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The hydrolysis of cyclopropyl acetate

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THE HYDROLYSIS OF CYCLOPROPYL ACETATE

by

Lee Robert Mahoney

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Signature was redacted for privacy.

Head of Major Department

Signature was redacted for privacy.

Dean of Graduate College

Iowa State University
of Science and Technology
Ames, Iowa

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INTRODUCTION

The study of small ring systems has in the past decade been a very fruitful area of research for the organic chemist. Due to the bizarre courses observed in many reactions of these compounds, unusual reactive intermediates have been postulated. Application of these reactive intermediates to systems with "less abnormal" steric and electronic enviornments have rationalized results and allowed predictions to be made in these latter systems. In addition to the above, due to their simplicity small rings may serve as models for the more advanced quantum mechanical descriptions of chemical systems. As is always the case, however, the first problem to be overcome is the preparation of such compounds.

Indeed it is surprising that cyclopropanol, a relatively simple alcohol had not, previous to this study, been prepared in the pure state. The present work was prompted by reports of the facile isomerization of crude samples of this interesting material. Having in mind an eventual synthesis of the pure material rate studies on the alcohol, generated in situ, lead to the discovery that the alcohol was relatively stable under some conditions. A straight forward synthesis of pure cyclopropanol was attempted and proved successful.

Preliminary studies of the isomerization of the pure al-

cohol have revealed some surprising and as yet unexplained solvent effects. It is hoped that this work will serve as a beginning, at least, to extensive research on cyclopropyl alcohol systems.

HISTORICAL

During the past fifty years a considerable amount of physical and chemical evidence has been presented to suggest a close analogy between the cyclopropane ring and the ethylenic double bond.

An examination of the spectroscopic properties of three membered rings tends to substantiate this view. A number of investigators[1] have shown that compounds containing a cyclopropyl-ethylene structure exhibit maximum absorption in the ultraviolet at a wavelength considerably higher than that of a simple ethylene, the value being closer to that of a conjugated diene.

Infra red studies on cyclopropane indicate that the high C-H stretching force constant for cyclopropane compared to the normal methylene group is due to a large amount of s character in the C-H bonds.[2] It was also noted by Roberts and Chambers[3] that the integrated extinction coefficients for

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[1](a) Klotz, J.M., J. Amer. Chem. Soc., 66, 88 (1944); (b) Mariella, R.P., ibid., 70, 1494 (1948); ibid., 74, 518 (1952); (c) Rodgers, M.T., ibid., 69, 2544 (1947); (d) Burt, E.P. and Carr, C.P., ibid., 40, 1590 (1918); (e) Roberts, J.D. and Green, C., ibid., 68, 214 (1946); (f) Smith, L.I. and Rogier, E.R., ibid., 73, 3840 (1951)

[2]Linnett, J.W., Nature, 160, 162 (1947)

[3]Roberts, J.D. and Chambers, V.C., J. Amer. Chem. Soc., 73, 5030 (1951)

The C-H bonds in cyclopropyl chloride and bromide were significantly lower than those of larger membered rings. Conjugative effects of substituted cyclopropanes have been studied by Cannon et al.[4]

Dipole moment measurements of three membered ring compounds by Rogers[5] and Roberts[5a] indicate that the C-C bond electrons are more weakly bound than the usual electrons and tend to exhibit the characteristics associated with mobile electrons.

The bond distances and geometry of cyclopropane have been investigated by several physical methods[6] and the results support the picture of a fully symmetrical ring with carbon atoms at the vertices of an equilateral triangle and the C^{H}_{H} planes bisecting the corresponding ring angle. As expected the C^{H}_{H} angle is close to 120°. The C-C bond distance is 1.526A° in cyclopropane, shorter than the normal C-C single bond distance of 1.544A°.

A molecular orbital interpretation of the physical data

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[4]Cannon, G.W., Santilli, A.A. and Shenian, P., J. Amer. Chem. Soc., 81, 1660 (1959)

[5](a) Rogers, M.T. and Roberts, J.D., ibid., 68, 843 (1946); (b) Rogers, M.T., ibid., 69, 1544 (1946)

[6](a) Skinner, H.A., Nature, 160, 902 (1947); (b) O'Gorman, J.M. and Schomaker, V., J. Amer. Chem. Soc., 68, 1138 (1946); (c) Pauling, L. and Brockway, L.O., ibid., 59, 1123 (1937)

on cyclopropane has been presented by Coulson and Moffitt.[7] These investigators introduced the concept of the bent bond; the endo ring orbitals are hybridized until the angle between them is 106° instead of 60°, the angle between the straight lines joining the nuclei. The smaller overlap between the atomic orbitals at an effective bond angle of 106° relative to that at 60° is compensated by the smaller bend required of the orbitals. One of the ring orbitals, ψR, may be written as

$$\psi R = 0.442[\psi(2S) + 2.03\,\psi(2p\sigma R)] \qquad \text{(Eq. 1)}$$

where $(2p\sigma R)$ is a 2p orbital in the ring. Since $(2.03)^2$ is equal to 4.12, the ring orbitals are $sp^{4.12}$. Similarly, the orbitals to hydrogen are

$$\psi CH = 0.552[\psi(2S) + 1.51\,\psi(2p\sigma CH)] \qquad \text{(Eq. 2)}$$

and these orbitals are $sp^{2.28}$.

It should be noted at this point that Trachtenberg and O'Dian[8] have recently suggested that the cyclopropane ring does not transmit conjugation. Their arguments are based on spectroscopic observations by Eastman *et al.*[9] and on the Hammett ρ values obtained in the acid ionization of trans-2-

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[7] Coulson, C.A. and Moffitt, E.W., Phil. Mag., 40, 1 (1949)

[8] Trachtenberg, E.N. and O'Dian, G., J. Amer. Chem. Soc., 80, 4018 (1958)

[9] (a) Eastman, R.H., ibid., 76, 4115 (1954); (b) Eastman, R.H. and Selover, J.C., ibid., 76, 4118 (1954); (c) Eastman, R.H. and Freeman, S.K., ibid., 77, 6642 (1955)

phenyl-cyclopropane carboxylic and β-phenylpropionic acids. The ρ values obtained were essentially the same, implying that the cyclopropyl ring is ineffective in transmitting conjugation. Fuchs and Bloomfield[10] have extended the study to the trans-cinnamic acids and also obtained ρ values for the ester hydrolysis. A resume of the results of both studies is presented in Table 1.

Table 1. Hammett ρ Values.

Series	p-Ester hydrolysis	p-Acid ionization
trans-Cinnamic	1.329	0.466
trans-2-Phenylcyclopropane	0.789	0.182
β -Phenylpropionic	0.489	0.212

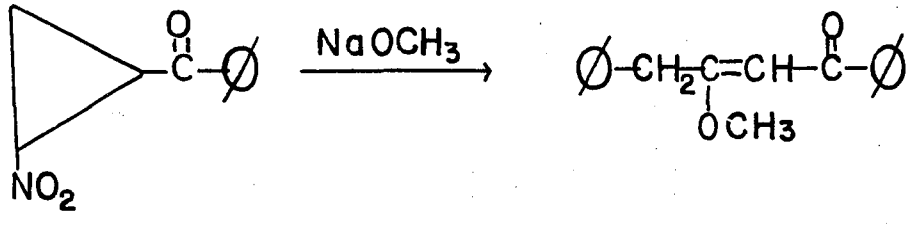
The work of Kohler et al.[11] on the addition of various electrophilic and nucleophilic reagents to substituted cyclopropanes revealed that both vinyl and cyclopropyl systems

[10] Fuchs, R. and Bloomfield, J.J., J. Amer. Chem. Soc., 81, 3158 (1959)

[11] (a) Kohler, E.P. and Conant, J.B., ibid., 39, 1404 1699 (1917); (b) Kohler, E.P. and Davis, T.L., ibid., 41, 992 (1919); (c) Kohler, E.P. and Steel, L.L., ibid., 41, 1093 (1919)

undergo addition reactions with many common reagents. In general, the products on addition of electrophilic reagents were determined by the Markownikoff rule while addition of many nucleophilic reagents to cyclopropyl carbonyl systems gave products analogous to those obtained in the unsaturated series. Recently Kierstead, Linstead and Weedon[12] have reported the 1-6 addition of the diethyl malonate anion to diethyl vinylcyclopropane-1,1-dicarboxylate.

Smith and Showell[13] have prepared a large number of nitro-substituted cyclopropanes and observed the action of base on the system. A ketonic function is necessary in compounds of this series for any reaction to take place.



(Eq. 3)

Although vinylcyclopropane[14] and dicyclopropane[15] fail

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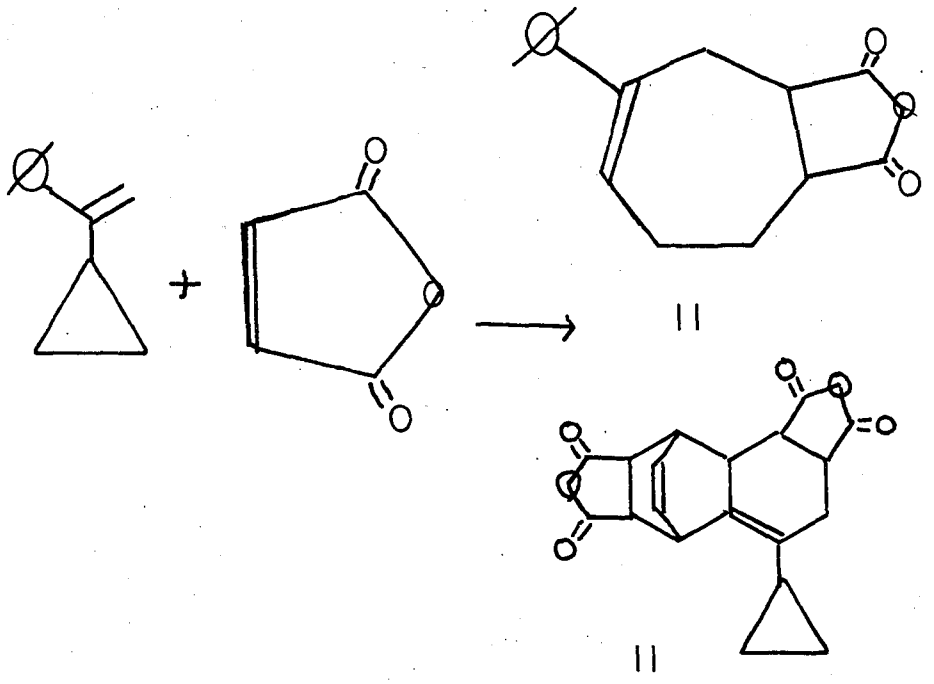
[12] Kierstead, R.W., Linstead, R.P. and Weedon, B.C.L., J. Chem. Soc., 3616 (1952)

[13] Smith, L.I. and Showell, J.J., J. Org. Chem., 17, 834 (1952)

[14] van Volkenburgh, R., Greenlee, K.W., Derfer, J.M. and Boord, C.E., J. Amer. Chem. Soc., 71, 172, 3595 (1949)

[15] Smith, L.I. and Rogier, E.R., ibid., 73, 3840 (1951)

to react with dienophiles, α-cyclopropylstyrene[16] reacts with maleic anhydride to give two products (I) and (II) of which (I) presumably arises by addition in a 1-5 manner.



(Eq. 4)

The observed stability of cationic, anionic and free radical species derived from the cyclopropyl system can be rationalized by the electronic description of the system.

Since the C-H bonds in cyclopropane possess a large amount of s-character relative to normal tetrahedral C-H bonds, the formation of the cyclopropyl carbanion should be relatively

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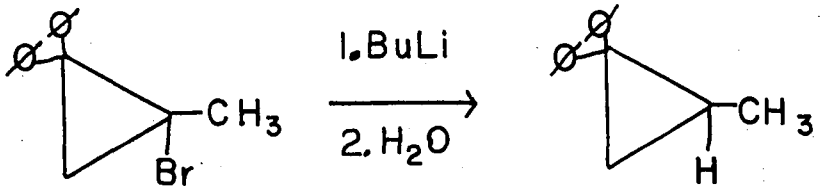
[16] Sarel, S. and Rreuer, E., J. Amer. Chem. Soc., 81, 6522 (1959)

facile. Lanpher, Redman and Morton[17] have recently reported the metalation of cyclopropane by amylsodium. Walborsky and Impastato[18] have studied the formation and stability of such species and have found that the carbanion derived from (III) retains its asymmetry to a large extent (71%) on neutralization. In the vinyl series Curtin and Harris[19] reported that trans-2-bromo-2-butene on treatment with butyl lithium at -15° followed by carbonation yielded the corresponding trans acid in 91% yield.



III (Eq. 5)

Although carbanions derived from asymmetric alkyl halides can under special conditions retain their asymmetry,[20] optically active 2-iodooctane[21] was metalated with sec-butyl lith-

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[17] Lanpher, E.J., Redman, L.M. and Morton, A.A., J. Org. Chem., 23, 1370 (1958)

[18] Walborsky, H.M. and Impastato, F.J., J. Amer. Chem. Soc., 81, 5835 (1959)

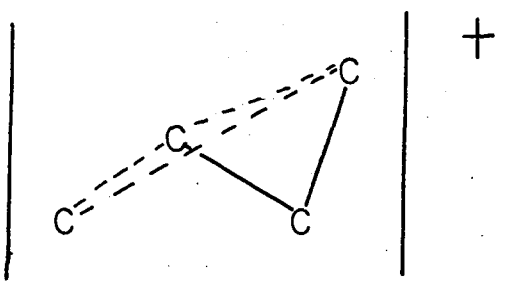
[19] Curtin, D.Y. and Harris, E.E., ibid., 73, 2716, 4519 (1951)

[20] Curtin, D.Y. and Kiehl, W.J., Chemistry and Industry, 262 (1960)

[21] Letsinger, R.L., J. Amer. Chem. Soc., 72, 4842 (1950)

ium at -70° and carbonated. The overall reaction proceeded with only 20% retention of optical activity.

