from the rubber. No wax-like material was found in the exuded resin, and since this is practically free of chlorophyll it might be considered as the true guayule resin. About 20% of the exuded resin was parthenyl cinnamate. The acetone extract of the rubber also yielded roughly 20% of crude parthenyl cinnamate.

Acknowledgment.—The author is indebted to the Rubber Laboratory, Navy Yard, Mare Island, California, for a supply of acetone extract of guayule rubber and to Dr. C. L. Ogg and assistants of the Microanalytical Laboratory for the analyses reported.

Summary

1. *Partheniol*, a new sesquiterpene alcohol, and *parthenyl cinnamate* were isolated from guayule resin, and some of their properties, including crystallographic optical properties, are described.

2. A crystalline waxlike substance and several fractions of volatile oils, probably sesquiterpenes, were prepared from acetone extracts of whole shrub, guayule foliage, and guayule rubber.

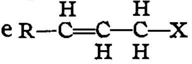
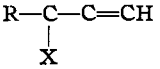
3. Retting of the shrub appears to make no change in the relative proportions of the constituents isolated from the resin.

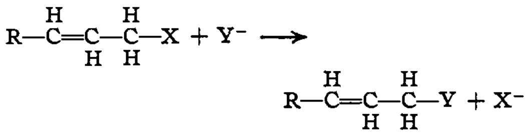
PHILADELPHIA, PA. RECEIVED DECEMBER 13, 1943

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

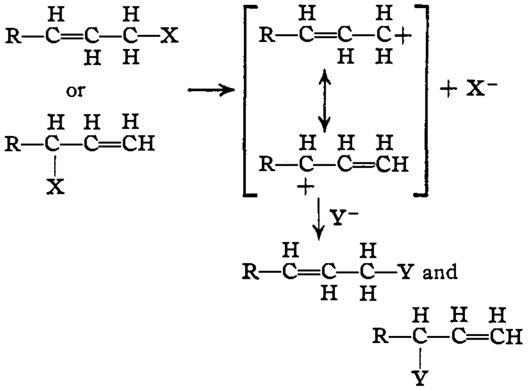
Allylic Rearrangements. XIV. The Hydrolysis of Butenyl Chlorides[1]

BY WILLIAM G. YOUNG AND LAWRENCE J. ANDREWS

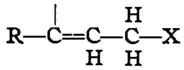
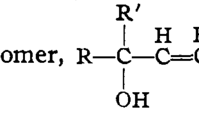
Recent work[2] on nucleophilic replacement reactions of allylic systems of the type  $R-\overset{H}{C}=\underset{H}{C}-\underset{H}{\overset{H}{C}}-X$ or  $R-\underset{X}{\overset{H}{C}}-\overset{H}{C}=\overset{H}{C}H$ indicates that bimolecular or S_N2 reactions produce unrearranged products (Equation 1). Unimolecular or S_N1 type reactions, involving an unfree carbonium ion intermediate, lead to a mixture of allylic isomers (Equation 2)

(1) 

$$R-\overset{H}{C}=\underset{H}{C}-\underset{H}{\overset{H}{C}}-X + Y^- \longrightarrow R-\overset{H}{C}=\underset{H}{C}-\underset{H}{\overset{H}{C}}-Y + X^-$$

(2) 

$$\begin{array}{c} R-\overset{H}{C}=\underset{H}{C}-\underset{H}{\overset{H}{C}}-X \\ \text{or} \\ R-\underset{X}{\overset{H}{C}}-\overset{H}{C}=\overset{H}{C}H \end{array} \longrightarrow \left[\begin{array}{c} R-\overset{H}{C}=\underset{H}{C}-\underset{H}{\overset{H}{C}}+ \\ \updownarrow \\ R-\underset{+}{\overset{H}{C}}-\overset{H}{C}=\overset{H}{C}H \end{array}\right] + X^- \xrightarrow{Y^-} R-\overset{H}{C}=\underset{H}{C}-\underset{H}{\overset{H}{C}}-Y \text{ and } R-\underset{Y}{\overset{H}{C}}-\overset{H}{C}=\overset{H}{C}H$$

The relative contributions of types (1) and (2) in a given reaction are readily influenced by the experimental conditions. With this in mind it was desirable to examine critically the apparently conflicting reports in the literature concerning the hydrolysis of alkenyl halides.[3] For example, halides of the type  $R-\overset{R'}{C}=\underset{H}{C}-\underset{H}{\overset{H}{C}}-X$ are reported to give primary alcohol, mixtures of alcohols or the pure allylic isomer,  $R-\underset{OH}{\overset{R'}{C}}-\overset{H}{C}=\overset{H}{C}H$. Although reaction (1) would account for the production of pure normal product and reaction (2) would give a mixture due to the formation of a resonating carbonium ion intermediate, neither (1) nor (2) should give a pure secondary alcohol from a pure primary halide.

