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Isomerization reactions of substituted cyclopropanes

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ISOMERIZATION REACTIONS OF SUBSTITUTED CYCLOPROPANES

by

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Signature was redacted for privacy.

Dean of Graduate College

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1964

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INTRODUCTION

Chemistry involving the three member carbon ring, cyclopropane has been a relatively recent addition to the field of organic chemistry. Upon scanning the literature, one is quickly impressed with the fact that before 1930, references to cyclopropane and its derivatives are relatively rare. However in recent years, the number of studies of this interesting and sometimes puzzling system has increased rapidly. The properties of cyclopropane containing compounds are often unique, and this perhaps offers a clue as to why much attention is being given them. Uniqueness is an appealing quality tending to attract for its own sake, however more importantly it is the unique situation which offers the most severe test of our theory and understanding, and this we cannot for long avoid. Cyclopropane is one of a number of highly strained compounds which is at present testing our concepts of hybridization, bonding and electronic properties of molecules.

This thesis is presented with the purpose of contributing, although only in a small way, to our growing fund of data, from which ultimately the correct conclusions will be drawn. In it will be found studies of the thermal geometric isomerization of three diarylcyclopropanes and discussions correlating them with earlier studies of other substituted cyclopropanes. Chemistry relating to the formation and stability of 1,2-diarylcyclopropanols will be discussed, along with some results of acid and base ring opening isomerization of these same compounds.

It is hoped that the reader will find this thesis enjoyable and interesting to read.

HISTORICAL

The observation of the uncatalyzed and purely thermal isomerization of cyclopropane to propylene (reaction 1) by Trautz and Winkler[1] in 1922

(1)

apparently drew little attention, for one can imagine many interesting variations if the reaction were to be proven general. In 1934, Chambers and Kistiakowski[2] did a detailed kinetic study of this same reaction, showing it to be homogeneous and unimolecular, and that $k_\infty = 10^{15.17}\exp(-65{,}200/RT)\ sec^{-1}$, where k_∞ is the rate constant extrapolated to infinite pressure.* Chambers and Kistiakowski proposed two possible mechanisms, one a C-C bond cleavage followed by a process formally analogous to the "disproportionation of free radicals" (Mechanism A), and the other a one step concerted type mechanism (Mechanism B).

Pritchard, Sowden and Trotman-Dickenson[3] verified the results of

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[1] M. Trautz and K. Winkler, J. Prakt. Chem., 104, 53 (1922).

[2] T. S. Chambers and G. B. Kistiakowski, J. Am. Chem. Soc., 56, 399 (1934).

[3] H. G. Pritchard, R. G. Sowden and A. F. Trotman-Dickenson, Proc. Roy. Soc., A217, 563 (1953).

*Kinetic pressure dependence in unimolecular gas phase reactions is general. According to this, a reactant molecule obtains the necessary energy by collision with a second molecule (reactant or inert gas). At sufficiently high pressures the Boltzman distribution is maintained and the rate determining step is the decomposition of the activated molecule. At very low pressure the distribution is not maintained and the slow step becomes the transfer of energy by collision.

Chambers and Kistiakowski and extended the study to lower pressures. They also showed that inert gases added to the system to increase the total pressure (while keeping the partial pressure of cyclopropane constant) increased the reaction rate. This verified the unimolecularity of the reaction, for while the inert gas would not directly be involved in the reaction, it would have the effect of aiding the maintenance of the Boltzman distribution through increased collisional frequency.

Slater[4], treating cyclopropane as a classical vibrating system, calculated the theoretical frequency factor and pressure dependence of reaction 1, using models suggested by the work of Chambers and Kistiakowski. Having available a complete vibrational analysis of cyclopropane[5], Slater calculated the amplitudes and phases of the internal co-ordinates for each of the normal modes of vibration of cyclopropane, and thus the reaction probability along various co-ordinates.

Assuming in the first case the model to be that of Mechanism B of Chambers and Kistiakowski[2], i.e., a concerted migration of H_5 to C_2 coincident with the breaking of C_2-C_3 (Fig. I), and thus the critical coordinate to be the non-bonded C_2-H_5 distance, Slater found the theoretical

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[2] T. S. Chambers and G. B. Kistiakowski, op. cit., p. 399.

[4] N. B. Slater, Proc. Roy. Soc., A218, 224 (1953); A194, 112 (1948); Trans. Roy. Soc. (London), A246, 58 (1953).

[5] B. D. Saksena, Proc. Indian Acad. Sci., 10, 448 (1939).

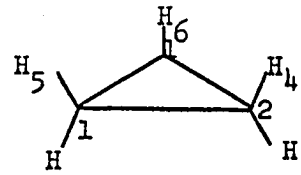

Fig. I. Cyclopropane

frequency factor to be 4×10^{14}.* This result is comparable to the experimental results of the previous workers, 14.8×10^{14}. Also the calculated pressure dependence was excellent.

In the second case, the model being that suggested by Mechanism A of Chambers and Kistiakowski[2], the reaction probability was calculated with the critical co-ordinate being a bonded C-C distance (Fig. II). The multiplicity here is three. The calculated frequency factor was 5.7×10^{13}, a poor correspondence with experiment, and the calculated pressure dependence was much different than that experimentally found. Using this co-ordinate of course ignores the possibility that disproportionation may be the controlling step or even that the transition state may be a more complex combination of Mechanisms A and B as later proposed by Schlag and Rabinovitch[6].

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[2] T. S. Chambers and G. B. Kistiakowski, op. cit., p. 399.

[6] E. W. Schlag and B. S. Rabinovitch, J. Am. Chem. Soc., 82, 5996 (1960).

*There are 11 other symetrically equivalent co-ordinates along which the reaction could occur. Slater took the reaction probability to be the sum of the 12 individual probabilities.

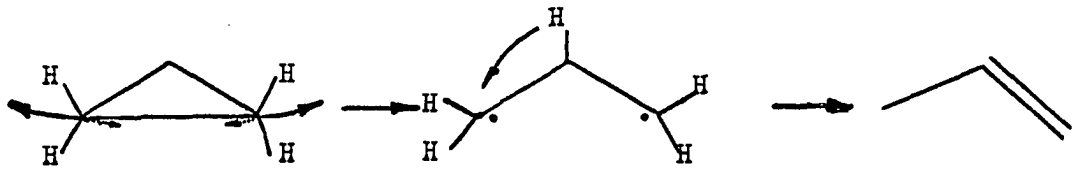

Fig. II. Mechanism A

It was on these results that Slater based his opposition to the intermediacy of the trimethylene biradical (Fig. II), and his support for Mechanism B (hydrogen migration) for this isomerization.

Weston[7] and Lindquist and Rollefson[8] have studied the kinetic isotope effect for the isomerization of cyclopropane-t_1. Both have studied the temperature effect and Weston determined a pressure dependence of the kinetic isotope effect.

The pressure dependence follows the theory of Lindeman[9], for the isotope effect for the reaction of activated molecules (the slow step at high pressures) would be expected to differ from unity, while the effect on the efficiency of collisional energy transfer (the slow step at low pressures) should be nearly unity. The kinetic isotope effect at lower pressures was indeed diminished. These results are not supported by later data of Schlag and Rabinovitch in which the kinetic isotope effect of the structural

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[7]R. E. Weston, Jr., J. Chem. Phys., 23, 988 (1955); 26, 975 (1957).

[8]R. H. Lindquist and Rollefson, J. Chem. Phys., 24, 725 (1956).

[9]For discussion, c.f. L. S. Kassel, The Kinetics of Homogeneous Gas Reactions, The Chemical Catalog Co., New York, 1932, Chap. 5.

isomerization of cyclopropane-d_2, given as $k_H/k_D = 2.18$ at 445° C, was not found to be pressure dependent. At 492° C, Weston found $k_H/k_D = 3.7 \pm 1.9$, in substantial agreement with the result of Lindquist and Rollefson. This was cited as evidence supporting Slater's choice of reaction co-ordinate, for if Mechanism A (non-concerted) were correct no isotope effect should be found.

Weston also determined the C_{13} isotope effect to be 0.0072 ± 0.0006 at 1 atm. pressure and 492° C, a piece of data from which he drew no conclusions.

Blades[10] has found the deuterium isotope effect for the structural isomerization of cyclo-C_3D_6 versus cyclo-C_3H_6 to be 1.96 at 482°. It was temperature and pressure dependent, although not quite disappearing at the lowest pressures studied.

A pertinent experiment was performed by McNesby and Gordon[11] ruling out the possibility that reaction 1 was a radical chain reaction (Fig. III). A mixture of cyclopropane and D_2 ($D_2/C_3H_6 = 1.35$) was pyrolyzed to propylene. The propylene and unreacted cyclopropane were separated by gas-liquid chromatography (GPC) and analyzed by mass spectrometry. A maximum of 0.9% of the propylene contained one D and the cyclopropane was essentially free of deuterium beyond natural abundance. If allyl and cyclopropyl radicals were present, the authors expected them to abstract D from the D_2 to a much larger extent than observed.

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[10] A. T. Blades, Can. J. Chem., 39, 1401 (1961).

[11] J. R. McNesby and A. S. Gordon, J. Chem. Phys., 25, 582 (1956).

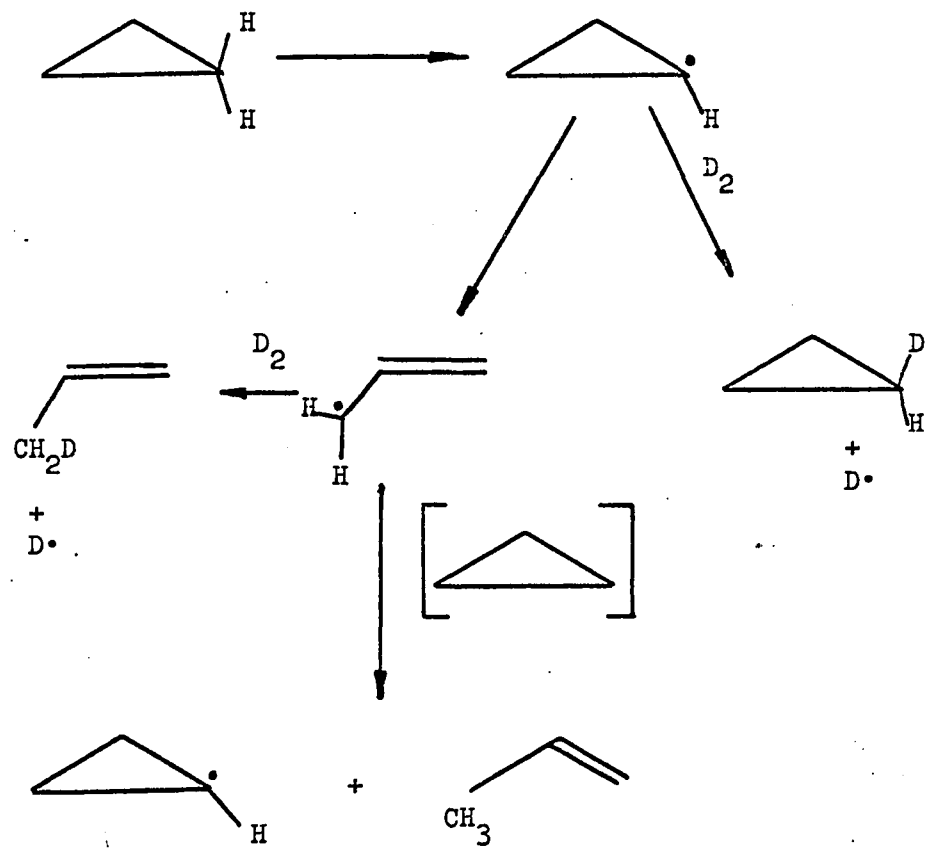

Fig. III.- Radical chain mechanism

Corner and Pease[12], whose kinetic work on the structual isomerization of cyclopropane (reaction 1) has been criticized and in part discredited, originally proposed that if a diradical intermediate did in fact exist then its reclosure to cyclopropane would need to be considered in the kinetic analysis. Rabinovitch, Schlag and Wiberg[13] observed what they

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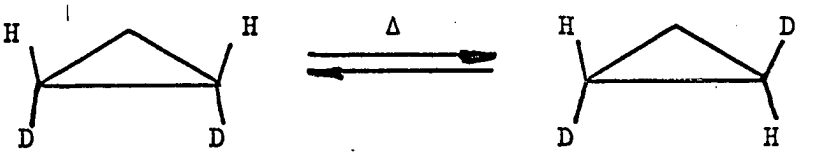
[12]E. S. Corner and R. N. Pease, J. Am. Chem. Soc., 67, 2067 (1945).

[13]B. S. Rabinovitch, E. W. Schlag and K. B. Wiberg, J. Chem. Phys., 28, 504 (1958).

considered to be an example of this reclosure step, the geometrical cis-trans isomerization of 1,2-dideuterocyclopropane (reaction 2). This



(2)

observation initiated new discussions concerning the mechanisms of structural and geometrical isomerizations, their relationship to one another, and the role of the trimethylene diradical. They listed three possible mechanisms for the geometrical transformation: (a) ring rupture and reversible recyclization; (b) intermolecular exchange reaction, radical or non-radical; (c) intramolecular hydrogen migration process. Mechanisms (b) and (c) were ruled out by the absence of $-d_1$, $-d_3$, or gem-dideutero products, as analyzed by mass spectrometry.

Structural isomerization (rate constant = k_s) was shown to be competitive with the geometrical isomerization (rate constant = k_g), however, somewhat slower: $k_g = 10^{16.0} \exp(-64{,}200/RT)$; $k_s = 10^{15.2} \exp(-65{,}500/RT)$. Of great interest in this system was the discovery that the pressure dependence characteristics of k_g and k_s were quite similar[6], which was interpreted to reflect a structural similarity in transition states. To support their previous[13] observation that the energies of activation for structural and geometrical isomerizations were alike, Rabinovitch and

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[6] E. W. Schlag and B. S. Rabinovitch, op. cit., p. 5996.

[13] B. S. Rabinovitch, E. W. Schlag and K. B. Wiberg, op. cit., p. 504.

co-workers[14] studied the isomerization of vibrationally excited cyclopropane-d_2 obtained by the reaction of methylene with ethylene-d_2 (Fig. IV).