Roberts and Mazur[22] carried out an extensive study of the solvolysis of cyclopropylcarbinyl, cyclobutyl, methylallyl and allylcarbinyl halides. The rate of unimolecular solvolysis was the greatest in all cases for the cyclopropylcarbinyl compounds. Again it was demonstrated that vinyl and cyclopropyl systems possess striking similarities since both accelerated the solvolysis and both gave rise to rearranged products. Rearrangements have been ascribed to the formation of a carbonium ion intermediate which in the case of the reaction of cyclopropylcarbinyl amine with nitrous acid[22] was initially pictured with the three methylene carbons equivalent. However, subsequent investigations by Roberts et al.[23] suggest that the intermediate has an unsymmetrical structure such as (IV).



IV (Eq. 6)

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[22]Roberts, J.D. and Mazur, R.H., J. Amer. Chem. Soc., 73, 2509, 3542 (1951)

[23]Mazur, R.H., White, W.N., Semenow, D.A., Lee, C.E., Silverand, M.S. and Roberts, J.D., ibid., 81, 320 (1959)

this observation has led to studies in rigid systems such as the i-steroids[24] and in cyclopropylcarbinyl systems with various leaving groups.[25]

In contrast to the reactivity toward solvolysis of cyclopropylcarbinyl and allyl systems is the relatively inert character of the cyclopropyl and vinyl p-toluene sulfonates and halides in solvolysis and displacement reactions.[26] Two explanations have been suggested for these phenomena. Roberts[26] prefers to explain the observations as being due to electronic effects, that is, either 1) the greater amount of s character in the C-X bond decreases the ionic character of the bond, or 2) delocalization of the unshared electron pairs on X increases the C-X bond strength. Brown et al.,[27] on the other hand, feel that the low reactivity of small ring halides is due to the greater steric strain in the ionization transition state than in the ground state of the molecule.

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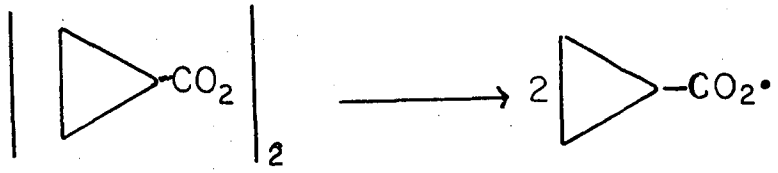
[24](a) Kosower, E.M. and Winstein, S., J. Amer. Chem. Soc., 78, 4347, 4354 (1956); (b) Pearson, R.C. and Langer, S.H., ibid., 75, 1065 (1953)

[25](a) Bergstrom, G.G. and Siegel, S., ibid., 74, 145 (1952); (b) Hart, H. and Sandri, J.M., ibid., 81, 320 (1959)

[26]Roberts, J.D. and Chambers, V.C., ibid., 73, 5035 (1951)

[27]Brown, H.C., Fletcher, R.S. and Johannesen, R.B., ibid., 73, 212 (1951)

Hart and Wyman[28] reported that the formation of the cyclopropyl radical from the decomposition of biscyclopropaneformyl peroxide (V) is very slow, being comparable in rate to the decomposition of benzoyl and acetyl peroxides.



(Eq. 7)

V

Decomposition in moist carbon tetrachloride with iodine present yields nearly equal amounts of cyclopropane carboxylic acid and cyclopropyl iodide. This observation is in contrast to the products formed from the decomposition of benzoyl peroxide and acetyl peroxide, which form benzoic acid and methyl iodide respectively under the same conditions. Whether the stability of the cyclopropanecarboxyl radical (compared with acetoxyl) is due to conjugation between the carboxy electron system and the cyclopropane ring, or whether it is due to reluctance to form the cyclopropyl radical, with sp^2 bonding in the ring, is a question which remains to be answered.

The ease of preparation of substituted cyclopropanes is consistent with the analogies drawn between the vinyl and cyclopropyl systems.

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[28] Hart, H. and Wyman, D.P., J. Amer. Chem. Soc., 81, 4891 (1959)

Nitro cyclopropane was prepared by Hass and Shechter[29] by means of the vapor phase nitration of cyclopropane by nitric acid or nitrogen dioxide. The compound is surprising in that it is stable to oxidation, bromination and action of alkaline reagents.

The preparation of methylene cyclopropane was achieved by Grayson et al. in 1953[30] by the action of zinc on 3-chloro-2 (2-chloromethyl)-1-propene. Several unsuccessful attempts to prepare the compound have been reported in the literature.[31]

Early attempts to prepare chlorocyclopropane[32] met with little success since the product reacts more readily with chlorine than does cyclopropane. Roberts and Dirstine[33] in 1945 prepared chlorocyclopropane by the thermal and photochemical chlorination of cyclopropane, employing flow methods.

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[29] Hass, H.B. and Shechter, H., J. Amer. Chem. Soc., 75, 1382 (1953)

[30] Grayson, J.T., Greenlee, K.W., Derfer, J.M. and Boord, C.E., ibid., 75, 3344 (1953)

[31] (a) Merzhkovskii, B.V., J. Russ. Phy. Chem., 45, 2072 (1913); (b) D'Jakanov, I.A., J. Gen. Chem., (U.S.S.R.); 10, 402 (1940); (c) Dem'janov, N.J. and Dojarenko, M., Ber., 56B, 2208 (1923)

[32] Gustavson, G., J. prakt. Chem. (2), 42, 496 (1890); ibid., 43, 396 (1891)

[33] Roberts, J.D. and Dirstine, P.H., J. Amer. Chem. Soc., 67, 1281 (1945)

Stevens[34] prepared by the thermal method and characterized 1, 1-dichloro-, 1,2-dichloro-, 1,1,2-trichloro- and 1,1,2,2-tetrachlorocyclopropane.

Since the action of bromine on cyclopropane results in ring opening, a different method had to be developed in order to obtain bromocyclopropane. Roberts and Chambers[35] obtained moderate yields of the material utilizing the Hunsdiecker reaction of silver cyclopropanecarboxylate and bromine.

Iodocyclopropane has not been fully characterized but was identified as the product of the decomposition of biscyclopropane-formyl peroxide in carbon tetrachloride containing iodine.[28] The product of the reaction formed a Grignard reagent with magnesium which on carbonation gave cyclopropane carboxylic acid.

Although available by conventional reactions from cyclopropanecarboxylic acid,[36] Roberts and Chambers[35] prepared cyclopropylamine in 70% yield by Beckman rearrangement of the benzenesulfonate of the oxime of cyclopropyl methyl ketone. The amine is prepared in the most direct manner by the method of Emmons,[37] utilizing the action of trifluoroacetic anhydride

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[34]Stevens, P.G., J. Amer. Chem. Soc., 68, 620 (1946)

[35]Roberts, J.D. and Chambers, V.C., ibid., 73, 3176 (1951)

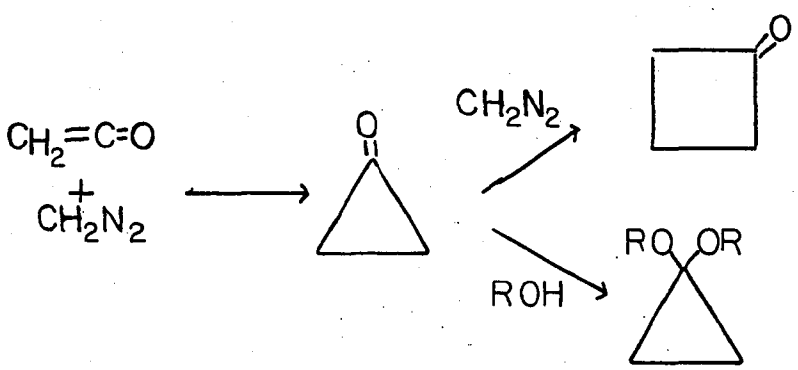
[36]Schatter, M.J., ibid., 63, 1733 (1941)

[37]Emmons, W.D., ibid., 79, 6522 (1957)

on the oxime of cyclopropyl methyl ketone.

Preparation of ether-substituted cyclopropanes offers no difficulty due to the relatively inert character of the ether linkage. The usual method is ring closure with zinc of 1,3-dihalo-2-propyl ethers.[38]

Although cyclopropanone has been demonstrated to be a possible intermediate in the Favorskii reaction in studies by Loftfield[39] and by Stork and Borowitz,[40] the ketone has never been isolated. Addition of methylene (via diazomethane) to ketene yielded cyclobutanone.[41] However if water or an alcohol was present, addition compounds could be isolated. The



(Eq. 8)

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[38](a) Krantz, J.C., Carr, C.V., Forman, S.E. and Evans, J.S., J. Pharmacol., 69, 207 (1940); (b) Olson, W.T., Hipsher, H.F., Buess, C.M., Goodman, I.A., Hard, J., Lamneck, J.H. and Gibbons, B.S., J. Amer. Chem. Soc., 69, 2451 (1947)

[39]Loftfield, R.B., ibid., 72, 632 (1950)

[40]Stork, G. and Borowitz, I.J., ibid., 82, 4301 (1960)

[41]Lipp, P., Buchkremer, J. and Seeles, H., Ann., 499, 1 (1932)

ethyl ketal of cyclopropanone has been characterized by McElvain and Weyna.[42] Thus we see that the ketone is very prone to the addition of nucleophilic reagents as is ketene, its vinyl analog.

Vinyl alcohol, suggested as the reactive intermediate in the reactions of acetaldehyde, is unknown. By analogy, cyclopropyl alcohol should be relatively unstable and should isomerize to propionaldehyde.

Numerous unsuccessful attempts to synthesize unsubstituted cyclopropyl alcohol have been reported. The earliest routes involve ring closure of 1,3-dihalo-2-propanols. Hubner and Muller[43] in 1871 and Tornoe[44] in 1891 obtained allyl alcohol from the action of sodium on the 1,3-dichloro compound. The same product was obtained by Aschan[45] on reaction of the corresponding dibromo compound.

Kishner[46] diazotized cyclopropylamine but also obtained only allyl alcohol.

The first report of the successful preparation of cyclo-

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[42] McElvain, S.M. and Weyna, P.L., J. Amer. Chem. Soc., 81, 2579 (1959)

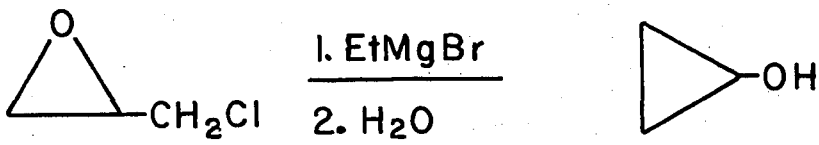
[43] Hubner, H. and Muller, K., Ann., 159, 168 (1871)

[44] Tornoe, H., Ber., 24, 2674 (1891)

[45] Aschan, O., ibid., 23, 1833 (1890)

[46] Kishner, N., Chem. Zentr., 1, 1704 (1905)

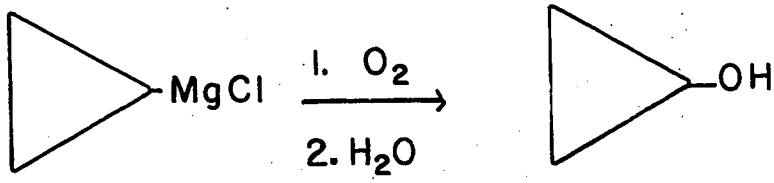
propyl alcohol was made by Magrane and Cottle[47] in 1942. The crude alcohol was isolated as a product of the reaction between epichlorohydrin and ethylmagnesium bromide. A number of



(Eq. 9)

interesting transformations of the alcohol were noted:[48] on repeated distillation it rearranged to propionaldehyde and on standing for several days over potassium carbonate 2-methyl-2-penten-1-al was formed.

In their study of small ring compounds, Roberts and Chambers[35] repeated the synthesis of cyclopropyl alcohol by the procedure of Cottle and also prepared the alcohol by the air oxidation of cyclopropylmagnesium chloride. Although the yield by this alternate method was very low (3%), the deriva-



(Eq. 10)

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[47] Magrane, J.K. and Cottle, D.L., J. Amer. Chem. Soc., 64, 484 (1942)

[48] Stahl, C.W. and Cottle, D.L., ibid., 65, 1782 (1943)

tives formed from the crude material were identical to those prepared via the Cottle procedure. There is little doubt that in each case the product consisted mainly of cyclopropyl alcohol, although it was never isolated in the pure state.

The formation of cyclopropyl esters also presented a problem for the preparative chemist. The electrolysis of potassium cyclopropanecarboxylate gave allyl, not cyclopropyl cyclopropanecarboxylate.[49] The same product was obtained when silver cyclopropanecarboxylate was reacted with iodine.[50]

Cottle[46] reported the formation of an acetate from the acetylation of cyclopropanol, but the material was not characterized. Roberts and Chambers[35] did identify the product as cyclopropyl acetate and reported its physical properties, although yields were very low.

A convenient preparation of the acetate had to await the development of a new reagent, since perbenzoic acid failed to give a Baeyer-Villiger reaction with methyl cyclopropyl ketone.[51] In 1955 Emmons and Lucas[52] prepared the acetate in good yield, utilizing peroxytrifluoroacetic acid as the oxi-

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[49](a) Hofer, H. and Moest, M., Ann., 323, 284 (1902) (b) Fichter, F. and Reeb, H., Helv. Chim. Acta, 6, 454 (1923)

[50]Lipp, P., Buchkremer, J. and Seeles, H., Ann., 499, 1 (1932)

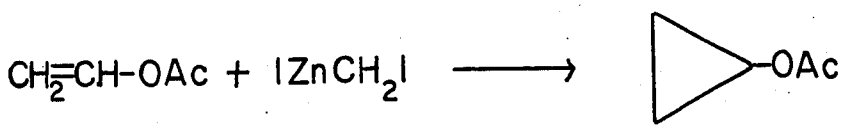
[51](a) Friess, S.L., J. Amer. Chem. Soc., 71, 14 (1949); (b) Friess, S.L. and Pinson, R., ibid., 74, 1302 (1952)

[52]Emmons, W.D. and Lucas, G.B., ibid., 78, 2287 (1955)

dizing agent.

