the piperazino-1,4-bis-(alkyl succinate) is 65 to 70% of the theoretical. These derivatives are soluble in dilute hydrochloric acid and are reprecipitated unchanged by the addition of alkali.

In an attempt at proof of structure, anhydrous piperazine and methyl bromosuccinate, prepared by the method of Volhard,[4] were refluxed in dioxane. Only piperazine dihydrobromide and methyl fumarate were formed. The former was identified by conversion into 1,4-dinitrosopiperazine[3] and the latter by a mixed melting point determination with an authentic sample. Piperazino-1,4-bis-(methyl succinate) was refluxed with excess alcoholic potassium hydroxide for an hour, piperazino-1,4-bis-(potassium succinate) crystallizing out from the hot solution. This potassium salt was boiled successively with alcohol and dioxane and dried for four hours at 105°. Subsequent analyses justified the formula assigned to the salt, and hence corroborated the structure of the piperazino esters.

TABLE I

PHYSICAL CONSTANTS AND ANALYSES OF THE PIPERAZINO-1,4-BIS-(ALKYL SUCCINATES)

Ester	M. p., °C., corr.	Solvent cryst.	Nitrogen analyses, % Calcd.	Found
Methyl	158.5–159	Dioxane	7.49	7.45
Ethyl	96–96.5	Dioxane	6.51	6.53
Isopropyl	90–90.5	Heptane	5.76	5.72
n-Propyl	88	Hexane	5.76	5.65
n-Butyl	48–48.5	Hexane	5.17	5.12
Benzyl	112–113	Methanol	4.13	4.11
Cyclohexyl	121	Hexane	4.33	4.20
Potassium (salt)	K, 33.24	33.04	5.95	6.04

(4) Volhard, *Ann.*, **242**, 148 (1887).

The authors wish to express their appreciation to Dr. H. G. Shaw and Mr. G. A. Barber for considerable analytical data presented in this paper.

Summary

1. The preparation and properties of compounds arising from the addition of piperazine to the ethenoid linkage of ethylene dicarboxylic esters have been described.

2. Syntheses involving mono-substituted piperazines and other amines with these and other unsaturated esters are in progress.

3. The reaction velocities of these syntheses are being studied.

GAINESVILLE, FLORIDA RECEIVED NOVEMBER 8, 1934

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Mechanism of Carbohydrate Oxidation. XVII.[1] The Preparation and Structure of Alpha-Methyl-*l*-arabinomethyloside[2]

BY DONALD ROBERT SWAN AND WM. LLOYD EVANS

The chemistry of the methyltetroses is far from complete. Of the eight possible configurations in this series only three have been reported in the literature. Ruff[3] prepared *l*-arabinomethylose[4] by the degradation of calcium rhamnonate with hydrogen peroxide and basic ferric acetate. This sugar was also reported by Fischer[5] as a degradation product of rhamnose (*l*-mannomethylose) by the Wohl reaction. Votoček[6,7] prepared *d*-arabinomethylose from isorhodeose (*d*-glucomethylose) by the Ruff reaction mentioned above, and *d*-lyxomethylose from rhodeose (*d*-galactomethylose, *d*-fucose) by the Wohl reaction. Deulofeu[8] obtained *l*-arabinomethylose osazone from rhamnonic amide by the Weerman degradation, but reported no data with reference to the yield.

None of these sugars have ever been obtained in crystalline form nor has a glycoside of any of them been reported previously. Likewise, the ring structure, although practically certain to be of the butylene oxide type, has not been proved.

In quantitative experiments carried out by us, α-methyl-*l*-arabinomethyloside showed the rapid hydrolysis characteristic of γ-glycosides[9] (Fig. 1). This new glycoside is of interest in that it is a key compound in the scheme of ring structure proof developed by Hirst, Haworth and others,[10] because a pyranose structure is excluded. We

(1) Contribution XVI of this series, THIS JOURNAL, **55**, 4957 (1933).

