3. The present results are in accord with those of Gilman and Harris, who isolated 2-phenyl-3-butenoic acid from the carbonation of cinnamylmagnesium chloride.

LOS ANGELES, CALIFORNIA

RECEIVED NOVEMBER 15, 1943

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Allylic Rearrangement in the Reaction of Cuprous Cyanide with Butenyl Halides[1]

BY JOHN F. LANE, JAMES FENTRESS AND L. T. SHERWOOD, JR.

That cuprous cyanide reacts smoothly with allyl halides to give good yields of 3-butenonitrile is well known.[2] Until the present time, however, the reaction has not been extended to α- and γ-substituted allyl halides; *i. e.*

$$\mathrm{R{-}CHX{-}CH{=}CH_2\ (I),\ R{-}CH{=}CH{-}CH_2X\ (II)}\qquad (\mathrm{X = Cl, Br})$$

In connection with studies being carried out in this Laboratory on the preparation and reactions of isomeric olefinic acids of the type

$$\mathrm{R{-}CH(CO_2H){-}CH{=}CH_2\ (III)}$$
$$\mathrm{R{-}CH{=}CH{-}CH_2CO_2H\ (IV)}$$

it seemed desirable to investigate the action of cuprous cyanide on a pair of allylic isomerides such as I and II in the hope of producing the nitriles

$$\mathrm{R{-}CH(CN){-}CH{=}CH_2\ (V)}$$
$$\mathrm{R{-}CH{=}CH{-}CH_2CN\ (VI)}$$

corresponding to the acids III and IV.

Replacement of halogen by cyanide in such a system might proceed either by normal (bimolecular) substitution to give the expected nitrile from each isomeride

$$(1)\quad \mathrm{R{-}CH{=}CH{-}CH_2X + CuCN \longrightarrow R{-}CH{=}CH{-}CH_2CN + CuX}$$

or by an "ionic" mechanism

$$(2)\quad \mathrm{R{-}CH{=}CH{-}CH_2X \longrightarrow X^- + [R{-}CH{\cdots}CH{\cdots}CH_2]^+} \xrightarrow{\mathrm{CN^-}} \begin{cases}\mathrm{R{-}CH{=}CH{-}CH_2CN}\\ \mathrm{R{-}CH(CN){-}CH{=}CH_2}\end{cases}$$
$$\mathrm{(VII)}$$

to give a mixture of the isomeric nitriles V and VI.[3] In the latter event the composition of the mixture obtained should be independent first of the isomeric halide (I or II) used, and second of the nature of X. There remains also the possibility that the replacement might proceed by an "inverse" (bimolecular) substitution process[3c] to give from each isomeric halide the nitrile corresponding to the other form

$$(3)\quad \mathrm{R{-}CH{=}CH{-}CH_2X + CuCN \longrightarrow R{-}CH(CN){-}CH{=}CH_2 + CuX}$$

Of these three types of substitution process, all of which are known in reactions involving allylic systems, the process 2 is most frequently encountered, since the high resonance energy of ions such as VII greatly facilitates reaction by this path.

We have investigated the action of cuprous cyanide on the butenyl halides ($\mathrm{R = CH_3}$, $\mathrm{X = Cl, Br}$) and have found that at 60–70°, regardless of the nature of the halide used, the same mixture of isomeric nitriles is always produced

$$\left.\begin{matrix}\mathrm{CH_3{-}CH{=}CH{-}CH_2X + CuCN}\searrow\\ \mathrm{CH_3{-}CHX{-}CH{=}CH_2 + CuCN}\nearrow\end{matrix}\right. \begin{cases}\mathrm{CH_3{-}CH{=}CH{-}CH_2CN}\\ \mathrm{CH_3{-}CH(CN){-}CH{=}CH_2}\end{cases} + \mathrm{CuX}$$

After the two pure isomers had been isolated, it was possible to estimate the composition of this mixture by measurement of the refractive index. By this means we have determined that the mixture produced in each instance consisted of 91.5 ± 0.5% 3-pentenonitrile and 8.5 ± 0.5% 2-methyl-3-butenonitrile.