The present investigation has been undertaken to show that under controlled conditions it is possible to account for the products of hydrolysis of the butenyl chlorides[4] in terms of the mechanisms given above. Reaction conditions were varied from those favorable to S_N1 type hydrolysis to those suitable for a bimolecular type (S_N2) reaction of the organic halide with hydroxide ion. From a consideration of the composition of the alcohols produced in these reactions (Table I) it was possible to compare the relative contributions of the S_N1 and S_N2 type processes to the hydrolysis of the two halides. The correctness of the estimated contributions of the mechanisms to these hydrolyses has been demonstrated by an investigation of the kinetics of the reactions.

The Products of Hydrolysis of the Butenyl Chlorides.—The reactions with silver oxide were studied to determine the composition of

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[1] This paper was presented before the Division of Organic Chemistry of the American Chemical Society, Memphis, April, 1942.

[2] (a) (XIII) Roberts, Young and Winstein, THIS JOURNAL, **64**, 1725 (1942); (b) Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

[3] (a) Claisen and Tietze, *Ber.*, **59**, 2344 (1926). (b) Claisen, *J. prakt. Chem.*, [2] **105**, 65 (1922). (c) Prévost, *Ann. chim.*, [10] **10**, 113 (1928). (d) Meisenheimer and Link, *Ann.*, **479**, 211 (1930). (e) Petrov, *J. Gen. Chem.* (U. S. S. R.), **11**, 713 (1941).

[4] In order to avoid complications arising from thermal rearrangement of the starting material the pure primary and secondary butenyl chlorides have been used rather than the corresponding bromides.

TABLE I

THE COMPOSITION OF BUTENOLS FROM THE HYDROLYSIS OF BUTENYL CHLORIDES[a,b]

Hydrolysis medium	Chloride used	Time of reaction, hr.	Composition of products % secondary alcohol		% primary alcohol		Yield,[c] %
Silver hydroxide suspended in water	Primary	1.5	54.7	54.8	45.3	45.2	57
		1.5	54.9		45.1		60
	Secondary	1.5	67.0	66.2	33.0	33.8	53
		1.5	65.5		34.5		72
0.5 N aqueous sodium carbonate; initial (OH^-) = 10^{-2} N	Primary	130	45.0		55.0		67
		49	45.0		55.0		64
	Secondary	120	65.2		34.8		65
0.8 N aqueous sodium hydroxide; initial (OH^-) = 0.8 N	Primary	123	39.9		60.1[d]		73
	Secondary	121	62.0		38.0		68
0.5 N solution of sodium carbonate in 45 volume % aqueous ethanol	Primary	96	31.8		68.2[d]		57
	Secondary	97	60.9		39.1		43

[a] All reactions were carried out at room temperature. [b] The designations primary and secondary are used for the crotyl and methylvinylcarbinyl radicals, respectively. [c] Yields are based on butenyl chloride assuming complete reaction. [d] This crotyl alcohol contains some *cis* isomer.

alcohols to be expected from the solvolytic (S_N1) type reaction. In this case both chlorides gave a predominance of secondary alcohol, 55% from the primary chloride and 66% from the secondary chloride. It might be expected that the same mixture of alcohols should be obtained from both chlorides in an S_N1 type process. This difference in composition of alcohols arising from the unfree carbonium ion[2a] probably should be attributed to the polarizing influence of the chloride ion on the carbon atom from which it is being removed rather than to contributions of a bimolecular type. The low solubility of silver oxide would leave little opportunity for a bimolecular reaction with hydroxide ion, and the rate of reaction was far too rapid to allow for bimolecular reaction of the organic halide with solvent.

