The authors are indebted to Dr. C. R. Noller, of Stanford University, who kindly furnished us with samples of decyl, undecyl and lauryl mercaptans for this work.

Summary

1. 2,4-Dinitrochlorobenzene, a reagent previously proposed by the authors, has now been studied more extensively and found to be valuable for both mono- and di-mercaptans.

2. Melting point and analyses are presented for eighteen 2,4-dinitrophenyl alkyl and aryl thio-ethers. In addition, data are presented for nine of the corresponding sulfones.

CHAPEL HILL, N. C. RECEIVED AUGUST 7, 1933
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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Mechanism of Carbohydrate Oxidation. XVI.[1] The Action of Aqueous Solutions of Potassium Hydroxide on *l*-Rhamnose

BY GALE FRANCIS NADEAU, MILDRED RATLIFF NEWLIN AND WM. LLOYD EVANS

Since *l*-rhamnose differs from *l*-mannose by having a methyl group in place of the primary alcohol group of the hexose sugar, it follows that the behavior of rhamnose toward aqueous solutions of potassium hydroxide must have certain restrictions placed upon it when this sugar is considered as a possible source of lactic acid through its reaction with the base. Among these limitations is the structural inability of the rhamnose molecule to form two molecules of glyceric aldehyde which in turn are partially converted into pyruvic aldehyde, the precursor of lactic acid. To determine the general extent to which the presence of the methyl group prevents *l*-rhamnose from acting like the hexose sugars in this respect was the first objective in this work.

It has been shown previously in this series of studies that the temperature employed and the concentration of the alkali used exercise marked effects in the yields of lactic acid obtained from certain sugars when they are subjected to the action of potassium hydroxide solutions, during forty-eight hours, a period of time which seemed sufficient to indicate the general tendency of the various sugars studied under these conditions.[2] To ascertain if this was equally true for *l*-rhamnose was the second objective in this work.

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(1) Contribution XV of this Series, THIS JOURNAL, **54**, 698 (1932).

(2) Evans and co-workers, (a) THIS JOURNAL, **48**, 2665 (1926); (b) **48**, 2703 (1926); (c) **50**, 486 (1928); (d) **50**, 1496 (1928); (e) **50**, 2543 (1928); (f) **52**, 294 (1930); (g) **52**, 3680 (1930); (h) **53**, 4384 (1931).

Experimental Part

(a) **Reagents.**—All the reagents used in these experiments were examined for their purity by the usual well-known laboratory procedures.

(b) **Rhamnose.**—Most of the rhamnose was prepared from lemon flavine by Walton's[3] method. The purity of the product (m. p. 92°, $[\alpha]_D^{20}$ 8.9°) was determined by the procedures of Pfanstiehl and Black.[4] Chlorides, alkaline earths and heavy metals were absent.

(c) **Apparatus and Analytical Procedures.**—The general and analytical procedures used throughout this work were essentially the same as those described in previous reports,[2b] except for the modification adopted in the method for the determination of lactic acid.

An amount of *l*-rhamnose equal to 2.2763 g. was weighed into a 150-cc. carbon dioxide flask. Twenty-five cc. of standard potassium hydroxide was added, the flask stoppered immediately, and placed in a thermostat at the desired temperature for forty-eight hours. The flasks were then removed, packed in ice, and 25 cc. of standard phosphoric acid added dropwise to the reaction mixture. Standard phosphoric acid solutions were prepared of the same molar strength as each of the potassium hydroxide solutions. The titer value of the acid solution against the corresponding alkali solution was determined by titrating 25 cc. of the alkali solution with the phosphoric acid, using methyl orange as indicator. The end-point appears when the primary potassium salt is formed. The color was compared with the color of an aqueous solution of primary potassium phosphate and methyl orange. There was considerable difficulty in observing the end-point when the solutions were stronger than two normal, due to the buffer action of the phosphates formed. In these cases the acid and alkali solutions were diluted, and the diluted solutions were titrated against each other. This procedure introduced no error and made the titration more accurate. The solution was transferred to a 500-cc. round-bottomed flask and the volatile products distilled off under reduced pressure at a temperature not exceeding 50°.