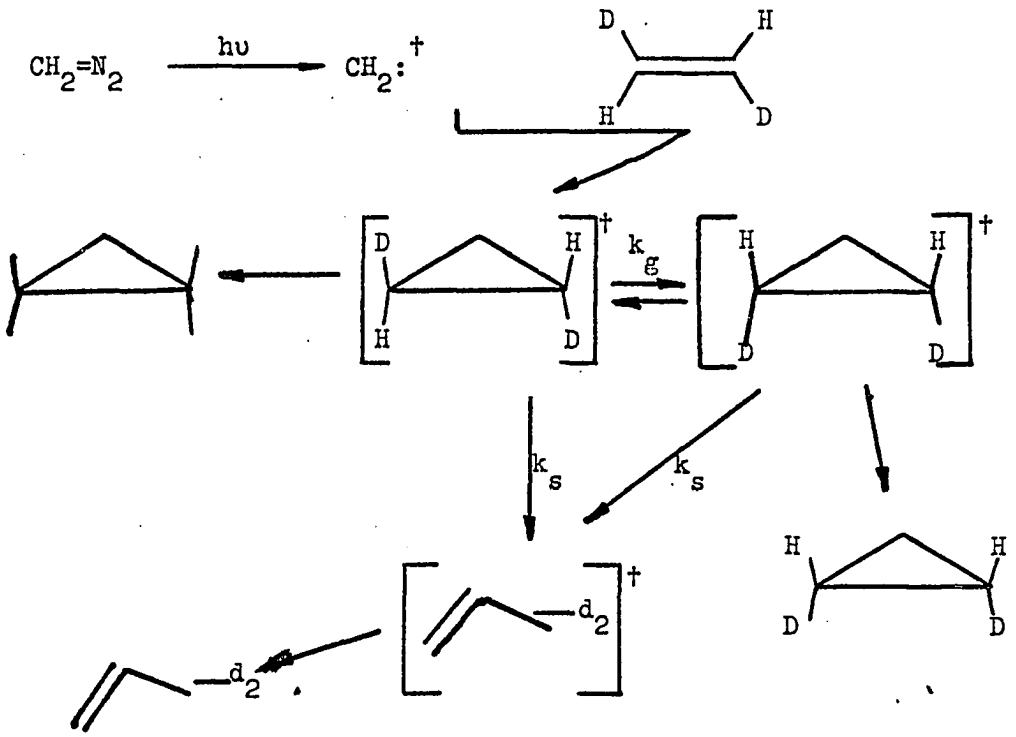

Fig. IV. Vibrationally excited cyclopropane-d_2

By varying the wavelength of irradiation the excess vibrational energy carried by the methylene and thus by the "hot" cyclopropane-d_2 could be controlled. It was found that the k_g/k_s ratio was neglibibly variant with respect to the total energy content of the reacting molecules. Thus the two processes were interpreted to be quite energetically similar,

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[14] B. S. Rabinovitch, E. Tschuikow-Roux and E. W. Schlag, J. Am. Chem. Soc., 81, 1081 (1959).

for if not one would have expected to find evidence of an isokinetic point reflected by changes in the rate ratio.

In refutation of the theory of Slater[4], Schlag and Rabinovitch[6] have observed that the kinetic pressure dependences of the rates of structural isomerization for both cyclopropane-d_2 and light-cyclopropane are identical. Slater has advanced the theory that the loss of symmetry with isotopic substitution would alter the fall-off shape. Studies with methylcyclopropane have also yielded the same objection[15,16].

With regard to the postulated structural similarity of transition states[6] and their similar energies[13,14] but with the realization that since different molecular processes and rates are involved they cannot be identical, Setser and Rabinovitch[17] have proposed the following mechanisms:

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[4] N. B. Slater, op. cit.

[6] E. W. Schlag and B. S. Rabinovitch, op. cit., p. 5996.

[13] B. S. Rabinovitch, E. W. Schlag and K. B. Wiberg, op. cit., p. 504.

[14] B. S. Rabinovitch, E. Tschuikow-Roux and E. W. Schlag, op. cit., p. 1081.

[15] J. P. Chesick, J. Am. Chem. Soc., 82, 3277 (1960).

[16] J. N. Butler and G. B. Kistiakowski, J. Am. Chem. Soc., 83, 1324 (1961).

[17] D. W. Setser and B. S. Rabinovitch, J. Am. Chem. Soc., 86, 564 (1964).

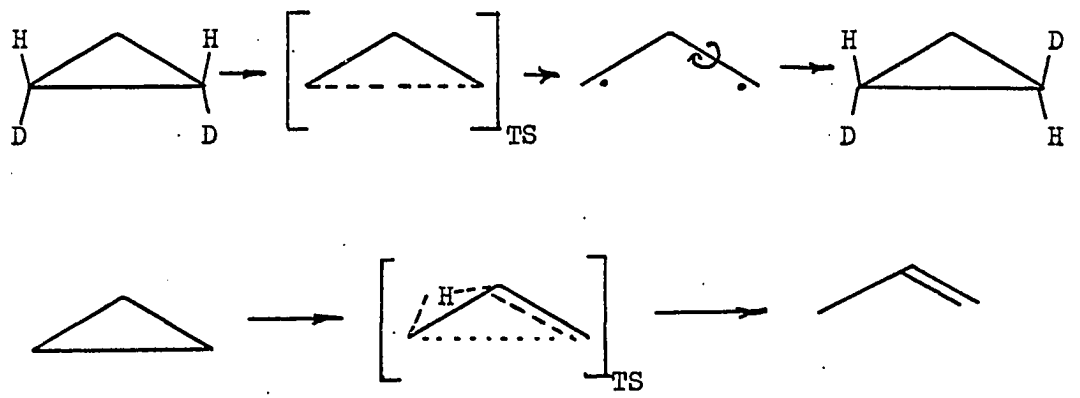

Fig. V. Mechanisms of isomerization

The experimental rate differences[13] must be primarily due to entropy differences, with geometric isomerization enjoying the more positive ΔS. From consideration of the above (Fig. V) transition states, the enhanced frequency factor of k_g, relative to that for k_s, could be due to developing freedom of internal rotation of the terminal methylenes, which is absent in the structural transition state[17]. Using the above transition state as a model for the structural isomerization, Rabinovitch[18] has reproduced theoretically the experimental kinetic isotope effect fall-off curves for cyclo-C_3D_6 and -C_3H_6.

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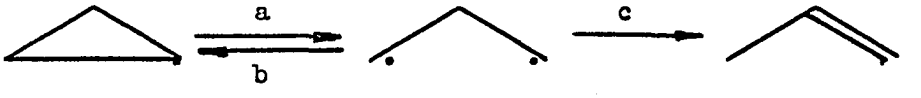
[13] B. S. Rabinovitch, E. W. Schlag and K. B. Wiberg, op. cit., p. 504.

[17] D. W. Setser and B. S. Rabinovitch, op. cit., p. 564.

[18] B. S. Rabinovitch, D. W. Setser and F. W. Schneider, Can. J. Chem., 39, 2609 (1961).

The theory that propylene cannot reasonably arise via trimethylene has been advanced by Blades[10] on the basis of the kinetic isotope effects for structural isomerization (vide supra). He argues that the following scheme proposed by Benson[19] from thermodynamical considerations is not consistent



with experimental findings. Benson[19] and Seubold[20] both propose that the trimethylene diradical reacts very rapidly with respect to molecular collisions, at least at the temperatures involved. This is consistent with the failure of all attempts to trap it (assuming it is indeed an intermediate)[3,13]. Blades argues that if this is true the observed pressure effects must occur in step a and since the observed deuterium isotope effects of necessity in this scheme occur in step c, one would not expect the isotope effect to be pressure dependent. He has found it to be pressure dependent[10]. Thus he concludes the above scheme could have no more than a small contribution to the kinetics.

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[3] H. G. Pritchard, R. G. Sowden and A. F. Trotman-Dickenson, op. cit., p. 563.

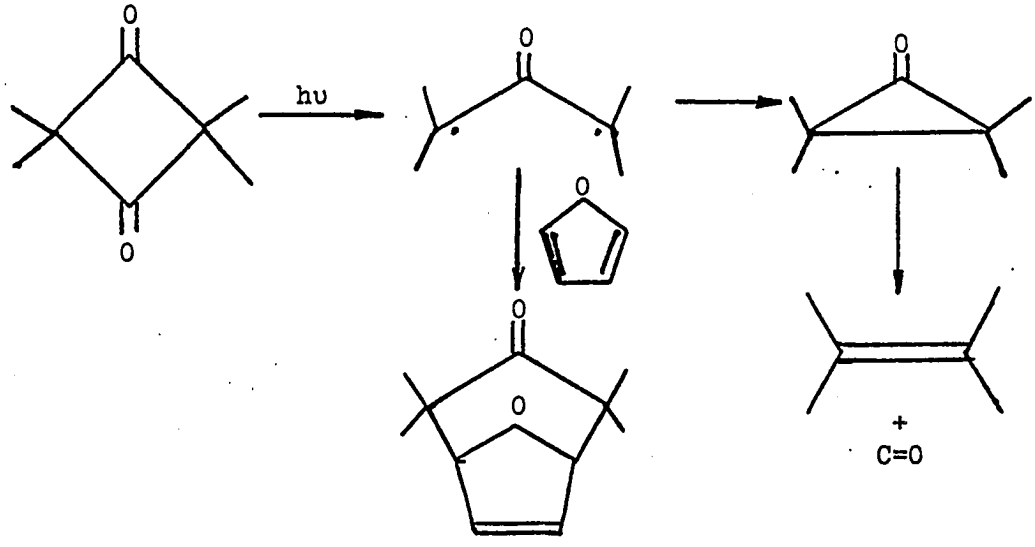
[10] A. T. Blades, op. cit., p. 1401.

[13] B. S. Rabinovitch, E. W. Schlag and K. B. Wiberg, op. cit., p. 564.

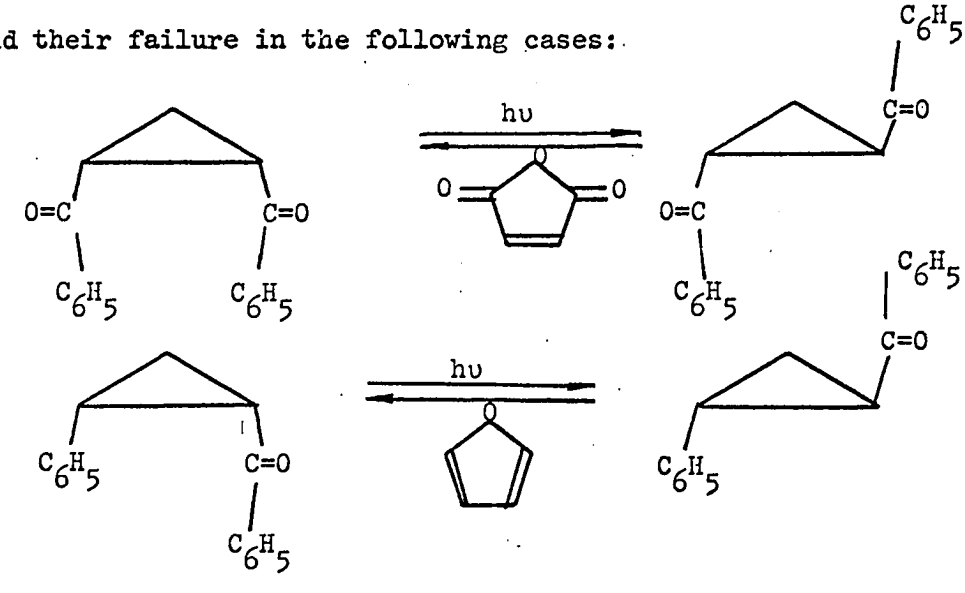
[19] S. W. Benson, J. Chem. Phys. 34, 521 (1961).

[20] F. H. Seubold, J. Chem. Phys., 22, 945 (1954).

Of interest with regard to the trapping of the diradical intermediate is the report by Cookson et al.[21] of having trapped a 1,3 diradical as shown,



and their failure in the following cases:



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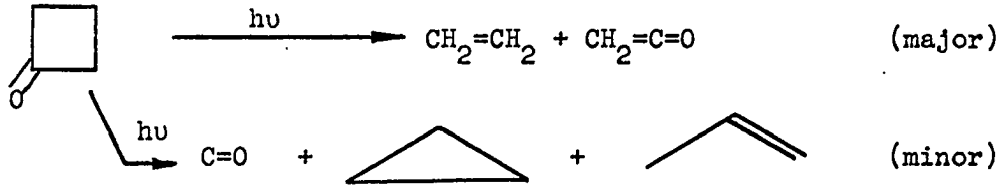
[21] R. C. Cookson, M. J. Nye and G. Subrahmanyam, Proc. Chem. Soc., 144 (1964).

Assuming that diradical intermediates do exist in these cases, they illustrate the interplay of developing angle strain and bond strength during cyclization in defining the relative lifetimes of the diradicals. This argument must however appear with qualification, for it is not clear whether the propanone diradical is singlet or triplet, although the singlet would appear more stable[21].

Bawn and Hunter[22] claim to have obtained propylene and cyclopropane directly from the trimethylene diradical generated from trimethylene bromide and elemental sodium by a flame diffusion method. However it is not clear that the propylene was not obtained from cyclopropane after initial cyclization[13].

Flowers and Frey[23] have argued against the intermediacy of the trimethylene diradical in the isomerization of cyclopropane with the results of the following experiments. The products of the photolysis of cyclobutanone are shown below. Frey assumes that ring rupture and loss of C=0



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[13] B. S. Rabinovitch, E. W. Schlag and K. B. Wiberg, op. cit., p. 564.

[21] R. C. Cookson, M. J. Nye and G. Subrahmanyam, op. cit., p. 144.

[22] C. E. H. Bawn and R. F. Hunter, Trans. Farad. Soc., 34, 608 (1938).

[23] M. C. Flowers and H. M. Frey, J. Chem. Soc., 2758 (1960).

yields the trimethylene diradical which then either cyclizes or rearranges to propylene. When the irradiation was carried out at 100° C. in the presence of large amounts of added ethylene, various C_5 olefins were obtained, indicating a bimolecular reaction with trimethylene. A mixture of cyclopropane and ethylene was thermally isomerized to propylene at 475° C. No pentenes were found and the authors suggested that trimethylene was not present under conditions which normally yield both geometrical and structural isomerization. It however has not been proven that the photolysis of cyclobutanone yields a diradical intermediate[24]. Also the temperature difference between the two experiments may merely indicate that a barrier to recyclization of trimethylene does exist. In fact, the interpretation these results as suggesting a diradical intermediate in the thermal isomerization is advanced by Rabinovitch[6].

Smith[25] has proposed an alternate transition state (Fig. VI) that involves no ring expansion for geometric isomerization. It is presented to

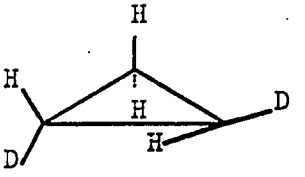

Fig. VI. Transition state with no ring expansion

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[6]E. W. Schlag and B. S. Rabinovitch, op. cit., p. 5996.

[24]R. Srinivasan, Cyclic Ketones. In W. A. Noyes, Jr., G. S. Hammond, J. N. Pitts, Jr., editors, Advances in Photochemistry, Interscience Publishers, New York, 1963, p. 96.

[25]F. T. Smith, J. Chem. Phys., 29, 235 (1958).

be compatible with the theory of Slater[4]. One methylene group is proposed to be excited through its "rocking" mode of vibration to such an amplitude as to become planar with the ring, at which point it may, with equal probability, go one to the other isomer or revert to the initial one. Benson[19] has criticized this picture because far higher energy requirements would be involved than are found experimentally. Setser and Rabinovitch[17] have also presented arguments against this mechanism (see discussion below on methylcyclopropane).

A critical feature of this transition state is the requirement that only consecutive rotation of methylene groups in a cyclopropane can occur. The transition state suggested by Rabinovitch (ring expansion) would allow for simultaneous rotations. No successful attempt to distinguish between these possibilities has yet been published. Smith later rescinded to allow for some ring expansion[6] thus making his differences with Rabinovitch more semantic, although he still would not allow free rotations in the transition state.