The other experiments were designed to increase the opportunity for a bimolecular reaction with hydroxide ion either by raising the hydroxide ion concentration or by decreasing the solvating power of the medium. In every case the composition of the butenols from the secondary chloride was close to that obtained in the runs with silver hydroxide. Aqueous sodium carbonate gave 65% secondary alcohol; aqueous sodium hydroxide gave 62% secondary alcohol. It thus appeared that the secondary chloride was not affected by conditions designed to promote the S_N2 reaction and instead reacted by an S_N1 process The primary chloride responded readily to conditions favoring the bimolecular reaction giving larger amounts of unrearranged product than obtained with silver oxide.

Additional evidence that a bimolecular reaction was being brought into play during the hydrolysis of the primary chloride arose through the fact that the crotyl chloride used must have contained some *cis* isomer. The S_N1 type hydrolysis of either the primary or the secondary chloride gave only *trans*-crotyl alcohol from the resonating carbonium ion. Similarly it has been observed that only *trans*-crotyl alcohol is formed when the secondary alcohol is rearranged by strong acid to produce primary alcohol by means of the intermediate carbonium ion.[5] However, when the conditions favored the bimolecular hydrolysis of the primary chloride, both *cis* and *trans* primary alcohols were formed (see Table I). The formation of *cis*-crotyl alcohol must be attributed to a bimolecular reaction of *cis*-crotyl chloride with hydroxide ion. This is the first evidence that the primary chloride contains some of the *cis* isomer[6]; however previous investigators did not prepare their chloride by chlorination of butene mixtures.

The Rate Expressions for Organic Halide Hydrolysis.—The rate of hydrolysis of an organic halide may be expressed by equation (3)

$$\frac{dx}{dt} = \underbrace{k_1(a - x)}_{\text{I}} + \underbrace{k_2(a - x)(b - x)}_{\text{II}} \qquad (3)$$

where a is the original concentration of organic halide, b the original concentration of hydroxide ion, and x the concentration of halide ion at time t. Term II represents the second order and bimolecular (S_N2) contribution to the rate. Term I does not necessarily represent only the S_N1 contribution to the reaction but also may account for any bimolecular reaction between the solvent and the halide which may occur. If term I disappears from the rate expression, a constant κ_2 equal to k_2, the specific second order rate constant, may be calculated by equation (4).

$$\kappa_2 = \frac{1}{t(a - b)} \ln [b(a - x)]/[a(b - x)] \qquad (4)$$

Similarly when only a first order reaction proceeds, κ_1 equal to k_1, the specific first order rate constant, is calculated by equation (5).

$$\kappa_1 = \frac{1}{t} \ln \frac{a}{a - x} \qquad (5)$$

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[5] Young, Warner and Andrews, unpublished work.

[6] Gredy, *Bull. soc. chim.*, [5] **2**, 1029 (1935), found only the *trans* isomer by measurement of the Raman spectrum of crotyl chloride prepared from methylvinylcarbinol and phosphorus trichloride.

In the event that first and second order reactions occur simultaneously values calculated for κ_1 and κ_2 during a run will show serious drifts.

Kinetic Studies of Butenyl Chloride Hydrolysis.—To verify the assumptions that the secondary chloride was hydrolyzed only by the S_N1 type reaction while the primary chloride could react by both S_N1 and S_N2 processes the kinetics of the hydrolysis of the butenyl chlorides were studied. The rate runs were made at 25.00° using dilute solutions of the halide and sodium hydroxide in approximately fifty volume per cent. aqueous ethanol.

As was expected, the rate of reaction of methylvinylcarbinyl chloride was independent of hydroxide ion over a range of 0.0 to 0.2 *N* hydroxide ion concentration. A typical run is summarized in Table II. During any given run using primary chloride in the presence of hydroxide ion values of κ_1 drifted downward while those of κ_2 drifted upward. This indicates that both first and second order reactions contribute to the total rate as was expected. Values of k_1 and k_2 were obtained by plotting x against t to obtain values of dx/dt at any time t. A plot of $(dx/dt)/a - x$ against $b - x$ gives a straight line according to equation (3). The slope of this line is k_2, and the intercept at $b - x$ equals zero is k_1. The values of k_2 and k_1 obtained from several runs in which the halide and sodium hydroxide concentrations were varied are in good agreement. The small variations in the rate constants may be the result of salt effects. The values of k_1 are also in good agreement with that obtained from a run in which no sodium hydroxide was used and the rate constant was calculated from equation (5). The rate constants for the hydrolysis of the primary and secondary chlorides are summarized in Table III.

