times 10^{-3} \pm 0.3146 \times 10^{-4}) + (56.85 \pm 0.3219)$$

16.56% optical purity at zero time

$$\frac{\text{inversion}}{\text{retention}} = 1.39$$

$$k_{(+)-I \to (-)-III} = 2.065 \times 10^{-6} \text{sec}^{-1}$$

$$k_{(+)-I \to (+)-III} = 2.885 \times 10^{-6} \text{sec}^{-1}$$

Refined rate constants were obtained in the same manner as for racemic material, with the rate constants obtained by the graphical method as trial rate constants. The kinetic scheme of Figure 14 provided the differential equations (shown on p. 80) to be solved. The same computer program was used as for racemic material, except for the substitution of a subroutine (given in Appendix I) containing the differential equations to be solved for this system. The experimental data are summarized in Table 23. The refined rate constants with their errors appear in Table 9. Table 24 contains a comparison of the specific rate constants as determined by graphical methods with those generated from the computer solution of the kinetic scheme of Figure 14.

Thermal Rearrangement of (-)-III. Twelve $\mu\ell$ of (-)-III ($[\alpha]_{578}^{25}$ -90.9°, $[\alpha]_{365}^{25}$ -293.3° (0.827°, 2.672°; c 0.9061, cyclohexane), (0.735°, 2.367°; c 0.8117, cyclohexane)) was heated for 12 hr at 217.8° ±0.3°. The recovered III (Column D: 120°, He 60 ml/min) showed $[\alpha]_{578}^{25}$ -88.8°, $[\alpha]_{365}^{25}$ -286.8° (0.371°, 1.199°; c 0.4180, cyclohexane). No other products were formed.

Table 23. Thermal Rearrangement of (+)-I and (-)-II at 217.8°C. Per Cent Composition vs. Time.

Time(sec)	(+)-I	(-)-I	(+)-II	(-)-II	(+)-III	(-)-III	IV
0	100.0	0.0	0.0	0.0	0.0	0.0	0.0
5400.	91.99	0.62	1.15	1.68	1.49	1.07	1.96
8100.	81.44	1.23	1.64	2.37	2.24	1.62	3.43
10800.	83.56	1.82	2.08	2.95	2.98	2.16	4.41
14400.	78.89	2.29	2.59	3.58	3.89	2.84	5.90
0	0.0	0.0	100.0	0.0	0.0	0.0	0.0
2700.	1.53	2.24	89.91	3.08	0.54	1.12	1.57
5400.	2.97	4.27	80.18	5.38	1.14	2.20	3.85
8100.	4.24	6.05	71.44	7.37	1.70	3.21	5.95
10800.	5.41	7.64	63.42	8.63	2.21	4.19	8.46
14400.	6.68	9.24	54.76	9.93	3.00	5.32	11.05

Table 24. Comparison of Specific Rate Constants for Figure   ,
as Obtained by Computer and Graphical Methods.

Specific Rate Constants[a]	Graphical Method	Computer Method
k_1	2.384	2.398
k_2	3.605	3.562
k_3	6.147	6.182
k_4	9.142	9.171
k_5	2.522	1.683
k_6	12.78	12.46
k_7	2.264	2.117
k_8	4.335	4.468
k_9	2.065	2.069
k_{10}	2.885	2.901
k_{11}	8.644	8.644
k_{12}	4.165	4.165

a All rate constants are in units of $10^{-6} sec^{-1}$.

Thermal Rearrangement of I and II in Lead Potash Tubes.

Two-$\mu\ell$ samples of I and II were heated in tubes of Corning 0120 glass (6.1 mm o.d. x 4 in.) for four hours at 217.8° $\pm 0.3°$. Analysis (Column E: 135°, He 35 psi) of the contents of the tubes by glpc gave for I: 81.2% I, 5.9% II, 6.6% III, and 6.2% IV; and for II: 64.6% II, 14.9%, I, 12.9% IV, 8.0% III.

