25% sodium hydroxide solution. Ten grams of nicotine base was dissolved in the hypochlorite solution followed by 0.25 g. of nickel sulfate in a little water. The mixture was heated to 50° and held at 50–55° until the available chlorine was practically exhausted (about three hours). The catalyst was filtered off, the solution was acidulated with sulfuric acid and heated to boiling to expel the carbon dioxide, then neutralized. An excess of copper sulfate solution was added and the copper nicotinate was filtered off. The nicotinic acid was isolated from the copper salt by the usual methods; yield, 4.54 g. (60%). After one recrystallization from water, about 90% pure acid was obtained; m. p. 235–236°.

Anal. Calcd. for $C_6H_5O_2N$: C, 58.54; H, 4.09; N, 11.38. Found: C, 58.81; H, 4.43; N, 11.32. No chlorine could be detected.

(*b*) *4-Amino-5-(3-pyridyl)-pyrazole.*—Ten grams of 4-amino-5-(3-pyridyl)-pyrazole dihydrochloride was dissolved in 125 cc. of 10% sodium hydroxide. A solution of 17.5 g. of sodium hydroxide and 13.5 g. of chlorine in 250 cc. of water was added, then 0.1 g. of nickel chloride as catalyst. The experiment was carried out as under (a). The yield of crude nicotinic acid was 2.9 g. (55%). This acid was of a poor quality yielding only about 65% pure acid on recrystallization from water.

Acknowledgment.—I am indebted to Dr. Max Tishler for valuable suggestions and interest, and to Messrs. J. P. Messerly, D. A. Lyttle and J. B. Ziegler for technical assistance.

Summary

Hypochlorites have been found to be efficient and economical oxidizing agents in the oxidation of aromatic sulfides to sulfones, nicotine and nicotine-like compounds to nicotinic acid, and diacetone sorbose to diacetone-2-keto-levo-gulonic acid in the Vitamin C synthesis.

RAHWAY, NEW JERSEY RECEIVED MARCH 17, 1945

NOTES

The Antibacterial Principle of *Allium sativum*. III. Its Precursor and "Essential Oil of Garlic"[1]

BY CHESTER J. CAVALLITO, JOHN HAYS BAILEY AND JOHANNES S. BUCK

In prior communications[1] a new type of antibacterial principle in garlic has been described and a tentative structure assigned. This substance (I) is relatively stable in aqueous solutions of 0.2% and less and is very unstable in the pure state. Nevertheless, it is present in whole garlic to the extent of 0.3–0.4% and appears to be stable therein over long periods of time. We have carried out the following experiments to arrive at an explanation of this behavior.

Whole garlic cloves and powdered Dry Ice were ground thoroughly under acetone in a mortar. The solid was filtered off, washed several times with acetone and dried at 70°. The acetone extracts upon evaporation yielded only minute quantities of residue and no sulfides, indicating the absence of free sulfides in the plant. The white garlic powder obtained constituted 30% of the weight of the whole garlic and contained all of the potential active principle. The powder had practically no odor, but upon addition of small quantities of water, the typical odor was detected and the antibacterial principle could be extracted and isolated. This demonstrates that neither I nor the allyl sulfides found in "Essential Oil of Garlic" are present as such in whole garlic.

Dry garlic powder, prepared as described, lost no potential activity when heated for three days at 85°. Heating to reflux in absolute ethanol, acetone or chloroform for one hour produced no inactivation. When the powder was heated to reflux for thirty minutes with a small volume of 95% ethanol, no activity could be demonstrated by addition of water to the insoluble residue or to the small amount of material extracted by the alcohol. When, however, a small quantity (1 mg. per cc.) of fresh garlic powder was added to the alcohol-insoluble fraction in water (20 mg. per cc.), the activity of the treated sample was shown to be equal to that of the original untreated powder (32 mm. diameter zone of inhibition *vs. S. aureus* by the Oxford cup method). The 95% ethanol treatment had inactivated the enzyme required for cleavage of the precursor and addition of a small quantity of fresh enzyme brought about the usual cleavage. The enzymatically catalyzed cleavage of the precursor proceeded at *p*H values of between 3 and 9. This shows that whole garlic contains the active principle in the form of a thermostable precursor (II) which is very rapidly broken down to yield I when the garlic cells are crushed. This conversion takes place only in the presence of an enzyme III and water. The precursor and enzyme are apparently present in different cells of the plant.