The simplest interpretation of these results is that the action of cuprous cyanide on halides such as I and II belongs to that class of allylic replacement reactions which are completely "ionic" in nature (mechanism 2 above). It has been pointed out,[3a] however, that assignment of such a mechanism may be most satisfactorily made only when the allylic reactants and products are not susceptible to thermal rearrangement under the conditions employed. While in the present investigation this requirement was fulfilled with respect to the products of the reaction, it could not be fulfilled with respect to the reacting halides. Even the butenyl chlorides, normally rather stable substances, are, under the conditions of the reaction (*i. e.*, at 60° in the presence of cuprous chloride), isomerized fairly rapidly to an equilibrium mixture containing 74.0 ± 0.5% 1-chloro-2-butene and 26.0 ± 0.5% 3-chloro-1-butene. The butenyl bromides, of course, are extremely labile substances which rearrange almost instantaneously at elevated temperatures to an equilibrium mixture containing 87% 1-bromo-2-butene and 13% 3-bromo-1-butene.[4]

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[1] Abstracted in part from Senior Theses presented to the Faculty of Princeton University by James Fentress and L. T. Sherwood, Jr., in partial fulfilment of the requirements for the degree of Bachelor of Arts.

[2] Bruylants, *Bull. Soc. Chim. Belg.*, **31**, 175 (1922); Breckpot, *ibid.*, **39**, 465 (1930); Supniewski and Salzberg, *Org. Syn.*, Coll. Vol. I, 38 (1932).

[3] (a) Young and Lane, THIS JOURNAL, **60**, 847 (1938); (b) Roberts, Young and Winstein, *ibid.*, **64**, 2157 (1942); (c) Hughes, *Trans. Faraday Soc.*, **37**, 627 (1941).

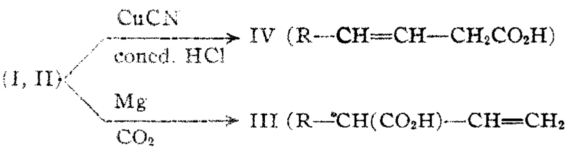
[4] Winstein and Young, THIS JOURNAL, **58**, 104 (1936).

We feel, however, that an alternative mechanism presuming initial rearrangement of the butenyl halides followed by reaction of each isomer in normal fashion (mechanism 1 above) is improbable. It is scarcely possible that such normal reactions of the two isomeric halides present at equilibrium in each case could proceed at precisely those rates necessary to give the same mixture of nitriles regardless of whether the reactants were butenyl bromides or butenyl chlorides. We prefer to assume, therefore, that the composition of the nitrile mixture is governed entirely by the relative rates of coördination of the entering cyanide ion at positions 1 and 3 in the mesomeric carbonium ion

$$[\mathrm{CH_3{-}CH{=}CH{=}CH_2}]^+ \quad (\mathrm{VII,\ R = CH_3})$$

We have also investigated the reaction of each of the two isomeric nitriles with concentrated hydrochloric acid according to the technique of Falaise and Frognier[5] for the preparation of 3-butenoic acid from 3-butenonitrile. It was found that while 3-pentenonitrile was readily converted to 3-pentenoic acid by this method, 2-methyl-3-butenonitrile was scarcely affected under the same conditions. Refluxing concentrated hydrochloric acid slowly attacked the latter nitrile to produce extensive charring but did not produce any appreciable amounts of the expected 2-methyl-3-butenoic acid.

From the results of this study it would appear that to derive an acid of type IV from either of the corresponding pair of halides (I, II) the proper procedure consists in treating the halides with cuprous cyanide and hydrolyzing the resulting nitrile with concentrated hydrochloric acid. On the other hand, the results previously reported[6] on the carbonation of butenylmagnesium bromide indicate that acids of type III will be exclusively produced when the corresponding halides (I, II) are converted to the Grignard reagent and the latter is treated with carbon dioxide. This may be summarized as follows



$$\begin{tikzcd} & \mathrm{IV\ (R{-}CH{=}CH{-}CH_2CO_2H)} \\ \mathrm{(I,\ II)} \arrow[ur, "\mathrm{CuCN}", "\mathrm{concd.\ HCl}"'] \arrow[dr, "\mathrm{Mg}", "\mathrm{CO_2}"'] & \\ & \mathrm{III\ (R{-}{}^{*}CH(CO_2H){-}CH{=}CH_2)} \end{tikzcd}$$

The general applicability of such methods to systems involving different alkyl and aryl groups R is being investigated.