Although now commerically available, a number of preparations of methyl cyclopropyl ketone, the precursor of cyclopropyl acetate, have been reported. Freer and Perkin[53] in 1887 prepared the ketone from ethyl acetoacetate and 1,2-dibromoethane. The action of alkyl magnesium bromides on cyclopropyl cyanide produces alkyl cyclcpropyl ketones in good yield.[54] The method of choice is the cyclization of 5-chloro-2-pentanone under the action of base.[55]

Recently a new synthesis of cyclopropyl acetate has been developed by Simmons and Smith,[56] utilizing a complex formed by the reaction of a zinc-copper couple with diiodomethane. The complex is formed in situ and reacts with vinyl acetate to form cyclopropyl acetate in moderate yield.



(Eq. 11)

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[53] Freer, P.C. and Perkin, W.H., J. Chem. Soc., 51, 820 (1887)

[54] (a) Bruylants, P., Rec. trav. chim., 28, 180 (1909) [C.A., 3, 2700 (1909)]; (b) ibid., Bull. Soc. Chim. Belg., 36, 519 (1927); [C.A., 22, 582 (1929)]

[55] (a) Zelinsky, N.D. and Dengin, E.F., Ber., 55, 3360 (1922); (b) Favorskaya, T.A., Kononova, K.A. and Titon, M.I., J. Gen. Chem. (U.S.S.R.), 29, 2854 (1959)

[56] Simmons, H.E. and Smith, R.D., J. Amer. Chem. Soc., 81, 4256 (1959)

There have been no studies on the rate of hydrolysis of cyclopropyl acetate and only one kinetic study of the hydrolysis of vinyl acetate has been reported.[57] No other enol acetates have been examined. This is rather surprising in view of the general interest in ester hydrolysis as a tool to evaluate electronic and steric effects in organic chemistry.[58]

Cyclopropyl alcohol is unique in that potentially it offers a system in which two problems can be investigated; ring-chain isomerization, and in the case of the base catalyzed isomerization, the problem of electrophilic substitution at saturated carbon.

The only reported study of isomerization in the hydroxycyclopropane system was the early work of Thorpe et al.[59] and Ingold.[60] Unfortunately, the structural assignments of the compounds were incorrect and were not α-keto acid hydroxycyclopropane isomers but, in fact, cis-trans isomers of the cyclic ether (VI). Recent infra red and nuclear magnetic

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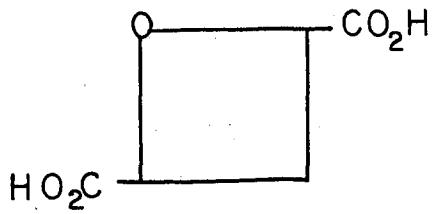
[57] Shrabal, A. and Zahorka, A., Monatsh., 48, 459 (1927)

[58] Taft, R.N. in Newman, M.S., ed. "Steric Effects in Organic Chemistry", John Wiley and Sons, Inc., New York, New York. 1956 p.556

[59] (a) Lanfear, E.W. and Thorpe, J.F., J. Chem. Soc., 123, 1683 (1923); (b) DesLapanda, S.S. and Thorpe, J.F., ibid., 121, 1430 (1922); (c) Barnes, L. and Thorpe, J.F., ibid., 123, 1206 (1923)

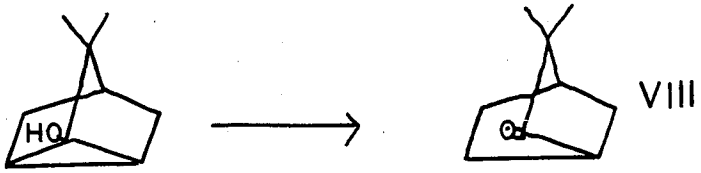
[60] Ingold, C.K., ibid., 119, 305 (1921), 121, 2676 (1922)

resonance studies by Wibert and Holmquist[61] have revealed this error.

VI  (Eq. 12)

A few reports of cyclopropanol isomerization to the corresponding carbonyl compound are to be found in the literature.

Lipp and Padberg[62] in 1921 reported the isomerization of the tricyclic system (VII) to the ketone (VIII) by means of either dilute sulfuric acid or heat.

VII  VIII (Eq. 13)

Julia and Tchernoff[63] have synthesized a large number of 2-phenoxy substituted cyclopropanes and noted the isomerization of several of these compounds under the influence of dilute acids.

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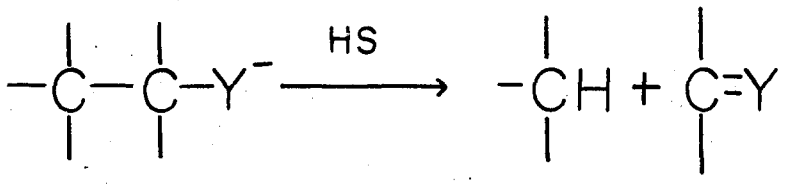
[61] Wibert, K.B. and Holmquist, H.N., J. Org. Chem., 24, 578 (1959)

[62] Lipp, P. and Padberg, C., Ber., 54, 1316 (1921)

[63] (a) Julia, M. and Tchernoff, G., Compt. rend., 249, 714 (1959); (b) Julia, M., Bull. Soc. Chim. France, 181, 184 (1956)

Cram et al.[64] have recently reported a very extensive study of the phenomena of electrophilic substitution at saturated carbon.



(Eq. 14)

Y^- was usually a negatively charged oxygen formed by the action of strong bases on the corresponding alcohol. Optically active materials were used to determine the stereochemical results of the reaction as a function of solvent, metal ion associated with the alkoxide and temperature.

The base catalyzed isomerization of cyclopropyl alcohol to propionaldehyde reported by Cottle may indeed involve a similar transformation, i.e. formation of cyclopropyl alkoxide followed by a ring opening reaction.

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[64](a) Cram, D.J., Langemann, A., Allinger, J. and Kopecky, K.R., J. Amer. Chem. Soc., 81, 5740 (1959); (b) Cram, D.J., Langemann, A. and Hauck, F., ibid., 81,5750 (1959); (c) Cram, D.J., Kopecky, K.P., Hauck, F. and Langemann, A., ibid., 81, 5754 (1959); (d) Cram, D.J., Langemann, A., Lavowski, W. and Kopecky, K.R., ibid., 81, 5760 (1959); (e) Cram, D.J., Hauck, F., Kopecky, K.R. and Nielsen, W.D., ibid., 81, 5767 (1959); (f) Cram, D.J., Mateos, J.L., Hauck, F., Langemann, A., Kopecky, K.R., Nielsen, W.D. and Allinger, J., ibid., 81, 5774 (1959); (g) Cram, D.J., Kingsbury, C.A. and Langemann, A., ibid., 81, 5785 (1959)

Study of this isomerization and possible isomerizations of substituted cyclopropyl alcohols potentially offers a scheme by which the electrophilic substitution at saturated carbon may also be investigated.

DISCUSSION

Choice of precursor for cyclopropyl alcohol

At the beginning of this investigation, there existed a dilema. In order to study the mode of transformation of cyclopropyl alcohol in basic solution, two alternate routes were open to the investigator.

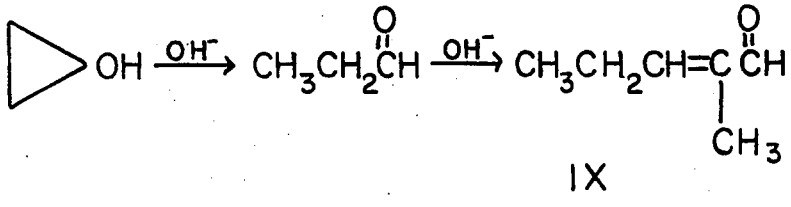
The first route was the synthesis of the pure alcohol. Although cyclopropanol had been prepared in two previous investigations[35,47] by tedious procedures, the material had not been obtained in the pure state; by active hydrogen analysis Cottle claimed a purity of only 87% for his best samples. Thus this route did not appear promising.

Purification of the alcohol would be avoided if it could be generated in situ by an unambiguous reaction from a known, easily purified compound. There are, however, relatively few compounds which could act as precursors of cyclopropyl alcohol. Cyclopropyl ethers, for example, although easily prepared, can only be transformed into the alcohol by the action of strong acids which simultaneously attack the ring.

The most promising class of compounds appeared to be cyclopropyl esters, since it had been demonstrated by several investigators that bond breaking in primary and secondary ester hydrolysis takes place with fission of the acyl-oxygen

bond.[65] Since the mode of isomerization of the alcohol in basic solution was of primary interest, cyclopropyl acetate was chosen as the source of cyclopropanol. Although the Baeyer-Villiger reaction of methyl cyclopropyl ketone with peroxytrifluoroacetic acid[52] does give moderate yields of cyclopropyl acetate, the method is expensive and tedious. However, since the recently reported reaction of zinc methylene iodide with vinyl acetate[56] proved most unsatisfactory, the former method was used.

On reaction with strong base the acetate gave 2-methyl-2-penten-1-al (IX) the same product reported by Magrane and Cottle[47] from the action of base on crude cyclopropyl alcohol this product almost certainly arises from the intermediate formation of propionaldehyde.



IX (Eq. 15)

Since it was hoped that the mode of isomerization of

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[65](a) Polanyi, M. and Szabo, A.L., Trans. Faraday Soc., 30, 508 (1934); (b) Datta, S.E., Day, J.N.E. and Ingold, C.K., J. Chem. Soc., 838 (1934); (c) Long, F.A. and Friedman, J., J. Amer. Chem. Soc., 72, 3692 (1950)

cyclopropyl alcohol could be elucidated by means of experiments in deuterated solvents, the isolation of propionaldehyde from the hydrolysis mixture seemed desirable. Removal of the aldehyde before it could undergo subsequent aldol condensation reactions was attempted by the use of a special apparatus, a complete description of which is found in the experimental section. The principles upon which the experiment was designed are the following: small amounts of cyclopropyl acetate were introduced into an excess of base with a rapid stream of nitrogen being bubbled through the solution. Since it seemed reasonable that the aldol condensation would be higher than first order in aldehyde in dilute solutions, the more dilute the solution, the less favorable the aldol condensation reaction. The most volatile material formed in the system is propionaldehyde which would be carried by the stream of nitrogen out of the solution into a cold trap or into a solution in which derivative of the aldehyde could be formed. The efficiency of the apparatus was tested by isolation of acetaldehyde formed from the hydrolysis of vinyl acetate at room temperature. (The boiling point of acetaldehyde is 21°C) A very high yield, 85% of acetaldehyde, isolated as its dimedone derivate, was obtained.

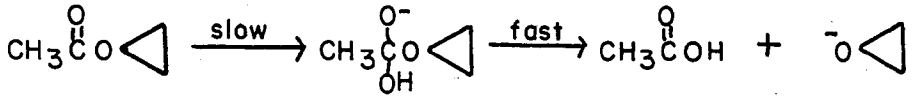
Cyclopropyl acetate was introduced in small portions into the apparatus at the same rate of flow of nitrogen as that used for the vinyl acetate reaction. The entire apparatus was

immersed in a constant temperature bath at 48°C, the boiling point of propionaldehyde. However, the yield of the dimedone derivative of propionaldehyde isolated from the hydrolysis of cyclopropyl acetate was only 15%. It was therefore decided at this point that a kinetic investigation of the series of reaction leading from cyclopropyl acetate to 2-methyl-2-pentenal should be undertaken.

Determination of rate of saponification of esters

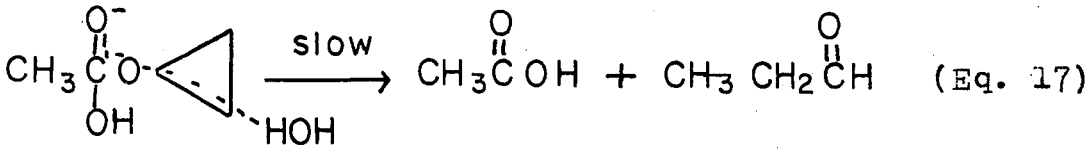
The first reaction of the series to be studied was the rate of hydrolysis of cyclopropyl acetate in aqueous base. Preliminary experiments indicated that the rate of saponification was rapid and could not be accurately determined by titrimetric techniques, even at 0°C. Consideration of other techniques led to the choice of conductimetry as the most elegant; all subsequent kinetic studies of ester hydrolysis were performed in this way.

If the reaction proceeded by a normal ester hydrolysis mechanism, the study of the hydrolysis of cyclopropyl acetate would not supply information concerning the stability of cyclopropyl alcohol, since the alkoxide if actually formed could isomerize rapidly or relatively slowly to propionaldehyde.



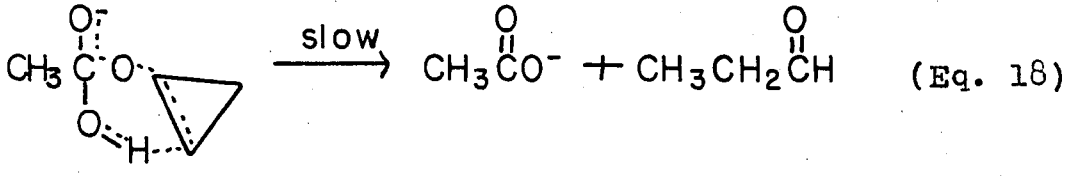
(Eq. 16)

However, a rather interesting possibility, considered at this point, was that of a concerted mechanism in which a species near the transition state of the hydrolysis of cyclopropyl acetate would collapse directly in the rate determining step to propionaldehyde. There are several unique ways in which a process of this type might occur. The first is a simple concerted process with solvent participation such as,



(Eq. 17)

Still another, more complex, pathway could be an intermolecular process after formation of the tetrahedronal intermediate.



(Eq. 18)

Other things being equal, such processes might give rise to activation parameters much different than those observed in the saturated series. However, in Table 2 are given the activation parameters at 20°C in aqueous solution for ethyl and cyclopropyl acetate and it is apparent that the differences are not large enough to be ascribed to any process other

than the electronic and steric differences in the two systems.

Table 2. Activation parameters for hydrolysis of ethyl and cyclopropyl acetate at 20°C.

