

1963

# Synthesis and reactions of substituted cyclopropanols

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SYNTHESIS AND REACTIONS  
OF SUBSTITUTED CYCLOPROPANOLS

by

Kenneth Lee Eilers

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DOCTOR OF PHILOSOPHY

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Approved:

Signature was redacted for privacy.

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Ames, Iowa

1963

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## INTRODUCTION

As cyclopropanol was shown to be isolable and as alkyl substituted cyclopropanols were being prepared and purified, we became intrigued with the possibility of using these alcohols for the study of some fundamental concepts. It appeared they would be ideal for a study of electrophilic substitution at saturated carbon, especially since a two prong attack on the problem appeared to be very possible.

Cyclopropanol was known to isomerize in basic media to propanol. As the most reasonable mechanism involves a carbanion we could examine the effect of solvent and substrate on the mode of protonation. If suitably substituted cyclopropanols could be synthesized, optical resolution might well be effected putting in our hands the most powerful tool for this type of study.

Secondly, cyclopropane derivatives are known to undergo substitution by acids, reportedly in a Markownikoff type addition. This has never been rigorously established but it is none the less quite interesting. Unfortunately, substitution and rearrangements possible in the reaction between acids and alkyl and aryl substituted cyclopropanes could make an exact and detailed analysis of reaction products difficult. Cyclopropanols would, on the other hand, if attacked by protons, give rise to a carbonium ion at or adjacent to the carbon atom bearing oxygen. This would lead to an aldehyde

or a ketone, depending on the alcohol, either directly or after a rearrangement of the carbon skeleton. These isomerization products would reduce the complexity of analysis and even facilitate analysis.

It was decided to attempt the preparation of some phenyl substituted cyclopropanols before proceeding. Alkyl substituted cyclopropanols were volatile liquids which are quite prone to isomerization. These properties make handling bothersome and quantitative work difficult. It was hoped that a phenyl substituent would stabilize the cyclopropanols and afford us with solid alcohols.

## HISTORICAL

All attempted preparations of cyclopropanol and substituted cyclopropanols prior to the last two decades have proven singularly unsuccessful. Huebner and Mueller<sup>1</sup> in 1871 and Tornoe<sup>2</sup> in 1891 attempted to cyclize 1,3-dichloropropan-2-ol with metallic sodium. Later, Aschan<sup>3</sup> tried a similar reaction with 1,3-dibromopropan-2-ol. In 1905 Kishner<sup>4</sup> treated cyclopropyl amine with nitrous acid and isolated only allyl alcohol, the only product isolated by all of these workers.

In 1907 Tiffeneau and Daufresne<sup>5</sup> reported the preparation of 2-*p*-methoxyphenylcyclopropanol from the reaction of 1-bromo-2-acetoxy-3-*p*-methoxyphenylpropane with alcoholic potassium hydroxide. It was claimed that the alcohol isomerized to 2-*p*-methoxypropanal upon distillation, treatment with acid or base or upon standing at room temperature.

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<sup>1</sup>Huebner, H. and Mueller, K., *Justus Liebigs Annalen der Chemie*, 159, 168 (1871).

<sup>2</sup>Tornoe, H., *Berichte der deutschen chemischen Gesellschaft*, 24, 2670 (1891).

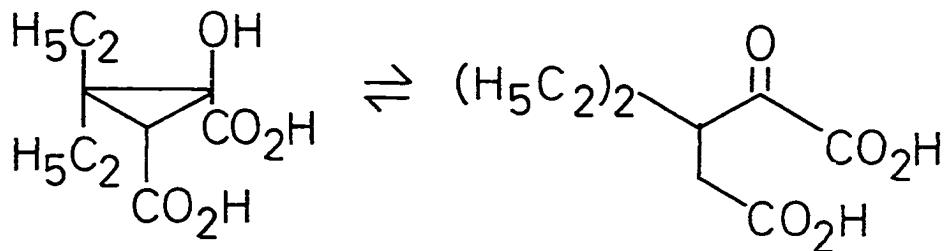
<sup>3</sup>Aschan, O., *Berichte der deutschen chemischen Gesellschaft*, 23, 1831 (1890).

<sup>4</sup>Kishner, N., *Chemisches Zentralblatt*, Series 1, 76, 1704 (1905).

<sup>5</sup>Tiffeneau, M. and Daufresne, M., *Comptes rendus hebdomadaires des seances de l'academie des science*, 144, 924 (1907).

Later<sup>6</sup>, they reported that it was not 2-p-methoxyphenylcyclopropanol that they had isolated but instead 2-methyl-2-p-methoxyphenylethanol. What really was isolated by these workers remains an unanswered question.

Ingold and Thorpe<sup>7</sup>, in a series of five papers, reported the preparation of a substituted cyclopropanol, 2,2-diethylcyclopropan-1-ol-1,3-dicarboxylic acid (A). This compound was supposedly in equilibrium with its tautomer, 3,3-diethyl-2-ketoglutaric acid (B). Wiberg<sup>8</sup> has unequivocally demonstrated, through the application of nuclear magnetic resonance spectroscopy (NMR), that these two compounds are in fact two stereoisomeric cyclic ethers (A' and B').

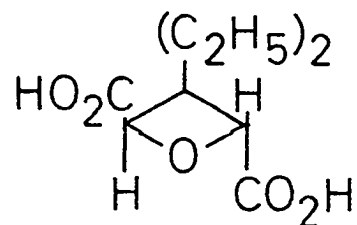
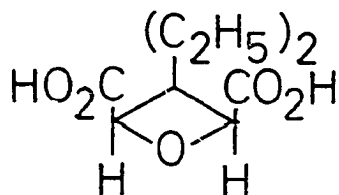


<sup>6</sup>Tiffeneau, M. and Daufresne, M., Comptes rendus hebdomadaires des seances de l'academie des science, 145, 628 (1907).

<sup>7</sup>(a) Ingold, C. K., Journal of the Chemical Society (London), 119, 305 (1921); (b) Deshapande, S. S. and Thorpe, J. F., Journal of the Chemical Society (London), 121, 1430 (1922); (c) Ingold, C. K., Journal of the Chemical Society (London), 121, 2676 (1922); (d) Bains, L. and Thorpe, J. F., Journal of the Chemical Society (London), 123, 1206 (1923); (e) Lanfear, E. W. and Thorpe, J. F., Journal of the Chemical Society, 123, 1683 (1923).

<sup>8</sup>Wiberg, K. B. and Holmquist, H. W., Journal of Organic Chemistry, 24, 578 (1959).





In 1942, while studying the effect of ethylmagnesium bromide on epichlorohydrin, Magrane and Cottle<sup>9</sup> isolated an alcohol which, by the process of elimination, had to be cyclopropanol. This method involves the reaction of epichlorohydrin with magnesium bromide and ethylmagnesium bromide in ether. Later, upon examining the reaction further, they discovered that ferric chloride was essential for the production of cyclopropanol and that magnesium bromide 1-bromo-3-chloro-2-propoxide could be substituted for epichlorohydrin<sup>10</sup>. The yields of cyclopropanol were low and the alcohol could never be isolated in a pure state. Acids, distillation and particularly bases readily converted cyclopropanol into its isomer, propanal, an inseparable impurity.

In 1951 Roberts and Chambers<sup>11</sup> repeated Cottle's work. They also prepared cyclopropanol from the air oxidation of cyclopropylmagnesium chloride and the hydrolysis of the

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<sup>9</sup>Magrane, J. K. and Cottle, D. L., *Journal of the American Chemical Society*, 64, 484 (1942).

<sup>10</sup>Stahl, C. W. and Cottle, D. L., *Journal of the American Chemical Society*, 65, 1782 (1943).

<sup>11</sup>Roberts, J. D. and Chambers, V. C., *Journal of the American Chemical Society*, 73, 3176 (1951).

resulting hydroperoxide. The yield in this case was very low, 3%, and again purification proved impossible. Derivatives prepared from the alcohol from both of these procedures were identical.

By treating 2,4-dibromo-2,4-diphenylpentan-3-one with so-called molecular silver or mercury in etheral solution Cogdell<sup>12</sup> reports the preparation of 2,3-dimethyl-2,3-diphenylcyclopropanone. This ketone supposedly yields 2,3-dimethyl-2,3-diphenylcyclopropanol, of unspecified configuration, when reduced with lithium aluminum hydride at 0°. Furthermore this cyclopropanol was reported to be converted into the corresponding chloride upon treatment with hydrogen chloride. The Grignard reagent was made from the chloride and carbonation of this yielded an acid which was identical to the acid formed from ethyl diazoacetate and 1,2-dimethyl-1,2-diphenylethene.

The first successful preparation and purification of cyclopropanol and monosubstituted cyclopropanols was reported by DePuy, et al.<sup>13</sup> Mahoney<sup>14</sup> prepared cyclopropanol by Cottle's method and by the lithium aluminum hydride reduction

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<sup>12</sup>Cogdell, J. F., Dissertation Abstracts, 19, 2751 (1959).

<sup>13</sup>DePuy, C. H., Mahoney, L. R. and Eilers, K. L., Journal of Organic Chemistry, 26, 3616 (1961).

<sup>14</sup>Mahoney, L. R., The Hydrolysis of Cyclopropyl Acetate. Unpublished Ph. D. Thesis. Ames, Iowa, Library, Iowa State University of Science and Technology, 1960.

of cyclopropyl acetate. He was able to obtain pure cyclopropanol by utilizing preparative vapor phase chromatography techniques, a development which started about the time of Robert's investigation. Dappen<sup>15</sup> has recently extended and improved upon Cottle's method to prepare cyclopropanol, 1-methylcyclopropanol, 2-methylcyclopropanol, 1-phenylcyclopropanol and, not too successfully, 2-phenylcyclopropanol. Further improvements have been made on this reaction by Klein who prepared, in addition, 1-p-methoxyphenylcyclopropanol and 1-p-toluylcyclopropanol and this work recently appeared in the literature<sup>16</sup>.

A review of the literature brings to light the unusual nature of the cyclopropane ring. Cyclopropane, per se, and derivatives of it undergo wide variety of reactions with radicals, acids and bases. Much of this work is incomplete or in need of re-examination so that few broad generalities can be made as to the course of reactions involving the three membered ring.

Walling<sup>17</sup> has re-examined the chlorination of cyclopropane and found that considerable ring opening does occur in

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<sup>15</sup>Dappen, G. M., Synthesis and Isomerization of Cyclopropanols. Unpublished Ph. D. Thesis. Ames, Iowa, Library, Iowa State University of Science and Technology, 1962.

<sup>16</sup>DePuy, C. H., Klein, R. A. and Dappen, G. M., Journal of Organic Chemistry, 27, 3742 (1962).

<sup>17</sup>Walling, C. and Fredricks, P. S., Journal of the American Chemical Society, 84, 3326 (1962).

contrast to the earlier published results of Roberts<sup>18</sup>. With the knowledge that Roberts' work is in error due to lack of suitable product analysis, the results of the reaction of cyclopropane with chlorine<sup>19</sup>, bromine<sup>20</sup>, iodine<sup>21, 22</sup> and methyl radicals<sup>23</sup> may well be questioned. Hammond<sup>24</sup> has found phenyl-, cyano- and acetylcyclopropane very inert toward free radicals and Haas and Schechter<sup>25</sup> have found nitrocyclopropane inert to acid, base, light, air, bromine in carbon tetrachloride and dilute potassium permanganate solution.

Alkyl- and arylcyclopropane derivatives give ring opened products when treated with Broensted-Lowry acids such that the carbon-carbon bond between the most and least substituted

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<sup>18</sup>Roberts, J. D. and Dirstine, P. H., Journal of the American Chemical Society, 67, 1281 (1945).

<sup>19</sup>Brown, H. C. and Borkowski, M., Journal of the American Chemical Society, 74, 1894 (1952).

<sup>20</sup>Kharasch, M. S., Fineman, M. Z. and Mayo, F. R., Journal of the American Chemical Society, 61, 2139 (1939).

<sup>21</sup>Benson, S. W. and Amano, A., Journal of Chemical Physics, 36, 364 (1962).

<sup>22</sup>Ogg, R. A., Jr. and Priest, W. S., Journal of Chemical Physics, 7, 736 (1939).

<sup>23</sup>Trotman-Dickenson, A. F. and Steacie, E. W. R., Journal of Chemical Physics, 19, 329 (1951).

<sup>24</sup>Hammond, G. S. and Todd, R. W., Journal of the American Chemical Society, 76, 4081 (1954).

<sup>25</sup>Haas, H. B. and Schechter, H., Journal of the American Chemical Society, 75, 1382 (1953).

carbon atoms of the ring is cleaved<sup>26</sup>. This permits an extension of Markownikoff's from the double bond to the cyclopropane ring as the proton will be attached to the least substituted carbon atom and the anion to the most highly substituted. Lawrence and Tipper<sup>27</sup> have studied the rate of dissolution of cyclopropane and propene into aqueous and alcoholic acid solutions and have found the rate to be faster for the former. If sulfuric acid-acetic acid is the solvent, cyclopropane yields 1-propyl acetate and propene yields 2-propyl acetate. Kharasch<sup>20</sup> reacted hydrogen bromide with cyclopropane under anhydrous conditions and found a radical mechanism in action. In the presence of water or alcohols the expected ionic reaction occurred.

Alkylation of aromatic compounds with cyclopropane under Friedel-Craft reaction conditions will give 1-arylpropanes whereas 1- and 2-halopropanes and propene will give 2-arylpropanes. 1,1,2,2-Tetramethylcyclopropane will slowly react with aqueous mercuric acetate in the expected mode of addition to yield 3-hydroxy-2,3,3-trimethylbutylmercury acetate<sup>28</sup>.

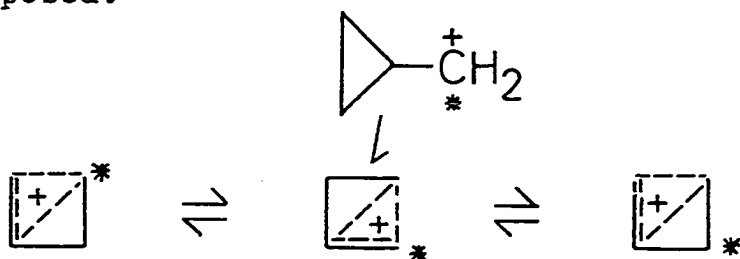
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<sup>26</sup>Smith, L. I., Record of Chemical Progress, 11, 65 (1950).

<sup>27</sup>Lawrence, C. D. and Tipper, C. F. H., Journal of the Chemical Society (London) 713 (1955).

<sup>28</sup>Levina, R. Ya. and Gladshtein, B. M., Doklady Akademii Nauk S.S.S.R., 71, 65 (1950). Original not available, abstracted in Chemical Abstracts, 44, 8321 (1950).