Thermal Rearrangement of (+)-II at 1 mm pressure. The thermal rearrangement was carried out in a 12-ℓ Pyrex flask treated in an air thermostat heated at 217°. A 40 mg sample of (+)-II ($[\alpha]_{578}^{25}$ +41.6°, $[\alpha]_{365}^{25}$ +143.0° (0.437°, 1.499°; c 1.0505, cyclohexane), (0.384°, 1.323°; c 0.9234, cyclohexane), 69.5% optically pure) was vacuum transfered within 5 min into the flask. After 240 min, the product was withdrawn quantitatively into a receiver cooled in liquid nitrogen. The recovered starting material (69.0%), had $[\alpha]_{578}^{25}$ +28.4°, $[\alpha]_{365}^{25}$ +97.3° (0.283°, 0.972°; c 0.9992, cyclohexane), (0.184°, 0.630°; c 0.6465, cyclohexane); (-)-I (16.3%) had $[\alpha]_{578}^{25}$ -20.2°, $[\alpha]_{365}^{25}$ -63.1°, (-0.100°, -0.312°; c 0.4944, cyclohexane); (-)-III (8.3%) had $[\alpha]_{578}^{25}$ -22.6°, $[\alpha]_{365}^{25}$ -73.1° (-0.050°, -0.162°; c 2216, cyclohexane). Acrylonitrile and butadiene (6.31%) were also formed.

Thermal Rearrangement of (+)-I and (+)-II in Acetonitrile.

A 50-mg sample of (+)-II ($[\alpha]_{578}^{25}$ +41.6°, $[\alpha]_{365}^{25}$ +143.0° (0.437°, 1.499°; c 1.0505, cyclohexane), (0.384°, 1.323°; c 0.9234, cyclohexane); 69.4% optically pure) was dissolved in 0.5 ml CH_3CN and sealed in a 6.8 ml, thick-walled Pyrex tube after three freeze-pump-thaw cycles.

The tube was heated for 240 min at 217.8° $\pm$0.3°. Analysis of the solution in the usual manner gave recovered II [60.7%; $[\alpha]_{578}^{25}$ +33.8°, $[\alpha]_{365}^{25}$ +116.0° (0.329°, 1.132°; c 0.9752, cyclohexane), (0.329°, 1.124°; c 0.9711, cyclohexane)], I [10.1%; $[\alpha]_{578}^{25}$ -14.5°, $[\alpha]_{365}^{25}$ -44.2° (-0.027°, -0.082°; c 0.1855, cyclohexane), III [12.7%; $[\alpha]_{578}^{25}$ -12.7°, $[\alpha]_{365}^{25}$ -40.2° (-0.059°, -0.187°; c 0.4646, cyclohexane)] and IV [16.43%].

A 200-mg sample of (+)-I [in 2.0 ml CH_3CN; $[\alpha]_{578}^{25}$ +160.2°, $[\alpha]_{365}^{25}$ +505.6 (1.032°, 3.280°; c 0.6504, cyclohexane), (1.307°, 4.144°: c 0.8191, cyclohexane); 87.4% optically pure] was treated in the same manner as II. Analysis of the mixture gave I [78.18%; $[\alpha]_{578}^{25}$ +153.8°, $[\alpha]_{365}^{25}$ +485.0° (1.215°, 3.834°; c 0.7905, cyclohexane), (1.630°;5.138°; c 1.0593, cyclohexane)], II [5.24%; $[\alpha]_{578}^{25}$ -5.5°, $[\alpha]_{365}^{25}$ -19.8° (-0.043°, -0.146°; c 0.7186, cyclohexane), (-0.018°, -0.069°; c 0.3575, cyclohexane)], III [10.0%; $[\alpha]_{365}^{25}$ +7.53° (0.055°; c 0.6737, cyclohexane), (0.094°; c 1.2788, cyclohexane)] and IV [6.55%].