The studies of these isomerizations have been extended to several methyl substituted cyclopropanes. Chesick[15], Butler and Kistiakowski[16]

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[4] N. B. Slater, op. cit.

[6] E. W. Schlag and B. S. Rabinovitch, op. cit., p. 5996.

[15] J. P. Chesick, op. cit., p. 3277.

[16] J. N. Butler and G. B. Kistiakowski, op. cit., p. 1324.

[17] D. W. Setser and B. S. Rabinovitch, op. cit., p. 564.

[19] S. W. Benson, op. cit., p. 521.

and Setser and Rabinovitch[17] have studied the reaction of methylcyclopropane, their results being in substantial agreement. Structural isomerization yielded the following products (relative rate)[15]: 1-butene (1.0), cis-2-butene (0.63), trans-2-butene (0.28), and isobutene (0.16). The relatively slower rate of isobutene formation has been used to support both a Smith type mechanism by relative inertias of the $C\begin{matrix}CH_3\\H\end{matrix}$ and $C\begin{matrix}H\\H\end{matrix}$ groups[16] (Fig. VII) and a ring expansion mechanism from a bond strength

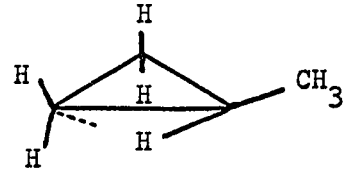

Fig. VII. Transition state with no ring expansion

argument[17] (Fig. VIII) where the bond opposite the methyl is the strongest*.

Fig. VIII. Transition state with ring expansion

Since the above discussions indicate that ring expansion is important, it

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[15] J. P. Chesick, op. cit., p. 3277.

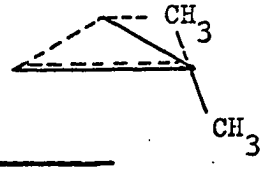
[16] J. N. Butler and G. B. Kistiakowski, op. cit., p. 1324.

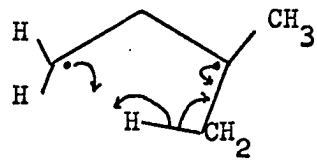
[17] D. W. Setser and B. S. Rabinovitch, op. cit., p. 564.

*Methyl substituents are well known to lower C-C bond energies.

would appear that a combination of these effects may be operative, for Setser and Rabinovitch have found deuterium isotope effects definitely to be present in the structural rearrangement of 2,3-dideutero-1-methylcyclopropane. This argues that both ring expansion and H-migration are important in the transition state. The rate of formation of 1-butene is faster than that of 2-butene only by a very small amount. It would appear that neither argument of radical reactivity nor of double bond stability would apply here concerning product ratios. The ratio of cis-2-butene/trans-2-butene is significantly larger than 1 in all studies made. The reason for this formation of the least stable isomer has not been explained although it would appear that some steric argument concerning a concerted mechanism must apply. Just how this should be so is not clear since in a study of the structural rearrangement of 1,2-dimethylcyclopropane, the ease of a H-migration to a methyl substituted carbon appeared to be independent from the cis-trans nature of that methyl group (see below).

Flowers and Frey[26] in their studies of the structural isomerization of 1,1-dimethylcyclopropane, found that 3-methylbut-1-ene and 2-methylbut-2-ene were formed in nearly equal quantities (1:0.96) at a combined rate of $k_\infty = 10^{15.05}\exp(-62{,}600)\sec^{-1}$. Small quantities ($\sim$1%) of 2-methylbut-1-ene were formed by either methyl migration or γ-H abstraction, the latter being the more likely mechanism.

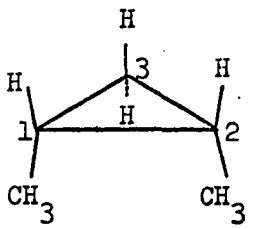




[26] M. C. Flowers and H. M. Frey, J. Chem. Soc., 3953 (1959).

Flowers and Frey have also studied the geometrical and structural isomerization of 1,2-dimethylcyclopropane[27,28]. This compound was shown to undergo cis-trans isomerization much faster than structural isomerization, analogous to the results for 1,2-dideuterocyclopropane[6,13] and 2,3-dideutero-1-methylcyclopropane[17]. The Arrhenius parameters for the thermal geometrical and structural isomerizations now known in the literature are given in Table I.

Of interest in the structural isomerization of 1,2-dimethylcyclopropane is the product formation. 2-methylbut-2-ene is formed at the same rate



from either cis or trans precursor. This requires the breaking of either C_1-C_3 or C_2-C_3 and the concommitant H-migration from C_2 to C_3 or C_1 to C_3. 2-methylbut-1-ene is formed by the same bond cleavages but with H-migration from C_1 to C_2 or C_2 to C_1 and its rate of formation is also independent of starting material. It is pertinent that H migration between C_1 and C_2 appears equally easy for cis and trans dimethyl, for this then cannot be a

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[6] E. W. Schlag and B. S. Rabinovitch, op. cit, p. 5996.

[13] B. S. Rabinovitch, E. W. Schlag and K. B. Wiberg, op. cit., p. 5996.

[17] D. W. Setser and B. S. Rabinovitch, op. cit., p. 564.

[27] M. C. Flowers and H. M. Frey, Proc. Roy. Soc., A257, 122 (1960).

[28] M. C. Flowers and H. M. Frey, Proc. Roy. Soc., A260, 424 (1961).

Table I. High pressure experimental rate parameters for cyclopropane isomerizations[17]

Compound	E_g(kcal mole^{-1})	log A_g (sec^{-1})	E_s(kcal mole^{-1})	log A_s (sec^{-1})
Cyclopropane[3]	---	---	65.0	15.17
Cyclopropane-d_2[6]	65.1	16.41	65.4	15.12
Methylcyclopropane-d_2[17]	60.5	15.35	62.3	14.43
Methylcyclopropane[15]	---	---	62.4	14.61
cis-1,2-dimethyl-cyclopropane[27,28]	59.4	15.25	61.7	14.60
1,1-dimethyl cyclopropane[26]	---	---	62.6	15.05
cis-1-ethyl-2-methyl-cyclopropane[29]	58.9	15.08	---	---

[3]H. G. Prichard, R. G. Sowden and A. F. Trotman-Dickenson, op. cit., p. 563.

[6]E. W. Schlag and B. S. Rabinovitch, op. cit., p. 5996.

[15]J. P. Chesick, op. cit., p. 3277.

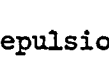
[17]D. W. Setser and B. S. Rabinovitch, op. cit., p. 564.

[26]M. C. Flowers and H. M. Frey, op. cit., p. 3953.

[27]M. C. Flowers and H. M. Frey, op. cit., p. 20.

[28]M. C. Flowers and H. M. Frey, op. cit., p. 424.

[29]C. S. Elliot and H. M. Frey, J. Chem. Soc., 900 (1964).

factor in determining the relative ease of C_1-C_2 cleavage for the cis and trans isomers. The fact that C_1-C_3 or C_2-C_3 cleavage in both cases is independent of starting material favors ring expansion in the transition state. If the Smith mechanism were operative with no expansion or only a small amount, the relief of methyl-methyl repulsion by rotation of  during H-migration should favor the reaction of cis-dimethylcyclopropane; expansion as the prominent process should offer little relief, as is consistent with observations.

Cis and trans-pent-2-enes are formed by scission of C_1-C_2 with subsequent H-migration. The trans-dimethyl forms products whose ratio is near the statistical value for all bond scissions and H-migrations. However the cis-dimethyl forms products whose percentage of cis-trans-pent-2-enes is nearly double the statistical value. The difference in rates of C_1-C_2 cleavage for cis and trans-dimethylcyclopropane corresponds to ΔE_a = 2 kcal/mole. Also the trans/cis ratio for the production of the pent-2-enes is the same for both cis and trans starting materials. Again postulation of considerable ring cleavage in the transition state explains these results. C_1-C_2 cleavage should be more favorable for the cis in order to relieve methyl-methyl repulsion, thus the preponderance of pentenes for this reactant. Ring expansion would allow for rotational equilibrium which supports the constancy of the trans/cis ratio of the pent-2-enes. This ratio is 1.26. The calculated equilibrium value at the temperatures involved for trans-pent-2-ene/cis-pent-2-ene is 1.15[28]. The experimental

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[28] M. C. Flowers and H. M. Frey, op. cit., p. 424.

difference from 1.15 is unexplained although it must be caused by subtle steric interactions during the H-migration.

1-ethyl-2-methylcyclopropane has been demonstrated[29] to undergo geometric isomerization (see Table I). The simultaneous formation of expected olefins did occur, however the authors infer that their rate of production relative to geometrical isomerization was much slower than found in the dimethylcyclopropane case, where they needed to consider the structural isomerization in order to analyze the kinetics of the geometrical transformation. In this case they pointed out that it was slow enough to be ignored.

Frey and Marshall[30] have reported the cis-trans isomerization of 1,2,3-trimethylcyclopropane which simultaneously yields cis and trans-3-methylpent-2-enes (ratio of cis/trans not given). The rate, k_g, is experimentally indistinguishable from that of 1,2-dimethylcyclopropane.

In a related type of reaction Chesick[31] has postulated allylic stablization of a 1,3 diradical intermediate. Kinetics followed from 197.2 to 233.8° C. for the reversible isomerization of 2-methylmethylenecyclopropane and ethylidenecyclopropane yielded $(k_1+k_2) = 10^{14.26}\exp(40{,}400/RT)$, where $K_{eq} = k_1/k_2$. Two approaches to the calculation of the barrier for this isomerization if resonance stabilization were not operative yielded 47 and 56.6 kcal/mole. Since the observed value is

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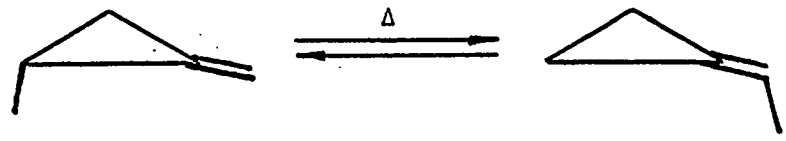
[29] Ibid, p. 900.

[30] H. M. Frey and D. C. Marshall, J. Chem. Soc., 5717 (1963).

[31] J. P. Chesick, J. Am. Chem. Soc., 85, 2720 (1963).



$$\Delta H = -0.5 \text{ kcal/mole}$$

$$\Delta S = -0.55 \text{ e.u.}$$

significantly less than this, he postulates that stabilization does indeed exist.

An analogous isomerization was discovered by Overberger and Borchert[32]. The thermal isomerization of vinylcyclopropane to cyclopentene may be postulated to traverse a diradical intermediate that recyclizes on the ends of the delocalized system. The analogous reactions of isopropenylcyclopropane[33] and 1-methylvinylcyclopropane[34] also have been studied. The rates are as follows: vinylcyclopropane, $k_\infty = 10^{13.5}\exp(-49{,}600/RT)$[35]; isopropenylcyclopropane, $k_\infty = 10^{13.9}\exp(-50{,}900/RT)$; 1-methylvinylcyclopropane, $k_\infty = 10^{14.1}\exp(-49{,}350/RT)$. The reverse reaction has been shown to proceed under irradiation[36].

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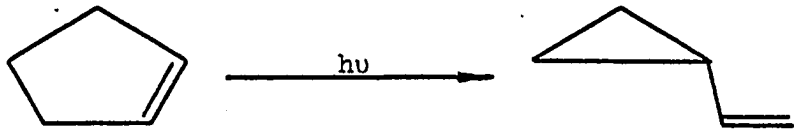
[32] C. O. Overberger and A. E. Borchert, J. Am. Chem. Soc., 82, 1007, 4891 (1960).

[33] H. M. Frey and D. C. Marshall, J. Chem. Soc., 3981 (1962).

[34] R. J. Ellis and H. M. Frey, J. Chem. Soc., 959 (1964).

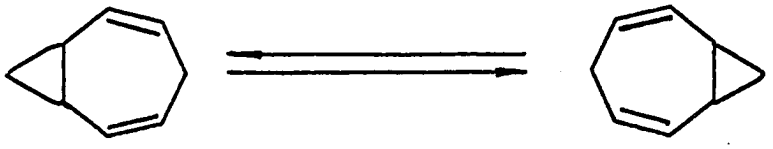
[35] M. C. Flowers and H. M. Frey, J. Chem. Soc., 3547 (1961).

[36] W. A. Gibbons, W. F. Allen and H. E. Gunning, Can. J. Chem., 40, 568 (1962).



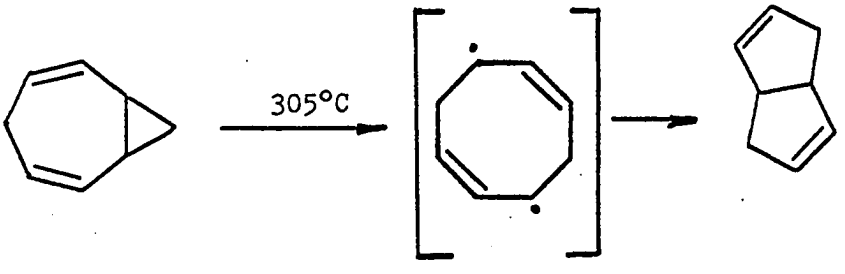
Vogel, Ott and Gajek[37], and Doering[38] have shown that cis-1,2-divinylcyclopropane isomerizes to 1,4-cycloheptadiene (Cope reaction) at temperatures as low as -40° C. The corresponding trans compound yields the same product only at above 190° C. indicating that the diallylic bond must break and rotation occur to maximize the electronic interactions.

A new and interesting concept is introduced with 3,4-homotropilidene.[38] Isomerization (reaction 3) yields a product which is identical to the



(3)

starting isomer. A study of the NMR signal temperature dependence has revealed that reaction 3 does indeed proceed. Above 350° C. however another process occurs.



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[37] E. Vogel, K. H. Ott and K. Gajek, Ann., 644, 172 (1961).

[38] W. von E. Doering and W. R. Roth, Angew. Chem., Int. Ed., 2, 115 (1963).

It has been estimated[38] that 3,4-homotropilidene isomerizes 1000 times per second at 180° C. and 1 time per second at -50° C. Molecules undergoing this very mobile process have been dubbed "fluctional structures"[38].

The extreme example of this type of molecule is tricyclo(3,3,2,$0^{4,6}$) deca-2,7,9-triene (Bullvalene)[38]. Schroder[39] has prepared this compound and found it to have the properties predicted by Doering and Roth[38], namely at 100° C. all protons are identical and the NMR spectra is only a sharp singlet at 5.8τ.