A further demonstration of the double bond character of the cyclopropane ring can be found in the cyclopropylcarbinyl cations. These are analogous to allyl cations but lead to a greater variety of products upon rearrangement. 2,2-Diphenylcyclopropyldiphenylcarbinol rearranges to 1,1,4,4-tetraphenylbuta-1,3-diene in sulfuric acid solution<sup>29</sup>. 2-Phenoxycyclopropyldiphenylcarbinol under similar conditions gives the two position isomers of 4,4-diphenylbutenal<sup>30</sup>. Roberts<sup>31</sup> has examined the rate of solvolysis of the cyclopropylcarbinyl system and found a definite increase in the rate over that of comparable aliphatic systems. C<sup>14</sup> labeled compounds give products with the labeled atom appearing in different positions. To account for this, three rapidly equilibrating isomeric non-classical unsymmetrical "cyclobutonium ions" have been proposed.

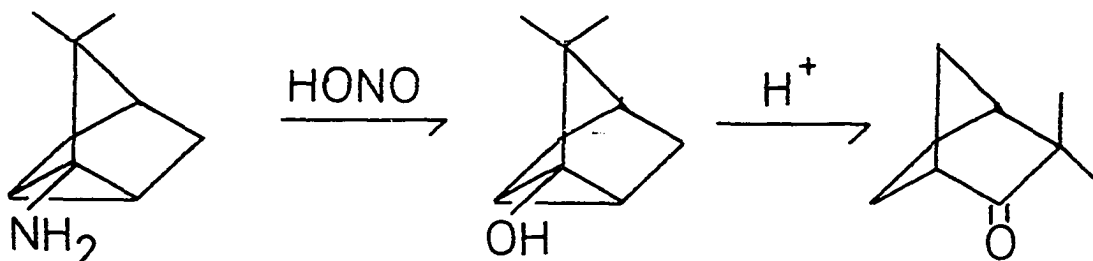


<sup>29</sup>Walborsky, H. M. and Pendleton, J. F., Journal of the American Chemical Society, 82, 1405 (1960).

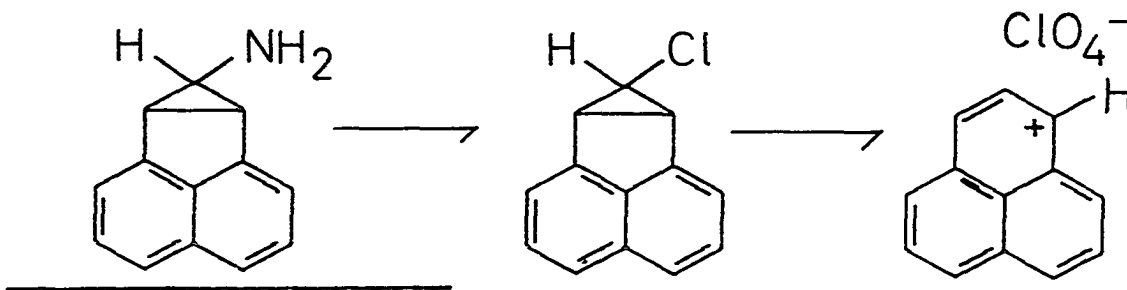
<sup>30</sup>Julia, M. and Tchernoff, G., Comptes rendus hebdomadaires des seances de l'academie des science, 249, 714 (1959).

<sup>31</sup>(a) Roberts, J. D. and Mazur, R. H., Journal of the American Chemical Society, 73, 2509 (1951); (b) Roberts, J. D. and Mazur, R. H., Journal of the American Chemical Society, 73, 3542 (1951); (c) Mazur, R. H., White, W. N., Semenov, D. A., Lee, C. C., Silver, M. S. and Roberts, J. D., Journal of the American Chemical Society, 81, 4390 (1959).

Lipp and Padberg<sup>32</sup> diazotized apotricycloamine in water and obtained apotricyclol, which could be further converted to camphenilone with acid. If the diazotization went through a carbonium-ion intermediate, camphenilone would be the expected product. Hart<sup>33</sup> redid this work and infers a concerted elimination of nitrogen from apotricyclyldiazonium hydroxide.



In the preparation of the very stable perinaphthenylium cation Petit<sup>34</sup> was able to convert 3'-amino-1:2-cyclopropanoacenaphthene into the corresponding chloride by diazotization in strong hydrochloric acid. As the chloride readily gave the perinaphthenylium cation when reacted with silver perchlorate the concerted reaction was again proposed.



<sup>32</sup>Lipp, P. and Padberg, C., *Verichte der deutschen chemischen Gesellschaft*, 54, 1316 (1921).

<sup>33</sup>Hart, H. and Martin, R. A., *Journal of the American Chemical Society*, 82, 6362 (1960).

<sup>34</sup>Petit, R., *Journal of the American Chemical Society*, 82, 1972 (1960).

Besides being soluble in acidic media it was discovered that cyclopropane slowly dissolves in ethereal lithium aluminum hydride<sup>35</sup>. Upon hydrolysis only saturated hydrocarbons were evolved.

Piehl and Brown<sup>36</sup> studied the benzylation of cyclopropyl phenyl ketone in benzene with either tritylsodium or sodamide as catalyst. They state that their results show that a proton adjacent to a carbonyl group, on a three membered ring is more difficult to remove than that of a straight chain analog. Schechter and Dessey<sup>37</sup> have studied the rate of deuterium exchange of this ketone in deuterium oxide-triethyl amine-dimethylformamide solvent and found that its rate is the highest compared to its larger alkyl ring analogs. This high rate is attributed to the great s-character of the carbon orbital directed toward the hydrogen atom (vide post). No comparison of the conflicting conclusions is justified because of the enormous differences between the two solvent systems.

Cyclopropane will undergo a complete intermetallation with amyl sodium in pentane in about a weeks time at room

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<sup>35</sup>Tipper, C. F. H. and Walker, D. A., Chemistry & Industry, 730 (1957).

<sup>36</sup>Piehl, F. J. and Brown, W. G., Journal of the American Chemical Society, 75, 5023 (1953).

<sup>37</sup>Schechter, H., Collis, M. J., and Dessey, R. E., Okuzumi, Y. and Chen, A., Journal of the American Chemical Society, 84, 2905 (1962).



temperature<sup>38</sup>. The anion does not rearrange to the allyl anion and its infrared spectrum is nearly identical to that of the parent hydrocarbon.

Piehl and Brown<sup>36</sup> also attempted to benzylate ethyl cyclopropanecarboxylate but only found cyclopropyl trityl ketone or cyclopropanecarboxamide, that is, ethoxide displacement rather than proton removal and benzylation. Wiberg, *et al.*<sup>39</sup> have found that ethyl trans-2-bromocyclopropanecarboxylate was smoothly converted to ethyl trans-2-tert-butoxycyclopropanecarboxylate by potassium tert-butoxide. The apparent ease of this transformation is ascribed to the elimination of hydrogen bromide to form the relatively stable cyclopropene-carboxylate, which then adds the elements of tert-butanol. The tert-butoxyacid undergoes an acid catalyzed rearrangement to butan-4-aloic acid<sup>40</sup>.

A number of reactions are known wherein the cyclopropane ring will act as if it were a double bond conjugated to a carbonyl group, as shown by Bone and Perkin<sup>41</sup> and Kierstead,

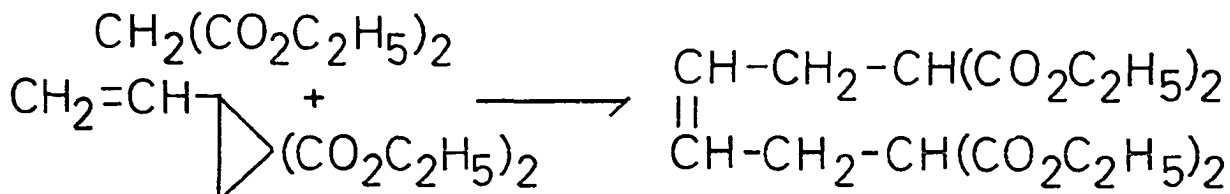
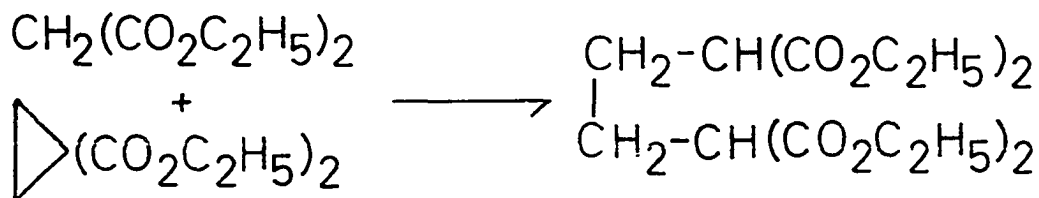
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<sup>38</sup>Lanpher, E. J., Redman, L. W. and Morton, A. A., *Journal of Organic Chemistry*, 23, 1370 (1958).

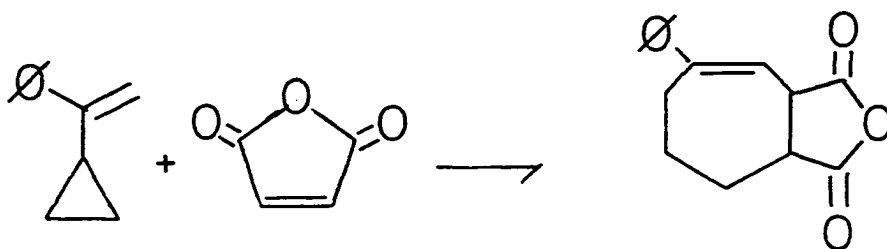
<sup>39</sup>Wiberg, K. B., Barnes, R. K. and Albin, J., *Journal of the American Chemical Society*, 79, 4994 (1957).

<sup>40</sup>Albin, J. R., *Dissertation Abstracts*, 19, 3119 (1959).

<sup>41</sup>Bone, W. A. and Perkin, W. H., *Journal of the Chemical Society (London)*, 67, 108 (1895).



et al.<sup>42</sup> Similarly cyclopropane can act as part of a diene system and undergo a Diels-Alder condensation.  $\alpha$ -Cyclopropylstyrene will condense with maleic anhydride in a 1,5-addition<sup>43</sup> but vinylcyclopropane<sup>44</sup> and dicyclopopyl<sup>45</sup> will not.



Numerous physical experiments have been conducted with cyclopropane and selected derivatives in an attempt to elucidate the true character of this entity, that is, to decide

<sup>42</sup>Kierstead, R. W., Linstead, R. P. and Weedon, B. C., *Journal of the Chemical Society (London)*, 3616 (1953).

<sup>43</sup>Sarel, S. and Breuer, E., *Journal of the American Chemical Society*, 81, 6522 (1959).

<sup>44</sup>van Volkenburgh, R., Greenlee, K. W., Defer, J. M. and Boord, C. E., *Journal of the American Chemical Society*, 71, 3595 (1949).

<sup>45</sup>Smith, L. I. and Rogier, E. R., *Journal of the American Chemical Society*, 73, 3840 (1951).

whether the three membered ring acts as a saturated carbon chain or like an unsaturated chain. Ultraviolet measurements by Klote<sup>46</sup> and Smith and Rogier<sup>47</sup> indicate that the cyclopropyl group has characteristics intermediate between a single and a double bond. The shift to higher wavelengths in these series has been interpreted as an extension of conjugation by

Compound	Wavelength (Å)	Epsilon
ethene	1850	----
vinylcyclopropane	2100	----
buta-1,3-diene	2150	----
ethylbenzene	2060	32,000
phenylcyclopropane	2200	8,400
styrene	2455	16,000

the cyclopropyl group. Considerable additional ultraviolet evidence has been reported by other workers<sup>48, 49</sup>.

Trachtenberg et al.<sup>50</sup> have examined the pK<sub>a</sub> values of a series of para-substituted phenyl carboxylic acids concluding that although cyclopropane might give rise to the extension of conjugation in an excited state, no conjugative effect was

<sup>46</sup>Klote, I. M., Journal of the American Chemical Society, 66, 88 (1944).

<sup>47</sup>Smith, L. I. and Rogier, E. R., Journal of the American Chemical Society, 73, 3840 (1951).

<sup>48</sup>Eastman, R. H. and Freeman, S. K., Journal of the American Chemical Society, 77, 6642 (1955). And references to earlier work contained therein.

<sup>49</sup>Perold, G. W., Journal of the South African Chemical Institute, 6, 22 (1955).

<sup>50</sup>Trachtenberg, E. N. and Odian, G., Journal of the American Chemical Society, 80, 4018 (1958).

transmitted in the ground state. Later, Fuchs<sup>51</sup> determined the  $pK_a$  values of a similar but larger series of acids both in water and in 50% ethanol. In addition he studied the rate of hydrolysis of the ethyl esters of this series. The Hammett  $\rho$ -values from these data are here tabulated.

Compound	Hammett $\rho$ -values for		
	$K(H_2O)$	$K(50\% EtOH)$	Ester hydrolysis
$\underline{p-X-O} \text{---} \text{CH}_2\text{---CH}_2\text{---CO}_2\text{H}$	0.212	0.344	0.489
$\underline{p-X-O} \begin{array}{c} \text{H} \\   \\ \text{---} \\   \\ \text{H} \end{array} \begin{array}{c} \text{H} \\   \\ \text{---} \\   \\ \text{CO}_2\text{H} \end{array}$	0.182	0.473	0.812
$\underline{p-X-O} \begin{array}{c} \text{CO}_2\text{H} \\   \\ \text{---} \\   \\ \text{H} \end{array} \begin{array}{c} \text{H} \\   \\ \text{---} \\   \\ \text{H} \end{array}$	---	0.436	0.014
$\underline{p-X-O} \text{---} \text{CH}=\text{CH} \text{---} \text{CO}_2\text{H}$	0.466	---	1.301
$\underline{p-X-O} \text{---} \text{CH}=\text{CH} \text{---} \text{CO}_2\text{H}$	---	---	1.122

<sup>51</sup>(a) Fuchs, R. and Bloomfield, J. J., *Journal of the American Chemical Society*, **81**, 3158 (1959); (b) Fuchs, R., Kaplan, C. A., Bloomfield, J. J. and Hatch, L. F., *Journal of Organic Chemistry*, **27**, 733 (1962).

The  $\nu$ -values imply an extension of conjugation in an excited or activated state but transmission of a conjugative effect in the ground state is slight if at all in existence.

Linnett<sup>52</sup> has noted an abnormally high force constant for the carbon-hydrogen stretch in cyclopropane. The value is nearer that of the force constant of ethene rather than a "normal" methylene group. Dipole moment measurements by Rogers<sup>53</sup> indicate that the electrons of the carbon-carbon bonds in cyclopropane are less tightly bound than usual  $\sigma$  electrons and are more like the mobile electrons of a  $\pi$  bond. Electron and X-ray diffraction work<sup>54</sup> shows that cyclopropane is an entirely symmetrical molecule. The carbon-carbon bond length of cyclopropane is 1.526 Å which is somewhat shorter than the bond length of ethane, 1.544 Å. The angle  $\angle \text{H-C-H}$  is calculated to be 116.4°.