Experimental Part

Materials.—1-Chloro-2-butene (n^{20}_D 1.4350), 2-chloro-1-butene (n^{20}_D 1.4150) and mixtures of these two butenyl chlorides were prepared by fractionation of a mixture containing approximately equal quantities of the two isomers which was purchased from the Shell Chemical Company. The composition of mixtures was determined before use in each instance by measurement of the refractive index. The mixture of butenyl bromides used in these experiments was prepared by the method of Claisen and Tietze[7] from a mixture of crotyl alcohol and methylvinylcarbinol purchased from the Shell Chemical Company. The cuprous cyanide employed in the preparation of nitriles was the Merck technical grade, dried for two hours at 110° before use. Cuprous chloride was prepared by the method of Marvel and McElvain,[8] washed successively with glacial acetic acid, alcohol, and ether, and dried in a vacuum desiccator over sulfuric acid before use.

Preparation of 3-Pentenonitrile and 2-Methyl-3-butenonitrile.—The method used was similar to that described by Bruylants, Breckpot and others[2] for the preparation of allyl cyanide from allyl halides. One hundred grams of a mixture of butenyl chlorides (n^{20}_D 1.4238: 56% 3-chloro-1-butene, 48% 1-chloro-2-butene) was mixed with dry cuprous cyanide (110 g.) in a flask equipped with a mechanical stirrer and an efficient reflux condenser protected by a calcium chloride tube. The mixture was heated on the water-bath with continuous stirring for one and one-half hours at 60–70°. The temperature of the bath was then increased to 95–100° for an additional half-hour in order to ensure complete reaction of the halide. The stirrer having been removed, the water-bath was replaced by an oil-bath, and at a bath temperature of 150–160° the volatile products were distilled under diminished pressure (200–100 mm.) into a trap immersed in an ice-salt bath. The crude product (70 g.) was dried over phosphorus pentoxide.

Fractionation of the product so obtained (200 g.) through a one meter column packed with glass helices, gave pure 3-pentenonitrile (133 g.); b. p. 146° (cor.); n^{20}_D 1.4228; d^{20}_4 0.8369[9]; M_D, calcd. 24.59, obs. 24.60, together with a low-boiling material, b. p. 120–143°. Systematic refractionation of this material gave pure 2-methyl-3-butenonitrile (22 g.); b. p. 126° (cor.); n^{20}_D 1.4063; d^{20}_4 0.8131; M_D, calcd. 24.59, obs. 24.57.

Anal. Calcd. for C_5H_7N: N, 17.26. Found: 3-pentenonitrile, N, 17.2, 2-methyl-3-butenonitrile, N, 17.5.

The identity of the low-boiling nitrile was further confirmed by preparation of an identical substance from 2-methyl-3-butenoamide[6] by dehydration with phosphorus pentoxide according to the technique of v. Auwers[9] for the preparation of 3-pentenonitrile from 3-pentenoamide. The nitrile so prepared boiled at 126° cor. and had n^{20}_D 1.4065; d^{20}_4 0.8131.

The refractive index of a mixture of the two nitriles was found to vary linearly with the composition. Mixtures of the two isomers could therefore be conveniently determined by measurement of this property.

TABLE I

REFRACTIVE INDICES OF MIXTURES OF 3-PENTENONITRILE AND 2-METHYL-3-BUTENONITRILE

Mixture	1	2	3
3-Pentenonitrile, %	30.0	50.0	74.0
2-Methyl-3-butenonitrile, %	70.0	50.0	26.0
n^{20}_D (calcd.)	1.4113	1.4146	1.4185
n^{20}_D (obs.)	1.4113	1.4146	1.4184

Action of Cuprous Cyanide on Different Butenyl Halides.—The procedure described above was repeated using (1) a mixture of butenyl chlorides (1 mole; n^{20}_D 1.4170) containing 90% 3-chloro-1-butene, 10% 1-chloro-2-butene; (2) pure 1-chloro-2-butene (1 mole, n^{20}_D 1.4350); (3) a mixture of butenyl bromides ($^2/_3$ mole, n^{20}_D 1.4781) containing 80% 1-bromo-2-butene, 20% 3-bromo-1-butene. These gave the following mixtures of nitriles: (1) 60 g., n^{20}_D 1.4215; (2) 58 g., n^{20}_D 1.4214; (3) 47 g., n^{20}_D 1.4212. The composition of the product in each instance was estimated first from the refractive index of the crude

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[5] Falaise and Frognier, *Bull. soc. chim. belg.*, **42**, 427 (1933).

[6] Lane, Roberts and Young, THIS JOURNAL, **66**, **543** (1944).