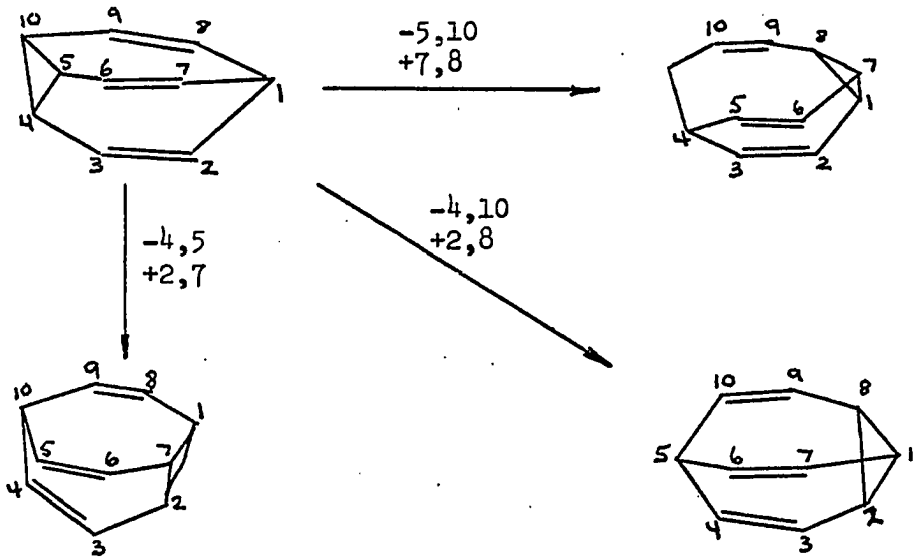

Fig. IX. Bullvalene rearrangements

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[38] Ibid., p. 115.

[39] G. Schroder, Angew. Chem., Int. Ed., 2, 481 (1963).

The most surprising fact is however that any isomer can be transformed into any other (Fig. IX) through a series of Cope rearrangements. With 10 carbon atoms there are more than 1.2 million combinations of Bullvalene, and since at 100° C. all protons are identical, all 1.2 million combinations must contribute to the structure at the same time. Since 10 points cannot be arranged on the surface of a sphere to form a fully symmetrical three dimensional figure, this must be a phenomenon of tautomerism and not of mesomerism[38].

There are several cases of these same types of isomerization in which heteroatoms are involved[40]. They will not be discussed here, for they are quite similar to the reactions already considered.

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[38] W. von E. Doering and W. R. Roth, op. cit., p. 115.

[40] For a review see E. Vogel, Angew. Chem., Int. Ed., 2, 1 (1963).

RESULTS AND DISCUSSION

Part I: Thermal Isomerization of Diarylcyclopropanes and Diarylcyclopropylacetates

As part of a continuing study of the chemistry of cyclopropanols it was proposed to synthesize a series of 2-aryl-1-phenylcyclopropanols. Since an efficient method for the reduction of cyclopropylacetates to the alcohols by methyl lithium had been worked out[41], it was felt that the best route would be through the acetates. Freeman[42] published a method of obtaining cyclopropylacetates and in fact had synthesized 1,2-diphenylcyclopropylacetate. The proposed total synthetic scheme is presented in Fig. X.

The lead tetraacetate oxidation would be expected to yield a mixture of cis and trans-pyrazolineacetates which would then yield cis and trans-cyclopropylacetates. Mixtures of cyclopropylacetates were obtained.

The mixture of cyclopropylacetates was in each case rich (70%) in the cis isomer*, which may be because during the oxidation the large $Pb(OAc)_4$ molecule could most effectively approach the pyrazoline from the "back side". The stereospecificity of the pyrazolineacetate pyrolysis however is not certain. However since it was later determined that the trans isomer was the most stable, these results suggest that this steric factor may be important.

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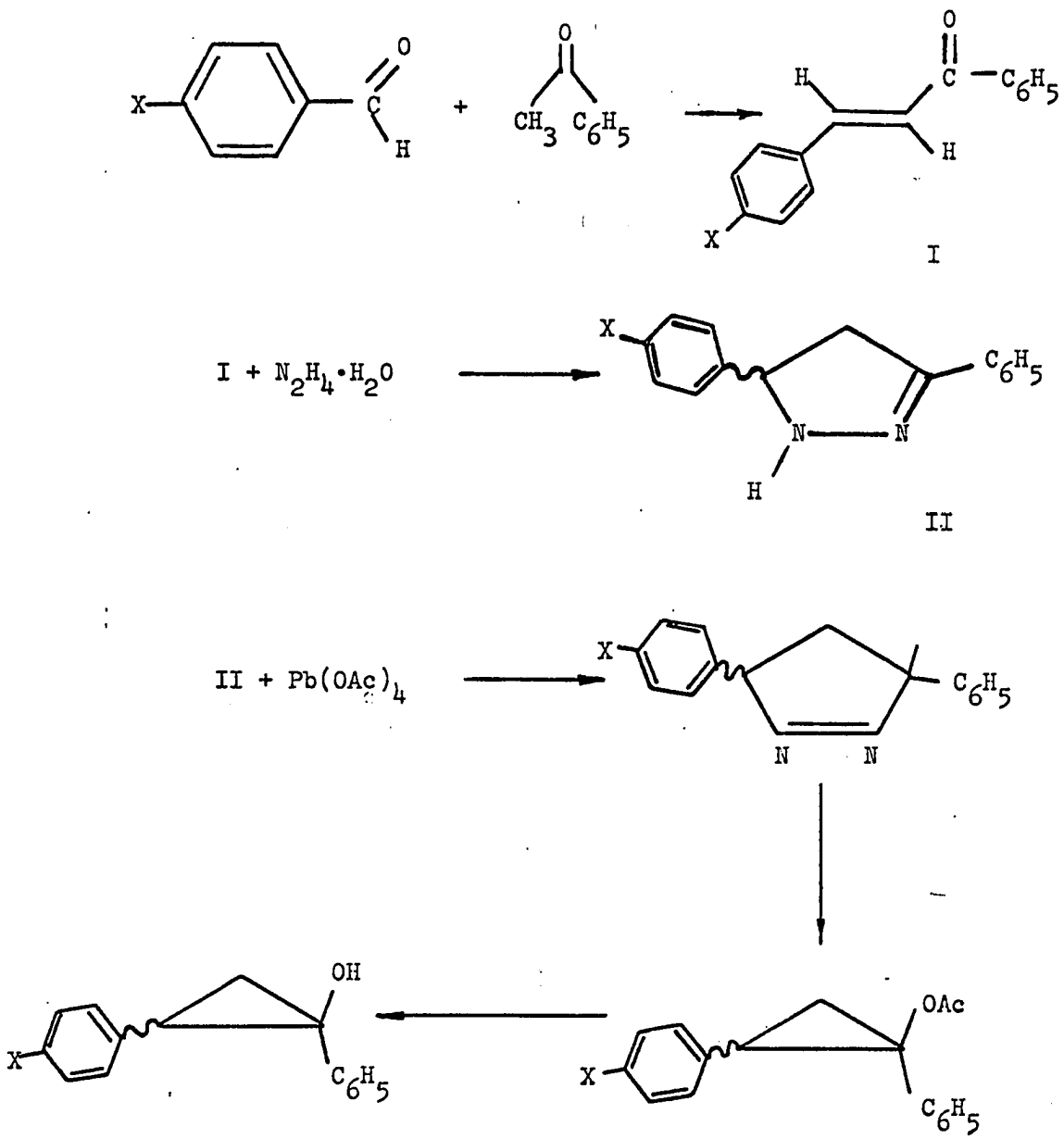
[41] C. H. DePuy, G. M. Dappen, K. L. Eilers and R. A. Klein, J. Org. Chem. (In press).

[42] J. P. Freeman, J. Org. Chem., 28, 885 (1963).

*The cis-trans relationship in this thesis will refer to the two phenyl groups.

Fig. X. Synthetic scheme for 1,2-diarylcyclopropylacetates and cyclopropanols



Synthetic scheme for 1,2-diarylcyclopropylacetates and cyclopropanols

Induced crystallization with hexane served to crystallize part of the cis isomer, leaving the mother liquor as an approximately 60/40 mixture trans/cis. A fractional distillation of these isomers was attempted. It was found that each fraction, although further enriched in one isomer, invariably yielded a mixture of isomers. Coupling this with the observation that even after careful recrystallization, the pure cis isomer yielded a gas phase chromatogram (temperature 190-200° C.) indicating a small percentage of trans isomer present, it was suggested that perhaps thermal cis-trans isomerization was occurring. Although it was later found that a very slow spinning band distillation under high vacuum was able to separate the isomers, this suggestion still served to initiate an experiment to determine this point. A sample of cis-1,2-diphenylcyclopropylacetate was determined to be pure by NMR and was heated at 190° C. for 24 hours. The NMR spectrum of the same sample was then found to be that of an approximately 60-40 mixture of trans and cis compound. The thermal isomerization which was evident as a result of this experiment was postulated to be analogous to the well documented geometric isomerizations of other substituted cyclopropanes (see Historical).

However in order to determine that the process was not of a different mechanism in which the acetate function played an integral role, cis and trans-diphenylcyclopropane were synthesized following the procedure of Beach, Turnbull and Wilson[43] (reaction 4). Heating the cis-1,2-diphenylcyclopropane at 190° showed that thermal geometric isomerization took place

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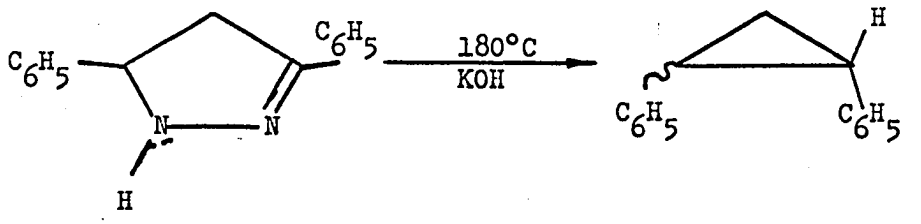
[43] S. G. Beach, J. H. Turnbull and W. Wilson, J. Chem. Soc., 4686 (1952).



(4)

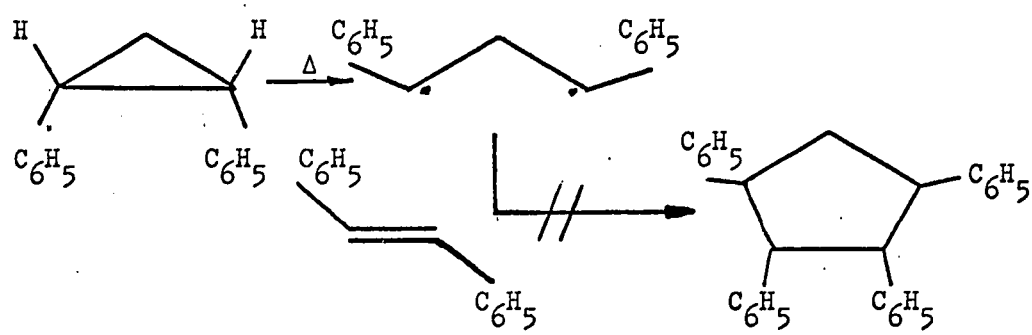
in this case also. It is thus not unreasonable to assume that the cyclopropylacetate isomerizes with the same mechanism as the cyclopropane, which must be but another example of the ring cleavage and recyclization mechanism postulated for this type of isomerization (see Historical). This is a reasonable mechanism, for ring cleavage would yield two benzylic radicals, and the comparatively low temperature at which this reaction occurs would seem to reflect their stability relative to alkane radicals.

The reaction was established as reversible by heating the trans isomer at the same temperature for several hours and producing cis isomer.

Since in previous work (see Historical) competitive structural isomerization had occurred along with geometric isomerization, it was considered unusual that no ring opened products had been found in any of the above experiments. A sample of cis-1,2-diphenylcyclopropane was heated in a sealed ampuole under nitrogen at 220° for 4 days ($t_{\frac{1}{2}}$ later determined to be 58 minutes). After this period an NMR revealed no other products and no olefin absorption appeared in the IR spectrum. This established the geometrical isomerization as clean with no side reactions.

Many attempts have been made to trap diradical intermediates in these thermal reactions. The failure of toluene and of even nitric oxide to

function as trapping agents has been attributed to the very short lived nature of the trimethylene radical with respect to intermolecular collisional frequencies[13,19,20]. In this case one might expect the postulated diradical to have a longer lifetime owing to the increased stability and consequent diminished reactivity of benzylic radicals relative to those studied in earlier aliphatic cases. Two experiments were performed with the hope of trapping the postulated intermediate. In the first trans-stilbene was combined with cis-1,2-diphenylcyclopropane and heated at 190° for several hours. No evidence of any intermolecular product (reaction 5) was found. In the second experiment the trapping agent used was maleic



(5)

anhydride. No trapped radical was detected (reaction 6) although the mixture did turn dark. The NMR showed no change.

Although McNesby and Gordon[11] (see Historical) had eliminated the

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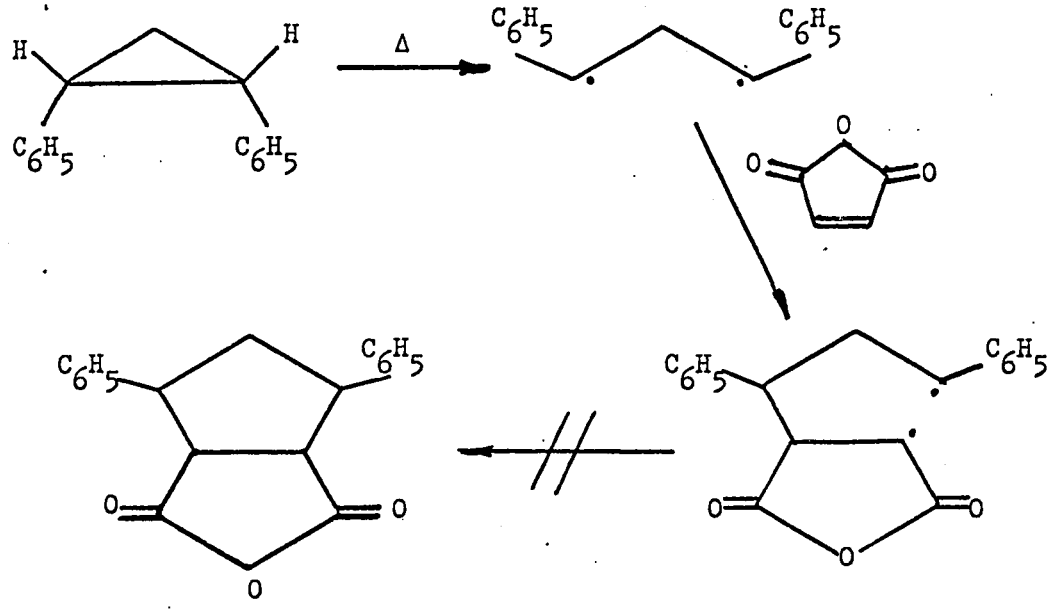
[11] J. R. McNesby and A. S. Gordon, op. cit., p. 582.