Coulson and Moffitt<sup>55</sup> have given a quantum mechanical

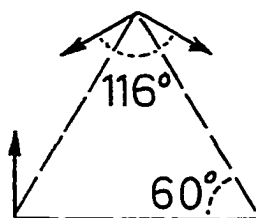
<sup>52</sup>Linnett, J. W., Nature (London), Series 2, 160, 162 (1947).

<sup>53</sup>(a) Rogers, M. T. and Roberts, J. D., Journal of the American Chemical Society, 68, 843 (1946); (b) Rogers, M. T., Journal of the American Chemical Society, 69, 2544 (1947).

<sup>54</sup>(a) Skinner, H. A., Nature (London), Series 2, 160, 902 (1947); (b) O'Gorman, J. M. and Schomaker, V., Journal of the American Chemical Society, 68, 1138 (1946); (c) Pauling, L. and Brockway, L. O., Journal of the American Chemical Society, 59, 1223 (1937).

<sup>55</sup>(a) Coulson, C. A. and Moffitt, W. E., Journal of Chemical Physics, 15, 151 (1947); (b) Coulson, C. A. and Moffitt, W. E., Philosophical Magazine, 40, 1 (1949).

treatment to the bonding of cyclopropane. They propose the use of the term "bent bond" to describe the ring orbitals of cyclopropane. Instead of the carbon orbital being directed along the line connecting the carbon nuclei they are directed outward, such that the angle between the lines representing the direction of the ring orbitals is  $116^\circ$ , not  $60^\circ$ . The overlap of the orbitals is then reduced but this is compensated for in the release of angle strain as the angle between the ring orbitals goes from  $60^\circ$  to  $116^\circ$ . On the basis of this model the calculated  $\angle \text{H-C-H}$  would be  $112 \pm 4^\circ$  which is in



good agreement with the experimentally determined value. In addition a shortening of the carbon-carbon bond is predicted. Instead of the usual  $sp^3$  hybridization of the carbon orbitals the calculated ring orbitals are  $sp^{4.12}$  and the exocyclic orbitals are calculated to be  $sp^{2.28}$ . This appears to be in accord with the chemical evidence for the  $\pi$  character of the  $\sigma$  bond electrons and the increased acidity of the hydrogen atoms.

## DISCUSSION

Synthesis of trans-2-Phenylcyclopropanol  
and 2-Phenyl-1-methylcyclopropanol

From the investigations of Mahoney<sup>14</sup> and Dappen<sup>15</sup> it has been shown that cyclopropanol and alkyl-substituted cyclopropanols are quite prone to rearrangement and decomposition. They are volatile, low boiling liquids, and are somewhat difficult to handle, especially quantitatively. The synthesis of phenyl-substituted cyclopropanols was undertaken with the hope that these compounds would be solids and somewhat more stable due to the presence of the phenyl group. trans-2-Phenylcyclopropanol was prepared. It was isolated as a white solid melting at 39° but the stability of this compound was not as great as was hoped. 2-Phenyl-1-methylcyclopropanol was also prepared and isolated as fine white needles melting at 82°. This compound was more stable than the other and proved more useful in this study.

The initial synthetic route attempted proved to be a successful one. trans-2-Phenylcyclopropanol was prepared from the known trans-2-phenylcyclopropanecarboxylic acid. Julia's procedure<sup>56</sup> for the preparation of this acid starts with the base catalysed condensation of diethyl malonate with styrene

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<sup>56</sup>Julia, M., Julia, S. and Bemont, B., Comptes rendus hebdomadaires des seances de l'academie des science, 245, 2304 (1957).

oxide.

Russell and Vander Werf<sup>57</sup> had studied the addition of diethyl malonate to styrene oxide in regard to the I-strain theory and concluded that the addition occurred exclusively at the terminal carbon atom of the side chain, to yield the lactone of 2-carboethoxy-4-hydroxy-4-phenylbutanoic acid (Ib) (see Figure 1). As proof, this compound was hydrolysed and decarboxylated and reported to give the lactone of 4-hydroxy-4-phenylbutanoic acid (IIb). The melting point of this compound was found to be 45° whereas the melting point given by Fittig and Jayne<sup>58</sup> who prepared the same lactone from styrylacetic acid, was 37°. The hydroxyacid derived from IIb melted 44° above that reported by the German workers and the only sound evidence for the structure of IIb was the fact that it could be oxidized to a ketoacid whose melting point was identical with that of 4-phenylbutan-4-onoic acid and showed no mixed melting point depression with an independently prepared sample.

When this reaction was carried out in this laboratory a melting point for the lactone was obtained which agreed with that reported by Russell and Vander Werf. A sample of the lactone, recrystallized from ethanol, was dissolved in carbon

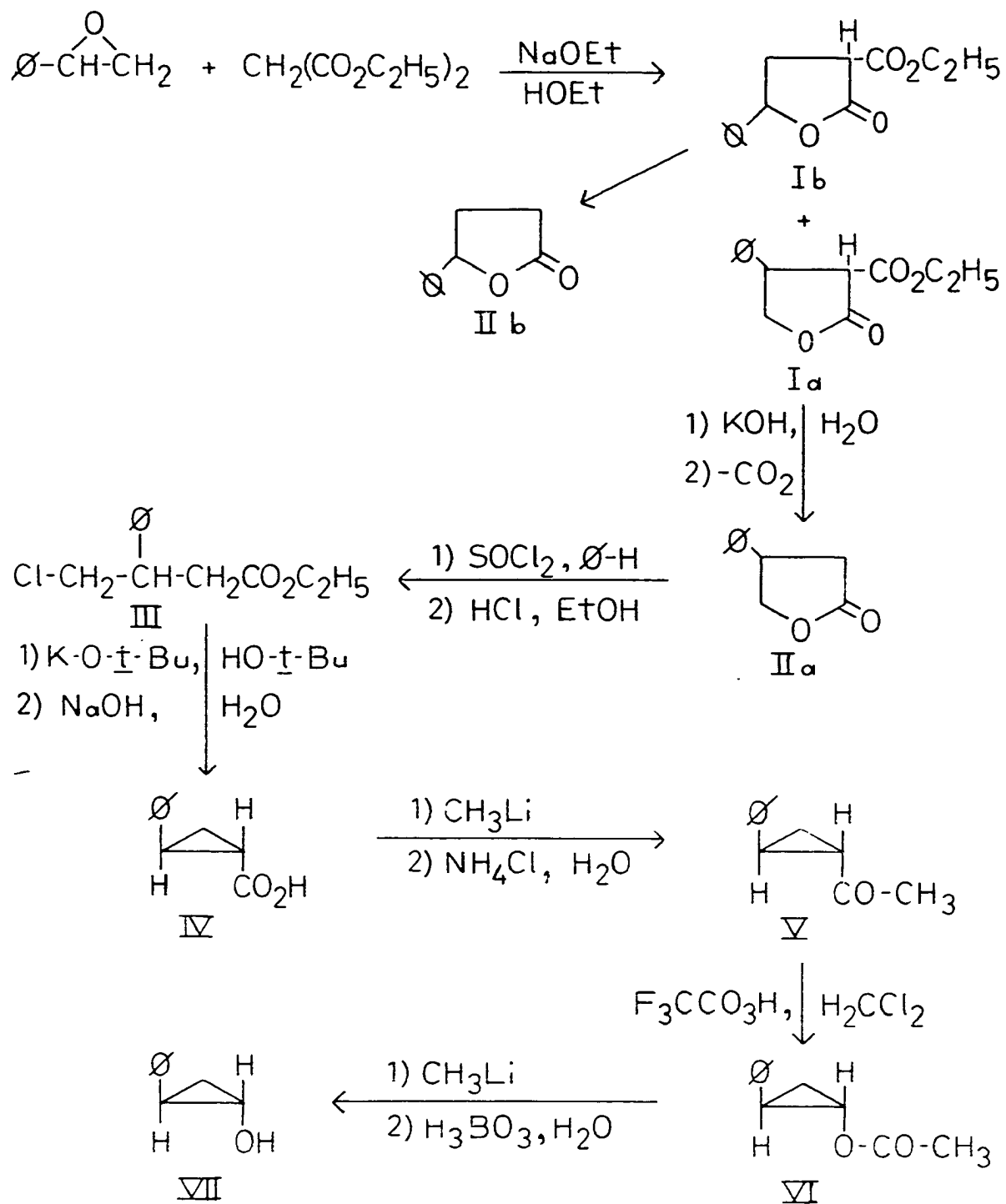
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<sup>57</sup>Russell, R. R. and Vander Werf, C. A., *Journal of the American Chemical Society*, 69, 11 (1947).

<sup>58</sup>Fittig, R. and Jayne, H. W., *Justus Liebigs Annalen der Chemie*, 216, 97 (1883).



Figure 1. Synthetic scheme

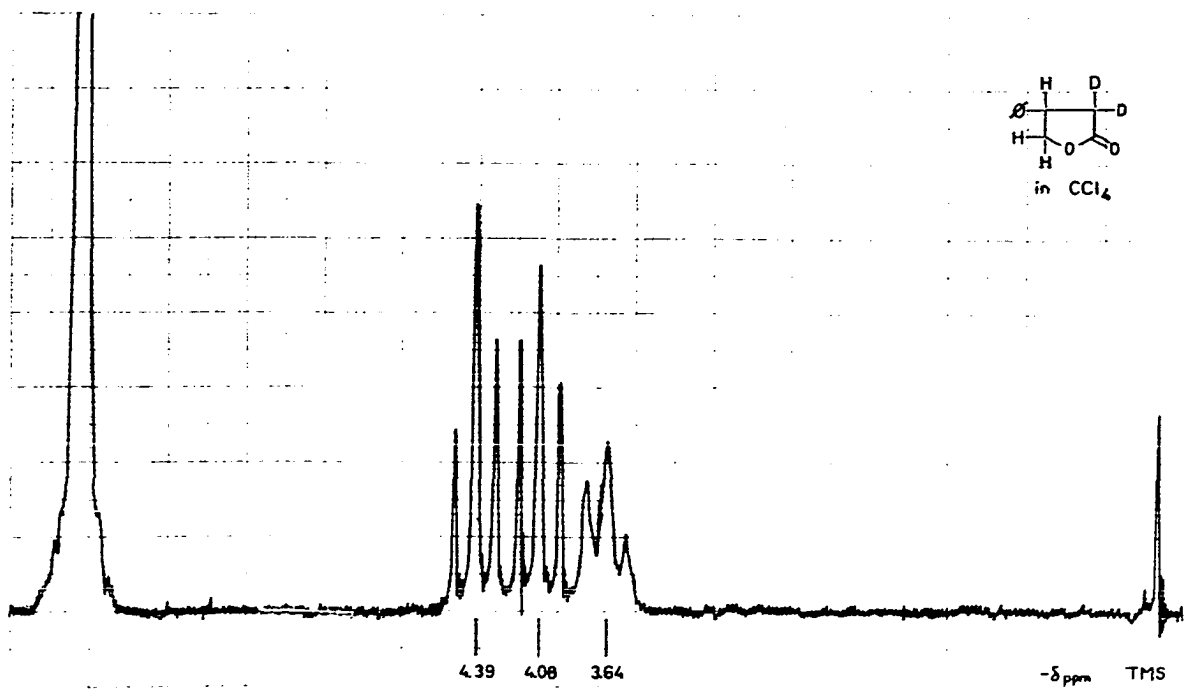
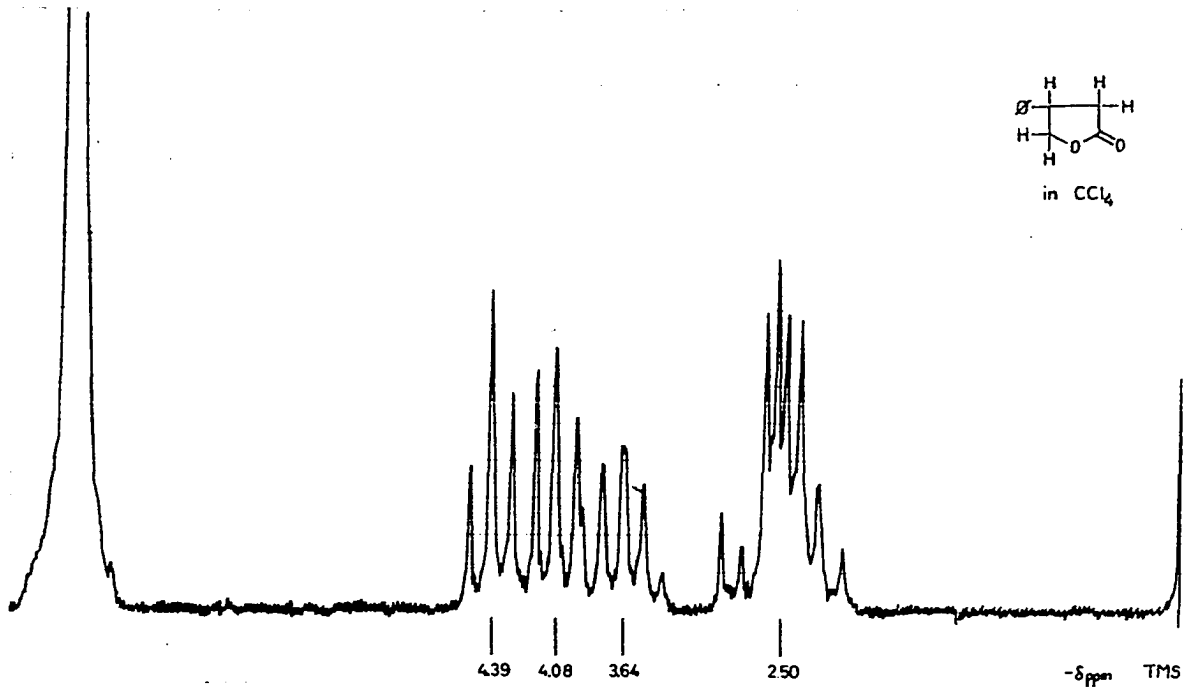


tetrachloride and prepared for NMR analysis. The NMR spectrum (Figure 2) showed triplets at 4.39 and 4.08 ppm, what appears to be a triplet with further splitting at 3.64 ppm, and an eight line pattern centered near 2.5 ppm which is the AB portion of an ABX spectra. Aromatic absorption at 7.2 ppm was also present. This was definitely not the spectra predicted for IIb but is more in line with the spectra one would expect from its position isomer, the lactone of 4-hydroxy-3-phenylbutanoic acid (IIa). The predicted spectra of IIb would show a complex pattern centered near 2.0 ppm attributed to the two adjacent methylene groups and a very complex pattern at about 5.0 ppm assigned to the lone proton on a benzylic carbon atom bearing an etheral oxygen atom.