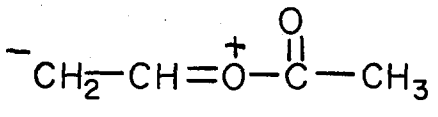
Compound	H (k. cal.)	S (e.u.)
cyclopropyl	12.1 0.5	-20.8 1.5
ethyl	11.0	-31.0

Since a striking number of similarities exist between the vinyl and cyclopropyl systems, it would be reasonable to assume that the mechanism of ester hydrolysis should be similar. Both classes of esters yield as a final product a carbonyl compound; involving in the case of the vinyl series a tautomerization from vinyl alcohol, in the case of cyclopropyl acetate, the formation of cyclopropyl alcohol with either a simultaneous or subsequent isomerization to propionaldehyde.

As pointed out previously, a survey of the literature revealed that there were no data on the saponification of enol acetates with the exception of one study on vinyl acetate. The rate constant reported was open to question since it had been determined in a borate buffer system, with acid and neutral hydrolysis simultaneously occuring at comparable rates. An attempt was made to apply correction factors for

the competing reaction paths.

Hine[66] has suggested that the reactivity of vinyl acetate may be ascribed to contribution of structures of the type



(Eq. 19)

which decrease the ability of the ether in oxygen atom to supply electrons to the carbonyl groups. The absorption maxima for the carbonyl stretching mode in the infra red tend to substantiate this view since vinyl esters and cyclopropyl esters have maximum absorption at 5.70 and 5.73 mμ respectively compared to saturated esters at 5.78. The lower wavelength indicates a higher force constant for the carbonyl function, hence less delocalization from the carbonyl double bond.

If concerted processes as suggested above were involved in the ester hydrolysis of enol acetates and cyclopropyl acetate, the energy of the transition state for each ester should be influenced by the stability of the corresponding enolate form of the final product. The observed rates of reaction are in the order: vinyl acetate $\gg$ 1-acetoxycyclopentene $>$ 2-acetoxypropene $>$ cyclopropyl acetate $\sim$ 1-acetoxycyclohexane.

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[66]Hine, J. in "Physical Organic Chemistry", John Wiley and Sons, Inc., New York, New York, 1956 p.274

Other factors being equal, the stability of the enolate form of a carbanion α to a keto group should be closely related to the stability of the enol form of the corresponding carbonyl compound. The equilibrium constants for keto-enol equilibrium of acetone, cyclopentanone and cyclohexanone increase in that order.[67] Since this order is not observed in the hydrolysis of the corresponding enol esters, it is clear that the stability of the leaving anion is not of primary importance in the determination of the hydrolysis rate.

The rates of acid hydrolysis of the enol acetates have not been determined, thus a treatment of the type used by Taft to evaluate steric and electron effects cannot be used. It was instructive, however, to make a plot of the enthalpy versus the entrophy of activation for the series of enol esters. Leffler[68] has shown that in a large number of reactions a series of similar compounds often yields a straight line when a plot of this type is made. He has suggested that such a treatment may in some cases serve as a diagnostic tool for mechanistic study. If for example, a good fit to a straight line is obtained for a series of related compounds, it is probable that all the compounds of this series react by the same mechanistic pathway.

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[67] Schwazenbach, G. and Wittiver, C., Helv. Chim. Acta., 30, 669 (1947)

[68] Leffler, J.E., J. Org. Chem., 20, 1202 (1955)

In Table 3 are summarized the enthalpies and entropies of activation at 20°C for the enol acetate used in this study.

Table 3. Activation parameters for hydrolysis of enol acetates at 20°C.

Compound	$\Delta H^{\ddagger}$ (k. cal.)	$\Delta S^{\ddagger}$ (e.u.)
vinyl acetate	12.8 ± 0.5	-12.7 ± 2.2
2-acetoxypropene	11.6 ± 0.5	-21.2 ± 1.5
1-acetoxycyclopentene	10.5 ± 0.5	-24.8 ± 1.2
1-acetoxycyclohexene	10.5 ± 0.6	-26.5 ± 2.3

In Table 4 is a summary of the same activation parameters of some formate esters in aqueous solution at 20°C as calculated from the data of Leimu et al.[69] A plot of the enthalpy versus entropy of activation for all these compounds is given in Fig. 1. The equation for the straight line from the enol acetates calculated by the method of least square is

$$\Delta H^{\ddagger} = 15000 + 239 \Delta S^{\ddagger} \qquad \text{(Eq. 20)}$$

[69] Leimu, R., Korte, R., Laaksonen, E., and Lehmuskoski, U., Suomen Kemistilehe, 19B, 93 (1946)

Table 4. Activation parameters for hydrolysis of formate esters at 20°C.

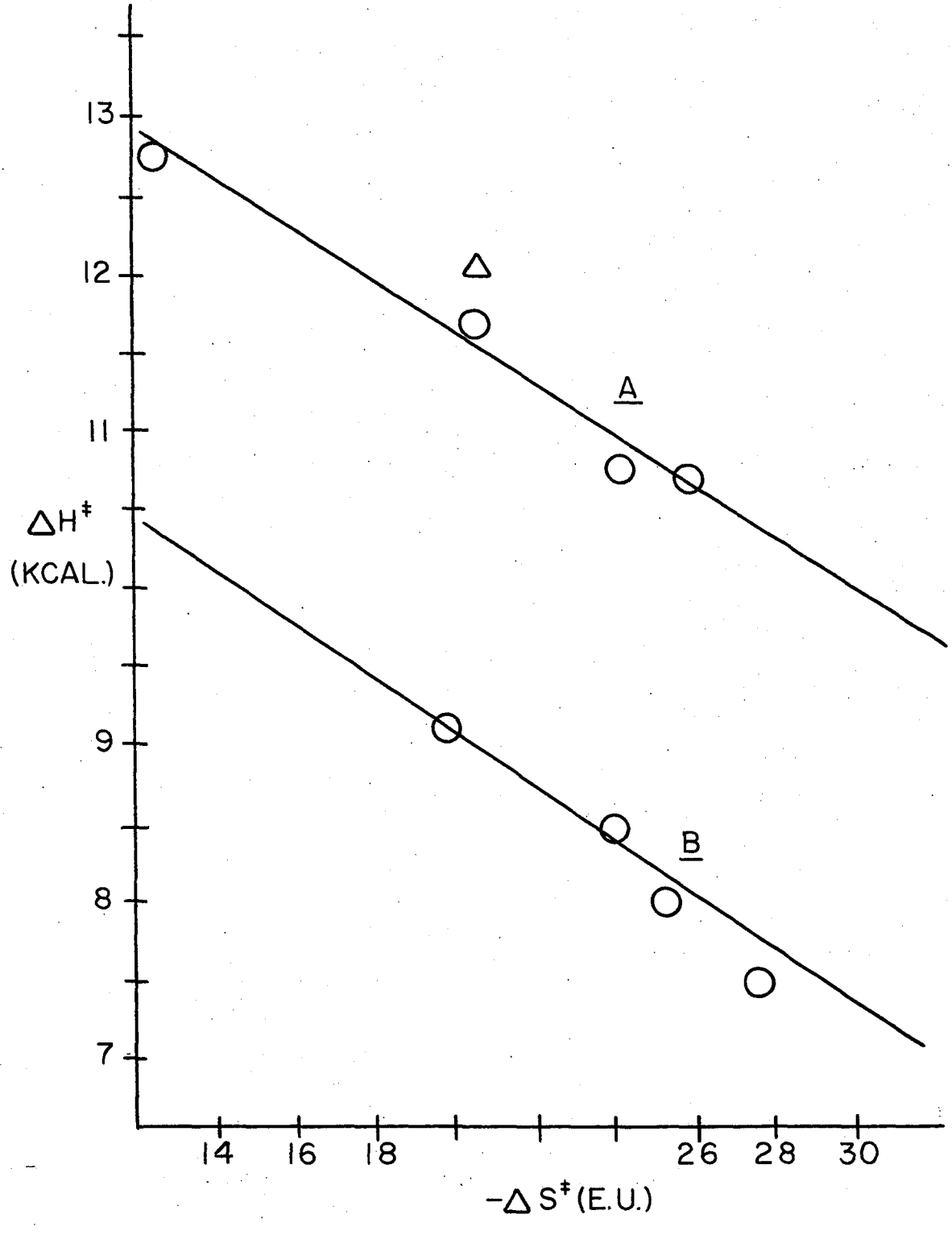
Formate	ΔH^* (k. cal.)	ΔS^* (e.u.)
methyl	9.0	-20.1
ethyl	8.3	-24.2
n-propyl	7.9	-25.6
1-butyl	7.4	-28.0

with correlation coefficient, r, equal to .988. The slope of the line β is called the isokinetic temperature and is 239 which is removed from the experimental temperature by 70°. If the isokinetic temperature and the experimental temperature are the same, then correlation by this technique is trivial since all rates would be the same. When β and T are far apart, the relationship may be invalidated by changes in ΔH^+ with temperature, β then having no physical meaning. In 32% of the reactions correlated by Leffler[68] β differed by at least 100° from T. Thus, it is reasonable to assume that this isokinetic relationship is valid in the case of the enol acetates.

For comparison, the saponification of alkyl acetates in 62% acetone yields a β equal to 270 with correlation coefficient 0.982. In Fig. 1 are plotted the activation parameters

Fig. 1. Isokinetic relationships

A. Enol acetates
B. Alkyl formates


13
12
11
9
8
7
ΔH‡
(KCAL.)
A
B
14
16
18
26
28
30
-Δ S‡ (E.U.)

for formates. For these, β is equal to 212 with correlation coefficient equal to .975. In the case of all these esters it is apparent that β is small; that is, the rate of reaction is governed by the entropy of activation. Since the same activation parameter governs the saponification of alkyl acetates, alkylformates and enol acetates in somewhat the same manner, it is likely that they all proceed by similar mechanism.

Cyclopropyl acetate was not included in the isokinetic correlation but is included in Fig. 1 for comparison. It is seen that the point for this acetate lies very close to the line for the enol acetates, the activation parameters being the same, within experimental error, as 1-acetoxypropene. Thus the basic hydrolysis of cyclopropyl acetate, although fast, very probably proceeds through a mechanism similar to that observed in the saturated series. The increase in rate can be ascribed to steric and electronic factors in the system and a concerted process is not indicated by the rate data.

Since there was no abnormality observed in the hydrolysis of cyclopropyl acetate, the subsequent reactions in the series leading to 2-methyl-2-penten-1-al were subjected to investigation.

Relative rates of formation of 2-methyl-2-penten-1-al from cyclopropyl acetate and propionaldehyde

The formation of propionaldehyde from cyclopropyl acetate

cannot be directly observed because of the subsequent aldol condensation reaction.

A number of investigators[70] have studied the reaction of acetaldehyde with base, and have found that the rate is a complex function of the concentration of aldehyde. For example, in concentrated solutions, the rate of disappearance of acetaldehyde is first order in both aldehyde and base. On the other hand, in more dilute solutions (ca. 0.1M in aldehyde) the reaction becomes second order in acetaldehyde but remains first order in base. These experimental observations are rationalized by assuming that in concentrated solutions the rate controlling step is the formation of the enolate anion, while in dilute solutions the slow step is its subsequent condensation. There have been no studies reported on the aldol condensation of propionaldehyde.

With the above facts in mind it was realized at the start of this portion of the study that it was improbable that complete kinetic description of the transformation from cyclopropyl acetate to 2-methyl-2-penten-1-al could be obtained. However, the relative rates of formation of the product from propionaldehyde and from cyclopropyl acetate should allow inferences to be made about the stability of cyclopropyl alcohol

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[70](a) Bell, R.P. and McTigue, P.T., J. Chem. Soc., 2983 (1960); (b) Broche, A. and Gilbert, R., Bull. Soc. chim. France, 131 (1955)

in basic solution. This has, in fact, been realized.

It was hoped that the main complications in the study of aldol condensation might be circumvented by studies of the initial rates of formation of product before reversible reactions and poly-condensation reactions became of importance. Thus, by following the formation of product to the first few percent reaction, a plot of the concentration of 2-methyl-2-penten-1-al versus time should yield a straight line whose slope m is the initial rate of formation of the material at a very nearly constant concentration of propionaldehyde and base. Since 2-methyl-2-penten-1-al shows strong absorption in the ultraviolet, spectrophotometric methods were used for following the rate. Preliminary experiments showed that the dehydration of the aldol of propionaldehyde to 2-methyl-2-penten-1-al was very rapid compared to the rate of formation of the material from propionaldehyde at the concentrations of base used in this study.

Although the kinetics of the aldol condensation are probably of mixed order (since good agreement over the entire range of concentrations studied was not obtained assuming either first or second order dependence in aldehyde) it is probable that the overall process is first order in base, as is the case with acetaldehyde. On this assumption, the ratio of the initial rate of formation of 2-methyl-2-penten-1-al (m) and the concentration of base should be a function only of the

concentration of propionaldehyde. Thus, the quantity m/OH^- in the third column of the tables is a direct measure of the rate of formation of 2-methyl-2-penten-1-al at a given concentration of propionaldehyde or from cyclopropyl acetate.

Table 5. Rate of formation of 2-methyl-2-penten-1-al from propionaldehyde and sodium hydroxide

Propionaldehyde	Sodium hydroxide	m/OH^- (sec^{-1})
2.85×10^{-3} M.	1.93×10^{-3} N.	4300×10^{-9}
1.62	174.0	1900
1.43	3.98	2950
1.29	5.70	1750
0.86	7.60	770

Table 6. Rate of formation of 2-methyl-2-penten-1-al from cyclopropyl acetate and sodium hydroxide

Cyclopropyl acetate	Sodium hydroxide	m/OH^- (sec^{-1})
1.85×10^{-3} M.	180×10^{-3} N.	21×10^{-9}
0.88	22	8.2
0.44	44	3.8

Comparison of the third column of the tables in which the concentrations of propionaldehyde and cyclopropyl acetate are similar is very striking. The rate of formation of 2-methyl-2-penten-1-al, m/OH^- is consistently 100 to 200 times higher from propionaldehyde than it is from cyclopropyl acetate. In the conversion of cyclopropyl acetate to propionaldehyde there must, therefore, be a relatively slow step.