Thermal Rearrangement of (+)-I in Benzene. A 200-mg sample of (+)-I [in 2.0 ml benzene; $[\alpha]_{578}^{25}$ +164.3°, $[\alpha]_{365}^{25}$ +518.2° (1.170°, 3.690°; c 0.7116, cyclohexane), (1.124°, 3.545°; c 0.6845, cyclohexane); 89.6% optically pure] was degassed and sealed in a 6.8 ml heavy walled Pyrex tube. The tube was heated for 4 hr at 217.8° $\pm$0.3° and the contents were analyzed in the usual way to give I [77.5%; $[\alpha]_{578}^{25}$ +150.3°, $[\alpha]_{365}^{25}$ +475.9° (0.943°, 2.987°; c 0.6230, cyclohexane)

(0.408°, 1.292°; c 0.2735, cyclohexane)], II [5.4%; $[\alpha]_{578}^{25}$ -5.1°, $[\alpha]_{365}^{25}$ -18.1° (-0.017°, -0.062°; c 0.3276, cyclohexane), (-0.026°, -0.088°; c 0.5092, cyclohexane)], III [10.9%; $[\alpha]_{578}^{25}$ +7.66°; $[\alpha]_{365}^{25}$ +24.6° (0.075°, 0.245°; c 0.9985, cyclohexane), (0.050°, 0.158°; c 0.6400, cyclohexane)], and IV [5.12%].

The results are summarized in Table 10.

Thermal Rearrangement of (-)-III in Acetonitrile. A sample of (-)-III [15 mg in 150 uℓ acetonitrile; $[\alpha]_{578}^{25}$ -90.9°, $[\alpha]_{365}^{25}$ -293.2° (-0.827°, -2.672°; c 0.9061, cyclohexane)] was heated in a heavy-walled Pyrex tube for 4 hr at 217.8° ±0.3°. Analysis of the contents gave only recovered III: $[\alpha]_{578}^{25}$ -89.8°, $[\alpha]_{365}^{25}$ -289.4° (-0.688°, -2.217°; c 0.7662, cyclohexane).

3-Bromocyclohexene.[66] Into a 250-ml flask fitted with a stirrer, nitrogen inlet tube and a reflux condenser were placed 16.4g (0.2 mol) of freshly distilled cyclohexene, 17.4g (0.1 mol) of N-bromosuccinimide, 0.1g of benzoyl peroxide and 125 ml of CCl_4. The reaction mixture was stirred and heated under reflux in a nitrogen atmosphere for 2 hours. The succinimide was removed by suction filtration and the CCl_4 removed under reduced pressure (120 mm). The residue was distilled (67°/30 mm) to give 8.2g (50%) of 3-bromocyclohexene.

3-Cyanocyclohexene.[67] A solution of 0.49g (0.01 mol) of NaCN in

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[66]M. D. Kellert and J. Sedak, Org. Syn., Col. Vol. IV, p. 108.

[67]M. Prochazka, V. Krestanova, J. Konicek, M. Smisek, Collect. Czeck. Chem. Comm., 35, 727 (1970).

0.5 ml of water was added dropwise with stirring to 1.6g (0.1 mol) of 3-bromocyclohexene in 1 ml of acetone. The stirring was continued for 90 min. The organic layer was separated, dried over $MgSO_4$ and distilled to give 0.5g of a liquid which was separated by gas chromotography (Column D, 150°, He 60 ml/min): ir (CCl_4) 2240 cm^{-1} (-C ≡ N); nmr (CCl_4) δ2.0 (m,6H), 3.3 (m,1H), 5.8 (m,2H). The retention time of 3-cyanocyclohexene 40.5 min (Column E, 135°, 35 psi) allowed its detection in 4-cyanocyclohexene (retention time 41.5 min) to 0.1%.