It appears that the primary chloride reacts by a bimolecular process much more readily than does the secondary chloride. To demonstrate further this difference in reactivity of the primary and secondary chlorides toward S_N2 type replacements a few rate runs were carried out with alcoholic sodium ethoxide in a manner similar to that previously described.[2a] The rate constants calculated from equation (4) are summarized in Table IV.

TABLE II

HYDROLYSIS OF METHYLVINYLCARBINYL CHLORIDE IN A 50 VOLUME % AQUEOUS ETHANOL SOLUTION OF SODIUM HYDROXIDE

Time, hours	(Halide) = a		(OH⁻) = b	
	x	$a - x$	$b - x$	k_1
0	0.00000	0.07165	0.05080	
2	.00715	.06450	.04365	0.0450
4¹/₂	.01360	.05805	.03720	.0432
7¹/₂	.02605	.05100	.03015	.0433
11	.02755	.04410	.02325	.0426
			Mean[a]	.0437

[a] Mean actually based on eleven observations.

TABLE III

RATE CONSTANTS FOR THE HYDROLYSIS OF BUTENYL CHLORIDES IN 50 VOLUME % AQUEOUS ETHANOL AT 25°

Halide	Halide concn.	OH⁻ concn.	k_1 hours⁻¹	k_2 hours⁻¹ g. mole⁻¹ l.
Secondary	0.1262	0.0000	0.0411	..
Secondary	.07165	.05080	.0437	..
Secondary	.04855	.05140	.0470	..
Secondary	.06902	.2143	.0461	..
Primary	.1224	.0000	.0532	..
Primary	.09375	.05140	.0525	1.16
Primary	.09913	.05140	.0511	1.11
Primary	.08941	.1024	.0480	1.05

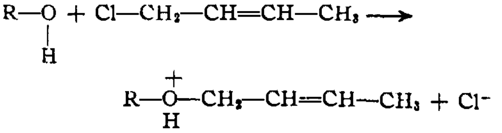
TABLE IV

THE REACTION OF BUTENYL CHLORIDES IN ALCOHOLIC SODIUM ETHOXIDE SOLUTION

(Butenyl chloride) = a			(NaOEt) = b	
Butenyl chloride	Temp., °C.	a	b	κ_2 hours⁻¹ g. mole⁻¹ l.
Secondary	40.00	0.1984	0.2110	0.0225
Secondary	40.00	.1984	.0937	.0276
Secondary	25.00	.1979	.2073	.00363
Primary	25.00	.2051	.2694	.201

At 25° the ratio of κ_2 for the primary chloride to that of the secondary chloride is 55/1. The effect of halving the sodium ethoxide concentration in the runs at 40° with the secondary chloride was to cause a 23% increase in the rate constant. This may be due to salt effects.

The Nature of the Solvolytic Reactions of the Butenyl Chlorides.—It is interesting to note that the first order constant for the hydrolysis of the primary chloride ($k_1 = 0.0532$) is slightly higher than that for the secondary chloride ($k_1 = 0.0411$). Similarly the first order constant for the solvolysis of the primary chloride in absolute ethanol at 25° ($\kappa_1 = 2.20 \times 10^{-4}$ hr.⁻¹) was found to be of the same magnitude as that for the secondary chloride at 40° ($\kappa_1 = 2.11 \times 10^{-4}$ hr.⁻¹). These facts are contrary to the usual observation that primary chlorides react much more slowly by an S_N1 type process than do secondary chlorides. It seemed quite possible, therefore, that the first order reaction of the primary chloride might be in part a bimolecular reaction with solvent giving rise to normal product, as represented by equation (6).



$$\underset{\text{H}}{\text{R—O}} + \text{Cl—CH}_2\text{—CH=CH—CH}_3 \longrightarrow \text{R—}\overset{+}{\underset{\text{H}}{\text{O}}}\text{—CH}_2\text{—CH=CH—CH}_3 + \text{Cl}^- \qquad (6)$$

It seemed like that in alcoholic solution, which is a poorer solvating medium than water, the primary chloride solvolysis might be completely bimolecular. This was found to be true when the primary chloride was refluxed with 90% aqueous ethanol in the presence of calcium carbonate giving a product containing at least 95.6% crotyl ethyl ether. It is, therefore, probable that the formation of normal product in the hydrolysis of the primary chloride in dilute basic media must result, in part, from a bimolecular reaction with solvent.