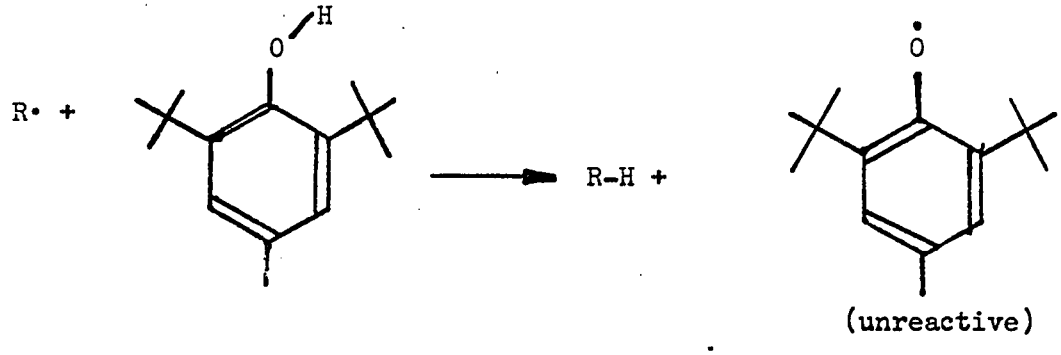
[13] B. S. Rabinovitch, E. W. Schlag and K. B. Wiberg, op. cit., p. 504.

[19] S. W. Benson, op. cit., p. 521.

[20] F. H. Seubold, op. cit., p. 945.



possibility of a chain radical mechanism for these isomerizations in the vapor phase, and the conditions for the diphenylcyclopropane isomerizations appear compatible with the diradical mechanism, the elimination of the radical chain possibility was desirable. 2,6-di-t-butyl-p-cresol is a good trapping agent for radicals due to the very stable nature of the radical it forms. If some impurity was acting as a radical initiator, the use of 2,6-di-t-butyl-p-cresol(III) should inhibit the radical reaction. One sealed ampuole was charged with cis-diphenylcyclopropane and another



with a 1:1 mixture of III and the cyclopropane. These ampuoles were heated at 190° for 3 hours and then removed from the oil bath. Analysis by NMR revealed that isomerization had taken place in both and to about the same extent (±5%). Thus it would appear that a radical chain mechanism is not operative.

In a preliminary kinetic experiment, cis-1,2-diphenylcyclopropane was heated under N_2 at 180° C. in a small tube fitted with a rubber septum. Samples were withdrawn directly with a micro-syringe and injected into the GPC. Peak areas were measured with a planimeter to obtain the cis/trans ratio. The kinetic analysis over the first 30% reaction revealed a first order reaction with a good straight line obtained from the following kinetic expression (see xperimental):

$$2.303 \log ((R+1)/R) = k_g t$$

R = ratio of starting isomer to product isomer

k_g = rate constant for geometric isomerization

At ∿30% reaction the apparent forward rate constant began to fall. The above kinetic expression does not take the equilibrium into account, and at this percent reaction the product isomer concentration has increased enough to make the reverse reaction noticeable. Of course the line must be a curved one even in the beginning stages of the reaction, however in that region the curvature is such as to be obscured by even small point scatter. In all subsequent kinetic runs the reactions were carried to no more than 10% completion and the rate constant determined by a least squares method of analysis.

Rate constants for the geometric isomerization of cis-1,2-diphenylcyclopropane were determined by this method at four different temperatures (165.8, 185.5, 197.0 and 220.1° C.). A plot of log k_g versus 1/T (°K) yielded a straight line. Determination of the slope ($=E_a/2.303RT$) and intercept by the method of least squares gave $E_a = 33.5 \pm 1.1$ kcal/mole and frequency factor $A = 10^{11.2 \pm 0.5}$ (Fig. XI). The kinetic temperature dependence of this reaction is thus given by the expression:

$$k_g\ (sec^{-1}) = 10^{11.2 \pm 0.5} \exp(-33{,}500 \pm 1{,}100/RT)$$

Esteban, Kerr and Trotman-Dickenson[44] have determined the energy of activation for the reaction

$$C_6H_5\text{-}CH_2\text{-}CH_3 \xrightarrow{\Delta} C_6H_5\text{-}CH_2\cdot + CH_3\cdot$$

to be $E_a = 70.1$ kcal/mole. The energy of activation for ethane homolysis to two methyl radicals is accepted as 83.3 kcal/mole[38]. Thus in the pyrolytic cleavage of the C-C bond, a single phenyl substituent will stabilize the transition state to the extent of 13.2 kcal/mole (83.3-70.1)*. In

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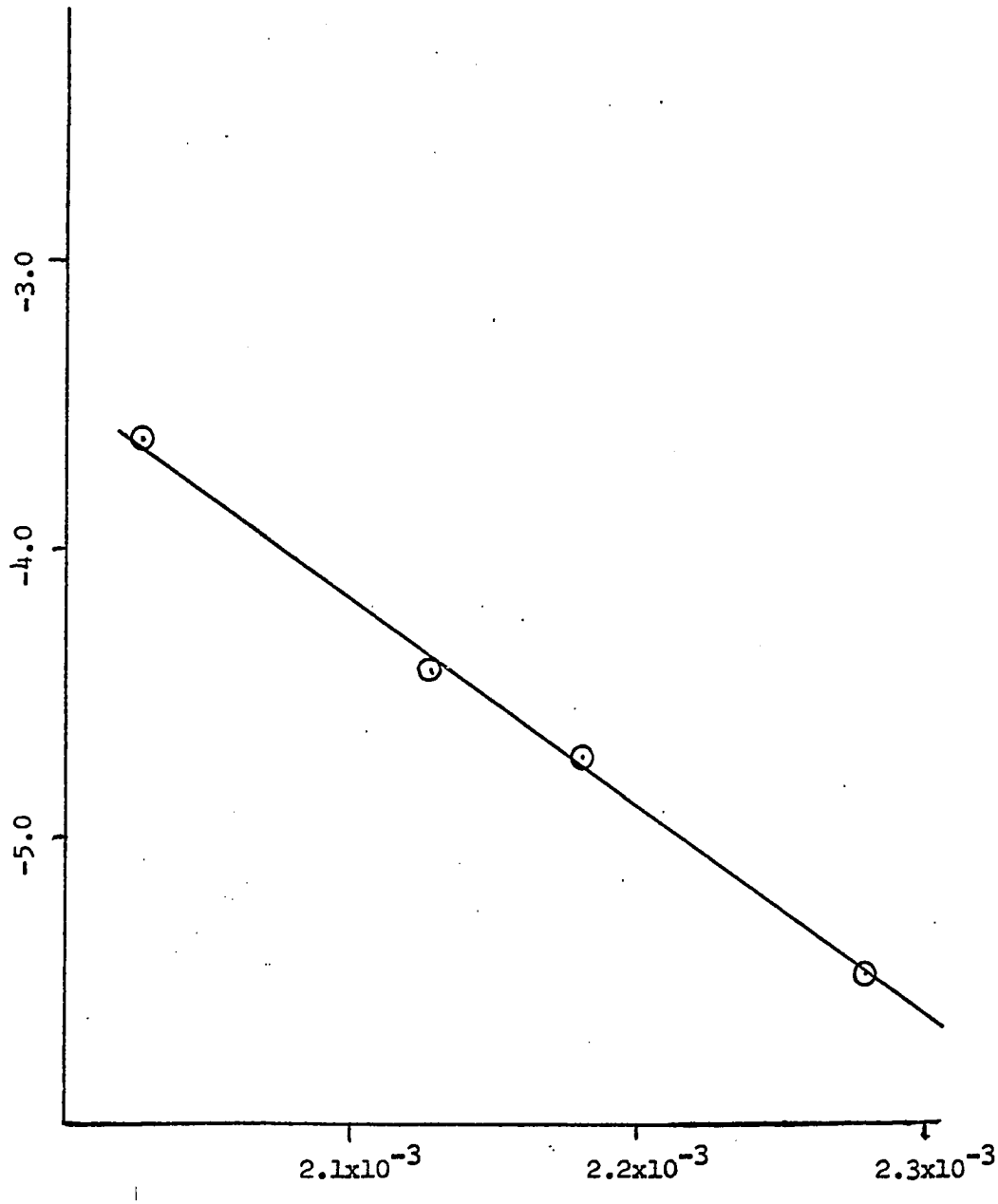
[38] W. von E. Doering and W. R. Roth, op. cit., p. 115.

[44] G. L. Esteban, J. A. Kerr and A. F. Trotman-Dickenson, J. Chem. Soc., 3873 (1963).

* A better model for the C-C bond cleavage stabilization energy in this case would be bibenzyl. However no data has been reported for the direct thermal homolytic cleavage of this molecule that isn't attendant with large experimental uncertainties.

Fig. XI. Log k_g *versus* 1/T (°K) for *cis*-1,2-diphenylcyclopropane



log k_g versus 1/T (°K.) for cis-1,2-diphenylcyclopropane

the diphenylcyclopropane cleavage above, the stabilization relative to cyclopropane cleavage should then be of the order of 26.4 kcal/mole (13.2 x 2). The E_a for cyclopropane cleavage is not available, however the energy of activation for geometric isomerization of cyclopropane-d_2 is known to be 64.2 kcal/mole. It is then seen that the electronic stablization may be expected to yield an energy of activation of 37.8 kcal/mole (64.2-26.4) on the basis of a diradical model. This value does not take into account the steric interaction energy of the cis diphenyls. This interaction energy was not specifically determined although the equilibrium constant was found to be 10 $\pm$ 0.5 at 193° C. If ΔS is assumed to be zero, ΔH may be approximated to be 2.2 kcal/mole. Making this adjustment the energy of activation of the diradical model would be 35.6 kcal/mole as opposed to 33.5 experimentally. This is reasonable agreement considering the approximations involved. It should be noted that this lends support not only to the diradical mechanism for this reaction, but since the energy calculations involved assumed the same transition state for cyclopropane-d_2, support is also given for the diradical mechanism for geometrical isomerization in that case.

The energy of activation for the reaction has also been determined[44],

$$C_6H_5\text{-}CH_2\text{-}CH_2\text{-}CH_3 \xrightarrow{\Delta} C_6H_5\text{-}CH_2\cdot + \cdot CH_2\text{-}CH_3$$

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[44] Ibid, p. 3873.

E_a = 68.6 kcal/mole. Subtracting this from 70.1, the value for the dissociation of ethyl benzene above, gives a value of 1.5 kcal/mole for the stablization of a developing radical by a methyl group. Using the same procedure as above, and employing the value of 1.1 kcal/mole for the cis-dimethyl interaction[27], a value of 60.1 kcal/mole is obtained for the geometric isomerization of cis-1,2-dimethylcyclopropane, in reasonable agreement with the experimental value of 59.4 kcal/mole[27].

It must be remembered that there are approximations involved in assuming energy additivity and in the models chosen, and that only rough correlations may be expected in these calculations. Even so, the above correlations support the hypothesis of a diradical intermediate for all of the geometric isomerizations.

The frequency factor of $10^{11.2}$ reflects a large negative entropy of activation (-8.9 e.u.) which most likely is a result of loss of rotational freedom of the two phenyl groups. They must be held planar to the developing radicals for maximum electron delocalization.

The lack of competitive structural isomerization may be best rationalized by considering the radical delocalization into the aromatic ring. This stabilizing delocalization has the converse effect of decreasing the radical reactivity so that attendant 1,2 hydrogen abstraction must be considered a "high energy" process. It may be hypothesized that the olefin would not be produced from the diradical, but would arise via a concerted process. If so the phenyls would have far less effect on the structural transition state than they do on the geometrical one, and thus the energy

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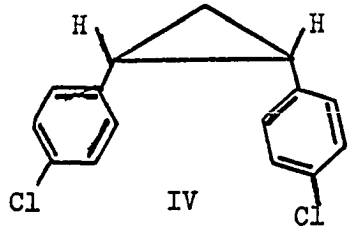
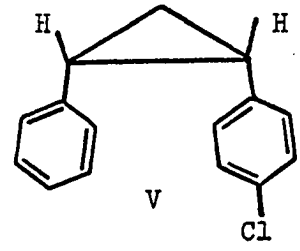
[27] M. C. Flowers and H. M. Frey, op. cit., p. 122.

of activation for structural isomerization would be effectively above the amount of energy available at the temperatures used for this work. This possibility seems the lesser likely of the two, although no differentiation between the two mechanisms is possible from the results in this thesis.

The two diarylcyclopropanes IV and V were synthesized by the same



IV



V

procedure as used for 1,2-diphenylcyclopropane. Determination of the rates of geometrical isomerization of cis-IV at four temperatures (169.2, 184.8, 196.3 and 219.7° C.) yielded

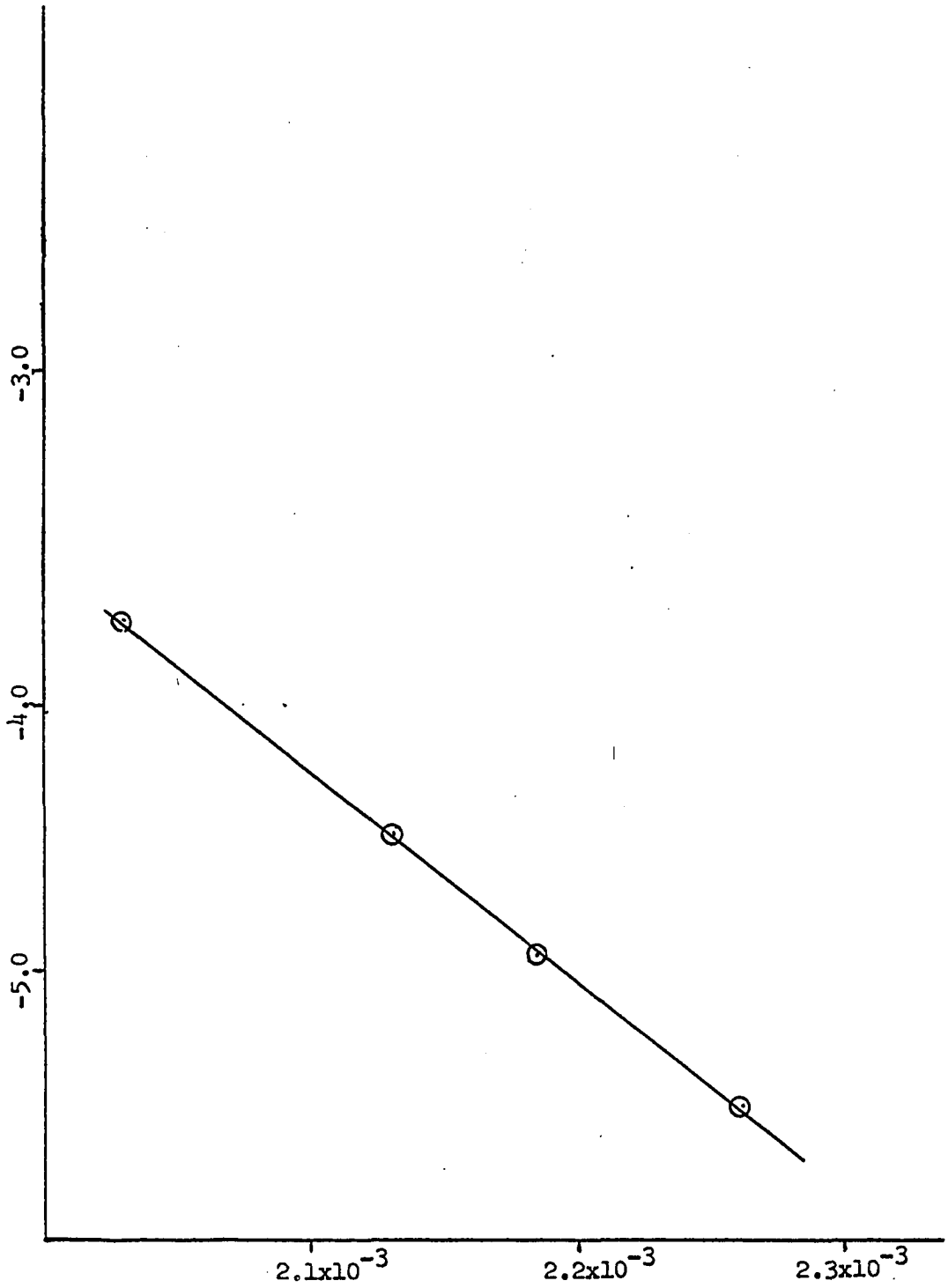
$$k_g = 10^{12.5 \pm 0.4} \exp(-36{,}400 \pm 800/RT).$$