APPENDIX I

GENERAL PROGRAM FOR SOLUTION OF RATE EQUATIONS

```
0001          DIMENSION Y(7),DERY(7),AUX(8,7),A(4),B(4),C(4),PRMT(4),
              RATE(12)
0002          DIMENSION TIME(201),CONC(7,201),TYME(10),VARY(12),CONA
              (7,10)
0003          DIMENSION CON(7,10),TERC(10),ERC(7,10),YINIT(7)
0004          DIMENSION DERC(7,10),SIGMAD(7),FINSIG(7)
0005          DATA A,B,C/.5,.2928932,1.707107,.1666667,2.,1.,
            1 1.,2.,.5,.2928932,1.707107,.5/
0006          READ (8,51) IDUR
0007          READ(8,56) NDIM,(YINIT(I),I=1,NDIM)
0008     56   FORMAT(I5,10F6.3)
0009          WRITE(6,56) NDIM,(YINIT(I),I=1,NDIM)
0010          READ (8,55) PRMT(4)
0011     55   FORMAT (F12.5)
0012          READ (8,51)NRATE
0013     51   FORMAT(I5)
0014          READ(8,510)(RATE(I),I=1,NRATE)
0015     510  FORMAT(8E10.4)
0016          WRITE(6,510)(RATE(I),I=1,NRATE)
0017          READ(8,66) XEND,STEP1
0018          WRITE(6,66) XEND,STEP1
0019     66   FORMAT(2F10.2)
0020          READ(8,5600)NTYME,(TYME(I),I=1,NTYME)
0021     5600 FORMAT(I5,7F10.2)
0022          WRITE(6,5600) NTYME,(TYME(I),I=1,NTYME)
0023          READ(8,51)NITER
0024          READ(8,5601)(VARY(I),I=1,NRATE)
0025          WRITE(6,51) NITER
0026          WRITE(6,5601) (VARY(I),I=1,NRATE)
0027          DO 5602 I=1,NTYME
0028          READ (8,5601) (CONA(J,I),J=1,NDIM)
0029          WRITE(6,5601)(CONA(J,I),J=1,NDIM)
0030     5601 FORMAT(8F10.5)
0031     5602 CONTINUE
0032          F=1./FLOAT(NDIM)
0033          DO 5000 IIJ=1,NITER
0034          STEP=STEP1
0035          NTIME=1
0036          X=0.0
0037          DO 5210 I=1,NDIM
0038          Y(I)=YINIT(I)
0039     5210 CONTINUE
0040          DO 1 I=1,NDIM
```

General Program, continued (2)

```
0041                DERY(I) = F
0042        1       AUX(8,I) =.06666667*F
0043        75      STEP = STEP * .5
0044                H = STEP
0045                XTEST = STEP * 2.
0046        60      CALL FCT( Y,DERY,RATE)
0047                IF(H*(XEND-X)) 38,37,2
0048        2       DO 3 I=1,NDIM
0049                AUX(1,I)=Y(I)
0050                AUX(2,I)=DERY(I)
0051                AUX(3,I)=0.
0052        3       AUX(6,I)=0.
0053                IREC=0
0054                H=H+H
0055                IHLF = -1
0056                ISTEP = 0
0057                IEND = 0
0058        4       IF((X+H*1.1-XEND)*H) 8,6,5
0059        5       H=XEND-X
0060                IF(ABS(H).LT.STEP*.01) H = STEP*.1
0061        6       IEND = 1
0062        8       ITEST = 0
0063        9       ISTEP = ISTEP+1
0064                J = 1
0065        10      AJ = A(J)
0066                BJ=B(J)
0067                CJ=C(J)
0068                DO 11 I=1,NDIM
0069                R1=H*DERY(I)
0070                R2=AJ*(R1-BJ*AUX(6,I))
0071                Y(I)=Y(I)+R2
0072                R2=R2+R2+R2
0073        11      AUX(6,I)=AUX(6,I)+R2-CJ*R1
0074                IF(J-4) 12,15,15
0075        12      J =J+1
0076                IF(J-3) 13,14,13
0077        13      X=X+.5*H
0078        14      CALL FCT( Y,DERY,RATE)
0079                GO TO 10
0080        15      IF(ITEST) 16,16,20
0081        16      DO 17 I=1,NDIM
0082        17      AUX(4,I)=Y(I)
0083                ITEST=1
0084                ISTEP=ISTEP+ISTEP-2
0085        18      IHLF= IHLF+1
0086                X=X-H
0087                H =.5*H
```