It has been possible to obtain crude preparations of II and III from garlic in such a manner as to prevent the formation of I. The absence of free I or of the allyl sulfides in such material indicates that the sequence of events in the usual preparation of "Essential Oil of Garlic" is: Precursor II + Enzyme III $\xrightarrow{H_2O}$ C_3H_5—SO—S—C_3H_5, which upon steam distillation yields C_3H_5—S—S—C_3H_5 and small quantities of other sulfides.

The closely related *Allium cipa* or onion does not contain I or II, but some varieties do contain an enzyme similar in action to III and will yield I from garlic precursor II. The red onion is more effective than the yellow in this respect, whereas the white varieties tested do not contain III.

It is of interest to note that garlic preparations in which the enzyme III has been destroyed do not possess the characteristic odor or flavor of garlic.

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(1) This is a continuation of previously published articles entitled "Allicin, the Antibacterial Principle of *Allium sativum*. I. Isolation, Physical Properties and Antibacterial Action" (THIS JOURNAL, **66**, 1950 (1944)) and "II. Determination of the Chemical Structure" (*ibid.*, **66**, 1952 (1944)). The name "allicin" has now been dropped in view of its possible confusion with certain well-established medicinal products.

The properties of the precursor II are being further investigated.

THE RESEARCH LABORATORIES
WINTHROP CHEMICAL COMPANY, INC.
RENSSELAER, NEW YORK RECEIVED FEBRUARY 28, 1945

Unsaturated Fatty Acid Benzylidene Glycerols[1]

BY B. F. DAUBERT

In our studies on the properties of synthetic glycerides, particularly those containing unsaturated fatty acids, it became necessary to prepare the oleyl and elaidyl esters of 1,3-benzylidene glycerol. Since the compounds are new and are not directly related to our present investigations, it was considered desirable to report their analytical constants at this time.

Experimental

1,3-Benzylidene Glycerol.—This acetal was prepared according to the method of Hibbert and Carter,[2] but with the changes suggested by Stimmel and King.[3] The acetal was also prepared from U. S. P. benzaldehyde and U. S. P. glycerol directly, to determine whether it was necessary to dry the reagents in advance. It was found that the condensation reaction required only an additional five minutes beyond the time necessary with dry reagents, and the yields were of the same magnitude as those obtained by Stimmel and King (m. p. 84.0°).

Acid Chlorides.—Oleyl and elaidyl chlorides were prepared from the corresponding highly purified fatty acids and oxalyl chloride by the method described previously.[4]

2-Elaidyl-1,3-benzylidene Glycerol.—Esterification of the 1,3-benzylidene glycerol with acid chloride was carried out essentially by the method of Bergmann and Carter.[5] The method is given in detail for 2-elaidyl-1,3-benzylidene glycerol.

1,3-Benzylidene glycerol (5 g.) was dissolved in 20 ml. of dry pyridine and the solution cooled to 5° in an ice-bath. Elaidyl chloride (8.4 g.) was added dropwise to the pyridine solution of the acetal, the temperature being maintained at 5° until the complete addition of the acid chloride. The mixture was allowed to stand at room temperature for twenty-four hours. After the addition of 200 ml. of ice water, the esterified acetal separated first as an oily liquid which later solidified on repeated washing with ice water. The solidified product was suction filtered and washed with ice water until the odor of pyridine was no longer perceptible. The product, after drying in a vacuum desiccator for several days, was dissolved in petroleum ether (b. p. 35–60°) and the resulting solution cooled to 5° for twenty-four hours. The crystalline mass was suction filtered and then recrystallized several times from a 1:1 mixture of petroleum ether and ethyl alcohol and finally from ethyl alcohol. The colorless, prismatic crystals melted at 43.5–44.0°; yield, 10 g. (82%); iodine value (Wijs), 56.6 (calcd. 57.1); mol. wt., 441 (calcd. 444).