To clarify this matter I(a or b) was hydrolysed and decarboxylated in deuterium chloride-deuterium oxide. This material was recrystallized and its NMR spectrum determined (Figure 3). This spectrum was identical to the other with one important exception, the entire pattern at 2.5 ppm was absent. By first order analysis we can now assign those missing lines to the methylene protons adjacent to the carbonyl group in structure IIa. Likewise on the basis of chemical shift the triplets at 4.39 and 4.08 ppm can be assigned to the protons on carbon bearing oxygen. Furthermore, the other "triplet" at 3.64 ppm is in this spectra considerably broadened due to the quadrupole moment of the two adjacent deuterium atoms.

Figure 2. NMR spectrum of the lactone of 4-hydroxy-3-phenylbutanoic acid

Figure 3. NMR spectrum of the lactone of 4-hydroxy-3-phenylbutan-2,2-d<sub>2</sub>-oic acid



From these NMR spectra and the disagreement of melting points of the lactone and its derivatives with those reported by Fittig and Jayne we must conclude that the correct structure for the lactone is IIa and that the addition of diethyl malonate to styrene oxide occurs primarily at the benzylic carbon atom. In further support of structure IIa, an NMR spectrum was made on the crude lactone and additional lines appeared at the 2.0 ppm region and at 5.3 ppm. Vapor phase chromatography of the crude lactone shows only a few per cent of IIb.

Lactone IIa can be converted into ethyl 4-chloro-3-phenylbutanoate (III) by treatment with thionyl chloride in refluxing benzene and then addition of absolute ethanol saturated with hydrogen chloride. The cyclization of III can be effected by treatment with potassium tert-butoxide in refluxing tert-butanol. Basic hydrolysis of the resulting ester yields trans-2-phenylcyclopropanecarboxylic acid (IV).

The cis- and trans-relationship of the phenyl and carboxyl group has been well established. Burger and Yost<sup>59</sup> heated ethyl diazoacetate in the presence of styrene and, after saponification, separated the two isomeric acids by fractional crystallization. All attempts to prepare the acid chloride or the amide of the acid obtained in lower yield,

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<sup>59</sup>Burger, A. and Yost, W. L., Journal of the American Chemical Society, 70, 2198 (1948).

12%, yielded the same derivatives obtained from the higher yield acid, and these derivatives could be converted to the other acid. The high yield acid, 74%, could not be transformed into the other by any means tried. As the trans-isomer would be the thermodynamically more stable isomer the relationship between them could be inferred. By comparing them to cyclopropane-1,2-dicarboxylic acids of known structure, de Waal and Perold<sup>60</sup> have ozonized and oxidized the phenyl group on these acids to a carboxyl group and established their configuration.

IV was converted to its corresponding methyl ketone, trans-2-phenylcyclopropyl methyl ketone (V), by the method of Tegner<sup>61</sup>. This method has been shown to be far superior to any previous method for converting carboxylic acids to methyl ketones. One equivalent of methyllithium converts the acid to the lithium salt and the second adds to the carbonyl group to form the dilithium salt of the ketone hydrate. Under anhydrous conditions this salt is quite stable and when hydrolysed gives near quantitative yields of ketones in many cases. Although the trans-relationship has not been rigorously established for V it can be reasonably inferred, as this configuration is the most stable and the reaction conditions are not those which

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<sup>60</sup>de Waal, H. L. and Perold, G. W., *Berichte der deutschen chemischen Gesellschaft*, 85, 574 (1952).

<sup>61</sup>Tegner, C., *Acta Chemica Scandinavica*, 6, 782 (1952).

would lead to inversion of the asymmetric center.

Although cyclopropyl ketones have been known for many years no oxidant could convert them to their corresponding esters. Emmons and Lucas<sup>62</sup> have developed peroxytrifluoroacetic acid as an oxidizing agent and have converted methyl cyclopropyl ketone into cyclopropyl acetate in good yield. This peracid, in disodium hydrogen phosphate buffered methylene chloride solution, nicely converts V into trans-2-phenylcyclopropyl acetate (VI). The stereospecificity of the Baeyer-Villiger oxidation has been well documented<sup>63</sup>.

The reduction of VI to trans-2-phenylcyclopropanol (VII) is the most difficult step and by far the lowest yield. Just as Mahoney<sup>14</sup> and Dappen<sup>15</sup> had difficulties reducing the isolating cyclopropanol from cyclopropyl acetate, the lithium aluminum hydride reduction of VI gave mostly aldehydic material and pure VII could not be obtained. Using methyl-lithium as the reductant, one could obtain small yields of VII upon repeated recrystallizations from pentane-ether at -78°. VII is a nominally stable white solid melting at 39° which can be characterized as a p-nitrobenzoate, l-naphthylurethan or tosylate. The NMR spectrum of VII (Figure 4)

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<sup>62</sup>Emmons, W. D. and Lucas, G. B., Journal of the American Chemical Society, 77, 2287 (1955).

<sup>63</sup>(a) Mislow, K. and Brenner, J., Journal of the American Chemical Society, 75, 2318 (1953); (b) Turner, R. B., Journal of the American Chemical Society, 72, 878 (1950).



is readily rationalized on the basis of chemical shift. The aromatic protons appear at 7.3 ppm and the hydroxyl proton as a broad singlet at 4.31 ppm. The remaining protons appear as three complex patterns centered at 3.52, 1.96 and 1.02 ppm. These have been assigned to the proton on a carbon atom bearing oxygen, the proton on a benzylic carbon atom and the two methylene protons on the cyclopropane ring.

Preliminary studies on VII spurred the preparation of 2-phenyl-1-methylcyclopropanol (VIII). VIII is prepared by the same series of reactions as VII. Diethyl malonate is condensed with styrene oxide but then the carbon atom between the carboethoxy groups is methylated by adding methyl iodide to the reaction (see Figure 6). The same steps are then followed as for the preparation of VII. Although it is of ultimate importance the spacial relationship of the phenyl, methyl and hydroxy groups of VIII remains unknown. An investigation is underway to determine this relationship.

VIII is obtained as a mass of fine white needles by recrystallizing the crude alcohol from ether-pentane at  $-78^{\circ}$ . The recrystallization was unsuccessful until a low density polyethylene bottle was used as a container for this step. The alcohol melts at  $82^{\circ}$  and is only somewhat more stable than VII, as it too will decompose in a sealed tube kept near  $0^{\circ}$  over a period of several weeks. The NMR spectrum of VIII (Figure 5) exhibits absorption peaks at 7.13 ppm, aromatic

Figure 4. NMR spectrum of trans-2-phenylcyclopropanol

Figure 5. NMR spectrum of 2-phenyl-1-methylcyclopropanol

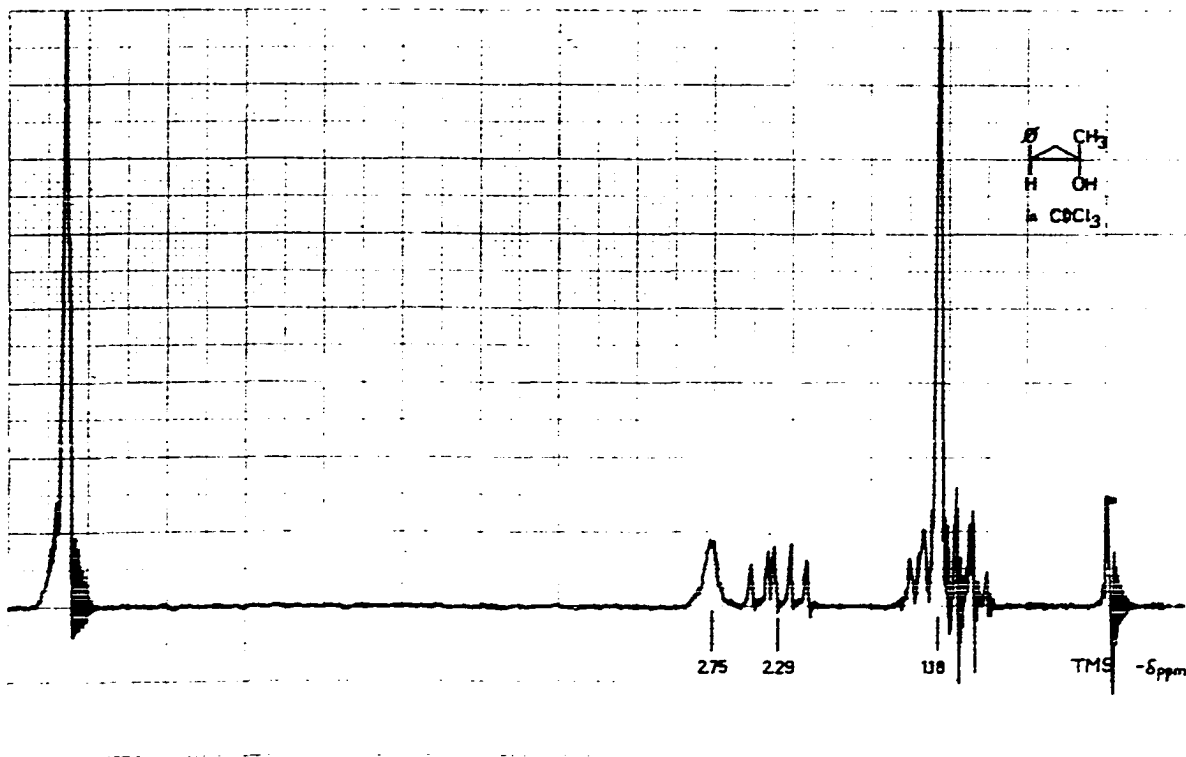
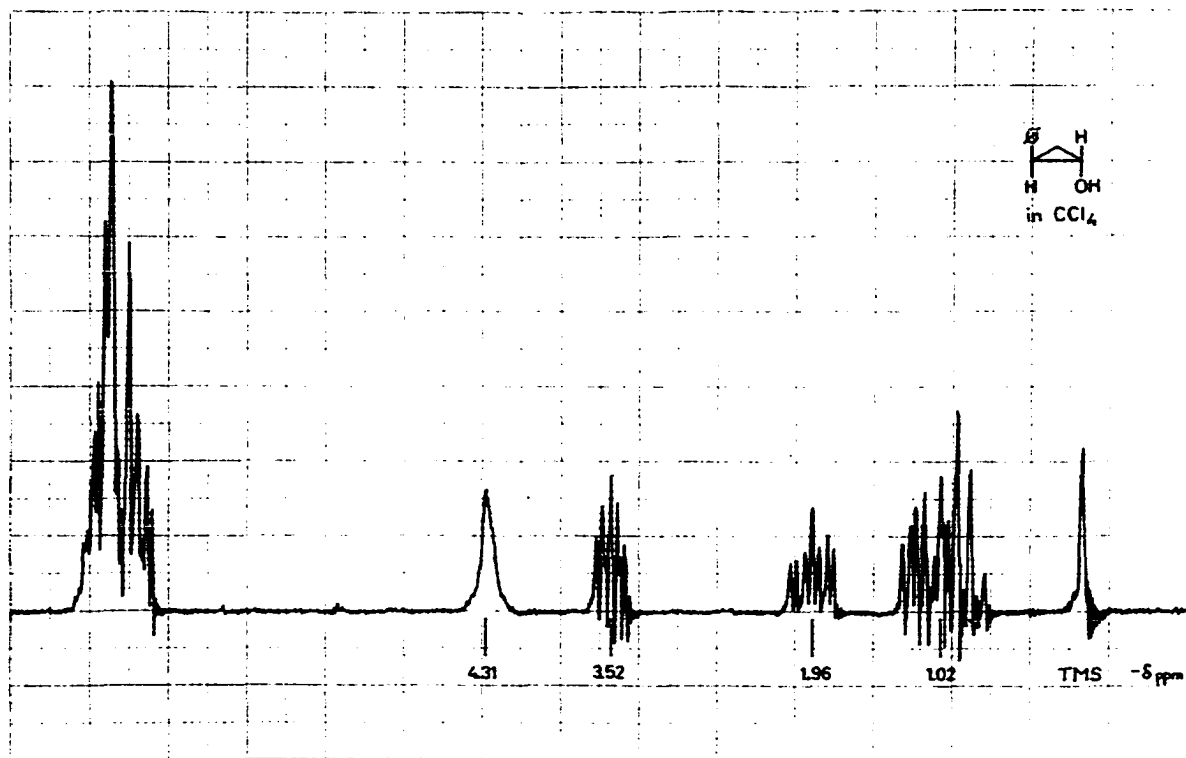
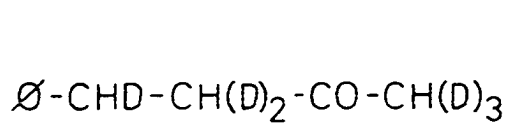
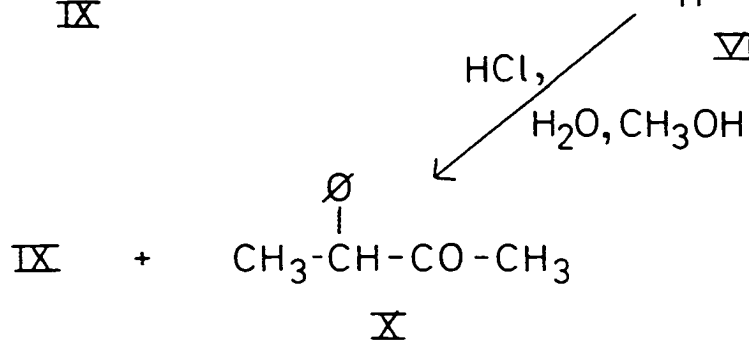
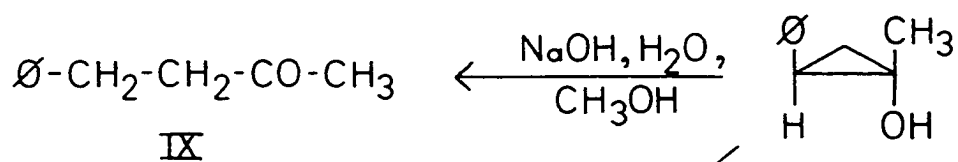
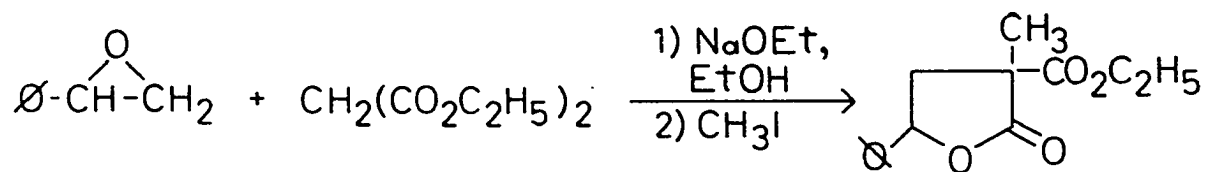
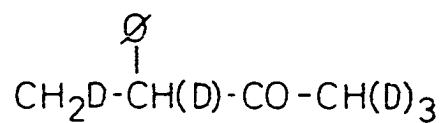


Figure 6. Synthetic scheme



IX-D

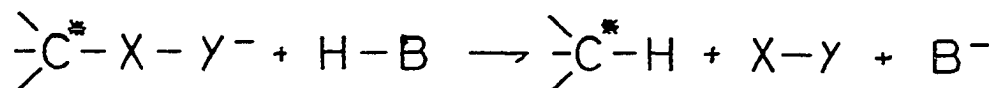


X-D

protons; 2.75 ppm, a singlet from the hydroxyl proton; an unsymmetrical pentuplet centered near 2.29 ppm from the benzylic proton; a sharp singlet at 1.18 ppm from the methyl group and centered about this are several lines from the two methylene protons. A p-nitrobenzoate derivative of this tert-alcohol could be prepared.