For the determination of lactic acid 60 cc. of water was added to the dry residue and the solution digested with norite for half an hour on a boiling water-bath. The material was then filtered, the residue washed with hot water and the filtrate evaporated sufficiently to be placed in a Soxhlet extractor. In a Sy flask was placed 75 cc. of water and an excess of zinc carbonate. The acid solution was extracted for forty-eight hours with U. S. P. ether. The Norite treatment removes a great deal of the tarry material which is otherwise extracted along with the ether-soluble acids and carried into the lower flask. The removal of the tar is not complete and the water solutions in the Sy flasks vary in color from a very pale straw color in the lower temperature runs to a dark amber in the runs at seventy-five degrees.

At the completion of the extraction the ether remaining in the Sy flask was evaporated. Norite was added to the material in the flask and the mixture boiled for several minutes to complete the reaction between the lactic acid and zinc carbonate. The solution was filtered from excess zinc carbonate and Norite, the residue washed with hot water and the filtrate evaporated to small volume on a water-bath. The second treatment with Norite serves further to decolorize the solutions, and although the runs with more dilute alkali at both 50 and 75° still retain some tar, it is not sufficient to interfere with the crystallization of the zinc lactate, and it is possible to wash the salt practically free from impurities.

When the zinc lactate had crystallized from the concentrated solutions, the material was cooled in ice and salt, then filtered into a weighed, porous-bottomed Gooch

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(3) Walton, THIS JOURNAL, **43**, 127 (1921).

(4) Pfanstiehl and Black, *Ind. Eng. Chem.*, **13**, 685 (1921).

crucible, washed with a little ice-water, then cold 95% alcohol, and finally ether, and air-dried. We found that zinc lactate tends to dehydrate by overnight drying *in vacuo* at 60–65°. The purity of the zinc lactate was determined in the usual way by roasting a sample to zinc oxide. The percentage carbon return as lactic acid with six different normalities of potassium hydroxide at 25, 50 and 75° are shown in Fig. 1.

As it appeared possible that either lactic acid or zinc lactate might be adsorbed by the Norite with a consequent lowering of the results, a run was made with glucose and 3 *N* alkali at 50°. Under these conditions Evans and O'Donnell[2e] report a carbon return as lactic acid equal to 45.1%. Using Norite as described above the yield of zinc lactate indicated a carbon return of 45.6%.

Before Norite was used the solutions of zinc lactate after extraction were always colored dark brown by the tar present. An attempt was made to get rid of this tar by placing these solutions in turn in the extractor and extracting again with ether. This removed part of the color, but apparently the tars are less soluble in ether after the reaction with zinc carbonate. The extract so obtained was dissolved in water. This solution gave no precipitate of zinc sulfide when treated with hydrogen sulfide in the presence of ammonia, indicating that none of the zinc salts had been extracted. This aqueous solution was acid to litmus and reduced Fehling's solution.

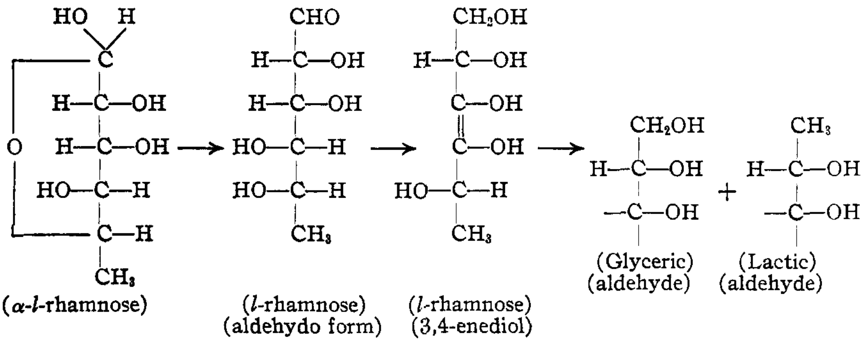
Some of the Norite was roasted to an ash which was taken up in dilute hydrochloric acid and tested for the presence of metallic ions. Analysis showed that the ash contained small amounts of iron, aluminum and zinc.