General Program, continued (3)

```
0088            DO 19 I=1, NDIM
0089            Y(I) = AUX(1,I)
0090            DERY(I)=AUX(2,I)
0091      19    AUX(6,I)=AUX(3,I)
0092            GO TO 9
0093      20    IMOD=ISTEP/2
0094            IF(ISTEP-IMOD-IMOD)21,23,21
0095      21    CALL FCT(  Y,DERY,RATE)
0096            DO 22 I=1,NDIM
0097            AUX(5,I)=Y(I)
0098      22    AUX(7,I)=DERY(I)
0099            GO TO 9
0100      23    DELT=0.
0101            DO 24 I=1,NDIM
0102      24    DELT=DELT+AUX(8,I)*ABS(AUX(4,I)-Y(I))
0103            IF(DELT-PRMT(4)) 28,28,25
0104      25    IF(IHLF-10) 26,36,36
0105      26    DO 27 I=1,NDIM
0106      27    AUX(4,I)=AUX(5,I)
0107            ISTEP=ISTEP+ISTEP-4
0108            X=X-H
0109            IEND=0
0110            GO TO 18
0111      28    CALL FCT(Y,DERY,RATE)
0112      62    DO 29 I=1,NDIM
0113            AUX(1,I)=Y(I)
0114            AUX(2,I)=DERY(I)
0115            AUX(3,I)=AUX(6,I)
0116            Y(I)=AUX(5,I)
0117      29    DERY(I)=AUX(7,I)
0118            IF(X.LT.XTEST-STEP*.99) GO TO 30
0119            TIME(NTIME) =X
0120            DO 600 I = 1,NDIM
0121      600   CONC(I,NTIME)= Y(I)
0122            NTIME = NTIME + 1
0123            XTEST = XTEST + STEP*2.
0124      30    DO 31 I=1,NDIM
0125            Y(I) = AUX(1,I)
0126      31    DERY(I)=AUX(2,I)
0127            IREC=IHLF
0128            IF(IEND) 32,32,39
0129      32    IHLF=IHLF-1
0130            ISTEP=ISTEP/2
0131            H =2.*H
0132            IF(IHLF)4,33,33
0133      33    IMOD=ISTEP/2
0134            IF(DELT-.02*PRMT(4))35,35,4
```

General Program, continued (4)

```
0135    35      IHLF = IHLF-1
0136            ISTEP= ISTEP/2
0137            H=2.*H
0138            GO TO 4
0139    36      WRITE(6,63)
0140    63      FORMAT('ERROR LIMIT TOO SMALL')
0141            GO TO 5002
0142    37      IHLF=12
0143            GO TO 39
0144    38      IHLF=13
0145    39      CONTINUE
0146    77      IF(XEND.LE.X) GO TO 5002
0147            WRITE(6,611)
0148    611     FORMAT('POSSIBLE ERROR',//)
0149            GO TO 75
0150    5002    DO 5001 ICHANG=1,NRATE
0151            RATE(ICHANG)=RATE(ICHANG)+VARY(ICHANG)*RATE(ICHANG)
0152    5001    CONTINUE
0153            DO 5003 IJJ=1,NTIME
0154            DO 5003 JJI=1,NTYME
0155            IF(TYME(JJI)-TIME(IJJ)) 5003,5004,5003
0156    5004    DO 5020 JJJ=1,NDIM
0157            CON(JJJ,JJI)=CONC(JJJ,IJJ)
0158    5020    CONTINUE
0159    5003    CONTINUE
0160            DO 5010 IA=1,NTYME
0161            WRITE(6,5011) TYME(IA),(CON(IB,IA),IB=1,NDIM)
0162    5011    FORMAT(6F12.5)
0163    5010    CONTINUE
0164            DO 5099 IJJ=1,NDIM
0165    5099    TERC(IJJ)=0.0
0166            DO 5100 IJJ=1,NTYME
0167            DO 5100 JJI=1,NDIM
0168            ERC(JJI,IJJ)=(CONA(JJI,IJJ)-CON(JJI,IJJ))/CONA(JJI,IJJ)
0169    5100    CONTINUE
0170            DO 5110 JJI=1,NDIM
0171            DO 5110 IJJ=1,NTYME
0172            TERC(JJI)=TERC(JJI)+ABS(ERC(JJI,IJJ))
0173    5110    CONTINUE
0174            TOTERR=0.0
0175            DO 5120 JJI=1,NDIM
0176            TOTERR=TOTERR+TERC(JJI)
0177    5120    CONTINUE
0178            DO 6100 IJJ=1,NTYME
0179            DO 6100JJI=1,NDIM
0180            DERC(JJI,IJJ)=CONA(JJI,IJJ)-CON(JJI,IJJ)
0181    6100    CONTINUE
```