(2) This paper was abstracted from the dissertation submitted in the Autumn, 1934, by D. R. Swan to the Graduate School of The Ohio State University for the Ph.D. degree. It was reported at the Cleveland Meeting of the American Chemical Society, September, 1934 (W. L. E.).

(3) O. Ruff, *Ber.*, **35**, 2362 (1902).

(4) According to the nomenclature proposed by Votoček for the methylpentoses [*Bull. soc. chim.*, [4] **43**, 18 (1928)] and extended by Micheel to the methyltetroses [*Ber.*, **63**, 347 (1930)], the methyltetrose having the *l*-arabinose configuration is named *l*-arabinomethylose. On this basis we have named the glycoside α-methyl-*l*-arabinomethyloside.

(5) Emil Fischer, *ibid.*, **29**, 1381 (1896).

(6) E. Votoček and C. Krauz, *ibid.*, **44**, 3287 (1911).

(7) E. Votoček, *ibid.*, **50**, 35 (1917).

(8) Deulofeu, *J. Chem. Soc.*, 2605 (1930).

(9) W. N. Haworth, *Ber.*, **65A**, 43 (1932).

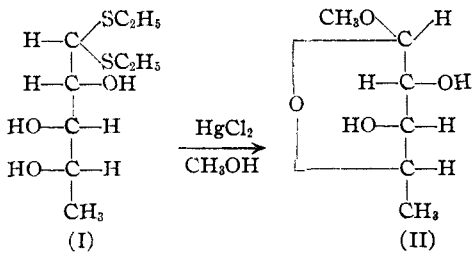
(10) W. N. Haworth, "The Constitution of Sugars," Longmans, Green and Co., New York, 1929.

have also found it useful in preparing a pure sample of the parent sugar, *l*-arabinomethylose. As shown recently by Hudson,[11] the methylglycosides serve as excellent intermediates for the preparation of pure sugars.

The new compound is of especial interest in a study of the action of alkalies and oxidizing agents on the sugars by reason of the presence of the methyl group in place of the primary alcohol one. It is obvious that the mechanism of such reactions could be traced more easily in compounds of this type.

The obscurity of the methyltetrose series has resulted in part from the methods employed in the isolation of these sugars. Previously the problem has always been attacked through hydrazone formation. The fact that the sugars exist only as sirups has been a great obstacle. The difficulty of working with them is shown by the gap existing in the literature between the trioses and the pentoses.

In the present work we have used as a crystalline derivative the ethyl mercaptal of *l*-arabinomethylose (I) prepared by Ruff.[3] This was converted to the glycoside (II) by means of mercuric chloride and methyl alcohol. The ring structure of the methylglycoside was then proved by conventional methods.[10]



(I) (II)

Experimental Part

Rhamnose.—The rhamnose used in this work was prepared from lemon flavin by the method of Walton.[12]

Calcium Rhamnonate.—The excellent electrolytic method of Isbell[13] served for the preparation of calcium rhamnonate. Rhamnose was electrolyzed in aqueous solution in the presence of calcium bromide and calcium carbonate. After filtering excess calcium carbonate the solution was evaporated to a small volume and the calcium rhamnonate precipitated with methanol. Thus prepared, the salt contains up to 20% of calcium bromide. This was usually removed with silver carbonate, although its presence appeared to have no appreciable effect on the yield obtained by the Ruff degradation.

Degradation of Calcium Rhamnonate.—In the degradation of calcium rhamnonate to *l*-arabinomethylose the Ruff reaction[3] as improved by Hockett and Hudson[14] was found to give good results.

Calcium rhamnonate (52 g. or 0.13 mole) in 600 cc. of water was treated with 73 cc. of 30% hydrogen peroxide in two portions at 40°. There was present in the solution[14] 2.58 g. of ferric acetate (0.015 mole) prepared *in situ*. When the oxidation was complete, the solution was filtered and evaporated *in vacuo* at 50° (bath temperature) to a volume of 60 cc. Methanol (400 cc.) was then added followed by 100 cc. of acetone. The salts thus precipitated were filtered with suction without using carbon. The solution was then evaporated to a thick, dark red, sweet tasting sirup. This product had the theoretical weight (34 g.), but it still contained calcium ion.