The phosphate solutions remaining after the ether extraction were tested, by the use of Fehling's solution, for the presence of reducing substances. In every case there was evidence of reduction, varying from copious precipitates of cuprous oxide from the twenty-five degree runs to a bare trace with the 7 *N* potassium hydroxide at 75°. No experiments were made to determine to what extent this reduction was due to unchanged sugar. Rhamnose is undoubtedly present especially at the lower alkalinities, because it has been previously shown that some of the sugar conversions caused by alkali go on for a long period of time.

Discussion and Summary

If aqueous solutions of potassium hydroxide react toward rhamnose in the same general manner as previously observed in the case of certain disaccharides,[2f,h] hexoses,[2d,e] pentoses[2g] and trioses[2b,c] then the data obtained from the interaction of the alkaline solutions of the methylpentose should be in accord with the enediol theory of carbohydrate chemical behavior. In these experiments various reaction mixtures were examined for their content of lactic acid while others were studied for their production of pyruvic aldehyde. The data with reference to these products are discussed in the following paragraphs.

***l*-Rhamose-3,4-enediol: (a) Lactic Acid.**—If rhamnose forms a 3,4-enediol in alkaline solutions of appropriate normality, then it is theoretically conceivable that this compound could undergo fission at the double bond and thus give rise to the formation of two different aldehydes, namely, glyceric and lactic. From this standpoint, the chief chemical interest lies in this latter possibility, because in the hexose sugar molecules such a change as that described would give rise to two molecules of one and the same aldehyde, namely, glyceric, while in rhamnose the products of such a reaction would be one molecule of glyceric aldehyde and one of lactic aldehyde. These changes in the *l*-rhamnose molecule are shown in the following reactions. It has been pointed out repeatedly that glyceric aldehyde is[2] an intermediate compound in the production of lactic acid formed through the interaction of certain sugars and alkalies. Hence, it follows that at least one-half of the *l*-rhamnose carbon should be found in these reaction mixtures as lactic acid if it were not for other changes taking place between the rhamnose molecule and its decomposition products and the aqueous solutions of the potassium hydroxide.



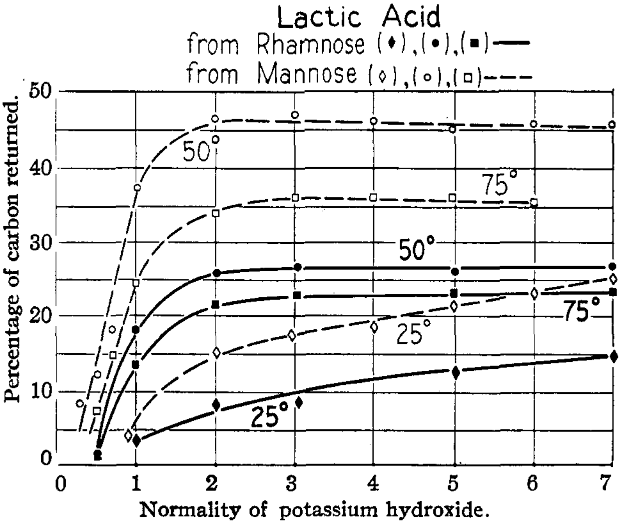


Fig. 1.

That lactic acid may actually be obtained in alkaline solutions of *l*-rhamnose is shown in Fig. 1, in which the data with reference to the experimental yields obtained at 25, 50 and 75° are conveniently recorded as functions of the *original* alkali normality, a value which will necessarily decrease due to the formation of acid in the reaction mixture. The general tendency of the yields of this acid at 75° to be lower than those at 50° is also characteristic of certain hexoses,[2e] pentoses[2g] and the trioses[2b,c] when these carbohydrates are subjected to the same experimental conditions as were employed with rhamnose. An examination of the lactic acid data shows that the production of this acid from *l*-rhamnose seems to be dependent upon the same general experimental factors, namely, temperature and alkali concentrations, as were observed in the case of other sugars previously studied. Shaffer and Friedemann[5] have shown that the concentration of the sugar itself is also an important factor governing the yields of lactic acid.