[7] Claisen and Tietze, *Ber.*, **59**, 2344 (1926).

[8] Marvel and McElvain, "Org. Syn.," Coll. Vol. I, 163 (1932).

[9] V. Auwers, *et al.*, *Ann.*, **432**, 70 (1923), report $n^{20}_{H_\alpha}$ 1.4230; d^{20}_4 0.841, for this nitrile.

mixture (method A) and then from the refractive indices and weights of the fractions obtained when the crude mixture was submitted to fractionation (method B). Thus, for mixture (1) the composition estimated by method A was 92.1% 3-pentenonitrile, 7.9% 2-methyl-3-butenonitrile, while fractionation gave the following results:

Fraction	Wt., g.	B. p. (755 mm.), °C.	n^{20}_D	3-Pentenonitrile (g.)	2-Methyl-3-butenonitrile (g.)
(a)[10]	10.7	119–140	1.4154	5.91	4.79
(b)	1.8	140–141.5	1.4220	1.71	0.09
(c)	45.8	141.5	1.4228	45.8	.00
Total				53.4	4.88

from which the estimated percentage composition (method B) was 91.7% 3-pentenonitrile, 8.3% 2-methyl-3-butenonitrile. The residue (2 g.) was a viscous tarry material. The compositions of the three mixtures as estimated by both methods are given in Table II. Regardless of the butenyl halide used, the reaction leads to a mixture of nitriles having the composition 91.5 ± 0.5% 3-pentenonitrile, 8.5 ± 0.5% 2-methyl-3-butenonitrile.

TABLE II

COMPOSITION OF THE NITRILE MIXTURE PRODUCED BY THE ACTION OF CUPROUS CYANIDE ON BUTENYL HALIDES

		Composition, %			
		3-Pentenonitrile		2-Methyl-3-butenonitrile	
Mixture	n^{20}_D (crude)	A	B	A	B
(1)	1.4215	92.1	91.7	7.9	8.3
(2)	1.4214	91.5	91.2	8.5	8.8
(3)	1.4212	90.3	91.6	9.7	8.4
Av.	1.4214	91.3±0.6	91.5±0.2	8.7±0.6	8.5±0.2

Action of Cuprous Cyanide on the Isomeric Nitriles.—To 8 g. of a mixture of 3-pentenonitrile (44.3%) and 2-methylbutenonitrile (55.7%), n^{20}_D 1.4136, was added an equal weight of cuprous cyanide. The mixture was heated for three hours with frequent agitation on the boiling water-bath. At the end of this time the water-bath was replaced by an oil-bath, and at a temperature of 140–150° the nitriles were distilled completely into a trap cooled by an alcohol–dry-ice mixture. The last traces of volatile material were removed from the cuprous cyanide at a pressure of 20 mm. The refractive index of the nitrile mixture so obtained was n^{20}_D 1.4137, corresponding, within the experimental error of the measurement, to the same composition as that of the starting material. It may therefore be concluded that under conditions such as those employed in their synthesis and purification these nitriles are quite stable and show no tendency toward interconversion.

Action of Cuprous Chloride on the Butenyl Chlorides.—The butenyl chloride (30 g.) was stirred mechanically under reflux at 60° with an equal weight of cuprous chloride. Five-ml. samples were removed at intervals and transferred to a small distilling flask. The chloride was then distilled completely from the copper salt at a temperature of 30–35° and a pressure of 15 mm. into a trap cooled in an alcohol–dry-ice mixture. The composition of the purified sample was determined by measurement of the refractive index. The results are summarized in Table III. It is evident that an equilibrium mixture of the two chlorides having the composition crotyl chloride 74.0 ± 0.5%, methylvinylcarbinyl chloride 26.0 ± 0.5% is rapidly produced over cuprous chloride at this temperature.