The Validity of Previously Reported Work.—The present investigation has shown that methylvinylcarbinyl chloride is hydrolyzed in dilute basic media by a first order process giving rise to a mixture of alcohols. Crotyl chloride reacts by a mixed first and second order process to give mixtures of alcohols, but the relative amount of normal product may be increased by raising the base concentration. In agreement with these findings are several reports in the literature that primary or secondary allylic halides hydrolyze in dilute basic media to give alcohol mixtures.[3c,d,e] In view of the rapid thermal rearrangement of butenyl bromides it is questionable just how much significance can be attached to the quantitative results reported for allylic bromide hydrolysis. The report of Claisen and Tietze[3a] that crotyl bromide is hydrolyzed in 10% sodium carbonate solution to give only crotyl alcohol must be regarded as erroneous. The reported conversion of 1-bromo-3-methyl-2-butene to 3-methyl-1-butene-3-ol in 10% sodium carbonate[3b] involves a rearrangement from a primary to a tertiary carbon atom. The present results indicate that complete conversion from one allylic isomer to the other is not to be expected from the hydrolysis of primary and secondary allylic halides. Therefore this report will be checked in this Laboratory.

Acknowledgment.—The authors wish to express their appreciation to Dr. S. Winstein for the many helpful suggestions which he made in regard to this work.

Experimental Part

Crotyl and Methylvinylcarbinyl Chlorides.—Mixtures of the chlorides obtained from the Shell Development Corporation or prepared from the alcohols as previously described[2a] were separated by fractionation on a six foot column packed with glass helices. The secondary chloride used had the properties: b. p. 63.4–63.5° (751 mm.), $n^{20}\text{D}$ 1.4151. The purity of the crotyl chloride samples was tested by measuring their rates of reaction with alcoholic sodium ethoxide.[2a] The sample used for rate work was prepared from methylvinylcarbinol and phosphorus trichloride and had the following physical properties: b. p. 45.2–45.4° (192 mm.), $n^{20}\text{D}$ 1.4352, κ_2 (alcoholic sodium ethoxide) 0.201. Other samples (from the Shell Development Corporation or prepared by the reaction of the butenols with concentrated hydrochloric acid) had somewhat higher refractive indices and rate constants. The properties of the primary chloride obtained from the Shell Development Corporation mixture were: b. p. 83.8–84.0° (750 mm.), $n^{20}\text{D}$ 1.4364, κ_2 0.225. It seems likely that the presence of *cis*-crotyl chloride in some of the samples is responsible for their varying physical properties.

The Hydrolysis of the Butenyl Chlorides in the Presence of Silver Hydroxide.—A mixture of freshly prepared silver hydroxide (258 g. or 1.1 moles), 250 ml. of water, and 100 g. (1.1 moles) of the chloride was stirred at room temperature, and the reaction flask was cooled by a water-bath. At the end of the reaction period the aqueous phase was filtered from the precipitate. The precipitate was washed several times with water, and the washings were added to the filtrate. The filtrate was distilled until the distillate no longer gave a bromine test for unsaturation. The alcohols were salted out from the distillate and dried over potassium carbonate. Analysis of the alcohol mixtures was accomplished by fractionation through a three foot Podbielniak type column. The refractive indices of samples of the pure chlorides in contact with silver chloride did not change over a long period of time nor did the pure butenols rearrange when in contact with silver residues taken from one of the runs.