Cis-V at four temperatures (161.9, 186.5, 196.4, and 220.0°C.) yielded

$$k_g = 10^{12.5 \pm 0.5} \exp(-36{,}800 \pm 1{,}000/RT).$$

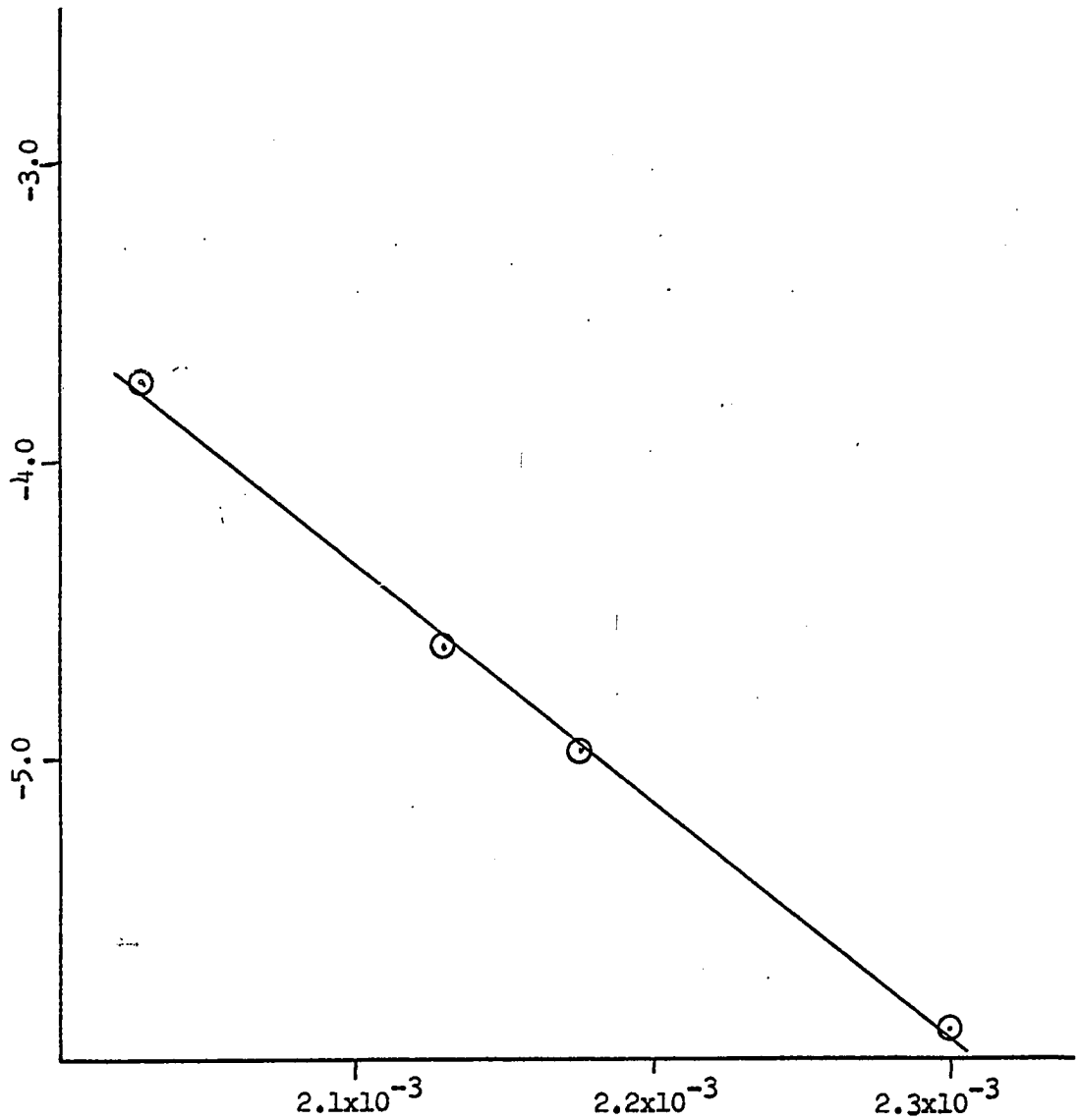
The Arrhenius parameters are seen to be identical within experimental error. It is an unexpected result that these energies of activation are higher than that for the diphenyl compound. (see Figs. XII and XIII). The equilibrium constants for these cis-trans isomerizations were found to be the same as for the diphenyl compound, namely 10.0 ± 0.5 at 193° C.

Fig. XII. Log k_g *versus* 1/T (°K) for *cis*-1,2-di-(4-chlorophenyl) cyclopropane



log k_g <u>versus</u> 1/T (°K) for <u>cis</u>-1,2-di-(4-chlorophenyl) cyclopropane

Fig. XIII. Log k_g *versus* 1/T (°K) for *cis*-1-phenyl-2-(4-chlorophenyl)-cyclopropane



log k_g <u>versus</u> 1/T (°K) for <u>cis</u>-1-phenyl-2-(4-chlorophenyl)-cyclopropane

Kinetic results by Leigh, Sehon and Szwarc[45] on the pyrolysis of substituted benzyl bromides indicate that any substituent on the benzene ring

$$C_6H_5\text{-}CH_2\text{-}Br \xrightarrow{\Delta} C_6H_5\text{-}CH_2\cdot + Br\cdot$$

will stablize the benzylic radical, although the authors did not come to that specific conclusion. The relative rates of reduction of substituted benzyl bromides (and some chlorides) with Cr(II) by Kochi and Davis[46] were

$$C_6H_5\text{-}CH_2\text{-}Br + Cr(II) \longrightarrow C_6H_5\text{-}CH_2\cdot + Cr(III)Br$$

also found to be slightly faster than benzyl bromide itself. For a p-Cl substituent the rate increase was by a factor of 1.3 (benzyl bromide) (1.26, benzyl chloride). These results indicate that IV and V should react with a lower energy of activation than their diphenyl analog. However it may be that an increased stabilization of the transition state is counterbalanced by other effects which tend to stabilize the reactant ground state. Substitution of chlorine for hydrogen on the phenyl rings increases the masses of these groups by ~50%. This should have a bond strengthening effect in that more energy would be needed to reach the

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[45] C. H. Leigh, A. H. Sehon and M. Szwarc, Proc. Roy. Soc., A209, 97 (1951).

[46] J. K. Kochi and D. D. Davis, Nature, 202, 690 (1964).

required vibrational amplitude for bond breakage (vibrational inertia). Another possible bond strengthening effect is suggested by consideration of the relative group electronegativities of the phenyl and 4-chlorophenyl groups. Kharasch[47] in a classic study of the relative rates of hydrolysis of substituted benzyl mercurials concluded that the electronegativity of a phenyl substituent was greater than that of a 4-chlorophenyl substituent. The same conclusion was reached by Brown[48] in a study of relative bond moments in simple molecules containing these groups. If this order is indeed correct then the 4-chlorophenyl substituents on the cyclopropane would allow for stronger ring C-C bonds relative to the phenyl substituents. This follows from increased orbital overlap from higher electron density in the bonding orbitals.

The rate constants for geometric isomerization of the diarylcyclopropylacetates were not determined, however observations of the NMR changes of these compounds relative to the diarylcyclopropanes on heating for various lengths of time have indicated that the isomerization of the cyclopropylacetates is a faster process. The equilibrium constants for the cis trans isomerizations in the cyclopropylacetates were approximately 1.5.

An attempt was made in the earlier stages of this work to effect the geometric isomerization of cis-1,2-diphenylcyclopropylacetate by photolysis. The irradiation was carried out in a quartz vessel in hexane solvent. Many products were obtained. Most likely photo-cleavage of the acetate

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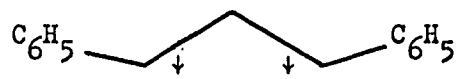
[47] M. S. Kharasch, J. Am. Chem. Soc., 48, 3130 (1926).

[48] H. C. Brown, J. Am. Chem. Soc., 61, 1483 (1961).

function led to these results. Further experiments were not performed.

Hammond and co-workers[49] have recently reported the sensitized reversible cis-trans photoisomerization of 1,2-diphenylcyclopropane. This reaction likely proceeds through a triplet diradical, as opposed to



the singlets likely involved in the thermolysis. Even though this should be a potentially trappable (long-lived) diradical, no trapped intermediates were reported.

Part II: Synthesis of 1,2-diarylcyclopropanols

There are now available several convenient methods of synthesizing cyclopropanols[41]. However at the time this work was undertaken most of the routes were not successful in producing pure stereoisomeric cyclopropanols, leading either to only one isomer or to a mixture of cis and trans cyclopropanols, whose separation would be indeed inconvenient.

A promising route appeared to be through cyclopropylacetates produced by a method reported in a recent communication by Freeman[42]. This method (see Fig. X), a lead tetraacetate oxidation of substituted pyrazolines,

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[41] C. H. DePuy, G. M. Dappen, K. L. Eilers and R. A. Klein, op. cit.

[42] J. P. Freeman, op. cit., p. 885.

[49] G. S. Hammond, P. Wyatt, C. D. DeBoer and N. J. Turro, J. Am. Chem. Soc., 86, 2532 (1964).

was able to produce directly cis and trans substituted cyclopropylacetates, more specifically in this case, 1,2-diarylcyclopropylacetates.

Even so, the large predominance of the cis-1,2-diarylcyclopropylacetates (70-80%) in the reaction product, along with the inability of obtaining complete separation by fractional distillation, made the production of the trans-cyclopropanols a rather low yield process.

However the discovery during the initial stages of this work that these cyclopropylacetates undergo cis-trans thermal equilibration to an approximately 60/40 (trans/cis) mixture, has offered a rather unique procedure for obtaining more difficultly accessible isomers of not only cyclopropylacetates but perhaps other types of substituted cyclopropanes. It should be possible to convert any one isomer almost entirely to another (assuming the equilibrium to be convenient). Since the high vacuum distillations normally reach temperatures at which either no or extremely slow isomerization takes place on the column, fractionation followed by thermal equilibration of the undesired isomer, refractionation, and even more cycles if necessary, should accomplish this conversion. This process indeed proved applicable for the diphenylcyclopropylacetate in obtaining quantities of the trans isomer (see below).

These cyclopropylacetates (except for two exceptions) were readily reduced by established means[41] to the cyclopropanols. These cyclopropanols were synthesized in order to provide compounds whose reactions might yield information of importance in determining the mechanisms of the acid and base catalyzed isomerizations of cyclopropanols to ring opened ketones.

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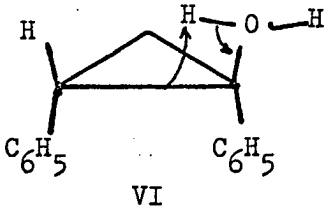
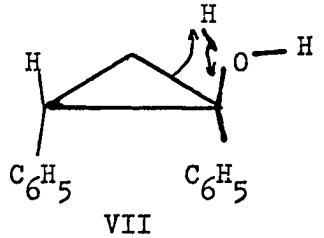
[41] C. H. Depuy, G. M. Dappen, K. L. Eilers and R. A. Klein, op. cit.

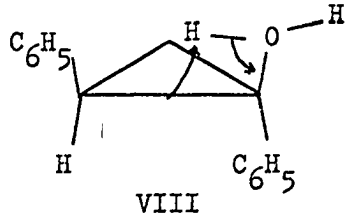
The acid catalyzed rearrangement is a bimolecular reaction[50] and presumably involves protium attack on the ring electrons. However one important possibility has not been ruled out and the compounds synthesized here may provide such information. The most basic spot in the cyclopropanol is the -OH group. It is likely that this group is protonated, however the importance of this bonded proton in determining the course of the reaction is unclear. It may be that a direct proton transfer from the -OH to the ring is of importance. If so, it might be expected that the reaction would be influenced by a β-phenyl group in either a <u>cis</u> or <u>trans</u> configuration to the -OH. This influence may very well be reflected in a shift of the ratio of products in going from <u>cis</u> to <u>trans</u> reactants. For instance the ratio of VI to VII should be reflective of inherent bond



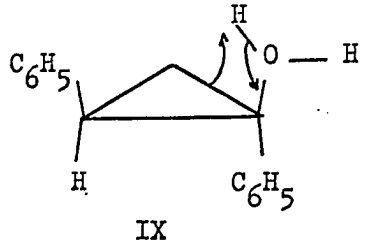
VI



VII



VIII



IX

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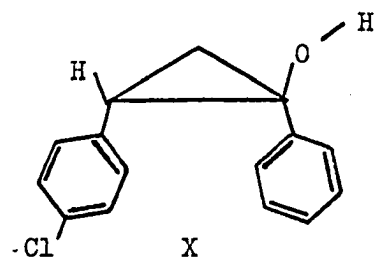
[50] C. H. DePuy and F. W. Breitbeil, J. Am. Chem. Soc., <u>85</u>, 2176 (1963).

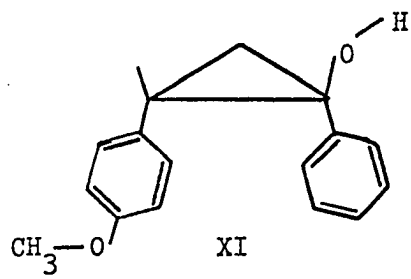
reactivities. However in considering VIII and IX one might expect the bulky phenyl group to inhibit VIII sterically and as such favor IX in the ratio of products.

This series of compounds with the 2-phenyl being variously substituted also provides for a study of the electronic supply and demand characteristics of the reaction at carbon 2. The correlation of such electronic influence is well grounded[51].

Of the cyclopropanols which were proposed to synthesize, 1-phenyl-2-(4-chlorophenyl)cyclopropanol (X) and its p-methoxy analog (XI) were not able to be made. Evidently the increased acidity of X due to the inductive



X



XI

effect of the chlorine group has made this compound completely unstable under conditions in which the phenyl and p-tolyl analogs are stable and give good yields. XI did yield some cyclopropanol as evidenced by IR spectra, however much ketone was present and no successful attempt at separation could be performed. This situation was reproducible. It is not clear why these difficulties occur.

The synthetic scheme (Fig. X) was a very convenient one. Many substituted benzaldehydes are readily available, as is acetophenone. With the addition of hydrazine and lead tetraacetate to this list, a variety

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[51] L. P. Hammett, Chem. Rev., 17, 125 (1935).

of cyclopropanols can be made inexpensively in quantity.