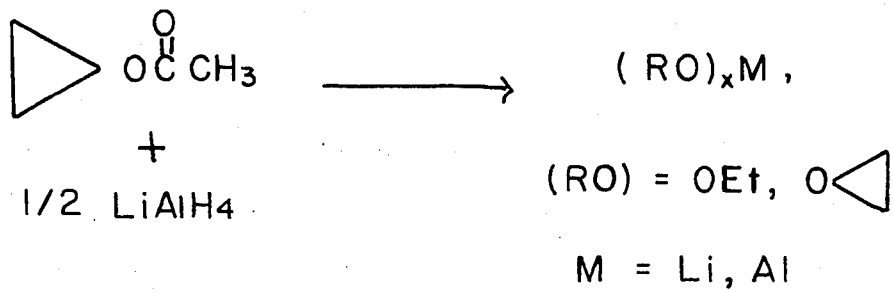
Consider the first entry from the Table 6. The concentration of acetate is 1.85×10^{-3}M. and sodium hydroxide is 180×10^{-3}M. The rate constant at 20°C for the hydrolysis is 1.78×10^{-1} liter-mole^{-1}-sec^{-1}. Calculation demonstrates that only 200 seconds are required for 99% of the acetate to be hydrolized. If the isomerization of cyclopropyl alcohol was simultaneous with, or a very fast reaction immediately after, hydrolysis of the acetate, the concentration of propionaldehyde would within a very short period be approximately 1.8×10^{-3}M. However, as noted above, the rate of formation of 2-methyl-2-penten-1-al is 100 to 200 times slower than would be observed from propionaldehyde at this concentration. One is lead inevitably to the conclusion that the slow step in the formation of propionaldehyde from cyclopropyl acetate is the isomerization of cyclopropyl alcohol. It is clear that cyclopropyl alcohol must have an appreciable lifetime in basic solution.

Synthesis of cyclopropyl alcohol

The results obtained above indicated that cyclopropyl alcohol is much more stable toward the action of base than was previously supposed, and a synthesis of the alcohol should be attempted.

There were several methods of synthesis of the alcohol which were considered. The most obvious is the saponification of the acetate in basic solution and isolation of the alcohol from the reaction mixture, since the rate studies had demonstrated that under these conditions the isomerization of cyclopropyl alcohol to propionaldehyde was relatively slow. There were several reasons why this method was not pursued. First of all, the properties of the crude alcohol reported by Cottle[47] and Roberts[35] indicated that it had a boiling point very similar to that of water and that the two liquids are completely miscible. The latter property would make extraction procedures very tedious, while the former property precludes use of distillation techniques.

The use of a reducing agent such as lithium aluminum hydride seemed to be the most feasible route. It is well known that oxygen-lithium and oxygen-aluminum bonds possess a certain degree of covalent character and in poorly ionizing solvents isomerization of the intermediate metal-cyclopropyl oxide (X) by means of a ring opening to propionaldehyde should be slow. It was therefore decided that the acetate would be



(Eq. 21)

reduced by the addition of a slight excess of lithium aluminum hydride in ether. Obviously, the amount of water used in the work up of the reaction mixture had to be kept to a minimum, due to the solubility of the product. This problem was circumvented by the use of a slurry of sodium sulfate-water which not only absorbed the basic salts formed by the action of water but also formed a precipitate which could be easily separated from the ether layer containing cyclopropyl alcohol.

In preliminary experiments n-propyl alcohol was chosen as the model compound for cyclopropyl alcohol in gas phase chromatographic separation experiments. A very excellent separation of n-propyl alcohol from ethyl alcohol and ethyl ether was obtained on a polyethylene oxide column at 80°C. The final isolation of cyclopropyl alcohol was accomplished using this column, after reduction of the volume of ether solvent used in the reaction. The yield of cyclopropyl alcohol was 55%. Cyclopropyl alcohol had a long retention time, nearly twice that of n-propyl alcohol on the column. The reason for this long retention time is obscure but it may be due to the

interactions of the cyclopropyl ring with the column packing, since allyl alcohol has a relatively long retention time under the same conditions. A study of this phenomena is now in progress.

Gas phase chromatographic analysis failed to reveal any n-propyl alcohol, the reduction product of propionaldehyde. Thus, it is improbable that any metal-cyclopropyl oxide isomerized during the reduction.

Distillation of ether may have resulted in some thermal isomerization of the alcohol, since the ether solution acquired a yellow color on distillation. In later reactions in which relatively small volumes of ether were used, requiring less distillation before gas phase chromatographic separation, the yield of alcohol markedly improved.

Micro boiling point determinations on the pure cyclopropanol revealed that it decomposed at its boiling point (100.5 - 101°C) to propionaldehyde. It is surprising that no decomposition was observed in the gas phase chromatographic separation; however, the lower temperature maintained on the column and the possibility that the mechanism of the decomposition may involve a complex configuration of the cyclopropyl alcohol molecule or molecules may explain the stability under the conditions of the separation.

The alcohol was identified by the preparation of derivatives which had the same melting point as those reported by

Cottle and Roberts. The infra red spectrum of the alcohol in solution and the vapor phase also give strong evidence for its structure. See Fig. 2. The C-H bond stretching absorptions are shifted to lower wavelengths than those observed in normal secondary alcohols and the markedly lower extinction coefficients of all the C-H vibrations are characteristic of the cyclopropyl system.

In addition to the above, the analytical data on the alcohol, the facile isomerization to propionaldehyde and the difference in retention time in gas phase chromatography from other alcohols confirm the identity of the alcohol as cyclopropanol. Finally, in the next section is given another strong argument based on the identical rate of formation of 2-methyl-2-penten-1-al from cyclopropyl acetate and cyclopropyl alcohol.

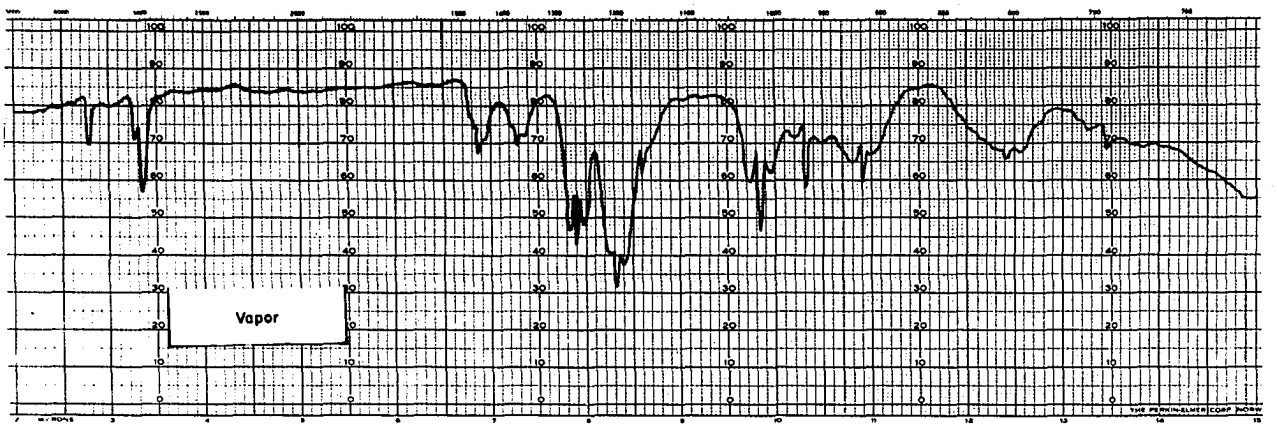
Rate of formation of 2-methyl-2-penten-1-al from cyclopropyl alcohol

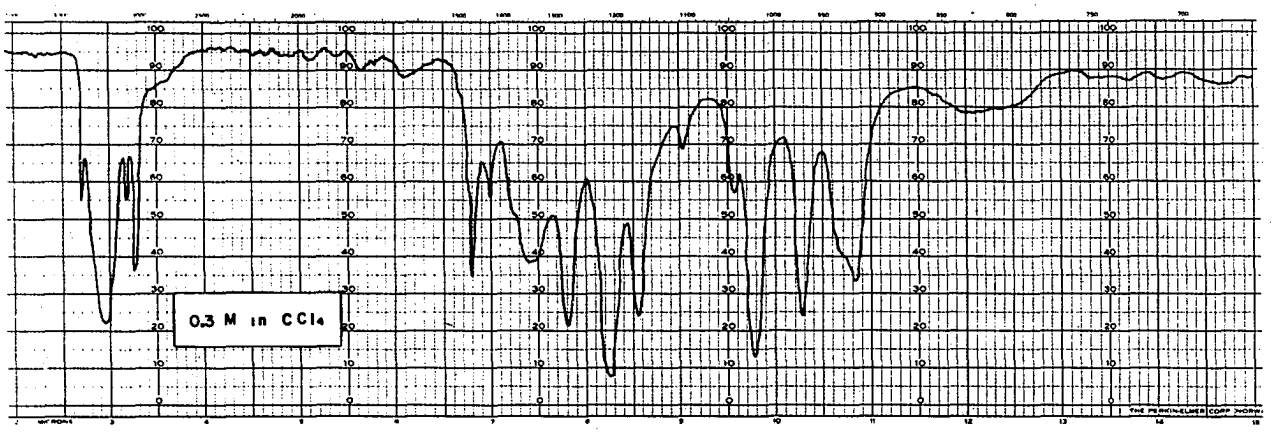
It was now possible, for the first time, to directly observe the stability of cyclopropyl alcohol in basic solutions.

Comparison of the relative rates of formation of the product from similar concentrations of cyclopropyl acetate and cyclopropyl alcohol is very satisfying since, within the range of experimental error, the rates are the same.

Fig. 2. Infra red spectra of cyclopropanol

Top. Vapor phase
Center. 0.3 M in carbon tetrachloride
Bottom. 0.3 M in carbon tetrachloride after 10 hours at 80°C


Vapor


0.3 M in CCl4

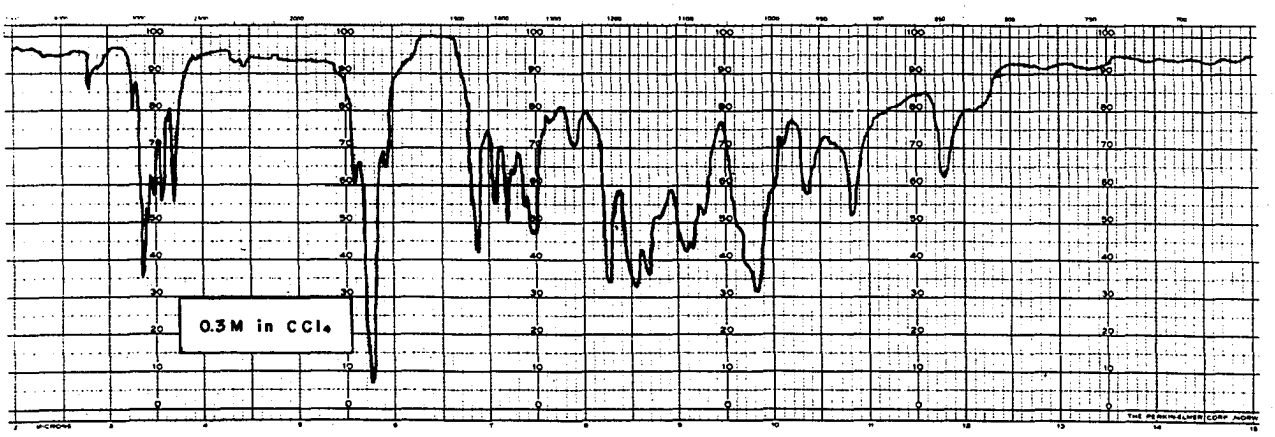

0.3M in CCl4

Table 7. Rate of formation of 2-methyl-2-penten-1-al

Compound	Sodium hydroxide N.	m/OH^- (sec^{-1})
	cyclopropanol	
1.90×10^{-3}	160×10^{-3}	31×10^{-9}
0.76	160	7.2
	cyclopropyl acetate	
1.85×10^{-3} M.	180×10^{-3} N.	21×10^{-9}
0.88	22	8.2
0.44	44	3.8

At this point one might be tempted to try to obtain a complete kinetic description of the series of reactions leading from cyclopropyl acetate to 2-methyl-2-penten-1-al. It would appear that a steady state assumption for the concentration of propionaldehyde is reasonable and that over the limited range of concentrations studied the rate of formation of product is, within experimental variations, first order in cyclopropyl alcohol or acetate and first order in base. However, late in the study a discovery was made which discouraged further attempts to study the kinetics of this transformation by this spectrophotometric method.

When 2-methyl-2-penten-1-al was allowed to stand in base (0.16N), a decrease in the absorption of the solution was

noted. The same significance is given to the symbol m/OH^-, except now it is a measure of the decrease in concentration of 2-methyl-2-penten-1-al.

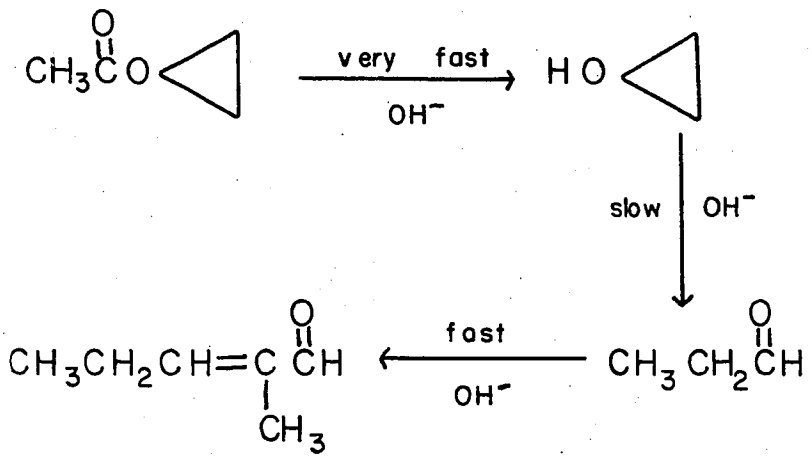
Table 8. Rate of decrease of concentration of 2-methyl-2-penten-1-al in sodium hydroxide solutions

NaOH	m/OH^-
160×10^{-3}	2.1×10^{-9}
97	1.8

It was also observed that the rate of decrease of absorption was independent of the concentration of 2-methyl-2-penten-1-al to high conversion. Although the rate of decrease was only a fraction of the rate of increase observed in the runs of cyclopropyl acetate and cyclopropyl alcohol, at similar concentration of base, this observation demonstrates that the formation of a material, even with a high molar absorption, is certainly not the most reliable method of obtaining rate data. Trace impurities and possible changes in mechanism of individual reaction due to concentration gradients in the rather extended series of reactions leading from cyclopropyl alcohol to 2-methyl-2-penten-1-al, in addition to the

lack of stability of the product, point out the inherent dangers in this technique. A much improved method would be that in which the disappearance of cyclopropyl alcohol could be followed. Experiments are now in progress on this problem.