#### Reactions of 2-Phenyl-1-methylcyclopropanol

In a survey of the literature D. J. Cram found that very little work had been done on electrophilic substitution at saturated carbon and that very little was known about the nature of reactions of carbanions at asymmetric centers. This is in contrast to the vast amount of work reported for nucleophilic substitution at saturated carbon and for the stereochemical course of carbonium ion reactions. He undertook a study of the system of the type



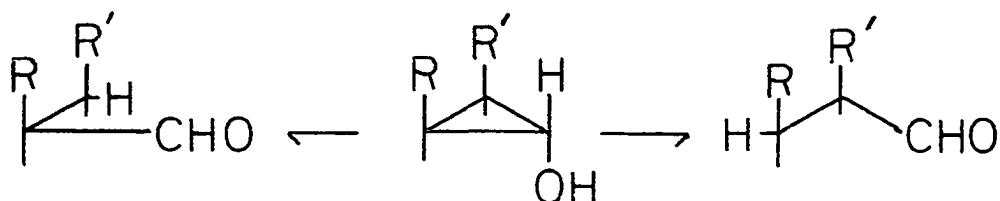
#### Reaction 1

where X was generally carbon, Y was usually oxygen and C\* was an asymmetrically substituted carbon. Usually this asymmetric carbon was substituted with an ethyl, methyl and phenyl group. A base catalyzed heterolytic cleavage of the C\*-X bond would yield 2-phenylbutane which possessed some degree of asymmetry. Cram was able to follow the stereochemical course of the protonation of the forming carbanion as a

function of substrate, solvent, base catalyst and temperature.

His work may be quickly summarized as follows. The course of the reaction is quite independent of substrate, base catalyst and temperature but it is exceedingly solvent dependent. This solvent dependence can lead to complete retention, complete racemization or predominant inversion of configuration about the asymmetric center. Proton donating solvents of low dissociating power, as tert-butanol, lead to retention. Solvents of high dissociating power unable to donate protons to the substrate, as dimethyl sulfoxide, lead to complete racemization and solvents of high dissociating power capable of donating protons, as ethylene glycol, lead to predominately inversion.

Cyclopropanols appeared to us to be a good substrate for another study of this fundamental concept. To obtain heterolytic cleavage, Cram was most often forced to use strong bases and temperatures about 200°. Cyclopropanols are in this way unique for they have a built-in driving force for cleaving the ring and that driving force is ring strain. This intrinsic factor facilitates the heterolytic cleavage such that the carbon-carbon bond breaks under base catalysis at room temperature. Another advantage of this system is that it would permit competitive reactions to be run within the same molecule (Reaction 2). Of course to study this reaction completely optically active alcohols become necessary. With



## Reaction 2

suitably substituted cyclopropanols resolution might be achieved, either directly with the alcohol or indirectly by resolving the carboxylic acid from which the alcohol is prepared and carrying out stereospecific transformations.

As mentioned in the Introduction a two prong attack at electrophilic substitution in this system was possible. The above described approach has its merits as it has an analogy in Cram's work but cyclopropanols will permit us to make a direct study. It has long been known that cyclopropane derivatives will undergo substitution reactions with acids. Reportedly the addition occurs in a Markownikoff type addition<sup>26</sup> but this has never been rigorously established. This substitution involves the formation of a carbon-hydrogen bond and the cleavage of a carbon-carbon bond, ideal electrophilic substitution. There is a definite advantage in studying cyclopropanols over other cyclopropane derivatives. Protonation of the three membered ring of a cyclopropanol would produce a carbonium ion either at or adjacent to the carbon



atom bearing the hydroxyl group. A carbonyl group would then immediately form or rearrangement would occur so that the formation of the carbonyl group would be possible. With alkyl- and aryl-substituted cyclopropanes one can easily envision the formation of substitution products and, as well, amounts of rearranged substitution products and olefins. The exact analysis of such a mixture would be far more difficult than the analysis of the isomerization products from cyclopropanols.

trans-2-Phenylcyclopropanol, VII, was the first phenyl substituted cyclopropanol available to us and therefore the first used to test some of the ideas stated above. Base and acid catalyzed ring opening studies, conducted in a manner which proved successful for 2-phenyl-1-methylcyclopropanol, VIII, were not analyzable by NMR probably due to the formation of condensation products of the resulting aldehydes. As the technique for preparing and isolating VIII had not yet been worked out, some studies were conducted with 2-phenyl-1-methylcyclopropyl acetate (XI). It was anticipated acetate XI would react as if it were the VIII or that VIII would be generated in situ. This was a reasonable assumption based on Mahoney's study<sup>14</sup>.

A small sample of acetate XI was dissolved in a solution of diglyme-water-sodium hydroxide and heated at reflux for eight hours. The solution was diluted with the water,

acidified and extracted with ether. The ether was removed and the residue was dissolved in carbon tetrachloride for NMR analysis. The NMR spectrum (Figure 7) shows one product which from NMR analysis is 4-phenylbutan-2-one (IX). The spectrum consists of an aromatic absorption peak equivalent to five protons, a typical  $A_2B_2$  pattern centered at 2.83 ppm equivalent to four protons attributed to the two nonequivalent methylene groups and a singlet at 1.96 ppm equivalent to three protons.

Another sample of acetate XI was dissolved in diglyme-water-hydrochloric acid, heated at reflux for eight hours and worked up in the same fashion. This NMR spectrum (Figure 9) has the same absorption peaks as above and some additional peaks attributed to the position isomer of IX, 3-phenylbutan-2-one (X). The doublet at 1.28 ppm is attributed to the methyl group on the benzylic carbon, the single peak adjacent to the 1.96 ppm methyl peak of IX is the corresponding methyl peak of X and the quartet centered at 3.58 ppm is the lone benzylic proton split by the methyl group. The integration of the NMR spectrum indicates a 55 to 45 ratio of X to IX.

A kinetic study was undertaken to determine the rate of hydrolysis and/or isomerization of acetate XI. A sample of XI was dissolved in methylene chloride-methanol-hydrochloric acid and placed in a constant temperature bath at 35°. At intervals samples were withdrawn, chilled and prepared for NMR

Figure 7. NMR spectrum of 4-phenylbutan-2-one

Figure 8. NMR spectrum of partially deuterated  
4-phenylbutan-2-one

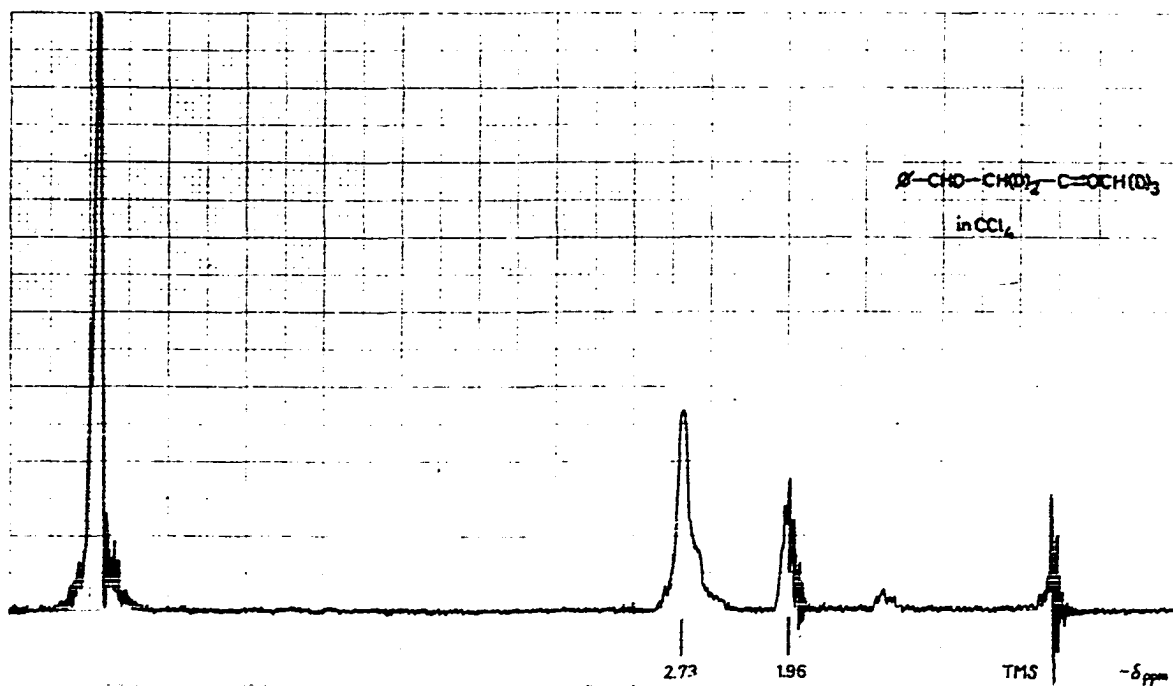
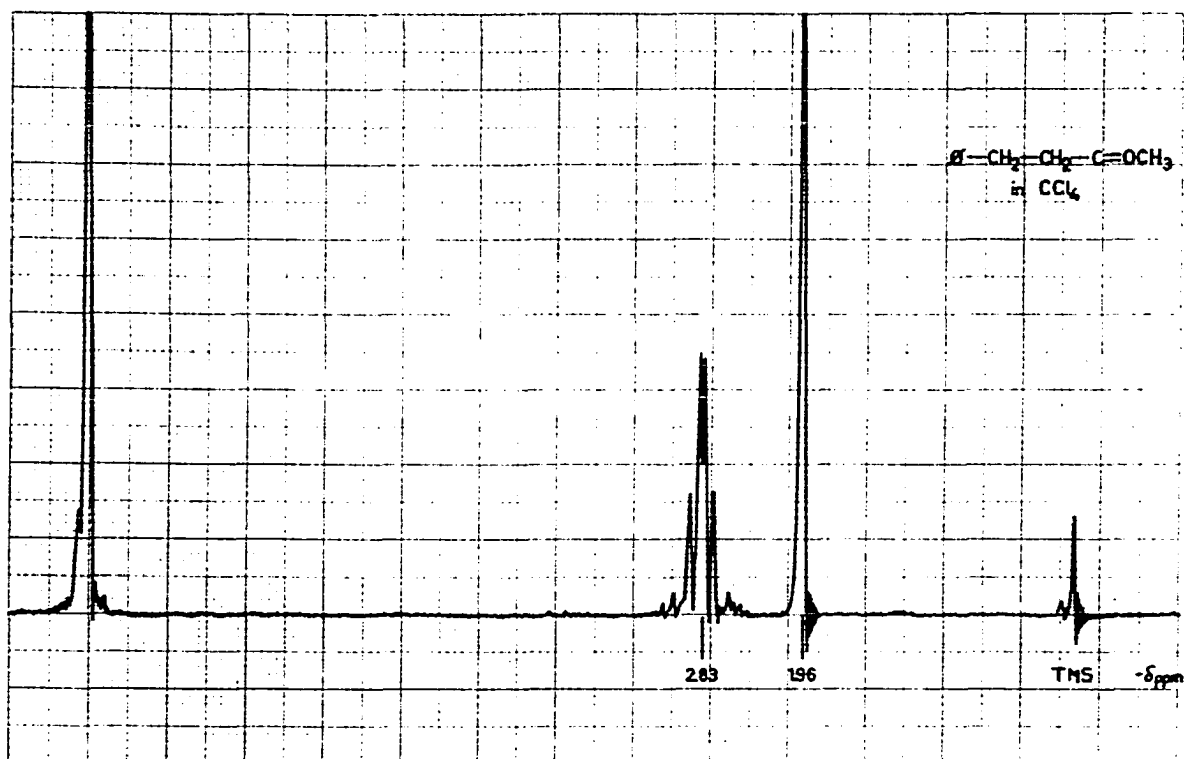
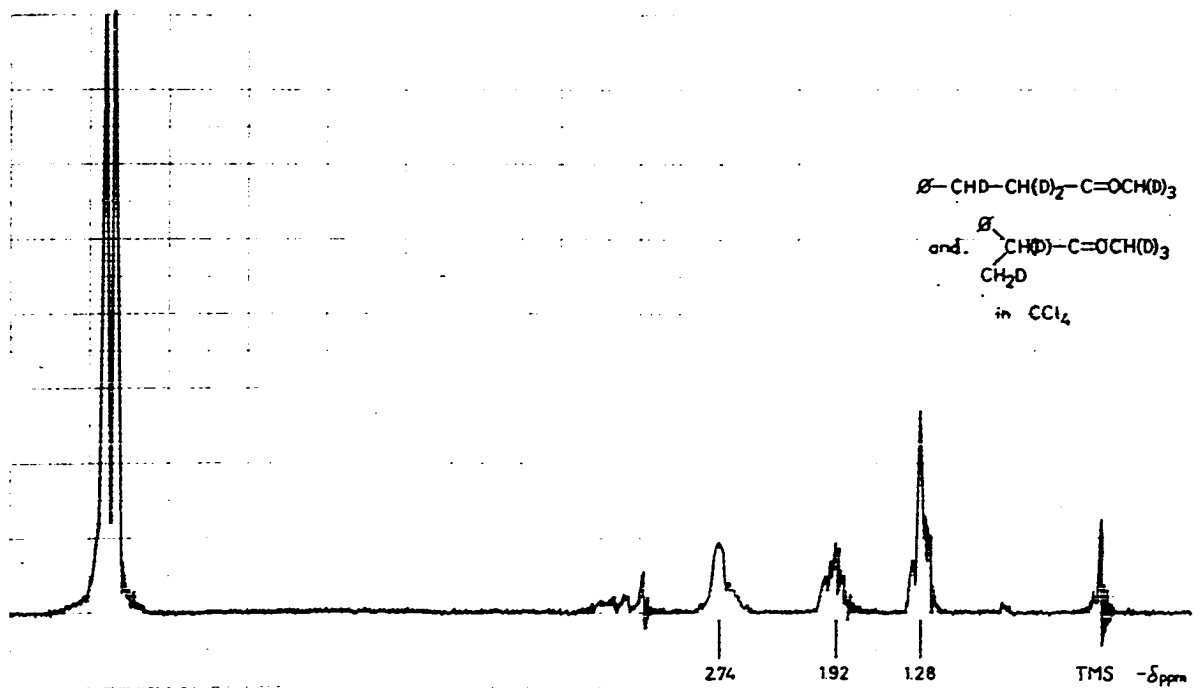
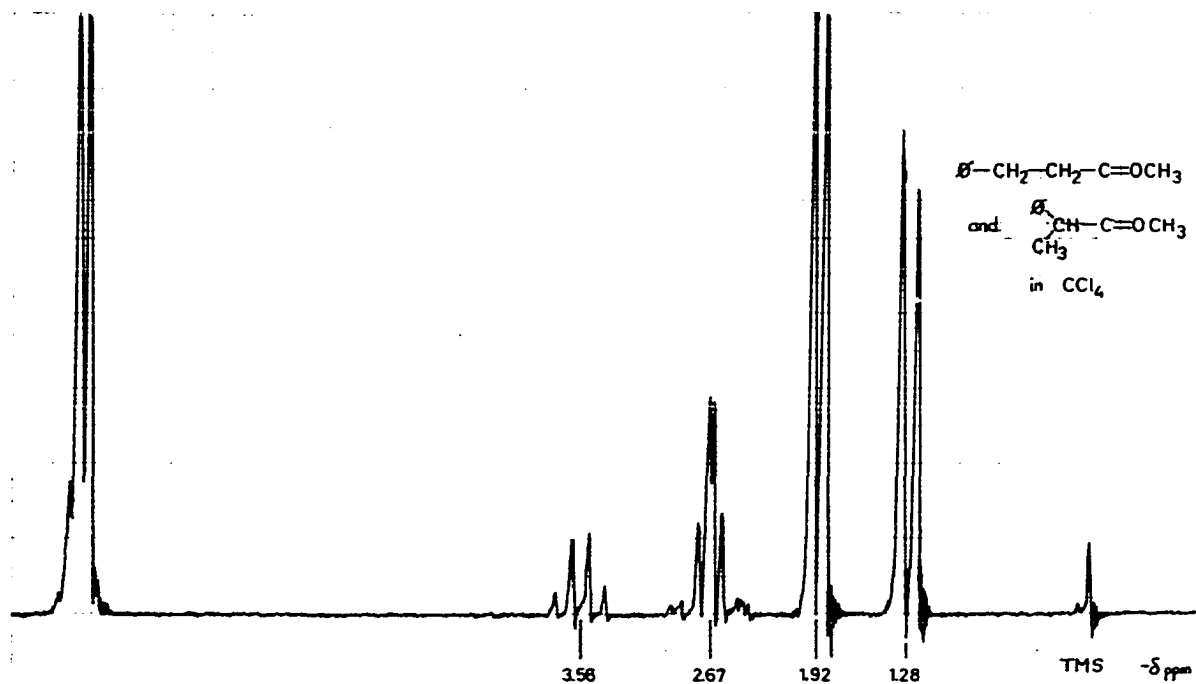