The initial condensation normally proceeds slowly requiring at least 24 hours. The solution acquires the yellow color attributable to the chalcone. The chalcone is best purified at this point because unreacted ketone and aldehyde will form azines with hydazine which will carry through and create problems of purification of the cycloprophylacetates.

After pyrazoline formation it has been found that haste is required in the work-up. A very exothermic decomposition of aryl substituted pyrazolines occurs in the presence of oxygen. Only 5-10 minutes are required to complete this decomposition if dry or damp crystals are left in the presence of oxygen. The most convenient solution is to forego purification and effect immediate lead tetraacetate oxidation.

The procedure for converting some cis isomer to trans is very straightforward. A spinning band distillation yielded initial fractions of cis isomer. The later fractions were trans. The fractions containing cis and those containing a mixture of isomers were placed in a round bottom flask with a reflux condenser and under nitrogen. The pot was heated for 2 days at 200°C. The mixture equilibrated over this time and was redistilled. More essentially pure fractions of trans isomer were obtained and these were combined with the trans initially obtained. If more trans had been desired, the process could have been repeated.

A very important procedure during the methyl lithium reduction is pre-acid washing of all glassware to be in contact with cyclopropanol. This procedure alone appears to increase the yield from 50-60% to 70-80%.

EXPERIMENTAL

Part I: 1,2-diarylcyclopropanols

Preparation of Materials

The following procedure was used to synthesize each of the substituted 1,2-diarylcyclopropanols used in this investigation and will be written for the general case.

Benzalacetophenones[52] One mole (120 grams) of acetophenone was combined with one mole of the appropriate substituted benzaldehyde in a 1 liter 2 necked round bottom flask, equipped with condenser and mechanical stirrer. To this was added 10 grams NaOH in 100ml water. The reaction pot was water cooled. The reaction was stirred for 24 hours and then neutralized with dil. HCl. The organic products were extracted with diethyl ether. The ether layer was washed with dil. $NaHCO_3$ and water. The solution was dried over anhydrous $MgSO_4$ and then filtered, and the solvent removed. Normally the substituted benzalacetophenones crystallized at this point and were recrystallized from absolute ethanol. However if crystals did not form, the oil was taken up in absolute ethanol from which the crystals formed in all cases. Yields averaged 55-65%.

3,5-diaryl-Δ^2-pyrazolines[43] The substituted benzalacetophenones prepared above were used in this reaction. Equimolar quantities of the appropriate benzalacetophenone and hydrazine hydrate were taken up in 1

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[43] S. G. Beach, J. H. Turnbull and W. Wilson, op. cit., p. 4686.

[52] H. Gilman and A. H. Blatt, Organic Syntheses, Coll. Vol. 1, 2nd edition, John Wiley and Sons, Inc., London, p. 78, (1956).

liter of absolute ethanol and this solution placed in a 2 liter 1 neck round bottom flask, fitted with a reflux condenser. The reaction was refluxed for 1 hour and the ethanol removed by distillation. The pyrazoline in all cases crystallized at this point. The crystals were filtered with a Buchner funnel, using a rubber dam. Precautions must be taken with aryl substituted pyrazolines due to their sensitivity to air oxidation. When the crystals were dry they were immediately dissolved in methylene chloride, without further purification, for use in the next reaction. Yields were essentially quantitative in all cases.

Formation and pyrolysis of 1-acetoxy-3,5-diaryl-Δ^2- pyrazolines

The following procedure is a general method of synthesizing cyclopropylacetates reported by Freeman[42]. An amount of lead tetraacetate equimolar to the benzalacetophenone used to make the 3.5-diaryl-Δ^2-pyrazoline above was used. A slurry of the lead tetraacetate and methylene chloride was placed in a 3 liter 3 neck round bottom blask equipped with condenser, mechanical stirrer and addition funnel. Using a cold water bath to hold the pot temperature at 15° C., the methylene chloride solution of the appropriate 3,5-diaryl-Δ^2-pyrazoline was slowly added to the slurry. The reaction was heated at flux for 2 hours following the addition. Water was added to destroy any remaining lead tetraacetate, the methylene chloride layer was then separated and washed until neutral with dil. $NaHCO_3$ and water. The solution was washed with saturated NaCl solution and dried over anhydrous $MgSO_4$. Removal of the solvent left the pyrazolineacetates, but in no case were these isolated and purified. The product obtained was

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[42] J. P. Freeman, op. cit., p. 885.

pyrolyzed in a round bottom flask fitted with a reflux condenser in turn attached to a bubbler to follow nitrogen evolution. A temperature of 190-200° C. was held until the nitrogen evolution stopped.

Cis and trans-1,2-diphenylcyclopropylacetate The crude product obtained from the above reaction series was induced to crystallization from hexane and only the cis isomer crystallized. The solvent was distilled from the mother liquor and the remaining product fractionally distilled. The first fraction yielded pure cis-1,2-diphenylcyclopropylacetate after two recrystallizations from hexane. Each of the remaining fractions was shown by NMR to be a mixture of cis and trans products. These were combined and refractionated through a 36" Nester-Faust Spinning Band Distillation Column. Fractions boiling at 105-106°C (0.1mm) were pure cis-1,2-diphenylcyclopropylacetate and those at 112-113°C (0.1 mm) were pure trans isomer, cis and trans referring to the phenyl substituents. Both isomers were crystallized from hexane. Attempts were made to separate the isomers by elution chromatography on Woelm grade #3 alumina and also on silica gel without success.

Cis-1,2-diphenylcyclopropylacetate, m.p. 52.0-52.5°C. (lit. m.p. 53.0-53.5°C)[42]. b.p. 105-106°C (0.1 mm); 145°C (0.35 mm).

Trans-1,2-diphenylcyclopropylacetate, m.p. 74.5-75.0°C. b.p. 112-113°C (0.1 mm). Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.91; H, 6.52*.

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[42] J. P. Freeman, op. cit., p. 885.

*Micro-analyses by Weiler and Strauss Microanalytical Laboratory, 164 Banbury Road, Oxford, England.

Cis and trans-1-phenyl-2-(4-methylphenyl)cyclopropylacetates

The mixture of isomers obtained by the procedure described above, but starting with p-tolualdehyde, was crystallized from hexane. Only the cis isomer crystallized. The product remaining in the mother liquor was fractionally distilled through a Nester-Faust 36" Spinning Band Distillation Column. Pure fractions were not obtained; however fractions boiling in the range 105-110°C (0.1 mm) were shown by GPC to be 90% cis and 10% trans isomer. Fractions boiling in the range 120-125°C (0.1 mm) were 90% trans and 10% cis. Crystallization and two recrystallizations from hexane of each of the sets of fractions yielded pure isomers. Final purification was effected by sublimation at 50°C and 0.1 mm pressure.

Cis-1-phenyl-2-(4-methylphenyl)cyclopropylacetate, m.p. 73.0-75.0°C. Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.18; H, 6.81. Found: C, 80.20; H, 6.90.

Trans-1-phenyl-2-(4-methylphenyl)cyclopropylacetate, m.p. 75.0-76.5°C. Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.18; H, 6.81. Found: C, 81.54; H, 6.96.

Cis-1-phenyl-2-(4-chlorophenyl)cyclopropylacetate The cis isomer of 1-phenyl-2-(4-chlorophenyl)cyclopropylacetate was obtained from the lead tetraacetate oxidation of the corresponding pyrazoline by crystallization of the crude product from hexane at 0°C. Recrystallization from hexane and subsequent sublimation yielded pure cis isomer. No trans isomer was obtained pure, however it was present in the mother liquor. The pure cis isomer had m.p. 74.5-75.5°C. Anal. Calcd. for $C_{17}H_{15}O_2Cl$: C, 71.21; H, 5.27. Found: C, 70.99; H, 5.32.

Cis-1-phenyl-2-(4-methoxyphenyl)cyclopropylacetate Crystallization of the crude product from hexane yielded the cis isomer. Recrystallization and sublimation yielded pure product. m.p. 64.5-66.0°C. Anal.

Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C 76.25; H, 6.65.

Cis and trans-1,2-diarylcyclopropanols[41]

Methyl Lithium To a 250 ml 3 neck round bottom flask fitted with N_2 inlet, condenser, addition funnel and magnetic stirrer 150 ml anhydrous diethyl ether (distilled from Lithium aluminum hydride) was added. This glassware had previously been flamed dry under a flow of N_2. To the ether was added 2 grams (0.29 mole) lithium wire, cut into small pieces. With magnetic stirring, 30 grams (0.21 mole) methyl iodide in 30 ml ether was added dropwise through the addition funnel, just fast enough to maintain reflux. A N_2 atmosphere was maintained. The contents of the flask were stirred for an additional 15 minutes after the addition was complete and then filtered through a glass wool plug into a 250 ml addition funnel which had previously been flamed dry under N_2. Any lithium hydroxide or nitride present was allowed to settle until the solution cleared. The sediment was removed through the stopcock of the funnel. Aliquots (1 ml) were titrated with standardized dil. HCl solution.

Acetate reduction A 250 ml 3 neck round bottom flask equipped with magnetic stirrer, condenser and N_2 inlet was flamed dry under N_2 flow. To 100 ml anhydrous ether was added the cyclopropylacetate to be reduced (usually 3-5 grams). The addition funnel containing the methyl lithium was placed in the third inlet position. A N_2 atmosphere was maintained. The calculated amount (2 molar equivalents) of methyl lithium/ether solution was added dropwise to maintain reflux. The reaction was stirred an

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[41] C. H. DePuy, G. M. Dappen, K. L. Eilers and R. A. Klein, op. cit.

additional 15 minutes after the addition was complete. To a 1 liter 3 neck round bottom flask equipped with mechanical stirrer, addition funnel and condenser was added 200 ml water and enough boric acid to saturate the solution and leave a large excess in suspension. The lithium alkoxide/ether solution was added to this mixture at a rapid rate maintaining maximum stirring speed. The 1 liter flask used here and all additional glassware to be used in the work-up should be prewashed with 5% HF followed by distilled water. The boric acid-ether solution was filtered through a large scintered glass filter to remove undissolved boric acid. The ether layer was separated. The water layer was washed two times with ether and the combined ether extracts washed with water. The ether layer was dried over anhydrous $MgSO_4$. All but about 20 ml of the ether was removed by distillation using a steam bath. The remaining solution was transferred to a 100 ml beaker and 2 ml of hexane* added. The remaining ether was evaporated under a stream of air filtered through a cotton plug. Hexane was added dropwise so that as the ether was evaporated the cyclopropanol would be left in 2-3 ml of hexane. Usually the cyclopropanol crystallized readily under these conditions. The hexane was filtered from the crystals and they were dissolved in a small amount of ether and the same process repeated. This was repeated until an IR of the dry crystals had no carbonyl absorption. The crystals were stored at -5°C in a tightly stoppered polyethylene bottle. Yields averaged 70-80%. These cyclopropanols are unstable

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*Hexane was purified by washing with conc. H_2SO_4, water, drying over $MgSO_4$ and distilling.

unless kept in the cold, and for this reason were not sent for analysis.

Cis-1,2-diphenylcyclopropanol, m.p. 75-77°C.

Trans-1,2-diphenylcyclopropanol, m.p. 69-71°C.*

Cis-1-phenyl-2-(4-methylphenyl)cyclopropanol, m.p. 75-77.5°C.*

Trans-1-phenyl-2-(4-methylphenyl)cyclopropanol, m.p. 62-64°C.*

Cis-1-phenyl-2-(4-chlorophenyl)cyclopropanol Cautious attempts were made three times to reduce the corresponding acetate to this cyclopropanol. Each time only ring opened ketone was obtained.

Cis-1-phenyl-2-(4-methoxyphenyl)cyclopropanol Two attempts were made to obtain this cyclopropanol by reduction of the acetate. Each time an oil was obtained which was indicated by IR to be a mixture of ring opened ketone and the cyclopropanol. This mixture resisted all attempted methods of separation.

Dioxane Dioxane was purified by heating at reflux over NaOH pellets for several days, distillation from NaOH, then redistillation through a Todd Distillation Assembly. The dioxane was stored by heating at continued reflux in a nitrogen atmosphere over NaOH and distilled as needed.

Perchloric Acid Perchloric acid (7.322 N) was made with distilled water and standardized by titration against standard NaOH solution. Composition table show that 7.3 N $HClO_4$ is 51.47% $HClO_4$ be weight, and that this solution has a density of 1.4285. Calculations indicate that 57.8 ml of 7.322 N $HClO_4$ contains 40 ml H_2O. This volume was used in making up 60/40 dioxane-water solutions for ring opening experiments.

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*Softened and yellowed during melting.

Hydrochloric Acid Concentrated hydrochloric acid (37%) was added to conductance water to make a solution approximately 2.5N. Titration with standard NaOH established the solution as 2.460 N. From the density and % HCl by weight for this concentration it was calculated that 41.8 ml of 2.460 N HCl contains 40.0 ml H_2O.

Ring opening experiments

Acid In all cases 60 ml dioxane was added to the calculated amount of either hydrocholoric or perchloric acid in order to make dioxane/water as 60/40 by volume. Volumes were measured with a buret. A regulated oil bath was held at either 50.2°C or 90.0°C for these experiments.

Base Base opening experiments were done in 95% ethanol with added aqueous NaOH.

Product Analyses Product analyses were by GPC retention time on a 5% SE-30 column against known compounds on hand and/or by NMR and IR.

Part II: Thermal Geometric Isomerization of Diarylcyclopropanes

Preparation of Materials

Cis and trans-1,2-diphenylcyclopropane These compounds were prepared by the method of Kishner[53] and Beach, Turnbull and Wilson[43] by P. Gettys[54]. The method is a pyrolysis of 3,5-diphenyl-Δ^2-pyrazoline over KOH. The isomers were separated on a Nester-Faust 36" Spinning Band

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[43] S. G. Beach, J. H. Turnbull and W. Wilson, op. cit., p. 4686.

[53] N. Kishner, Zhur. Russ. Fiz.-Khim. Obscheh., 47, 1104 (1915).

[54] P. Gettys, Senior Research Program, Iowa State University of Science and Technology, 1963.

Distillation Column[55]. Isomeric structure was confirmed by NMR. The trans isomer yielded an A_2B_2 type multiplet, with one half broadened as is typical of benzylic protons. $\delta_A = 1.27$; $\delta_B = 2.07$. The cis isomer yielded an ABX_2 type multiplet with the X_2 portion broadened from being benzylic. $(\delta_A + \delta_B)/2 = 1.36$; $\delta_X = 2.39$. The chemical shift values above are only approximate since a complete analysis was not done.

Cis-1,2-diphenylcyclopropane, m.p. 37.0-37.5°C* (lit. m.p. 38.0-38.5°C)[55] b.p. 95°C (0.08 mm) (lit. b.p. 126.5-129°C (3.8 mm))[55].

Trans-1,2-diphenylcyclopropane, b.p. 100-101°C (0.08 mm) (lit. b.p. 144-145°C (3.8 mm))[55].