It is clear that in the presence of an appropriate oxidizing agent the two fragments resulting from the fission of the rhamnose 3,4-enediol should yield glyceric and lactic acids. In the absence of an oxidizing agent, however, lactic aldehyde would probably be incapable of existence by reason of its rearrangement into acetol. It is planned to study any possible effects of the small amount of atmospheric oxygen contained in the reaction flask in the formation of reaction products, such as formic and acetic acids. Nef[6] showed that acetol under the influence of alkalies would form resins *without the production of lactic acid.* This observation has been verified recently by Dworzak and Prodinger,[7] who found that crystalline lactic aldehyde in 4% sodium hydroxide solution gave a brown sirup. The distillate in our work gave only the faintest odor of iodoform with the usual alkaline iodine reaction.

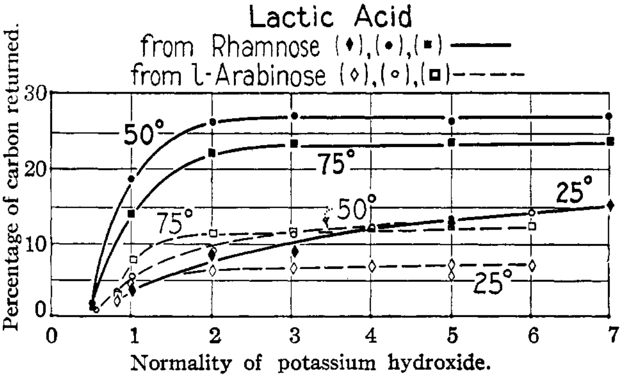


Fig. 2.

Since the arabinose molecule has the possibility of yielding but one molecule each of glyceric aldehyde and glycol aldehyde, rhamnose one each of glyceric and lactic aldehydes, and that of mannose two molecules of glyceric aldehyde, one would expect that the yields of lactic acid from rhamnose would resemble more nearly those of arabinose than those of

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[5] Shaffer and Friedemann, *J. Biol. Chem.*, **86**, 345 (1930).

[6] Nef, *Ann.*, **335**, 254 (1904).

[7] Dworzak and Prodinger, *Monatsh.*, **50**, 459–475 (1928).

mannose if all the conditions within the reacting mixtures were ideal, *i. e.*, if these various sugars reacted with the same degree of ease toward the alkali present. In Fig. 2 a comparison of the yields of this acid obtained from *l*-arabinose and *l*-rhamnose at 50° shows that relatively the rhamnose seems to react more like a hexose sugar than a pentose one. It is known that the yields of lactic acid arising from the alkaline degradation of glucose and mannose[2e] at 50° are of about the same order of magnitude, while the yields obtained from glucose, mannose and fructose[2d,e] at 75° are also approximately the same. Therefore, these data and those plotted in Figs. 1 and 2 show that the yields of lactic acid from rhamnose lie between those of the above named hexoses and arabinose[2g] at 50 and 75°. In the case of xylose[2g] the yields of lactic acid are still higher than those from arabinose. Since *l*-rhamnose, *l*-isorhamnose and the unknown *l*-2-keto-rhamnose (or in the more convenient nomenclature of Votoček[8] *l*-manno-methylose, *l*-gluco-methylose and *l*-fructo-methylose) are related to each other in the same way as glucose, mannose and fructose, and since the relation of the lactic acid curves at 50 and 75° are related to each other like those of these well-known hexose sugars, it is very probable that the 75° lactic acid curve of *l*-rhamnose is approximately that for the other two related methyl pentoses.