With these complications in mind, however, the relative rates of the series of reactions from cyclopropyl acetate to 2-methyl-2-penten-1-al can be estimated as illustrated in Eq. 22.



(Eq. 22)

The poor yield of propionaldehyde observed in the hydrolysis of cyclopropyl acetate could then be explained by the rapid formation of cyclopropanol and its slow conversion to propionaldehyde, followed by a fast condensation step.

Preliminary studies on the isomerization of cyclopropyl alcohol in solution

As noted above, pure cyclopropyl alcohol decomposes to propionaldehyde at its boiling point. It seemed of interest

to study this phenomena under controlled conditions.

A carbon tetrachloride solution of the alcohol was prepared and infra red absorption spectra of the solution was obtained. The solution was then sealed in a glass vial which was placed in a 80°C constant temperature bath. After 10 hours the spectrum of this solution was recorded and found to be identical with that of propionaldehyde. Both spectra are reproduced in Fig. 2.

A preliminary study of the effect of solvent on this isomerization led to some striking observations. The solvents investigated were carbon tetrachloride, water, methylcyclohexane and acetonitrile. The course of reaction in each solvent was followed by spectrophotometric methods.

The isomerization in carbon tetrachloride was very facile, the half life of cyclopropyl alcohol at 80°C in this solvent being approximately one hour. In contrast to carbon tetrachloride, the alcohol appeared to be relatively stable in other solvents studied. After 3 days at 80°C in water, an absorption at 2650A° was observed which was not propionaldehyde (2800A°) or 2-methyl-2-penten-1-al (2355A°). There was no change in the spectra after this period although the spectra was recorded daily for one week. The ultraviolet and infra red spectra of solutions of the alcohol in methyl cyclohexane did not change after eight days at 80°C. Solutions of the alcohol in acetonitrile at 80°C did not change after three

days. At the end of seven days, a weak absorption in the infra red at 4.9 mμ was observed.

It is of interest, in passing, to compare the appearance of the absorption maxima in the infra red spectrum in solution of the alcohol which are ascribed to the bonded and non-bonded hydroxyl stretching modes at 28 mμ and 3 mμ respectively. A 0.3M. solution in carbon tetrachloride exhibits strong absorptions in both these regions. In methyl cyclohexane at the same concentration there is a complete absence of the non-bond stretching absorption maximum, with a broad bonded absorption. Solutions of the alcohol in acetonitrile show a complete absence of bonded and non-bonded hydroxyl stretching vibrations. Because of the strong hydrogen bonding characteristics of water it would be expected that the hydroxyl function on the alcohol would be involved with hydrogen bonding to water molecules exclusively, thus there would be a relatively low concentration of non-bonded hydroxyl function in water solution.

The effect of solvent on the isomerization could be ascribed to a number of factors. It would be reasonable, however, to assume that a definite configuration of one or more molecules must be obtained during isomerization. A variation in equilibrium constants with solvent for various hydrogen bonded aggregates in solvent could rationalize the above observations.

An extensive kinetic study of the isomerization as a function of solvent, temperature and catalysts is now in progress.

EXPERIMENTAL

Gas phase chromatography

All gas phase chromatography analyses were conducted by means of a Perkin-Elmer Vapor Fractometer Model 154C on 2 meter x 15 mm. 30% Ucon LB550X on 60/80 mesh firebrick.

Cyclopropyl Acetate

Cyclopropyl acetate was prepared by the procedure of Emmons and Lucas.[52] A solution of peroxytrifluoroacetic acid was prepared from 67.6 ml (0.48 mole) of trifluoroacetic anhydride and 10.8 ml of 90% hydrogen peroxide. This was added over a 30 minute period to a well stirred mixture of 142 grams of anhydrous sodium dibasic phosphate and 16.8 grams (0.20 mole) of methyl cyclopropyl ketone in 200 ml of methylene chloride. After addition was complete the mixture was heated under reflux for one hour. The mixed salts were collected on a filter and washed with methylene chloride (100 ml). The combined filtrates were washed with 150 ml of 10% sodium carbonate and dried over anhydrous sodium sulfate. Most of the solvent was removed by distillation and the residual liquid was dissolved in a mixture of 180 ml of methyl alcohol and 20 ml of acetic acid containing 37.4 grams of Girard's reagent P. The resulting solution was refluxed for 16 hours and poured into 600 ml of ice water. The mixture was partially neutral-

ized with 25.2 grams of sodium bicarbonate in 100 ml of water and was then extracted with six 100 ml portions of methylene chloride. The extracts were washed with 50 ml of 10% sodium bicarbonate, dried, and most of the solvent removed by distillation at atmospheric pressure. The residual liquid on fractionation gave 3.5 to 11.0 grams (16 - 55% yield) of cyclopropyl acetate, b.p. 110.2 - 111.0° n_{20}^{D} 1.4084.[52] (lit. b.p. 109 - 111° n_{25}^{D} 1.4060) The higher yields were obtained in preparations where the trifluoroacetic anhydride had been distilled under anhydrous conditions immediately before use.

Attempted preparation of cyclopropyl acetate by an alternate route

An alternate route to cyclopropyl acetate was the method of Simmons and Smith,[56] who reported a 30% yield from the reaction of vinyl acetate with a zinc diiodomethane complex previously formed from a zinc - copper couple and methylene iodide in ether.

Mallinckrodt A.R. wireform cupric oxide (30 grams) was ground in a mortar and mixed with 240 grams of Mallinckrodt A.R. zinc dust. The mixture was placed in a Vycor combustion boat and the boat was sealed in a pyrex tube with thermocouple. The entire apparatus was then placed in a muffle furnace. A mixed gas (H_2 65 liters/hour, N_2 25 liters/hour) was passed through the tube while the temperature was raised to 500°C

during 4 hours. The mixture was kept at 500°C for 30 minutes, and the tube was then allowed to cool to room temperature in a hydrogen atmosphere. The fine gray powder was utilized in the addition reaction.

Seventy-five grams (0.30 mole) of methylene iodide was dissolved in 150 ml of anhydrous ether. To this solution was added 25.0 grams (0.35 mole) of the zinc - copper couple and 47.7 grams (0.50 mole) of vinyl acetate. The mixture was stirred under reflux for 22 hours, the reaction mixture allowed to cool, washed sucessively with 100 ml of cold 5% ammonium chloride and 150 ml of 1:1 ammonium hydroxide and dried over anhydrous magnesium sulfate. The ether was distilled and the residual liquid fractionated; a 2 gram fraction boiling from 107 - 111°C was collected. The yield base on the limiting reagent, zinc - copper couple was 5%. The purity checked by gas phase chromatography was 95%.

Numerous variations in reaction time, molar ratio of reactants and addition of I_2 to initiate the reaction failed to improve the yield. Duplication of the above procedure failed to yield any cyclopropyl acetate. The only explanation which one may offer for the failure of the preparation was lack of reactivity of the zinc - copper couple.

1-Methyl cyclopropyl acetate

Zinc - copper couple (18 grams, .25 mole), prepared by

the thermal method, was added to 53.0 grams (0.20 mole) of methylene iodide in 150 ml of anhydrous ether. To this mixture 2.5 grams (0.01 mole) of resublimed iodine was added and the mixture stirred until disappearance of the iodine color. At this point 40 grams (0.4 mole) of isopropenyl acetate was added and the mixture stirred under reflux for 68 hours. The reaction mixture was cooled, washed sucessively with 100 ml of 5% ammonium chloride and 150 ml of 1:1 ammonium hydroxide, dried over anhydrous magnesium sulfate, and the ether distilled at atmospheric pressure. The residual liquid was then distilled under vacuum. Gas phase chromatography at 100°C indicated that the fraction collected at 33°- 38°/40mm contained a material whose retention time was 1.55 that of isopropenyl acetate. This material was then collected from the column. The yield of material collected from the gas phase chromatography separation amounted to 0.7 gram (2.5%). B.p. 112.5 - 113.0° (760 mm.) The infra red spectrum had an absorption maximum at 5.71 m .

Anal. Caled. for $C_6H_{10}O_2$: C, 63.10; H, 8.84. Found: C, 62.53; H, 9.10.

Identification of product from reaction of cyclopropyl acetate in concentrated sodium hydroxide.

Three drops of cyclopropyl acetate were added to 8 drops of concentrated sodium hydroxide. Vigorous evolution of heat

took place after a short induction period and the odor of propionaldehyde was noted. The solution was then neutralized with hydrochloric acid and extracted with chloroform. The infra-red spectrum had a strong carbonyl absorption maximum at 5.95 m .

The above procedure was duplicated with one gram of cyclopropyl acetate and 5 ml of concentrated sodium hydroxide. The neutralized solution was extracted with ether. The ether was distilled and the semicarbazone derivative of 2-methyl-2-penten-1-al, formed by conventional methods, was obtained. After two recrystallizations from 50% ethyl alcohol - water the derivative melted at 186.5 - 187.0°. A mixed melting point with an authentic sample of 2-methyl-2-penten-1-al (vide-infra) semicarbazone melted at 186.0 - 187.5°C.

Preparation of 2-methyl-2-penten-1-al

The procedure of Doebner and Weissenborn[71] was used for the preparation of 2-methyl-2-penten-1-al. Eighty grams (1.38 moles) of propionaldehyde was cooled to 0° and 20 ml of 10% sodium hydroxide was added slowly over a 30 minute period. After 10 minutes of stirring the mixture was neutralized with dilute sulfuric acid. The two-phase mixture was then steam distilled. The distillate was shaken with saturated sodium

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[71]Doebner, Von O. and Weissenborn, A., Ber., 35, 1144 (1902)

chloride, dried over anhydrous calcium chloride and fractionally distilled at atmospheric pressure in an atmosphere of nitrogen. The yield of 2-methyl-2-penten-1-al was 25.2 grams (37%) b.p. 134.0 - 135.5°. n_D^{20} 1.4487

Recovery of propionaldehyde from basic hydrolysis of cyclopropylacetate

A special apparatus was designed in order to recover the propionaldehyde generated by the action of base on cyclopropylacetate. The apparatus consisted of a glass cylinder, (2 cm x 10 cm) the base of which was a coarse sinstered glass disk, through which purified nitrogen could be passed at a rapid rate. Two side arms were provided near the top of the cylinder, through which solutions could be injected by means of a syringe. The top of the cylinder was fitted with a standard tapered joint which was connected to a series of gas wash bottles used as traps for material carried by the nitrogen stream. The cylinder was immersed in a constant temperature bath 48 0.5°C.

By means of a micro syringe, 0.010 ml of cyclopropylacetate was injected into 5 ml of 0.15N sodium hydroxide solution at 15 minute intervals until 0.050 ml had been added. One ml of 0.75N sodium hydroxide was then added and 5 more injections of 0.01 ml of the ester were then made at 15 minute intervals. During the injections and for an additional 8 hours after the

last injection, nitrogen was bubbled through the apparatus at a rate of 50 ml/minute into 2 gas bottles, connected in series, containing aqueous 5:5-dimethylcyclohexa-1:3-dione solution (0.2%). The gas bottles were then stoppered and allowed to stand two days. At the end of this time, the white crystals which had precipitated were filtered on a weighed sintered glass filter funnel. The yield of the dimedone derivative of propionaldehyde was 0.035 g(15%). m.p. 154.5 - 155.0°C (lit. 155°).

The efficiency of the apparatus was determined by hydrolyzing vinyl acetate at room temperature (25 - 27°) in the apparatus under the same gas flow. An 85% yield of the dimedone derivative of acetaldehye was obtained. m.p. 138.5 - 139.5 (lit. m.p. 140).

Determination of rates of saponification of esters

Materials. All esters were subjected to gas phase chromatographic analysis and in all cases, with the exception noted below, were greater than 99% pure.

Vinyl acetate. Eastman (practical) vinyl acetate was distilled, the center fraction with constant boiling point was collected, b.p. 72.5 (750 mm) n_D^{20} 1.3944 (lit. 72.0 (740 mm), n_D^{20} 1.3942).[72] The ester was utilized in the kinetic run with-

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[72] Hagemeyer, H.S. and Hill, D.C., Ind. Eng. Chem., 41, 2920 (1949)

in one half hour after the distillation.

2-Acetoxypropene. Matheson, Coleman and Bell (practical) was fractionally distilled, the middle fraction with constant boiling point was collected, b.p. 95.8 (740 mm) n_D^{20} 1.3993 (lit. b.p. 96.6 (748 mm) n_D^{20} 1.4001)

1-Acetoxycyclohexene. 1-acetoxycyclohexene was obtained from G.E. Hunt, prepared by the procedure of Machinskaya.[73] The compound was repeatedly fractionated at reduced pressure, the middle fraction collected during each distillation. b.p. 68.5 - 69.0°C (12 mm) n_D^{20} 1.4532 (lit. 72.0°C (15 mm) n_D^{25} 1.4560) Gas phase chromatographic analysis indicated a (ca. 3%) impurity of cyclohexanone.

1-Acetoxycyclopentene. 1-acetoxycyclopentene was prepared by the procedure of Hagemeyer and Hill[72] from the reaction of isopropenyl acetate and cyclopentanone with a catalytic amount of p-toluene sulfonic acid. The product was fractionated at reduced pressure and the center fraction, b.p. 77.5 - 78.0°C (50 mm) n_D^{20} 1.4456 was collected. (lit. b.p. 156 - 158°C (760 mm)[74]

Cyclopentyl acetate. Cyclopentyl acetate was prepared by the esterification of cyclopentanol (Eastman Kodak White

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[73]Machinskaya, I.V., J. Gen. Chem. U.S.S.R., 22, 1205 (1952)

[74]Mannich, C. and Hancu, V.H., Ber., 41, 522 (1908)

Label) with acetic anhydride in pyridine. The acetate was fractionated at reduced pressure and the middle fraction which had a constant boiling point was collected. b.p. 50.0° (13mm) n_D^{20} 1.4305 (lit. b.p. 52 - 53° (12mm)[75]

Cyclopropyl acetate. Cyclopropyl acetate was prepared by method of Emmons as described above, b.p. 110.5 - 111.0°C (740 mm) n_D^{20} 1.4084.