Figure 9. NMR spectrum of 4-phenylbutan-2-one and 3-phenylbutan-2-one

Figure 10. NMR spectrum of partially deuterated 4-phenylbutan-2-one and 3-phenylbutan-2-one



analysis. The resulting spectra were too complex for any quantitative analysis as the lines of the starting material and products overlapped. One salient feature of the spectra was the appearance of the absorption peak due to the methyl group of the alcohol. This indicated that the ester was hydrolysing at a faster rate than the isomerization of either the ester or the alcohol.

One additional experiment was conducted with acetate XI. Since cyclopropene and methylenecyclopropane had been prepared we attempted to prepare methyl-phenylcyclopropene by the acetate pyrolysis of XI. Acetate pyrolysis occurred at 525° but no olefin was evident and the extent of charring in the pyrolysis apparatus discouraged any additional pyrolyses.

With pure 2-phenyl-1-methylcyclopropanol, VIII, an experiment was conducted in the same manner as Dappen conducted his isomerization experiments with cyclopropanol and alkyl-substituted cyclopropanols. A sample of VIII was heated for eight hours in the presence of air in deuteriochloroform. On the basis of Dappen's work we would expect to find only isomerization products from this experiment but very surprisingly the NMR spectrum of this sample showed no isomerization products. This fact is difficult to reconcile with the facile isomerization of other cyclopropanols and no explanation can be given at this time.

The acid and base catalyzed ring-opening isomerizations

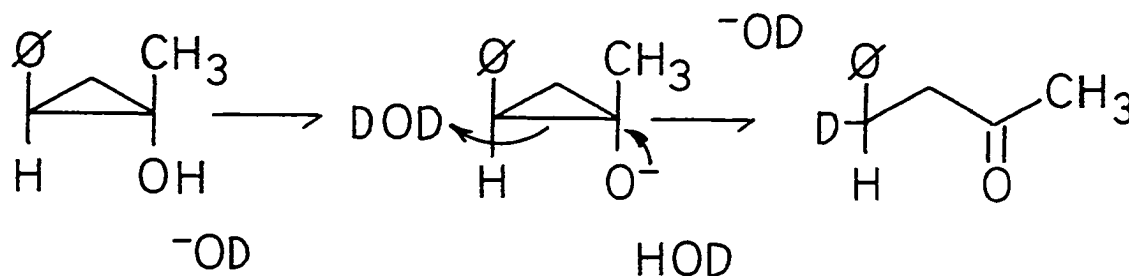
of VIII were now undertaken. A small sample of the alcohol was dissolved in methanol-water-sodium hydroxide, sealed in a tube and heated at 80° for ten hours. To preclude the loss of any isomerization products the contents of the tube were carefully transferred to a micro heavier-than-water continuous extractor, diluted with water, acidified and continuously extracted with carbon tetrachloride for one hour. All the organic material is extracted in one hour as a sample extracted for over twenty-four hours led to the same analysis. The carbon tetrachloride extract was filtered and the carbon tetrachloride was removed at reduced pressure. Other work with similar compounds showed no differential loss of the various components due to differences in volatility or solubility. The residue was dissolved in carbon tetrachloride and its NMR spectrum recorded.

The results with the alcohol were the same as with the acetate. To check for other possible isomerization products a VPC analysis was made. Four different VPC columns were used in an attempt to find any compounds other than 4-phenylbutan-2-one but none were found. From the acid catalyzed reaction we know that 3-phenylbutan-2-one is easily separated and detected. Under the analysis conditions another component amounting to .01% of IX could have been easily detected.

The base catalysed reaction was also carried out in a methanol-d-deuterium oxide-sodium deuterioxide. The integration

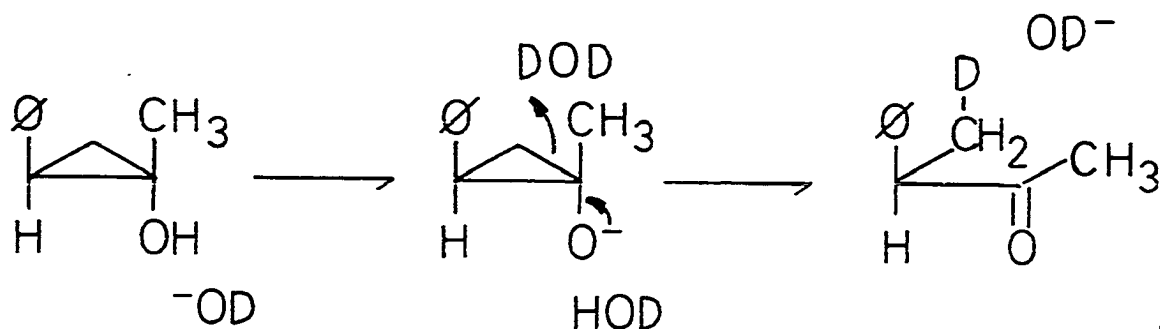


of the NMR spectrum (Figure 8) may be interpreted to indicate that deuterium has been incorporated into the benzylic position. The area under the methylene peak integrates to 1.62 protons. Assuming one proton and one deuterium on the benzylic carbon atom of IX, 70.0% deuterium exchange per proton has occurred at the methylene carbon atom adjacent to the carbonyl group. This is in line with the 71.6% deuterium exchange which has occurred at the methyl group. This of course bears out the mechanism of the type expected (Reaction 3). What is



Reaction 3

amazing is that only one product is formed whereas two are reasonably expected (Reactions 3 and 4).

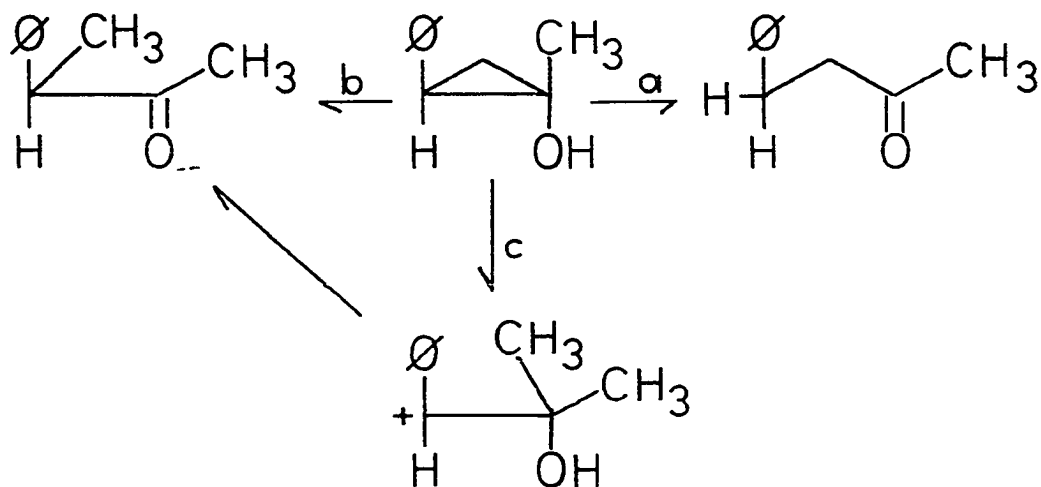


Reaction 4

Two factors could have a controlling influence over the direction of the ring opening, 1) solvation of the forming

carbanion and 2) stabilization of the forming carbanion. Cram found that solvation was very important in his study and such might be expected here. If solvation were more important, X-D (Reaction 4) would be expected to predominate over IX-D (Reaction 3) as solvation would be greater at the unsubstituted carbon atom than at the benzylic. If stabilization of the carbanion were more important one might expect the opening to occur in the manner observed. Any carbanion character in the transition state would be stabilized by the phenyl group at the benzylic carbon but there would be no stabilization at a primary carbon atom. If no other factors are important the stabilization of the carbanion must predominate. A study with an optically active alcohol may clarify this point for if resonance stabilization is important racemization should occur regardless of the solvent.

The acid catalyzed ring opening experiments were conducted just as the base catalyzed experiments except the solvent was methanol-water-hydrochloric acid. The NMR spectrum (Figure 9) was identical to that obtained from the acetate under similar conditions, with 3-phenylbutan-2-one, X, and 4-phenylbutan-2-one, IX, in a 55 to 45 ratio. VPC analysis confirms this ratio and indicates that no other products are present. These two isomerization products can be envisioned to arise in three ways (Reaction 5). 1,2-Cleavage would yield the straight chain ketone IX (Reaction 5a) and 1,3-cleavage



## Reaction 5

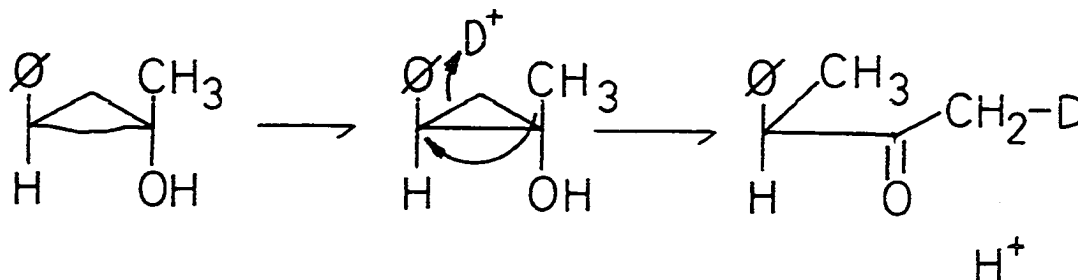
would yield the branched chain ketone X (Reaction 5b). 2,3-Cleavage would, after the migration of a methyl group, give the branched isomer X (Reaction 5c).

The possibility of X being formed by two different reactions, 2,3- and 1,3-cleavage, was tested in the following way. The isomerization was carried out in diglyme-deuterium oxide-hydrochloric acid- $d_4$ . The NMR spectrum at the products was integrated and analyzed. The analysis indicated that 79% of the possible hydrogen in the benzylic methyl group was present, or, 60% of the deuterium that could be incorporated into this position was incorporated. VPC analysis showed no change in the overall product ratio of IX to X.

As some protons are always present in the deuterated

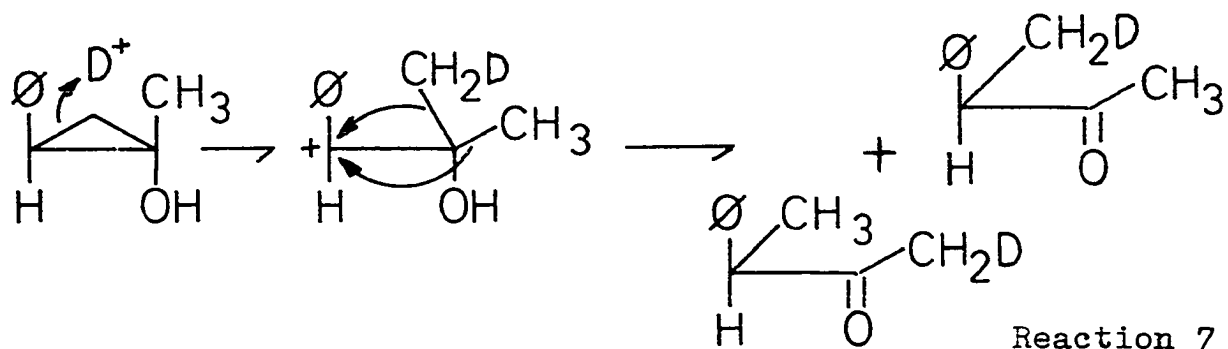
solvents a check was made to determine if any large isotope effect was present. If the effect of a proton is much greater than that of a deuteron, or the reverse, the above figures would not be valid. A sample of alcohol VIII was isomerized in methanol-d whose analysis showed only 85% deuterium. The NMR spectrum (Figure 9) of the isomerization products was integrated and indicated that 82% of the benzylic protons were present, or, 54% deuterium incorporation. Within experimental error these are the expected figures if no isotope effect is present.