TABLE III

ISOMERIZATION OF BUTENYL CHLORIDES OVER CUPROUS CHLORIDE AT 60°

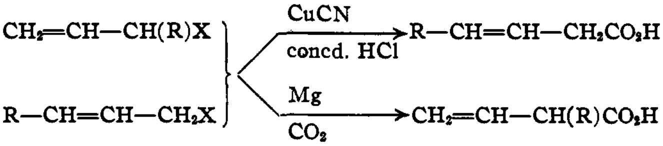
			Composition, %	
Expt.	Time, hr.	n^{20}_D of butenyl chloride mixture	Crotyl chloride	Methylvinylcarbinyl chloride
	0	1.4168	9.0	91.0
I	1.5	1.4298	74.0	26.0
	3.0	1.4299	74.5	25.5
	0	1.4331	90.5	9.5
II	1.0	1.4301	75.5	24.5
	2.0	1.4299	74.5	25.5
	3.0	1.4297	73.5	26.5

Preparation of 3-Pentenoic Acid from 3-Pentenonitrile.—3-Pentenonitrile (81 g.) was treated with concentrated hydrochloric acid (100 ml.) in the manner described by Falaise and Frognier[6] for the conversion of 3-butenonitrile to 3-butenoic acid. After twenty-five minutes the reaction mixture was diluted with water, saturated with salt and extracted four times with ether. The acid was obtained from the ethereal extract by alkaline extraction as previously described[6] for the isolation and purification of 2-methyl-3-butenoic acid. It distilled completely at 93° (14 mm.): m. p. −0.5°; n^{20}_D 1.4362; d^{20}_4 0.9876; M_D calcd. 26.36, obs., 26.50; eq. wt., calcd. 100.1, obs., 101. The melting point of the product was not depressed by admixture with 3-pentenoic acid prepared by the method of Linstead, Noble and Boorman.[11] When the acid was treated with bromine in carbon disulfide solution, the crystalline dibromide,[12] m. p. 64°, was obtained. The yield of pure acid was 70 g., 70% of the theoretical amount. This yield may be somewhat bettered when large quantities of the acid are to be prepared, since unreacted 3-pentenonitrile may then be profitably recovered from the neutral ethereal extracts of several runs and subjected again to hydrolysis in the manner described.

Attempted Hydrolysis of 2-Methyl-3-butenonitrile.—The experiment described above was repeated using 2-methyl-3-butenonitrile (10 g.) and 15 cc. of concentrated hydrochloric acid. On treatment of the reaction mixture by the purification methods described almost all of the nitrile was recovered in the neutral fraction (9 g.). The sodium carbonate extract was acidified and extracted with ether as before, but no appreciable amount of product was obtained on evaporation of this ethereal extract. When the nitrile (4 g.) was refluxed for one-half hour with concentrated hydrochloric acid, extensive charring took place. On working up the reaction mixture a neutral fraction of 3 g. was obtained. Less than 0.1 g. of acidic material was obtained by ether extraction of the acidified carbonate extract.

Summary

Cuprous cyanide acts on crotyl and methylvinylcarbinyl halides to produce a mixture of isomeric nitriles containing 91.5 ± 0.5% 3-pentenonitrile and 8.5 ± 0.5% 2-methyl-3-butenonitrile. It is suggested that this reaction belongs to that type of allylic replacement reaction which proceeds through a mesomeric carbonium ion.



$$\left.\begin{array}{l} CH_2{=}CH{-}CH(R)X \\ R{-}CH{=}CH{-}CH_2X \end{array}\right\} \begin{array}{l} \xrightarrow[\text{concd. HCl}]{\text{CuCN}} R{-}CH{=}CH{-}CH_2CO_2H \\ \xrightarrow[CO_2]{Mg} CH_2{=}CH{-}CH(R)CO_2H \end{array}$$

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[10] Direct estimation of halogen by a slightly modified Volhard procedure, standardized against the pure butenyl halides, indicated that this fraction and the corresponding first fractions for mixtures (2) and (3) contained in each instance less than 0.2% unreacted butenyl halide.

(11) Linstead, Noble and Boorman, *J. Chem. Soc.*, 557 (1933).

(12) Thiele and Jehn, *Ber.*, **35**, 2320 (1902); Goldberg and Linstead, *J. Chem. Soc.*, 2243 (1928).

It has been further shown that of the two isomeric nitriles produced by this reaction only 3-pentenonitrile is susceptible to acid hydrolysis.

These results and those of a previous study[6] on the carbonation of butenylmagnesium bromide indicate that either an α or γ-substituted butenoic acid may be prepared from either of a given pair of α- and γ-substituted allyl halides by an appropriate choice of method, as shown.

PRINCETON, NEW JERSEY RECEIVED OCTOBER 30, 1943

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NORTH CAROLINA]

Fish Poisons from *Ichthyomethia Piscipula*. I

BY ALFRED RUSSELL AND E. A. KACZKA[1]

Since the occurrence of toxic principles in various species in many genera of the family *Fabaceae* is well established and covered in several review articles,[2] it is unnecessary to give here a general survey of the field.