1-Butyl acetate. Commercial n-butyl acetate (Matheson, Coleman and Bell) was fractionated and a center fraction was taken which had a constant boiling point, 125°C (740 mm) n_D^{20} 1.3955. (lit. b.p. 124 - 125°C).[76]

Conductivity water. The water used in this study was obtained from a mixed anion-cation resin column (Amberlite MB 300). In all runs the specific resistance of the water was greater than 400,000 ohms cm^{-1} as measured in the conductivity cell.

Apparatus. The conductance cell was constructed similarly to those of Jones and Bollinger[77] with two modifications; only one opening was provided for filling and a capillary gas

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[75]Godchot, M. and Taboury, F., Compt. rend., 152, 881 (1904)

[76]Lieben, A. and Rossi, A., Ann., 158, 169 (1871)

[77]Jones, G. and Bollinger, G.M., J. Amer. Chem. Soc., 53, 411 (1931)

inlet in the base was added in order to flush the cell with purified nitrogen.

The conductivity bridge was of commercial construction, manufactured by Industrial Instruments Inc., Model RCIB 60 cycle.

For kinetic runs at 0.2°C and 20.0°C a refrigerating bath was employed. The model is the "Lo Temp. Bath" with built in thermoregulator manufactured by Wilkens-Anderson Co.

Preparation of sodium hydroxide solutions. Since the sodium hydroxide solutions employed in this study were very dilute, absorption of carbon dioxide became a serious source of error. It was found necessary to prepare the solution of base immediately before each kinetic run by the following technique. A capillary tube, diameter 1.5mm, was filled with sodium by boring the tube into a freshly cut piece of the metal. The tube was then dropped, under a nitrogen atmosphere into a volumetric flask filled with conductivity water. The base was then standardized by delivering an aliquot of the base into an excess of standard hydrochloric acid and back-titration of the excess with dilute sodium hydroxide using phenolphthalein as an indicator. All titrations were carried out under a purified nitrogen atmosphere.

Solutions and pippettes used in the standardization and kinetic run were equilibrated in the constant temperature bath before use.

Kinetic measurement. A flask of the base was placed in the constant temperature bath. The latter was set at 0.20° using a thermometer calibrated by the National Bureau of Standards. Ester solutions of a definite concentration were prepared by weighing out the requisite amount of ester into "S" shaped capillary tubes. Each tube was dropped into a volumetric flask containing conductivity water equilibrated at the bath temperature. The flask was closed with a rubber stopper through which a glass rod extended almost to the bottom. The capillary tube was crushed, the flask shaken until the ester dissolved and the flask then replaced in the constant temperature bath. The conductance cell was then flushed with purified nitrogen and 4.94 ml of ester solution was delivered into the conductivity cell by means of a calibrated pippette. Timing was started when one half of the base was added from a 2.42 ml fast delivery pippette.

The value of the conductivity at zero time was obtained prior to each run by delivering 2.42 ml of the sodium hydroxide solution into the cell containing 4.94 ml of conductivity water. The value of the conductance at infinite time was obtained from experimental measurements of a standard solution of sodium acetate. The values obtained by this method agreed within 2% for those reactions which went to completion in a reasonable time.

It was found necessary to clean the cell after each run

with a hot concentrated sulfuric-nitric acid mixture. If this precaution was not taken, erratic results were obtained, probably due to accumulation of organic material on the electrode surfaces which ordinary cleaning methods did not remove.

Method of calculation and results. The method of calculation of the concentration of base was the following: It is assumed that the reciprocal of the resistance of a solution of a uni-univalent electrolyte is proportional to its concentration, e.g.

$$\frac{1}{R_x} = \delta C_x \qquad \text{(Eq. 23)}$$

When δ is a constant, C_x is the concentration of X, R is the resistance of the solution.

In a solution containing sodium acetate and sodium hydroxide, at any time, t

$$\frac{1}{R_t} = aC^t_{NaOAc} + bC^t_{NaOH}$$

since

$$C^o_{NaOH} = C^t_{NaOAc} + C^t_{NaOH} \qquad \text{(Eq. 24)}$$

$$\frac{1}{R_t} = (a-b)\, C^t_{NaOH} - bC^o_{NaOH}$$

and

$$C^t_{NaOH} = \frac{1}{a-b}\left[\frac{1}{R_t} - bC^o_{NaOH}\right] \qquad \text{(Eq. 25)}$$

where C^{o}_{NaOH} is the initial concentration of sodium hydroxide, C^{t}_{NaOH} and C^{t}_{NaOAc} are the concentrations of sodium hydroxide and sodium acetate respectively at time t.

The integrated expression for a second order reaction was used in the calculation of the rate constant, that is,

$$k_2 t = \frac{1}{C^{o}_{Ester} - C^{o}_{NaOH}} \; 2.303 \log_{10} \frac{C^{o}_{NaOH} \times C^{t}_{Ester}}{C^{o}_{Ester} \times C^{t}_{NaOH}} \qquad \text{(Eq. 26)}$$

where t is time in seconds, C^{o}_{Ester} and C^{t}_{Ester} are the concentrations of the ester at time t equal to zero and time t respectively.

The heats of activation were calculated by the Arrhenius equation.

$$2.303 \log \frac{k_{T_2}}{k_{T_1}} \qquad \frac{\Delta E}{R(T_2 - T_1)} \qquad \text{(Eq. 27)}$$

where $\Delta H^{*} = \Delta E^{*} - RT$

Entropies of activation were calculated from the absolute rate equation, where the symbols have their usual significance.

$$k = \frac{kT}{h} e^{-\Delta H/RT} e^{\Delta S/R} \qquad \text{(Eq. 28)}$$

In tables 9 through 12 are presented typical data from individual kinetic runs. Table 13 summarizes the results of all the ester hydrolysis.

Table 9. Saponification of vinyl acetate at 0.20°C

?	C_{OH^-} x 10^3	C_{ester} x 10^3	t (sec)	k_2 x 10
3660	0.817	0.999	0	----
3850	0.759	0.941	125	5.87
3950	0.726	0.908	199	6.04
4050	0.698	0.880	262	6.21
4300	0.620	0.811	445	6.41
4450	0.593	0.775	571	6.15
4550	0.569	0.751	655	6.31
4700	0.535	0.717	785	6.31
4850	0.504	0.686	909	6.41
5000	0.475	0.657	1053	6.31
5200	0.439	0.621	1255	6.39
5400	0.405	0.587	1450	6.41
5550	0.381	0.561	1643	6.18
5600	0.373	0.553	1698	6.17
5800	0.344	0.526	1938	6.28
6000	0.316	0.498	2233	6.24
6200	0.291	0.473	2483	6.24
6400	0.268	0.450	2788	6.26

ave. k_2 - $.625 \pm 0.005$ ($mole^{-1}$-liter-sec^{-1})

Table 10. Saponification of 2-acetoxypropene at 20.0°C

R	C_{OH^-} x 10^3	C_{ester} x 10^3	t (sec)	K_2 x 10
1420	1.313	3.817	0	----
1535	1.123	3.627	213	3.18
1600	1.029	3.533	261	3.14
1650	0.978	3.482	327	3.19
1710	0.908	3.412	380	2.95
1755	0.858	3.362	453	3.25
1805	0.802	3.306	563	3.18
1900	0.710	3.214	633	3.18
1955	0.661	3.165	769	3.35
2025	0.602	3.106	840	3.12
2100	0.541	3.045	999	3.19
2200	0.468	2.972	1169	3.20

ave. k_2- .318 ± 0.003 ($mole^{-1}$-liter-sec^{-1})

Table 11. Saponification of cyclopropyl acetate at 20.0°C

R	C_{OH^-} x 10^3	C_{ester} x 10^3	t (sec)	k_2
1140	1.587	3.537	0	----
1190	1.468	3.418	123	.182
1240	1.356	3.306	254	.177
1310	1.215	3.165	437	.182
1360	1.124	3.074	568	.184
1410	1.038	2.988	703	.186
1465	0.951	2.901	869	.186
1500	0.897	2.847	993	.182
1575	0.794	2.744	1232	.182
1625	0.740	2.690	1377	.182
1700	0.641	2.611	1655	.187
1750	0.584	2.534	1863	.183
1800	0.533	2.483	2076	.182

ave. k_2 - (1.83 ± 0.01) x 10^{-1}

Table 12. Saponification of 1-acetoxycyclopentene at 40.0°C

R	C_{OH}-x 10^3	C_{ester} x 10^3	t (sec)	k_2
925	1.570	2.055	0	----
1240	.905	1.390	103	3.22
1280	.846	1.331	121	3.13
1335	.770	1.255	145	3.13
1382	.709	1.194	167	3.10
1420	.664	1.149	191	3.00
1460	.619	1.104	210	3.03
1500	.575	1.060	236	3.08
1550	.525	1.010	263	2.95
1600	.477	0.962	290	2.97
1625	.459	0.944	314	2.97
1705	.386	0.871	367	3.05
1740	.359	0.844	395	3.05

ave. k_2 - 3.06 ± .03

Table 13. Summary of results of saponification of esters

C^o_{ester} x 10^3	C^o_{NaOH} x 10^3	k_2 x 10	ave. k_2 x 10
	Vinyl Acetate at 0.20°C		
0.999	0.817	6.25	
1.358	0.907	6.43	6.1 ± 0.3
1.795	1.415	5.68	
	Vinyl Acetate at 20.0°C		
1.245	1.027	31.3	
1.172	1.066	35.0	32.8 ± 1.3
1.038	0.865	32.2	
	2-Acetoxypropene at 0.20°C		
1.571	0.754	.595	
1.853	1.173	.700	.648 ± .024

Table 13 (Continued).

$C^{o}_{ester} \times 10^3$	$C^{o}_{NaOH} \times 10^3$	$k_2 \times 10$	ave. $k_2 \times 10$
2.275	1.328	.650	.648 ± .024
2.513	1.558	.645	
	2-Acetoxypropene at 20.0°C		
3.817	1.313	3.18	3.01 ± 0.15
3.405	2.055	3.00	
4.665	1.962	2.86	
	1-Acetoxycyclopentene at 20.0°C		
3.408	1.975	7.96	8.55 ± .38
3.468	1.475	8.88	
2.856	1.255	8.82	
	1-Acetoxycyclopentene at 40.0°C		
1.409	1.245	27.8	28.6 ± 1.2
1.972	1.085	27.5	
2.055	1.570	30.6	
	1-Acetoxycyclohexene at 20.0°C		
2.832	1.854	1.75	1.78 ± .03
3.295	1.712	1.81	
	1-Acetoxycyclohexene at 40.0°C		
3.68	3.62	5.64	5.64 ---
	Cyclopropyl at 20.0°C		
4.818	1.531	1.69	1.78 ± .06
4.080	2.130	1.83	
6.100	1.347	1.83	
	Cyclopropyl at 40.0°C		
3.115	1.515	7.23	7.17 ± .07
3.758	1.386	7.10	

Table 13 (Continued).

C^{o}_{ester} x 10^3	C^{o}_{NaOH} x 10^3	k_2 x 10	ave. k_2 x 10
	Cyclopentyl at 20.0°C		
2.84	1.51	.251	.260 ± .009
2.86	1.93	.269	
	Cyclopentyl at 40.0°C		
4.000	2.086	.893	.893 ---
4.455	2.605	.893	
	1-Butyl at 20.0°C		
4.70	2.72	.643	.653 ± .009
2.89	1.93	.664	
	1-Butyl at 40.0°C		
4.32	1.56	1.87	
4.32	1.56	2.03	1.95 ± .06
4.07	2.53	1.96	

Ultraviolet absorption spectra

All untraviolet absorption spectra were recorded by means of a Cary Model 14 recording spectrophotometer, manufactured by the Applied Physics Corporation.

Rate of formation of 2-methyl-2-penten-1-al from the reaction of propionaldehyde in sodium hydroxide solution

Standard solutions of propionaldehyde in water were prepared by weighing the aldehyde into "S" shaped capillary tubes

(1.5 mm diameter), which were then dropped into volumetric flasks filled to the mark with conductivity water and crushed with a glass rod. The flasks were placed in an air conditioned room (20 ± 2.0°C) along with standard solutions of sodium hydroxide.

An aliquot of the sodium hydroxide was added to the propionaldehyde solution. When one half of the base had been added an electric timer was turned on. After thorough shaking, the solution was pippetted into a ground glass stoppered quartz Beckman cell. The absorbance of the solution from 3000°A to 2000°A was then recorded at various time intervals. The absorption maximum at 2355 (ϵ=17,700) was used to calculate the amount of 2-methyl-2-penten-1-al formed.

In the case of solutions where the hydroxide concentration was high (ca. 0.1 normal) the reaction was followed by taking aliquots of the reaction mixture, diluting and the time recorded when dilution was made. The spectrum of the diluted sample was then recorded as before and later recorded again. In no cases was it necessary to correct for reaction after dilution.

Rate of formation of 2-methyl-2-penten-1-al from the reaction of cyclopropyl acetate in sodium hydroxide solution

The procedure used was exactly the same as that used in the reaction of propionaldehyde with base, as outlined above.

Aliquots of the reaction mixtures of base and ester were sealed in glass tubes and placed in an 80° temperature bath for 2 days. At the end of this period the tubes were opened and diluted, the spectrum was determined from 3000A° - 2000A° and approximately 80-85% of the theoretical yield of 2-methyl-2-penten-1-al was obtained as calculated from absorption maximum at 2355A°.