The Hydrolysis of the Butenyl Chlorides in Dilute Basic Media.—In the aqueous sodium carbonate runs the hydrolysis medium was a solution of 58 g. (0.5 mole) of sodium carbonate in 2 liters of water. In the runs using aqueous ethanol 58 g. of sodium carbonate was dissolved in a solution of 1142 ml. of water and 858 ml. of 95% ethanol. In the runs with sodium hydroxide the medium contained 65 g. (1.63 moles) of sodium hydroxide in 2 liters of water. To these solutions were added 100 g. (1.1 moles) of the chloride, and the mixtures were stirred at room temperature until the halide layer had disappeared. The products from the runs in aqueous media were isolated and analyzed in a manner similar to that used in the runs with silver hydroxide. The products from the runs in aqueous ethanol were isolated by distillation from their solution and dried as before. The ethanol and the constant boiling mixtures of ethanol and the ethyl ethers of the primary and secondary chlorides[7] were removed from the butenols by distillation through a three foot column packed with glass helices. When all of the low boiling material was removed, the column was washed down with 50 ml. of ether. Fractionation of the combined boiler residues and ether washings was carried out on the three foot column of the Podbielniak type.

Properties of the Butenols Prepared from the Butenyl Chlorides.—The methylvinylcarbinol produced in these reactions had the following properties: b. p. 97°, $n^{25}\text{D}$ 1.4125, m. p. of 3,5-dinitrobenzoate 54°. The crotyl alcohol obtained from the hydrolysis of methylvinylcarbinyl chloride and that obtained from the hydrolysis of crotyl chloride in the presence of silver hydroxide or in aqueous sodium carbonate solution appeared to be predominantly the *trans* isomer. Its properties were as follows: b. p. 121°, $n^{25}\text{D}$ 1.4270, m. p. of 3,5-dinitrobenzoate 70.5°. The crotyl alcohol isolated from the reaction of crotyl chloride with aqueous sodium hydroxide and with an aqueous ethanol solution of sodium carbonate always distilled over a range of 121–122°. The refractive index of material taken at the end of these distillations was high. A sample of such material of $n^{25}\text{D}$ 1.4302 gave a 3,5-dinitrobenzoate which melted from 54–56°. These properties indicated that this sample contained an appreciable quantity of *cis*-crotyl alcohol. The properties of *cis*-crotyl alcohol which had been prepared in this Laboratory by other methods[8] were b. p. 121°, $n^{25}\text{D}$ 1.4330, m. p. of 3,5-dinitrobenzoate 54–56°.

Rates of Reaction of Butenyl Chlorides with 50 Volume % Aqueous Ethanol Solutions of Sodium Hydroxide.—To a 100-ml. volumetric flask was added 50 ml. of a standardized aqueous solution of sodium hydroxide and enough anhydrous ethanol to fill the flask to within about 0.5 ml. of the mark. This solution was brought to temperature in the thermostat, and the butenyl chloride was added to the mark by means of a weight pipet. Aliquot portions were withdrawn from time to time and titrated with alcoholic hydrogen chloride or in runs where no sodium hydroxide was used with aqueous sodium hydroxide to the phenolphthalein end-point.

Rate of Conversion of Butenyl Chlorides to Ethyl Ethers.—To a 100-ml. volumetric flask was added the proper volume of a standardized solution of sodium ethoxide in absolute ethanol. The flask was filled to within 5 ml. of the mark with absolute ethanol, and a 2-ml. sample of the organic halide was added from a weight pipet. The flask was filled to the mark with absolute ethanol, shaken and immersed in the thermostat. Aliquot portions were removed from time to time and analyzed as described above. All liquids were brought to thermostat temperature before they were mixed.

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[7] Lépingle, *Bull. soc. chim.*, [4] **39**, 864 (1926).

[8] Young and Siegel, unpublished work.

The Solvolysis of Crotyl Chloride in 90% Aqueous Ethanol.—A mixture of 75 g. (0.83 mole) of crotyl chloride, 200 ml. of absolute ethanol, 20 ml. of water, and 95 g. of calcium carbonate was stirred and refluxed on an oil-bath (85°) for one hundred hours. The calcium carbonate was filtered out and washed with 50 ml. of ethanol, and the washings were added to the filtrate. The alcoholic solution of the product was added to 1.5 liters of water. The mixture was extracted with a total of 400 ml. of carbon disulfide and dried briefly over potassium carbonate. Fractionation of this material was carried out on the three foot Podbielniak type column. Fractions containing other than carbon disulfide, alcohol and water were

Fr. 1	1.9 g.	48.0–76.0° (uncor.)	n^{20}D 1.5030
Fr. 2	2.0 g.	76.0–98.6°	n^{20}D 1.4010
Fr. 3	24.9 g.	98.6–99.0°	n^{20}D 1.4049 (crotyl ethyl ether)

It was estimated that not more than 1.2 g. of methylvinylcarbinyl ethyl ether (b. p. 77.6°, n^{21}D 1.3751)[2a] out of a total of 27.6 g. of ether was formed in this reaction. The yield of ether was 33%.