Cis and trans-1,2-(4-chlorophenyl)cyclopropane The method is the same as for the diphenyl compound above. A mixture of 70 gms (0.5 mole) p-Cl-benzaldehyde and 77 gms (0.5 mole) p-Cl-acetophenone was condensed with NaOH to yield 1,3-bis(4-chlorophenyl)propenone (see Experimental, Part I). The pyrazoline was made in absolute ethanol using 25 gms (0.5 mole) hydrazine hydrate. The ethanol was distilled and the residue dried on a Rotovac. Anhydrous KOH (1.5 gms) was added to the impure pyrazoline, the atmosphere replaced by N_2 and the pot heated at 185°C in an oil bath

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[55] D. Y. Curtin, H. Gruen, Y. G. Hendrickson and H. E. Knipmeyer, J. Am. Chem. Soc., 83, 4838 (1961).

*All melting points were determined with either a Fischer-Johns melting point block or a Hershberg melting point apparatus and are reported here uncorrected.

heated with a hot plate*. Nitrogen was evolved and observed by a bubbler. After N_2 evolution stopped, the pot was cooled and the contents dissolved in methylene chloride. The methylene chloride solution was extracted with dil. HCl and dried over anhydrous $MgSO_4$. The solvent was removed and the residue crystallized immediately. A triangular fractional recrystallization procedure with 95% ethanol such as that used by James[56] for separating rare earth salts yielded pure isomers. The NMR patterns of these isomers were the same as for the diphenylcyclopropanes above, and were consistent with the desired products.

Trans: $\delta_A = 1.27$, $\delta_B = 2.04$; Cis: $(\delta_A + \delta_B)/2 = 1.32$, $\delta_X = 2.62$. There is some discrepancy in the melting points below and those reported by Overberger and Anselme[57], however combustion analyses agreed well with the theoretical, and the compounds were shown to be pure by GPC.

Cis-1,2-(4-chlorophenyl)cyclopropane, m.p. 64.0-64.7°C (lit. m.p. 50-52°C[57]. Anal. Calcd. for $C_{15}H_{12}Cl_2$: C, 68.46; H, 4.60. Found: C, 68.33; H, 4.42.

Trans-1,2-(4-chlorophenyl)cyclopropane, m.p. 83.3-83.8°C (lit. m.p.

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[56] C. James, J. Am. Chem. Soc., 30, 184 (1908).

[57] C. G. Overberger and J. Anselme, J. Am. Chem. Soc., 86, 658 (1964).

*Caution must be exercized here for the base-catalyzed pyrolysis is very exothermic and very rapid if heated above 190°C.

83.0-83.5°C[57]. Anal. Calcd. for $C_{15}H_{12}Cl_2$: C, 68.46; H, 4.60. Found: C, 68.44; H, 4.43.

Cis and trans-1-phenyl-2-(4-chlorophenyl)cyclopropane These compounds were prepared by the same procedure as for the dichloro compounds above. They were separated by fractional distillation on the 36" Nester-Faust Spinning Band Distillation Column. NMR spectra of both isomers yielded the ABXY type multiplets expected.

Cis-1-phenyl-2-(4-chlorophenyl)cyclopropane, b.p. 94-95°C (0.07 mm). Anal. Calcd. for $C_{15}H_{13}Cl$: C, 78.77; H, 5.73. Found: C, 78.57; H, 5.86.

Trans-1-phenyl-2-(4-chlorophenyl)cyclopropane, b.p. 107-108°C (0.07 mm). Anal. Calcd. for $C_{15}H_{13}Cl$: C, 78.77; H, 5.73. Found: C, 77.98; H, 5.85.

Kinetics

Regulatory equipment A 5" o.d. pyrex glass jar (6" deep) was fitted into a larger wooden box which was then filled with mica for insulation. The box was wrapped for further insulation, and the whole apparatus placed in a draft free hood. The jar was filled with silicon oil. Its circulation was maintained with a mechanical stirrer.

The bath was heated with two 125 watt heating blades. One was connected to a Variac which was adjusted so that this one heating device would keep the bath at a "background" temperature of 140°C. The other was connected to a Niatrol Proportional Control from Niagra Electron Labs, Andover, New York. The temperature difference between 140° and the

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[57] Ibid, p. 658.

desired bath temperature was maintained with this control. A thermocouple sensor supplied with the "Niatrol" was immersed in the bath just "downstream" from the two heaters. Occasional checks with a Beckman thermometer indicated that over a period of several hours the temperature was easily maintained at ± 0.05°C.

Physical measurements The bath temperature for each kinetic run was determined with a National Bureau of Standards calibrated thermometer if the temperature was below 200°C. Both calibration and stem corrections were used. If the temperature was above 200°C, an Anschutz* thermometer was used.

Time was measured with an electronic timer from Precision Scientific Co., Chicago, Illinois.

Peak areas for gas phase chromatograms were measured with a planimeter.

Preparation of samples Samples were heated in 1 1/2" Pyrex tubes sealed on one end and fitted on the other with tight fitting rubber septums. The atmosphere in the tubes was replaced by nitrogen. Each tube was carefully cleaned before use with 5% HF solution, washed with distilled water, acetone and then ether. It was then flamed dry under a stream of nitrogen. During the run the tubes were supported in the bath to within 1/3" of the top with a thermometer clamp. In each case pure cis isomer was used as the starting material.

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*Anschutz thermometers are a set of accurately calibrated thermometers covering -10-360°C in 60° increments.

Kinetic Analyses The integrated first order rate equation is

$$2.303 \log \frac{a_o}{a_o - x} = kt$$

where a_o = initial concentration of reactant

x = concentration of product at time = t

k = first order rate constant.

This equation may be rewritten

$$2.303 \log \frac{1}{1 - a_o/x} = kt$$

If we define

$$R = \frac{\text{concentration of reactant}}{\text{concentration of product}}$$

then

$$R = \frac{a_o - x}{x} \qquad (7)$$

or

$$x/a_o = 1/(R+1)$$

Substituting this result into (7) and rearranging we find

$$2.303 \log (R+1)/R = kt$$

This is the form of the rate equation used in this work. For this equation to hold, the reverse rate of the equilibrium must be negligible (see Discussion).

Chemical Analyses Gas phase chromatography was chosen as the method of obtaining the value of R for each kinetic point. The ratio of

the areas of the peaks obtained gives R after correcting for the non-linearity of the detector. An Aerograph Model 600-C GPC from Wilkens Instrument and Research, Inc. was used for these kinetics. Its flame ionization detector was calibrated as discussed below. Purified N_2 was used as a carrier gas. It was found that a 5' column of either 5% Dow-11 or 5% SE-30 would effect all separations required within convenient temperature ranges. The conditions for each diarylcyclopropane were established for separation of the isomers. The possibility of isomerization on the column was in each case eliminated by injecting a sample of pure cis isomer and observing no trans peak.

Calibration of Detector To correct for the non-linearity of the detector, samples of known isomer ratio but with an approximate 10:1 excess of cis isomer over trans were prepared. Pure cis and pure trans portions were individually weighed and combined; this combination was melted together if necessary and mixed well. Into 0.1 ml of solvent (cyclohexane or ether) 5.0 µl of the mixture was placed. With the attenuator on a standard (for this work) setting, 1 µl of this solution was injected and the ratio of areas on the chromatograph determined. The correction factor was determined from this area ratio and the known weight ratio. Kinetic point injection samples were prepared in the same way, namely by removing 5 µl from the reaction vial and injecting into 0.1 ml solvent. It must be assumed that there will be a small variation of this correction factor with the ratio, R, as the reaction proceeds. However this was considered negligible and the single correction factor for each diarylcyclopropane as determined above was used throughout each run. Also, small errors of this kind in R effectively cancel in the function

log (R+1)/R.

Calibration of Attenuator In order to determine the ratio when the trans isomer concentration was still very low, it was necessary to decrease the attenuation for the trans peak while keeping the setting at the "standard" setting for the cis peak. The changes were calibrated against an internal standard.

Results The kinetic runs were carried out by taking samples (as described above) at several time intervals and analyzing for the cis/trans ratios, using all the correction factors described above to obtain the numbers. 2.303 log (R+1)/R was plotted versus t (t = time) to insure that a straight and not a curved line was obtained. If so k was determined by the method of least squares. Tables II - XIII give the numerical data for each run.

Table II. Geometric isomerization of cis-1,2-diphenylpropane (Temperature = 220.1°C)

Point	Time (min.)	R	log (R+1)/R
1	27.83	2.15	0.16687
2	35.45	1.60	.21085
3[a]	43.32	0.87	---
4	50.38	1.26	.25374
5	57.57	1.03	.29466
6	64.72	0.88	.37107
7	92.50	0.57	.44003
8	107.66	0.45	.50816
9	121.62	0.41	.53644
10	138.26	0.34	.59562
			$k = 2.29 \times 10^{-4}$ sec^{-1}

[a]Point 3 omitted

Table III. Geometric isomerization of cis-1,2-diphenylcyclopropane (Temperature = 197.0°C)

Point	Time (min.)	R	log (R+1)/R
1	40.82	10.42	0.03980
2	51.74	8.44	0.04863
3	61.88	6.09	0.06603
4	74.85	5.65	0.07077
5	83.89	4.97	0.07961
6	96.58	4.13	0.09417
		$k^a = 3.71 \times 10^{-5}$ sec^{-1}	

[a]Determined by method of least squares

Table IV. Geometric isomerization of cis-1,2-diphenylcyclopropane (Temperature = 185.5°C)

Point	Time (min.)	R	log (R+1)/R
1	50.52	17.54	0.02408
2	83.00	11.24	0.03701
3	99.99	10.37	0.03998
4	120.63	9.66	0.04278
5	147.93	6.18	0.06513
6	183.26	4.175	0.09336
		$k^a = 1.82 \times 10^{-5}$ sec^{-1}	

[a]Determined by the method of least squares

Table V. Geometric isomerization of cis-1,2-diphenylcyclopropane (Temperature = 165.8°C)

Point	Time (min.)	R	log (R+1)/R
1	0	∞	0.00000
2	325	12.54	0.03332
3	584	8.51	0.04824

$k^a = 3.20 \times 10^{-6}$ sec^{-1}

[a]Determined by the method of least squares

Table VI. Geometric isomerization of cis-1,2-di-(4-chorophenyl)cyclopropane (Temperature = 219.7°C)

Point	Time (min.)	R	log (R+1)/R
1	1.03	87.11	0.00496
2	2.10	43.99	0.00977
3	3.18	27.59	0.01546
4	4.56	18.63	0.02271
5	6.15	13.43	0.03119
6	9.26	8.17	0.05013

$k^a = 2.11 \times 10^{-4}$ sec^{-1}

[a]Determined by the method of least squares

Table VII. Geometric isomerization of cis-1,2-di-(4-chlorophenyl)cyclopropane (Temperature = 196.3°C)

Point	Time (min.)	R	log (R+1)/R
1	7.33	82.31	0.00525
2	19.90	26.67	0.01599
3	26.17	18.89	0.02240
4	34.48	14.19	0.02958
5	46.30	10.68	0.03887
6	56.60	8.53	0.04816

$k^a = 3.33 \times 10^{-5}$ sec^{-1}

[a]Determined by the method of least squares

Table VIII. Geometric isomerization of cis-1,2-di-(4-chlorophenyl)cyclopropane (Temperature - 184.8°C)

Point	Time (min.)	R	log (R+1)/R
1	18.25	83.24	0.00519
2	40.25	38.12	0.01125
3	74.73	20.71	0.02048
4	89.94	15.61	0.02697
5	108.56	12.68	0.03297

$k^a = 1.16 \times 10^{-5}$ sec^{-1}

[a]Determined by the method of least squares

Table IX. Geometric isomerization of cis-1,2-(4-chlorophenyl)cyclopropane (Temperature = 169.2°C)

Point	Time (min.)	R	log (R+1)/R
1	56.9	119.8	0.00361
2	100.4	67.75	0.00636
3	156.6	27.96	0.01526
4	216.1	25.06	0.01699
5	268.6	19.88	0.02131
6	312.8	17.36	0.02432

$k^a = 3.09 \times 10^{-6}$ sec^{-1}

[a]Determined by the method of least squares

Table X. Geometric isomerization of cis-1-phenyl-2-(4-chlorophenyl)cyclopropane (Temperature - 220.0°C)

Point	Time (min.)	R	log (R+1)/R
1	1.09	253.9	0.00171
2	2.23	67.78	0.00636
3	3.57	34.03	0.01258
4	6.52	16.08	0.02620

$k^a = 1.74 \times 10^{-4}$ sec^{-1}

[a]Determined by the method of least squares

Table XI. Geometric isomerization of cis-1-phenyl-2-(4-chlorophenyl)cyclopropane (Temperature = 196.4°C)

Point	Time (min.)	R	log (R+1)/R
1	10.02	60.01	0.00718
2	22.34	26.61	0.01603
3	29.98	19.30	0.02194

$k^a = 2.40 \times 10^{-5}$ sec^{-1}

[a]Determined by the method of least squares

Table XII. Geometric isomerization of cis-1-phenyl-2-(4-chlorophenyl)-cyclopropane (Temperature = 186.5°C)

Point	Time (min.)	R	log (R+1)/R
1	15.65	83.49	0.00518
2	39.95	32.63	0.01311
3	67.20	19.53	0.02169

$k^a = 1.06 \times 10^{-5}$ sec^{-1}

[a]Determined by the method of least squares

Table XIII. Geometric isomerization of cis-1-phenyl-2-(4-chlorophenyl)-cyclopropane (Temperature - 161.9°C)

Point	Time (min.)	R	log (R+1)/R
1	52.70	225.1	0.00192
2	93.60	144.4	0.00299
3	159.10	100.2	0.00431
4	205.85	70.5	0.00612
5	251.65	54.47	0.00790
6	512.10	27.54	0.01549

$k^a = 1.22 \times 10^{-6}$ sec^{-1}

[a]Determined by method of least squares

Activation parameters Activation parameters were obtained by plotting log k versus 1/T (°K). The slope and intercept were obtained by the method of least squares. From these the activation parameters are readily calculated. Error terms for these parameters are obtained from the following equations[58]:

$$s_E^2 = \Sigma(Y - \hat{Y})^2/(n-2)$$

where Y = log k at T°

$\hat{Y}$ = least squares value of log k at T°

n = number of points

$$s_{b_1}^2 = s_E^2 / \Sigma(X - \bar{X})^2$$

where $\pm s_{b_1}$ = desired error term for slope

[58]B. Ostle, Statistics in Research, Iowa State University Press, Ames, Iowa, 1963, pp. 159-170.

$$X = 1/T$$

$$\overline{X} = (\Sigma 1/T)/n$$

$$s_{b0}^2 = s_E^2 \, (1/n + \overline{X}^2 \, / \, \Sigma(X - \overline{X})^2)$$

where s_{b0} = desired error term for intercept.

SUMMARY

The thermal geometric isomerizations of 1,2-diphenylcyclopropane, 1,2-di-(4-chlorophenyl)cyclopropane, and 1-phenyl-2-(4-chlorophenyl)cyclopropane have been studied. They are shown to undergo reversible isomerization in the temperature range 160-220°C., and to exhibit no side reactions. Their Arrhenius parameters are given and discussed.

Calculations are given which support a diradical intermediate for this cis-trans isomerization. The lack of competing structural isomerization to propylene systems, was attributed primarily to the delocalized nature of the benzylic radical.

Description is given of the synthesis of 1,2-diarylcyclopropanols and of their properties and chemical stability.

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