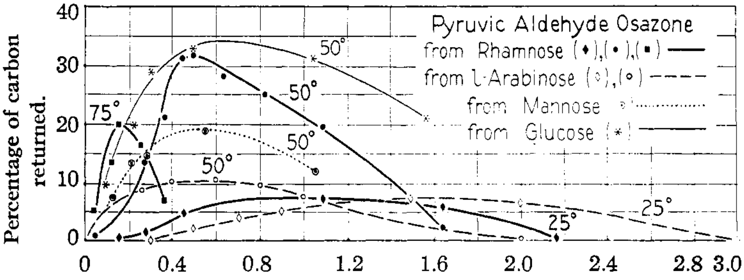

Fig. 3.

(b) **Pyruvic Aldehyde.**—If the behavior of rhamnose in alkaline solutions of appropriate normality is correctly expressed by the above equation, then it follows that there are two different possible sources for the formation of pyruvic aldehyde. (1) It is well known that glyceric aldehyde will form this compound under the experimental conditions employed. (2) Since lactic aldehyde will yield the same phenyl-osazone as pyruvic aldehyde and acetol then it is to be expected that rhamnose should more nearly resemble the hexose sugars in this respect than it does the pentose ones.

In Fig. 3 it is shown that rhamnose seems to have undergone the necessary transformations to yield pyruvic aldehyde osazone and that the yields are influenced by the temperature and the concentration of the alkali

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[8] Votoček, *Bull. soc. chim.*, [4] **43**, 1 (1928).

employed. At 75° the maximum is much lower than at 50°. This is in harmony with the relative yields of lactic acid obtained from this sugar. Furthermore, it is evident that rhamnose and glucose[2e] at 50° will yield pyruvic aldehyde osazone in amounts that are of the same general magnitude. There is no way to differentiate between glyceric and lactic aldehydes as the sources of pyruvic aldehyde osazone in the case of rhamnose. It is clear from Fig. 3 that rhamnose is more like the hexoses than it is arabinose in this respect. Evans and Conaway have shown that arabinose and xylose are likewise much the same. The interest that attaches to the comparison with mannose lies in the fact pointed out above, namely, the substitution of the primary alcohol group in mannose for the methyl group of rhamnose—the asymmetrical portion of each molecule being the same.

Concerning the mechanism suggested by Evans and Hass[2e] for the conversion of glyceric aldehyde to pyruvic aldehyde, it has been pointed out by Mr. Harry Gehman of this Laboratory that the same end could be attained through the hydrogen of the water molecule reducing the primary alcohol group and the oxygen forming an aldehyde group on the other terminal carbon atom of the postulated intermediate oxidic ring.[9]

Acknowledgment.—In conclusion the authors wish to acknowledge their great indebtedness to The Cyrus M. Warren Fund of The American Academy of Arts and Sciences for very valuable assistance rendered during the progress of these experiments.

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[9] *Cf.* Bernhauer, "Grundzüge der Chemie und Biochemie der Zuckerarten," Verlag von Julius Springer, Berlin, 1933, p. 118.

COLUMBUS, OHIO

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The Reaction of Phthaloylnaphthol with Hydroxylamine and with Diazomethane[1]

BY LOUIS F. FIESER

The exact nature of the two carbonyl groups of phthaloylnaphthol is still an open problem. The Grignard reagent appears to attack only one of the two ketonic groups,[2] and a further peculiarity is to be found in the anomalous, and still unexplained, course of the oxidation.[3] It thus seemed of interest to study the action of some other carbonyl reagent, and hydroxylamine was selected for the purpose. It was found that phthaloylnaphthol may be converted in an alkaline medium into either one or the other of two monoximes, and that a dioxime is not formed under any of the conditions investigated. The most striking observation to be recorded in this

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[1] Seventh paper. Sixth paper: THIS JOURNAL, **55**, 3342 (1933).

[2] Fieser, *ibid.*, **53**, 3546 (1931).

[3] L. F. and M. Fieser, *ibid.*, **55**, 3010 (1933).