Summary

The hydrolysis of crotyl and methylvinylcarbinyl chlorides has been studied using a variety of experimental conditions designed to produce different ratios of S_N1 and S_N2 replacement reactions, and the compositions of butenols from these reactions have been determined. The secondary chloride appears to react only by the S_N1 type process to give a mixture of allylic isomers while the primary chloride responds readily to changes in experimental conditions, giving relatively larger amounts of normal product as the medium becomes more suitable for a bimolecular reaction.

Kinetic studies of the reaction of the isomeric chlorides in dilute solutions of sodium hydroxide in aqueous ethanol showed that the secondary chloride reaction rate was independent of hydroxide ion; the primary chloride, however, showed both first and second order kinetics. Evidence was obtained that the first order reaction of the primary chloride is in part a bimolecular reaction with solvent.

LOS ANGELES, CALIFORNIA RECEIVED SEPTEMBER 7, 1943

[CONTRIBUTION FROM THE NUTRITIONAL RESEARCH DEPARTMENT, ABBOTT LABORATORIES]

The Hydrolysis of Pantothenate: A First Order Reaction.[1] Relation to Thiamin Stability

BY DOUGLAS V. FROST AND FLOYD C. MCINTIRE

A rapid polarimetric method for following the hydrolytic decomposition of pantothenate in aqueous solution was described recently in a paper from this Laboratory.[2] Reaction rate analyses applied to the data of this earlier publication clearly show that at the temperature studied, 60°, pantothenate hydrolysis follows the pattern of a first order reaction with respect to pantothenate concentration. The effect of varying *p*H at that temperature demonstrates that pantothenate stability is good in the *p*H range 5.5–7, but that hydrolysis proceeds at an increasing rate with increase in acidity below *p*H 5.5. The present study deals with the temperature variation of the rate of pantothenate destruction at constant *p*H.

Procedure.—A *p*H of 3.7–4.0 was chosen since the formation of pantoyl lactone is rapid and complete in this range.[2] The specific rotation of 1% calcium pantothenate at *p*H 3.8 was found to be +24.2°. A standard reference curve was therefore plotted from −27.5 to +24.2° and estimations of residual pantothenate were made as previously described.[2]

Two solutions of 1% calcium pantothenate, one buffered with 3% monosodium phosphate, the other unbuffered, were studied in parallel. Addition of small amounts of concentrated hydrochloric acid was required at the start and from time to time during the experiments to maintain a *p*H of 3.8 as closely as possible. Since the necessary additions of acid were small, no corrections were made for dilution. The various temperatures of reaction were maintained constant within 0.5°. Samples were withdrawn from the reaction vessels to make the rotation measurements.

The results obtained are shown in Table I.

Discussion.—When the logarithm of the concentration of pantothenate was plotted against time, straight lines, characteristic of a first order reaction, were obtained at each of the temperatures studied. The values of *k* in Table I have therefore been calculated using the standard first order equation.

The rate of destruction of pantothenate was slightly greater in the buffered solutions than in the unbuffered ones. The effect of phosphate buffer, as well as other substances, in catalyzing pantothenate destruction is more pronounced at higher *p*H,[2] than at the relative low *p*H of this study. The values for the unbuffered and buffered solutions in this case are close enough to serve as a partial check against one another.

In Table II the average values for *k* at different temperatures are shown, together with a calculation of the half-life period for each. When the values for log *k* are plotted against $1/T$, the results are seen to follow the Arrhenius equation in yielding a straight line, as shown in Fig. 1. From the slope of this line an activation energy of 19,000 ±1000 cal. may be calculated. By extrapolation of the data the value for the half-life at 0° is found to be 6030 days, while at 110 and 120° it is 0.174 and 0.096 day, respectively.

Studies also were made to determine whether

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[1] Reported in part before the American Chemical Society at Pittsburgh, Pa., September 9, 1943.

[2] D. V. Frost, *Ind. Eng. Chem., Anal. Ed.*, **15**, 306 (1943).