General Program, continued (5)

```
0182              DO 6140 JJI=1,NDIM
0183      6140    SIGMAD (JJI)=0.0
0184              DO 6150 JJI=1,NDIM
0185              DO 6150 IJJ=1,NTYME
0186              SIGMAD (JJI)=SIGMAD(JJI)+(DERC (JJI,IJJ))**2
0187      6150    CONTINUE
0188              DO 6160 JJI=1,NDIM
0189              FINSIG(JJI)=SQRT(SIGMAD(JJI)/(NTYME-1))
0190      6160    CONTINUE
0191              IF(IDUR.EQ.1) GO TO 6161
0192              DO 5130 IJJ=1,NTYME
0193              WRITE (6,5131)(ERC(JJI,IJJ),JJI=1,NDIM)
0194      5130    CONTINUE
0195              WRITE (6,5131)(TERC(JJI),JJI=1,NDIM)
0196              WRITE(6,5131) TOTERR
0197      5131    FORMAT(7F10.6)
0198              GO TO 5000
0199      6161    DO 6170 IJJ=1,NTYME
0200              WRITE (6,5131)(DERC(JJI,IJJ),JJI=1,NDIM)
0201      6170    CONTINUE
0202              WRITE(6,5131)(FINSIG(JJI),JJI=1,NDIM)
0203              WRITE(6,510)(RATE(I),I=1,NRATE)
0204      5000    CONTINUE
0205              CALL EXIT
0206              END
```

ROUTINES CALLED:
FLOAT , FCT   , ABS   , SQRT   , EXIST

SWITCHES = /ON

```
BLOCK         LENGTH
MAIN.   6519   (031356)*

**COMPILER ---- CORE**
    PHASE      USED   FREE
DECLARATIVES 00687 04882
EXECUTABLES  01167 04402
ASSEMBLY       02314 06172
```

General Program, continued (6)

```
0001        SUBROUTINE FCT (C,D,R)
0002        DIMENSION C(7),D(7),R(12)
0003        D(1) =-R(1)*C(1)-R(2)*C(1)-R(5)*C(1)-R(12)*C(1)-R(9)*C(1)-
           NR(10)*C(1)+R(3)*C(3)+R(4)*C(4)+R(5)*C(2)
0004        D(2) =-R(1)*C(2)-R(2)*C(2)-R(5)*C(2)-R(9)*C(2)-R(10)*C(2)-
           NR(12)*C(2)+R(3)*C(4)+R(4)*C(3)+R(5)*C(1)
0005        D(3) =-R(3)*C(3)-R(4)*C(3)-R(6)*C(3)-R(7)*C(3)-R(8)*C(3)-
           NR(11)*C(3)+R(1)*C(1)+R(2)*C(2)+R(6)*C(4)
0006        D(4) =-R(3)*C(4)-R(4)*C(4)-R(6)*C(4)-R(7)*C(4)-R(8)*C(4)-
           NR(11)*C(4)+R(1)*C(2)+R(2)*C(1)+R(6)*C(3)
0007        D(5)=R(10)*C(1)+R(9)*C(2)+R(7)*C(3)+R(8)*C(4)
0008        D(6)=R(9)*C(1)+R(10)*C(2)+R(7)*C(4)+R(8)*C(3)
0009        D(7)=R(12)*C(1)+R(12)*C(2)+R(11)*C(3)+R(11)*C(4)
0010        RETURN
0011        END
```

SUBROUTINE CONTAINING RATE EQUATIONS FOR RACEMIC I AND II

```
        SUBROUTINE FCT (C,D,R)
        DIMENSION C(10), D(10), R(10)
        D(1) = -R(1)*C(1) + R(2)*C(2) -R(3)*C(1) -R(4)*C(1)
        D(2) = -R(2)*C(2) + R(1)*C(1) -R(5)*C(2) -R(6)*C(2)
        D(3) = R(3)*C(1) + R(5)*C(2)
        D(4) = R(4)*C(1) + R(6)*C(2)
        RETURN
        END
```

APPENDIX II

(

MICRONS

FREQUENCY (CM⁻¹)

ABSORBANCE