In connection with another study[3] there was collected on Key Largo, Florida, several hundred pounds of the roots, and wood, including bark, of the Jamaica dogwood. The powdered bark of the roots has been used extensively throughout tropical and subtropical America to narcotize fish but no exact information is available as to the nature of the toxic materials present.

The Jamaica dogwood has now been identified as *Ichthyomethia piscipula* (L) A. Hitchc. and it appears to be the same species as *Piscidia erythrina* L. Although six species in genus *Ichthyomethia* are stated[4] to occur in tropical and subtropical America, *I. piscipula* is the only member native to the United States.

E. Hart[5] separated, from a commercial liquid extract of *Piscidia erythrina*, a substance of m. p. 192° which he claimed was the toxic principle and named it piscidia. Freer and Clover[6] denied this, stating that Hart's product was not toxic and was not a chemical individual but a mixture of two distinct compounds, one melting at 201° and the other at 216°. They obtained a number of products from *Piscidia erythrina* "bark" by extraction with water and with petroleum ether. None of these was positively identified and apparently no toxicity tests were made since none was claimed to be toxic.

A drug known as "Cortex Piscidiae erythrinae," claimed to be an extract of the bark of *Piscidia erythrina*, was examined by Dankwortt and Schütte.[7] Ten assorted products were isolated by these workers and they came to the conclusion that the toxic principle was an amorphous saponin. Finally, Hauschild[8] made an examination of the bark of *Piscidia erythrina* and concluded that the toxic substance was a crystalline material m. p. 72° and not the saponin of Dankwortt and Schütte.

Obviously there is no way of correlating this earlier work since it appears that four different initial materials were used—root bark, tree bark, a commercial liquid extract and "Cortex Piscidiae erythrinae."

The physiological properties associated with *Piscidia erythrina* may be summarized: Ott[9] states that it is a direct sedative, producing narcotic effects that are refreshing and not followed, like those produced by opium, by hyperaemia of the brain, nausea and general nervous disturbance. It is claimed, also by Ott,[10] to be of value in treatment of bronchitis, asthma, nervous cough, writer's cramp, muscular spasms, chorea, tetanus and toothache. According to Reko[11] some quantity of *Piscidia erythrina* is included in "Sinicuichi"—a Mexican drink which causes rapid stupefaction. Drake and Spies[12] and Hauschild[8] report that an extract of the bark is toxic to goldfish.

In the present work, a few preliminary tests showed that the powdered root bark and root wood were very toxic to goldfish, two grams of either sprinkled into four liters of water producing death in a few minutes. Neither the powdered wood nor the powdered bark of the tree were noticeably toxic. Accordingly the work has been confined to a study of the extractives of the root bark and root wood.

Extraction of the ground bark with cold water followed by evaporation at low temperatures gave a large quantity (30% of the weight of the bark) of a dark colored resinous vitreous material. This extract was toxic to goldfish, the extracted bark was not. No satisfactory analytical separation of the components of aqueous extract could be achieved and the procedure was abandoned. Extractions with methanol, acetone and ethyl

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(1) From a dissertation submitted to the Faculty of the University of North Carolina in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1943.

(2) H. King, *Ann. Rep.*, **29**, 186 (1932); LaForge, Haller and Smith, *Chem. Rev.*, **12**, 182 (1933), etc.

(3) Russell, *et al.*, "Natural Tanning Materials of the Southeastern United States," *J. Am. Leather Chem. Assoc.*, part I, XXXVI, 340 (1942); part II, XXXVIII, 30 (1943); part III, XXXVIII, 144 (1943); part IV, XXXVIII, 235 (1943); part V, XXXVIII, 355 (1943).

(4) Small, "Manual of the Southeastern Flora," New York, N. Y., 1933.

(5) E. Hart, *Am. Chem. J.*, **5**, 39 (1883).

(6) Freer and Clover, *ibid.*, **25**, 405 (1901).

(7) Dankwortt and Schütte, *Arch. Pharm.*, **272**, 701 (1934).

(8) Hauschild, *ibid.*, **274**, 388 (1936).

(9) Ott, *Detroit Lancet*, June, 1880.

(10) Ott, *Archives of Medicine*, February, 1881.

(11) Reko, *Pharm. Monatsh.*, **16**, 155 (1937).

(12) Drake and Spies, *J. Econ. Entomol.*, **25**, 129 (1932).