The 79% figure can only mean that some methyl group migration is occurring but there are two possible mechanisms by which this can happen. A concerted mechanism (Reaction 6) would have a deuterium-carbon bond formed with the simultaneous migration of a methyl group from the 1-position to the benzylic or 2-position to yield X-D. In this case no deuterium would be incorporated into the benzylic methyl group. The

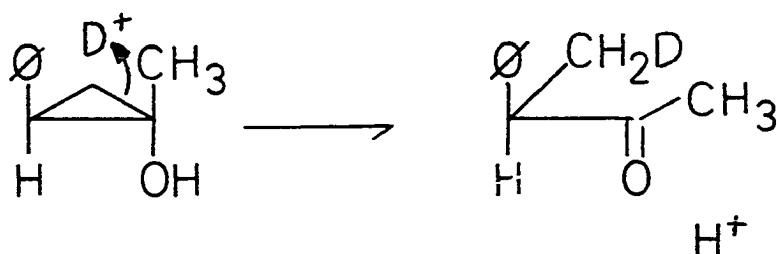


Reaction 6

other possible mechanism involves a "free" benzylic carbonium ion (Reaction 7). The formation of a "free" carbonium ion



would permit rotation within the molecule causing the probability of  $-\text{CH}_3$  group migration to become equal to  $-\text{CH}_2\text{D}$  migration. In the analysis the benzylic methyl group would then contain one-half of a deuterium atom or 83.3% of possible hydrogen. The 1,3-cleavage would leave the benzylic methyl group with in deuterium in it or 66.7% of possible hydrogen (Reaction 8).



The ratio of 1,3-cleavage to concerted 2,3-cleavage to "free" carbonium ion 2,3-cleavage might reasonably be determined. This would involve the synthesis of 2-phenyl-1-methyl- $\text{d}_3$ -cyclopropanol (XII) and the use of NMR integration

which has an accuracy of better than 2%. Three variables are present; alcohol, VIII and XII; solvent, deuterated and undeuterated and cleavage mechanism. By considering all possible combinations of these three variables one can calculate the fraction of observable hydrogen in the benzylic methyl group for any alcohol, solvent and mechanism. These fractions can be used as weighting constants (Table 1).

Table 1. Weighting constants

Run	Solvent	Alcohol	1,3- Cleavage	Concerted 2,3- cleavage	"Free" carbonium ion 2,3- cleavage
1	H	VIII	1.00	1.00	1.00
2	H	XII	1.00	0.00	0.50
3	D	VIII	0.67	1.00	0.83
4	D	XII	0.67	0.00	0.17

Let  $\underline{A}$  be the fraction of 1,3-cleavage,  $\underline{B}$  the fraction of concerted 2,3-cleavage and  $\underline{C}$  the fraction of "free" carbonium ion 2,3-cleavage.  $\underline{T}_n$  will be the total scaled integration for run  $\underline{n}$  referred to the phenyl protons as a standard. The combination of appropriate terms leads to four simultaneous equations in four unknowns (Table 2).

Table 2. Simultaneous equations

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$$1.00A + 1.00B + 1.00C = T_1 = 1.00$$

$$1.00A + 0.00B + 0.50C = T_2$$

$$0.67A + 1.00B + 0.83C = T_3$$

$$0.67A + 0.00B + 0.17C = T_4$$

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## EXPERIMENTAL

## Synthetic and Experimental Conditions

Boiling points

All boiling points are uncorrected and in degrees Centigrade. The pressures associated with low pressure distillations were read from a McLeod gauge.

Melting points

All melting points are corrected and in degrees Centigrade. All were taken on a Fisher-Johns Melting Point Apparatus between two glass slides.

Infrared spectra

All infrared spectra were recorded on a Perkin-Elmer Model 21 infrared spectrophotometer as carbon tetrachloride solutions in 0.5 mm sodium chloride cells and only the carbonyl absorption maxima is given, unless otherwise noted.

Vapor phase chromatography (VPC)

All vapor phase chromatography analyses were performed on a Perkin-Elmer Vapor Fractometer Model 154C or a F&M Scientific Corporation Model 500 Programmed Temperature Gas Chromatograph.

Nuclear magnetic resonance spectra (NMR)

All nuclear magnetic resonance spectra were recorded on a Varian Associates HR-60 high resolution spectrometer at 60 megacycles.



Elemental analyses

Elemental analyses were performed by Midwest Microlab, Inc., Indianapolis, Indiana or Spang Microanalytical Laboratory, Ann Arbor, Michigan.

The lactone of 3-phenyl-4-hydroxybutanoic acid  
( $\beta$ -phenyl- $\gamma$ -butyrolactone)

In a five liter round bottom flask equipped with a condenser and a mechanical stirrer 50 gm (2.2 moles) of sodium was dissolved in 2000 ml of absolute ethanol. After 325 gm (2.0 moles) of diethyl malonate was added the solution was heated to reflux. Over a two hour period 240 gm (2.0 moles) of styrene oxide was added. After heating for two additional hours 40 gm (1.0 mole) of sodium hydroxide in 2000 ml of water was cautiously added. The ethanol was allowed to distill off. Concentrated hydrochloric acid (300 ml, 3.6 moles) was carefully added and the organic material was extracted with methylene chloride. The methylene chloride was removed and the residue was heated over 140° to decarboxylate it. When the evolution of carbon dioxide ceased the material was distilled to give 200 gm (1.2 moles, 62%) of  $\beta$ -phenyl- $\gamma$ -butyrolactone, bp 103-105°/0.25 mm (literature bp 126.0-126.5°/0.8 mm).

Analysis      Calculated for  $C_{10}H_{10}O_2$ : C, 74.05; H, 6.22.  
Found: C, 73.84; H, 6.15. Infrared: 5.58  $\mu$  ( $1790\text{ cm}^{-1}$ ).

Ethyl 4-chloro-3-phenylbutanoate

Charged to a 5000 ml round bottom flask equipped with a reflux condenser were 251 gm (1.4 moles) of  $\beta$ -phenyl- $\gamma$ -butyrolacetone, 300 gm (2.5 moles) of thionyl chloride and 1000 ml of benzene. The solution was heated to reflux for six hours and after it had cooled to room temperature 500 ml of absolute ethanol saturated with anhydrous hydrogen chloride was slowly added. The solution was then heated at reflux for four hours after which the bulk of the solvent was allowed to distill off. The remaining material was distilled under reduced pressure until the temperature of the column rose to 150°. Low pressure distillation gave 286 gm (1.3 moles, 90%) of ethyl 4-chloro-3-phenylbutanoate, bp 104-105°/0.25 mm.

Analysis      Infrared: 5.77  $\mu$  ( $1736\text{ cm}^{-1}$ ).

trans-2-Phenylcyclopropane carboxylic acid

In a 5000 ml round bottom flask equipped with a reflux condenser and a mechanical stirrer was dissolved 80 gm (2.0 moles) of potassium in 2000 ml of absolute tert-butanol. The solution was heated at reflux and 308 gm (1.3 moles) of ethyl 4-chloro-3-phenylbutanoate was added dropwise over a one hour period. Heating was continued for four more hours after which 40 gm (1.0 mole) of sodium hydroxide in 2000 ml of water was cautiously added. The tert-butanol was allowed to distill off and then the flask was cooled in ice-water. Concentrated hydrochloric acid (300 ml, 3.6 moles) was added and the

organic material was extracted with methylene chloride. The methylene chloride solution was washed twice with saturated aqueous sodium chloride solution. The methylene chloride was removed and the residue distilled to yield 188 gm (1.2 moles, 89%) of trans-2-phenylcyclopropane carboxylic acid, bp 104-105°. A sample of the acid was recrystallized from water to give a mat of fine white needles, mp 90.5-91.5° (literature mp 93.0°).

Analysis      Calculated for  $C_{10}H_{10}O_2$ : C, 74.05; H, 6.22. Found: C, 74.18; H, 6.22. Infrared: 5.91  $\mu$  (1692  $cm^{-1}$ ) in  $CHCl_3$ .

(trans-2-Phenylcyclopropyl) methyl ketone

Methylolithium (approximately 2.5 moles) was prepared according to the method of Gilman. To 1500 ml of anhydrous ether in a 5000 ml round bottom flask, equipped with a high capacity internal cooling coil condenser and a mechanical stirrer, was added 43 gm (6.1 moles) of lithium wire previously pounded flat, cut into 5 to 10 mm pieces and washed with ether. Added at a rate to maintain a moderate reflux was 400 gm (2.8 moles) of methyl iodide. When the reaction was complete the solution was filtered through a coarse glass wool plug into an addition funnel.

Into a 5000 ml round bottom flask equipped with a reflux condenser, as described above, and a mechanical stirrer was charged 189 gm (1.2 moles) of trans-2-phenylcyclopropane

carboxylic acid and 200 ml of anhydrous ether. The methyl-lithium solution was then added dropwise to maintain a steady reflux, suitable precautions being taken to vent the resulting methane. When the addition was complete saturated aqueous ammonium chloride solution was added dropwise with vigorous stirring to destroy any excess methyl-lithium. The addition was continued until two clear layers formed. The ether layer was separated, washed once with saturated aqueous ammonium chloride solution, twice with water and dried over anhydrous magnesium sulfate. The ether was removed and the residue distilled to yield 140 gm (0.88 mole, 75%) of (trans-2-phenylcyclopropyl) methyl ketone, bp 85-87°/0.25 mm.

Analysis Infrared: 5.89  $\mu$  ( $1700\text{ cm}^{-1}$ ).

A 2,4-dinitrophenylhydrazone derivative of the ketone was prepared by the diglyme method of Shine. The derivative was recrystallized from 95% ethanol giving fine orange needles, mp 137.0-138.0°.

Analysis Calculated for  $\text{C}_{17}\text{H}_{16}\text{O}_4\text{N}_4$ : C, 59.99; H, 7.74; N, 16.46. Found: C, 59.98; H, 4.80; N, 16.61.

#### trans-2-Phenylcyclopropyl acetate

Peroxytrifluoroacetic acid was prepared by the method of Emmons and Lucas. To 500 ml of methylene chloride in a 1000 ml glass stoppered Erlenmeyer flask was added 460 gm (2.2 moles) of trifluoroacetic anhydride and then in 5 ml portions 57 ml (2.2 moles) of 90% hydrogen peroxide. The reaction was

moderated as necessary by immersing the reaction vessel in ice-water.

The peracid solution was added dropwise over a two hour period to a 5000 ml round bottom flask containing a stirred slurry of 140 gm (0.88 mole) of trans-2-phenylcyclopropyl methyl ketone, 600 gm (4.2 moles) of disodium hydrogen phosphate and 500 ml of methylene chloride. This reaction was moderated with ice-water so that it was just at or below reflux temperature. When the addition was complete the reaction was allowed to stir at room temperature for several hours. Next the solids were filtered, washed with methylene chloride and discarded. The methylene chloride solution was washed twice with water, then with saturated aqueous sodium bicarbonate solution until free from acid and then twice again with water. The methylene chloride was removed and the residue distilled to give 109 gm (0.6 mole, 77%) of trans-2-phenylcyclopropyl acetate, bp 84.85°/0.25 mm.

Analysis      Infrared: 5.71  $\mu$  ( $1752 \text{ cm}^{-1}$ ).

#### trans-2-Phenylcyclopropanol

Approximately 0.3 mole of methylolithium was prepared. This solution was added dropwise to a 1000 ml round bottom flask, equipped with stirrer and internal cooling coil condenser, containing 20 gm (0.113 mole) of trans-2-phenylcyclopropyl acetate in 200 ml of ether. After stirring ten minutes saturated aqueous boric acid solution was added dropwise until

the excess methyllithium was destroyed and then rapidly until two clear phases separated. The ether layer was separated, washed twice with water, dried over anhydrous magnesium sulfate and removed at reduced pressure. The remaining liquid was distilled to give 12.0 gm (0.089 mole, 79%) of trans-2-phenylcyclopropanol, bp 73-74°/0.25 mm.

The alcohol was then recrystallized from 50 ml ether-pentane (1:1 by volume) at -78°. The resulting white precipitate was quickly vacuum filtered into a Buchner funnel.

The material was redissolved in 50 ml ether-pentane (1:1) and again cooled to -78°. Again it was filtered and redissolved in 40 ml ether-pentane (1:2). After the crystals appeared again more pentane was added until it was apparent that no more alcohol was crystallizing out of solution. Filtration gave a white solid material which was dried at room temperature at 1.0 mm. Yield, 3.2 gm (0.0238 mole, 26.8%) of trans-2-phenylcyclopropanol, mp 41.5-42.0°.

Analysis      Calculated for C<sub>9</sub>H<sub>10</sub>O: C, 80.56; H, 7.51.  
Found: C, 80.17; H, 7.67. Infrared: 2.76  $\mu$  (3630 cm<sup>-1</sup>) unbonded hydroxyl; 3.00  $\mu$  (3333 cm<sup>-1</sup>) bonded hydroxyl; 6.23  $\mu$  (1607 cm<sup>-1</sup>) phenyl.

A 1-naphthylurethan derivative was prepared<sup>64</sup> and recrystallized twice from carbon tetrachloride and twice from hexane, mp 130.0-130.5°.

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<sup>64</sup>Tipson, R. S., Journal of Organic Chemistry, 9, 235 (1944).

Analysis      Calculated for  $C_{20}H_{17}NO_2$ : C, 80.56; H, 7.51. Found: C, 79.29; H, 7.60.

Also a p-nitrobenzoate derivative was prepared<sup>64</sup> and recrystallized five times from 95% ethanol, mp 102.0-102.4°.

Analysis      Calculated for  $C_{16}H_{13}NO_4$ : C, 67.84; H, 4.63; N, 4.95. Found: C, 67.38; H, 4.59; N, 4.84.

A p-toluenesulphonate derivative was prepared<sup>65</sup> and recrystallized from ether-pentane at -78°, mp 97.0-98.0°.

Analysis      Calculated for  $C_{16}H_{16}O_3S$ : C, 66.67; H, 5.55; S, 11.10. Found: C, 66.44; H, 5.53; S, 11.15.

The lactone of 2-methyl-3-phenyl-4-hydroxybutanoic acid  
( $\alpha$ -methyl- $\beta$ -phenyl- $\gamma$ -butyrolactone)

In a five liter round bottom flask equipped with condenser and a mechanical stirrer 55 gm (2.4 moles) of sodium was dissolved in 200 ml of absolute ethanol. After the addition of 310 gm (1.9 moles) of diethyl malonate the solution was heated to reflux. Over a two hour period 230 gm (1.9 moles) of styrene oxide was added. After heating for two additional hours 320 gm (2.2 moles) of iodomethane in 200 ml of absolute ethanol was slowly added. One hour later 40 gm (1.0 mole) of sodium hydroxide in 1700 ml of water was cautiously added. The ethanol was then allowed to distill. Concentrated

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<sup>65</sup>Shriner, R. L. and Fuson, R. C., The Systematic Identification of Organic Compounds. 2nd edition. New York, John Wiley and Sons, Inc. 1940.

hydrochloric acid (300 ml, 3.6 moles) was carefully added and the organic material was extracted with methylene chloride. The methylene chloride was removed and the residue heated above 140° to decarboxylate it. When the evolution of carbon dioxide ceased the material was distilled to give 258 gm (1.4 moles, 71%) of  $\alpha$ -methyl- $\beta$ -phenyl- $\gamma$ -butyrolactone, bp 105-108°/0.25 mm.