Preparation of cyclopropyl alcohol

To a solution of 6.20 grams (.062 mole) of cyclopropyl acetate in 35 ml of anhydrous ether in a three neck round bottomed flask, cooled to 0°C, 35 ml of 1.1 F. lithium aluminum hydride solution in ether was added dropwise. The rate of addition was controlled by evolution of heat by the reaction; as refluxing of ether subsided, dropwise addition was resumed. The total time of addition was 5 minutes. Approximately 5 grams of sodium sulfate saturated with water was added to the mixture immediately after addition of the hydride was complete. The ether solution was filtered to remove the basic salts and dried over anhydrous sodium sulfate. The solvent was removed by distillation through a twelve inch packed column until the volume of the residual liquid was 5 ml. The residual liquid was then analyzed by G.P.C. on the L.B. 550X column at 80°C. The analysis indicated that the mixture contained three components; ether, retention ratio 1.00, ethyl

alcohol, retention ratio 3.00 and a third component, retention ratio 10.0. This third component was neither n-propyl alcohol whose retention ratio under these conditions is 6.00 nor allyl alcohol whose retention time is 8.00. The unknown component was isolated by collecting the effuent gas from the vapor fractometer. It was possible to use samples as large as 1.00 ml on the initial injection into the instrument. A yield of 53%, 1.9 grams, of the compound was isolated. The material was identified by its infra red spectrum in carbon tetrachloride as an alcohol (2.80 mμ). See Fig. 2. The phenyl urethan formed by conventional methods and recrystallized 3 times from carbon tetrachloride had m.p. 101.5 - 102.5°C (lit. 101.5 - 102.0)[35] and α-napthyl urethan m.p. 101.0 - 102.0°C (lit. 101.5 - 102°C)[35] identified the compound as cyclopropyl alcohol. Range of b.p. by micro method was 100.5 - 101.0°C with decomposition and odor of propionaldehyde. (lit. 100 - 103)[35]

Anal. Calcd. for C_3H_6O: C, 62.03; H, 10.41. Found: C, 61.60; H, 10.76

Rate of formation of 2-methyl-2-penten-1-al from the reaction of cyclopropyl alcohol in sodium hydroxide solution

Samples for the rate determination were prepared in the same manner as described above. Infinity points were determined by the sealed tube method exactly as described above in the cyclopropyl acetate reaction.

Stability of 2-methyl-2-penten-1-al in sodium hydroxide solutions

An aqueous solution of 2-methyl-2-penten-1-al was prepared in the usual manner and then diluted to ca. 5×10^{-5} M. After the ultraviolet absorption spectrum of the solution was recorded, aliquots of concentrated base were added so that the final concentration of 2-methyl-2-penten-1-al was 4×10^{-5}M in 0.2 N sodium hydroxide. The absorption spectrum of this solution was then recorded at various time intervals.

Calculation of the relative rates of formation of 2-methyl-2-penten-1-al

The concentrations of 2-methyl-2-penten-1-al as calculated from its absorption maximum at 2355A° were plotted versus time. Fig. 3 and Fig. 4 are typical plots obtained by this technique.

Preliminary experiments on the isomerization in solution of cyclopropyl alcohol to propionaldehyde

Purification of solvents. Carbon tetrachloride (Baker Reagent Grade) was purified by the procedure of Gunther, et al.[78] Purification of acetonitrile (Matheson, Coleman and

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[78]Gunther, P., von der Horst, H.D. and Cronheim, G., Z. Elektrochem., 34, 616 (1928)

Fig. 3. Concentration of 2-methyl-2-penten-1-al as a function of time

A. 2.98×10^{-3}N sodium hydroxide
2.14×10^{-3}M propionaldehyde

B. 5.70×10^{-3}N sodium hydroxide
1.29×10^{-3}M propionaldehyde

C. 7.60×10^{-3}N sodium hydroxide
0.86×10^{-3}M propionaldehyde

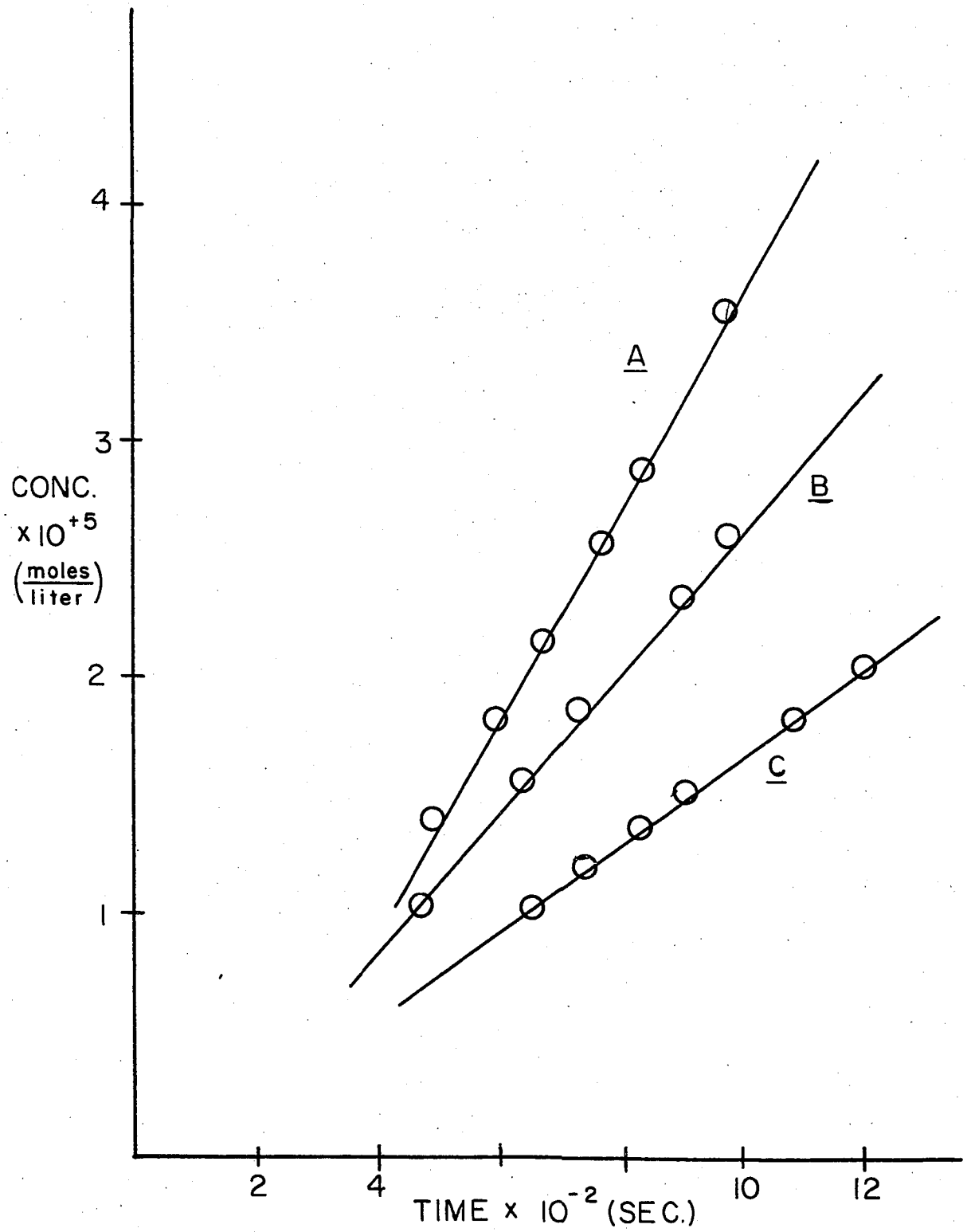
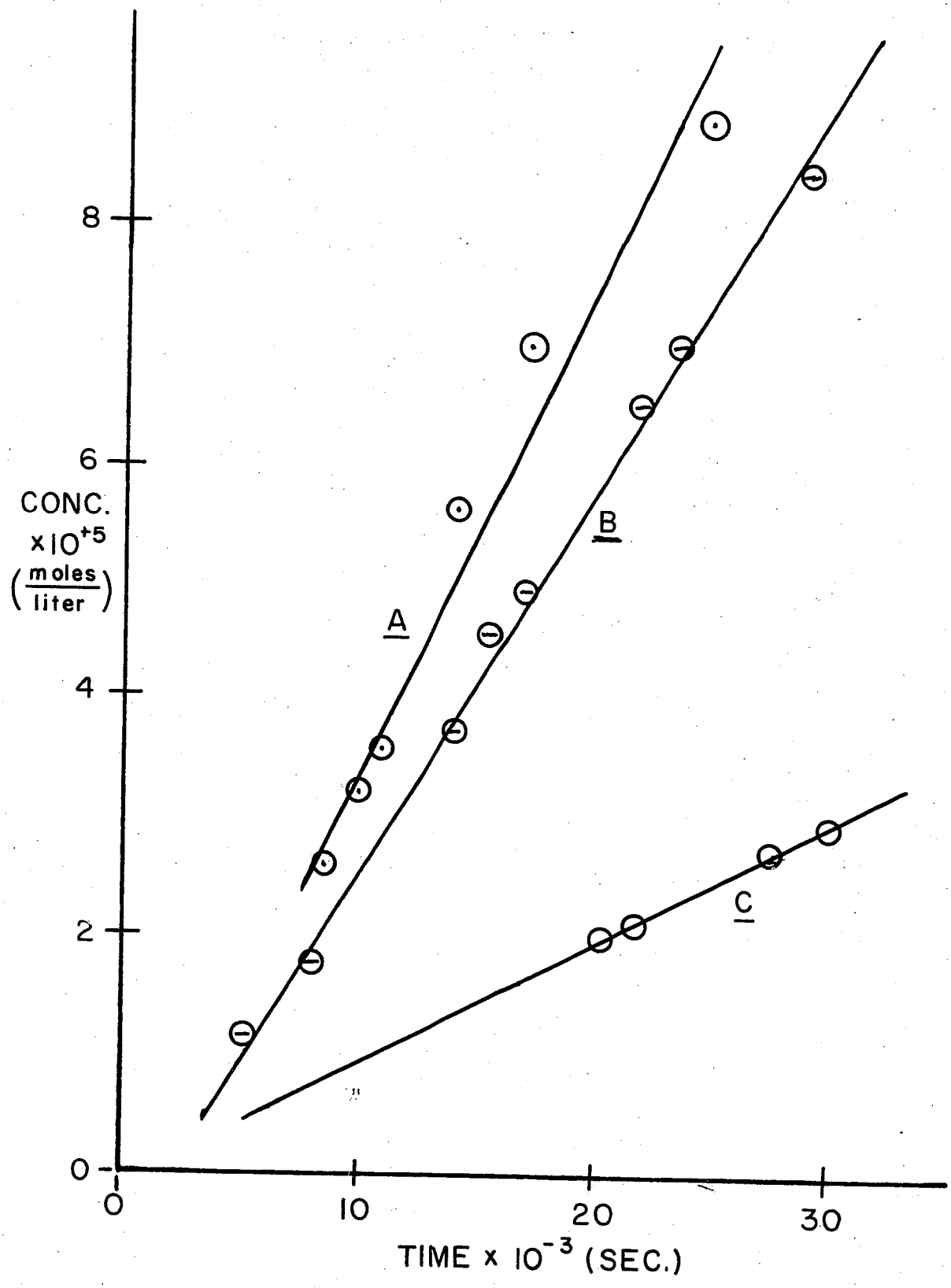

4
3
2
1
CONC.
x 10+5
(moles/liter)
A
B
C
2
4
10
12
TIME x 10-2 (SEC.)

Fig. 4. Concentration of 2-methyl-2-penten-1-al as a function of time

A. 180×10^{-3}N sodium hydroxide
1.85×10^{-3}M cyclopropyl acetate

B. 160×10^{-3}N sodium hydroxide
1.90×10^{-3}M cyclopropyl alcohol

C. 160×10^{-3}N sodium hydroxide
0.76×10^{-3}M cyclopropyl alcohol


8
6
4
2
0
CONC.
x10+5
(moles/liter)
A
B
C
0
10
20
30
TIME x 10-3 (SEC.)

Bell) was carried out as described by Lewis and Smyth.[79] Spectral grade methyl cyclohexane (Matheson, Coleman and Bell) was used without further purification.

Infra red spectra. All infra red spectrum was recorded by means of a Model 21 infra red Spectrophotometer manufactured by Perkin Elmer Corporation. Solution spectra were recorded in sodium chloride cells with light path of 0.5 mm. Gas phase spectra were recorded utilizing a gas sodium chloride cell Model 127-XX03 with path length of 7.5 cm and volume of 25 cc also manufactured by Perkin Elmer Corporation.

Glassware. All glassware, (tubes, vials and volumetric flasks) used in this study were subjected to the action of concentrated sulfuric-nitric acid at 100°C for periods of not less than one hour. The glassware was then rinsed successively with conductivity water and dilute ammonium hydroxide and finally was rinsed with copious amounts of conductivity water. Just prior to use the surface of the glass was freed of moisture by "flaming" with a glass torch.

Technique. Solutions of cyclopropyl alcohol were prepared by weighing the alcohol into "S" shaped capillary tubes, which were then placed in volumetric flasks filled to

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[79]Lewis, G.L. and Smyth, C.P., J. Chem. Phys., 7, 1085 (1939)

the mark with solvent. The tubes were then crushed and flask vigorously shaken.

Glass vials were filled with the solutions, sealed, and placed in a 80°C constant temperature bath. At various time intervals, the vials were withdrawn from the bath and rapidly cooled by means of an ice bath. The vials were then opened and in the case of acetonitrile, carbon tetrachloride and methylcyclohexane, the infra red spectrum of the solution was recorded. Ultraviolet absorption spectrum were recorded in runs in which water and methylcyclohexane were the solvents.

SUMMARY

Cyclopropyl alcohol has been prepared for the first time in the pure state. The synthesis was the result of a kinetic investigation of the series of reactions, catalyzed by base, leading from cyclopropyl acetate to 2-methyl-2-penten-1-al. It was strongly suggested by kinetic arguments that the isomerization of cyclopropyl alcohol to propionaldehyde was less facile than previously suggested. Based on this evidence a relatively simple synthesis of the alcohol was attempted and proved successful. The kinetic arguments were verified when the action of base on pure cyclopropyl alcohol was studied.

In conjunction with the above, a rate study of the saponification of a number of enol acetates was made. The results indicate that the mechanism of basic hydrolysis of enol acetates is of the same type as that observed in the series of saturated alkyl acetates.

A preliminary investigation of the facile thermal isomerization of cyclopropyl alcohol in solution has revealed an interesting and as yet unexplained solvent effect on the rate of the isomerization.

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