Anal. Calcd. for $C_{28}H_{44}O_4$: C, 75.63; H, 9.97. Found: C, 75.58, 75.61; H, 9.88, 9.92.

Constants for the 2-oleyl-1,3-benzylidene glycerol prepared in an analogous manner are as follows: m. p., 4.0–5.0°; iodine value (Wijs), 56.7 (calcd. 57.1); mol. wt., 440 (calcd. 444).

Anal. Calcd. for $C_{28}H_{44}O_4$: C, 75.63; H, 9.97. Found: C, 75.55, 75.51; H, 9.85, 9.87.

Hydrogenation of the Esterified Acetals.—Reduction with hydrogen of both 2-elaidyl- and 2-oleyl-1,3-benzylidene glycerol in ethyl alcohol solution with palladium black as the catalyst[5] resulted in the isolation of 2-monostearin (m. p. 74.5°). Mixed melting points of the 2-monoesters obtained by the separate reduction of the two esterified acetals showed no melting point depression.

Although other conditions of hydrogenation with many different catalysts have been used, the fully saturated 2-monoester was always obtained. It is planned to study further the conditions of hydrogenation and hydrogenolysis which will lead to the removal of the benzylidene group without at the same time affecting the double bond of the unsaturated fatty acid.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF PITTSBURGH
PITTSBURGH, PENNSYLVANIA RECEIVED MARCH 12, 1945

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[1] The generous aid of the Buhl Foundation is gratefully acknowledged.

[2] Hibbert and Carter, THIS JOURNAL, **51**, 1601 (1929).

[3] Stimmel and King, *ibid.*, **56**, 1724 (1934).

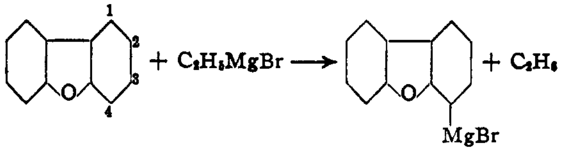
[4] Wood, Jackson, Baldwin and Longenecker, *ibid.*, **66**, 287–289 (1944).

[5] Bergmann and Carter, *Z. physiol. Chem.*, **191**, 211 (1930).

Interconversion Reactions with Some Aluminum Compounds[1]

BY HENRY GILMAN AND A. H. HAUBEIN

Dibenzofuran has been metalated in the 4-position irrespective of the metalating agent: organometallic compounds, inorganic salts or metals. The rate and extent of metalation is markedly influenced by the reactivity of the organometallic compound: that is, the more highly active organoalkali compounds effect metalation most rapidly and can give di-metalation.[2] Organoaluminum compounds are relatively low in reactivity, and we have observed that triethylaluminum does not metalate dibenzofuran. However, the moderately reactive Grignard reagent does effect metalation in the 4-position.



The metalation of an aromatic ether under forced conditions by means of Grignard reagents was to have been expected in view of earlier studies by Challenger and Miller[3] with anisole and phenetole.

Inasmuch as "mixed" organoaluminum compounds appear to be more reactive in some reactions than the simple compounds which contain no halogen, dibenzofuran was treated under forced conditions with ethylaluminum iodides [$(C_2H_5)_2AlI + C_2H_5AlI_2$]. Metalation did occur, but the product isolated subsequent to carbonation and hydrolysis was 2-dibenzofurancarboxylic acid. This anomalous behavior suggested that one of the active agents might have been aluminum iodide, present in the mixture

$$(C_2H_5)_2AlI + C_2H_5AlI_2 \rightleftarrows (C_2H_5)_3Al + AlI_3$$

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[1] Paper LXI in the series: "The relative reactivities of organometallic compounds"; the preceding paper with Brown is in THIS JOURNAL, **67**, 824 (1945).

[2] Gilman and Young, *ibid.*, **57**, 1121 (1935), and *J. Org. Chem.*, **1**, 315 (1936). See, also, pp. 533–538 of Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943.

[3] Challenger and Miller, *J. Chem. Soc.*, 894 (1938).