Analysis Infrared: 5.64 (1772  $\text{cm}^{-1}$ ) in  $\text{CHCl}_3$ .

Ethyl 4-chloro-2-methyl-3-phenylbutanoate

Charged to a 5000 ml round bottom flask equipped with a reflux condenser were 258 gm (1.4 moles) of  $\alpha$ -methyl- $\beta$ -phenyl- $\gamma$ -butyrolactone, 300 gm (2.5 moles) of thionyl chloride and 900 ml of benzene. The solution was heated at reflux for eight hours. After it had then cooled to room temperature 500 ml of absolute ethanol saturated with anhydrous hydrogen chloride was slowly added. The solution was again heated at reflux for four hours after which the bulk of the solvent was allowed to distill. The remaining material was distilled at reduced pressure until the temperature of the column rose to 150°. Low pressure distillation yielded 223 gm (1.0 mole, 70%) of ethyl 4-chloro-2-methyl-3-phenylbutanoate, bp 104-106°/0.25 mm.

Analysis Infrared: 5.78 (1735  $\text{cm}^{-1}$ ).



2-Phenyl-1-methylcyclopropane carboxylic acid

In a 5000 ml round bottom flask equipped with a reflux condenser and a mechanical stirrer was dissolved 50 gm (1.3 moles) of potassium in 1200 ml of tert-butanol. The solution was heated to reflux and 270 gm (1.1 moles) of ethyl 4-chloro-2-methyl-3-phenylbutanoate was added over a one hour period. Heating was continued for four more hours after which 25 gm (0.6 mole) of sodium hydroxide in 1500 ml of water was cautiously added. The tert-butanol was allowed to distill off and then the flask was cooled in ice-water. Concentrated hydrochloric acid (300 ml, 3.6 moles) was added and the organic material was extracted with methylene chloride. The methylene chloride solution was washed twice with saturated sodium chloride solution. The methylene chloride was removed and the residue was heated above 250° to pyrolyze any tert-butyl ester present. This material then was distilled at low pressure to yield 133 gm (0.76 mole, 72%) of 2-phenyl-1-methylcyclopropane carboxylic acid, bp 118-120°/0.25 mm. A sample of the acid was recrystallized from water to give a mat of fine white needles, mp 79.5-80.0°.

Analysis      Calculated for  $C_{11}H_{12}O_2$ : C, 74.97; H, 6.84.  
Found: C, 75.03; H, 6.72. Infrared: 5.93 ( $1687\text{ cm}^{-1}$ ) in  $CHCl_3$ .

2-Phenyl-1-methylcyclopropyl methyl ketone

Methyl lithium (approximately 2.1 moles) was prepared

according to the method of Gilman from 320 gm (2.2 moles) of methyl iodide and 21 gm (3.0 moles) of lithium wire in 2000 ml of ether.

In a 5000 ml round bottom flask equipped with a high capacity internal cooling coil condenser and a mechanical stirrer was charged 159 gm (0.91 mole) of 2-phenyl-1-methylcyclopropane-carboxylic acid and 200 ml of anhydrous ether. The methyllithium solution was then added dropwise to maintain a steady reflux, suitable precautions being taken to vent the resulting methane. After the addition was complete the reaction was allowed to stir for an additional one half hour. Saturated aqueous ammonium chloride solution was added dropwise to destroy any excess methyllithium. The addition was continued until two clear layers formed. The ether layer was separated, washed once with saturated aqueous ammonium chloride solution, twice with water and dried over anhydrous magnesium sulfate. The ether was removed and the residue distilled to yield 118 gm (0.68 mole, 75%) of 2-phenylcyclopropyl) methyl ketone, bp 74-76°/0.25 mm.

Analysis Infrared: 5.91  $\mu$  ( $1692\text{ cm}^{-1}$ ).

A 2,4-dinitrophenylhydrazone derivative was prepared by the diglyme method of Shine. The derivative was recrystallized from 95% ethanol to give fine orange crystals, mp 165.0-165.5.

Analysis Calculated for  $\text{C}_{18}\text{H}_{18}\text{N}_4\text{O}_4$ : C, 61.01; H, 5.12; N, 15.81. Found: C, 60.92; H, 5.07; N, 15.91.

2-Phenyl-1-methylcyclopropyl acetate

Peroxytrifluoroacetic acid was prepared by the method of Emmons and Lucas. To 300 ml of methylene chloride in a 1000 ml glass stoppered Erlenmeyer flask was added 200 gm (0.95 mole) of trifluoroacetic anhydride and then in 5 ml portions 25 ml (0.97 mole) of 90% hydrogen peroxide. The reaction was moderated as necessary by immersing the reaction vessel in ice-water.

The peracid solution was added dropwise over a one hour period to a 5000 ml round bottom flask containing a slurry of 38 gm (0.22 mole) of 2-phenyl-1-methylcyclopropyl methyl ketone, 200 gm (1.4 moles) of disodium hydrogen phosphate and 400 ml of methylene chloride. This reaction was moderated by immersing in ice-water so that it was just at or below reflux temperature. When the addition was complete the reaction was allowed to stir at room temperature for several hours. Next the solids were filtered, washed with methylene chloride and discarded. The methylene chloride solution was washed twice with water, then with saturated aqueous sodium bicarbonate solution until free from acid and twice again with water. The methylene chloride was removed and the residue distilled to give 30 gm (0.16 mole, 72%) of 2-phenyl-1-methylcyclopropyl acetate, bp 70-72°/0.25 mm.

Analysis      Infrared: 5.73  $\mu$  ( $1746\text{ cm}^{-1}$ ).

2-Phenyl-1-methylcyclopropanol

Approximately 0.11 mole of methyllithium was prepared. This solution was added dropwise to a 1000 ml round bottom flask, equipped with an internal cooling coil condenser and stirrer, containing 9.5 gm (0.050 mole) of 2-phenyl-1-methylcyclopropyl acetate and 50 ml of anhydrous ether. The flask was cooled externally with ice-water throughout the addition. Stirring was continued for thirty minutes after the addition was complete. Then saturated aqueous boric acid solution was added dropwise to destroy any excess methyllithium and continued until two clear layers formed. The ether layer was separated, washed thrice with water, diluted with one-half its volume of pentane and extracted twice more with water. After drying over anhydrous magnesium sulfate the solution was concentrated to one-fifth of its volume, transferred to a polyethylene bottle and packed in solid carbon dioxide. Several hours later the crystals were filtered, yield 1.0 gm. The mother liquors were concentrated, diluted somewhat with pentane and cooled again. The second crop of crystals amounted to 1.4 gm. Total yield, 2.4 gm (0.016 mole, 32.4%) of 2-phenyl-1-methylcyclopropanol, mp 81.5-82.0°.

Analysis Infrared: 2.70  $\mu$  ( $3700\text{ cm}^{-1}$ ) unbonded hydroxyl; 2.94  $\mu$  ( $3450\text{ cm}^{-1}$ ) bonded hydroxyl; 6.19  $\mu$  ( $1613\text{ cm}^{-1}$ ) phenyl.

A p-nitrobenzoate derivative was prepared by heating a

sample of the alcohol with p-nitrobenzoyl chloride in anhydrous pyridine at 80° for one hour. Recrystallization from 95% ethanol gave colorless monoclinic crystals, mp 107.5-108.5°.

The base catalyzed isomerization of  
2-phenyl-1-methylcyclopropyl acetate

A 200 mg sample of 2-phenyl-1-methylcyclopropyl acetate was dissolved in a solution of 8 ml of diglyme, 2 ml of water and 0.5 gm of sodium hydroxide. The solution was heated at reflux for eight hours. It was acidified with concentrated hydrochloric acid and extracted with several small portions of ether, the total volume of ether was 70 ml. The ether solution was washed twice with water and dried over anhydrous magnesium sulfate. The ether was removed and the residue was prepared for NMR analysis. The NMR spectrum showed just one compound to be present, 4-phenylbutan-2-one.

The acid catalyzed isomerization of  
2-phenyl-1-methylcyclopropyl acetate

A 200 mg sample of 2-phenyl-1-methylcyclopropyl acetate was dissolved in a solution of 8 ml of diglyme, 2 ml of water and 10 drops of concentrated hydrochloric acid. The solution was heated at reflux for eight hours. It was extracted with several small portions of ether, total volume of ether was 50 ml. The ether solution was dried over anhydrous magnesium

sulfate. The ether was removed and the residue prepared for NMR analysis. The NMR spectrum showed 3-phenylbutan-2-one and 4-phenylbutan-2-one to be present in an approximate 55 to 45 ratio.

#### The pyrolysis of 2-phenyl-1-methylcyclopropyl acetate

Four 0.25 ml samples of 2-phenyl-1-methylcyclopropyl acetate were pyrolyzed<sup>66</sup>, each under slightly varying conditions. The first sample was admitted to the pyrolysis column which was at 450°. The pyrolysate trap was kept at temperatures near -50°. After the sample had been admitted to the column, the column was cooled to room temperature and washed down with carbon tetrachloride. The washings were further washed with sodium bicarbonate solution and water and dried over anhydrous sodium sulfate. The infrared spectrum of the pyrolysate was identical to that of the acetate indicating little pyrolysis. At 525° another sample was pyrolyzed. The infrared spectrum showed a reduction in the acetate carbonyl absorption but charred material was not observed on the column. At 550° the infrared spectrum indicated a majority of the sample had pyrolyzed but no indication of an olefin was present. The amount of charred material on the column indicated that any pyrolysis product had decomposed at these

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<sup>66</sup>For a complete description of the pyrolysis apparatus and nominal reaction conditions see: DePuy, C. H. and King, R. W., Chemical Reviews, 60, 431 (1960).

temperatures. The fourth sample of acetate was dissolved in three ml of toluene and admitted to the column which was at 550°. Toluene is known to reduce decomposition of pyrolysis products by trapping free radicals which may arise under the reaction condition and lead to the decomposition. Again charring occurred and the pyrolysis was abandoned.

The base catalyzed isomerization of  
2-phenyl-1-methylcyclopropanol

In methanol A 100 mg sample of 2-phenyl-1-methylcyclopropanol was dissolved in 1.5 ml of methanol. To this solution was added 0.2 ml of approximately 6 M sodium hydroxide solution. This was sealed in a glass tube and heated for ten hours at 80°. It was transferred to a micro heavier-than-water continuous extractor, acidified and extracted with carbon tetrachloride for one hour. The carbon tetrachloride was removed and the residue prepared for NMR analysis. The NMR spectrum (Figure 7) showed but one compound, 4-phenylbutan-2-one. Careful checking and re-examination of the reaction and work up conditions and techniques precludes the loss of any other reaction product.

As NMR analysis may not detect a component which is less than 10% of the main product a VPC analysis was made. This technique, under the conditions used, should detect another component which is 0.01% of the main product. The VPC column used for this and following analyses was a one meter Pyrex

column packed with UCON LB 550X 1:4 on 60/80 mesh Regular W Chromosorb. This column proved to efficiently separate all products detected. The most satisfactory conditions for separation are 180° and a helium flow rate of 50 ml per minute.

The VPC analysis also indicated that only one isomerization product was present. Three other columns were used at various temperatures and helium flow rates but none of these gave any indication of other components. These columns were packed with Apiezon L 1:10 on 20/40 mesh firebrick, TCEP (tris-(2-cyanoetoxy)-propane) 1:3 on 60/80 mesh firebrick and Carbowax, Perkin Elmer column K.

In methanol-d A 100 mg sample of 2-phenyl-1-methylcyclopropanol was dissolved in 1.5 ml of methanol-d. To this solution was added 0.2 ml of approximately 5 M sodium deuteriooxide solution. The isomerization and work up were carried out as above. The NMR spectrum (Figure 8) showed considerable exchange as expected. Analysis of the integration of the spectrum shows 72% exchange at the methyl group and of the four methylene protons possible only 1.62 are present.

The acid catalyzed isomerization of  
2-phenyl-1-methylcyclopropanol

In methanol A 100 mg sample of 2-phenyl-1-methylcyclopropanol was dissolved in 1.5 ml of methanol and 0.2 ml of approximately 9 M hydrochloric acid. The solution was



sealed in a glass tube and heated for ten hours at 80°. The work up was the same as above. The NMR spectrum (Figure 9) was recorded and integrated. Two compounds are clearly indicated, 3-phenylbutan-2-one and 4-phenylbutan-2-one in a 55 to 45 ratio. A VPC analysis on the UCON LB 550X column confirmed this ratio and showed no other compounds were present. The three other columns also showed only two components.

In dioxane A 100 mg sample of alcohol VIII was dissolved in 1.5 ml of dioxane and 0.2 ml of approximately 9 M hydrochloric acid-d. The solution was sealed in a tube and heated for four hours at 75°. The solvent was then removed, the residue dissolved in chloroform, dried with anhydrous magnesium sulfate and filtered. The chloroform was removed and the residue prepared for NMR analysis. The integration of the NMR spectrum showed 79% of the possible hydrogen is present in the benzylic methyl group, that is, 60% deuterium incorporation.

In methanol-d, 85% pure A 100 mg sample of alcohol VIII was dissolved in 1.5 ml methanol-d and 0.2 ml of approximately 9M hydrochloric acid-d. By NMR analysis this methanol-d was only 85% pure and the hydrochloric acid-d was 99.5+% pure. The isomerization and work up were carried out the same as with methanol. The NMR spectrum (Figure 10) was integrated and indicated 82% of the possible protons were present. The increase of 39% over the 79% observed above is accounted for

by assuming a negligible isotope effect and the dilution of deuterons by protons. The 15% dilution times the 33% possible observable incorporation leaves a maximum increase of 5% in the integration.

## SUMMARY

trans-Phenylcyclopropanol and 2-phenyl-1-methylcyclopropanol have been synthesized. During the synthesis it was discovered that the reported addition of diethyl malonate to styrene oxide is incorrect. The addition occurs predominantly at the  $\alpha$  rather than at the  $\beta$  position of the styrene oxide side chain.

2-Phenyl-1-methylcyclopropanol proved to be more stable and of greater interest than trans-2-phenylcyclopropanol and several reactions attempted with it are described. The alcohol isomerizes in basic media to a single product, 4-phenylbutan-2-one. In contrast to the facile isomerization of cyclopropanol and alkyl-substituted cyclopropanols in chloroform the alcohol gives no indication of isomerizing in this solvent. The pyrolysis of 2-phenyl-1-methylcyclopropyl acetate yielded only carbonaceous material.

The alcohol isomerizes in acidic media to 4-phenylbutan-2-one and 3-phenylbutan-2-one in nearly equal amounts. When the isomerization was catalyzed by hydrochloric acid-d the results indicated that carbon-carbon bond cleavage occurred between all three bonds of the cyclopropane ring. A method of determining the ratio of the three cleavages is described.

This work has shown that cyclopropanols are an excellent system for the study of electrophilic substitution at

saturated carbon. More detailed studies along this line are being pursued by others.

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