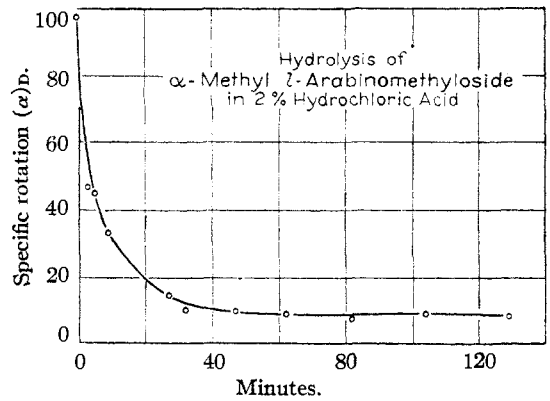


Fig. 1.

Separation of *l*-Arabinomethylose as the Mercaptal.—The sirup (34 g.) was treated with 60 cc. of concentrated hydrochloric acid and 48 g. of ethyl mercaptan (1 mole excess). After shaking for two minutes, the mixture became warm and viscous. On adding a few small pieces of ice the whole mass crystallized. The mercaptal was then filtered, washed with a little ice water and recrystallized from hot water. After one more recrystallization it melted at 109°; yield 11.8 g. of the once recrystallized mercaptal, or 18%. (Ruff obtained 6.1% as the benzylphenylhydrazone.)

Preparation of Alpha-Methyl-*l*-arabinomethyloside.—Pacsu[15] had described the preparation of α- and β-methylglucosides from glucose ethyl and benzyl mercaptals. Our procedure, which follows, is based on that of Pacsu.

l-Arabinomethylose ethyl mercaptal (13.88 g. or 0.058 mole) was dissolved in 300 cc. of boiling C. P. methanol and treated with 47 g. (1 mole excess) mercuric chloride in 100 cc. of hot methanol. A white precipitate of HgClSEt (34.6 g., calcd., 34.3 g.) separated immediately. The mixture was held at the boiling point on the water-bath for fifteen minutes, cooled and filtered with suction. Dry hydrogen sulfide was then passed in, carboraffin added and the mercuric sulfide filtered with suction. The solution was then neutralized with silver carbonate, carboraffin added and filtered with suction. On evaporating

(11) C. S. Hudson and K. L. Jackson, THIS JOURNAL, **56**, 958 (1934).

(12) C. F. Walton, *ibid.*, **43**, 129 (1921).

(13) Isbell, *Bur. Stand. J. Research*, **6**, 1145 (1931).

(14) R. C. Hockett and C. S. Hudson, THIS JOURNAL, **56**, 1632 (1934).

(15) E. Pacsu, *Ber.*, **58**, 511 (1925).

in vacuo at 35° bath temperature, there remained 7.4 g. of sulfur-free, white, crystalline substance, representing 87%. This material is evidently a mixture of alpha and beta *l*-arabinomethylosides. Once recrystallized from chloroform and petroleum ether it gave $[\alpha]_D$ −73.9° in chloroform. Since at constant rotation the product showed $[\alpha]_D$ −129.2°, the latter is the more levorotatory form, and according to the nomenclature of Hudson[16] is to be considered the alpha glycoside.

The substance dissolves readily in water (hygroscopic), methanol, ethanol, ethyl acetate, chloroform and ether. It can be recrystallized from chloroform with addition of petroleum ether or from hot carbon tetrachloride. From the latter a constant rotation is reached more quickly. $[\alpha]_D^{31°}$ −129.2° (α −18.37°; 0.925 g. in 26.02 cc. of U. S. P. $CHCl_3$, 4-dm. tube); m. p. 89–90°; b. p. 133–137° (5 mm.).

Anal. Calcd. for $C_5H_9O_3(OCH_3)$: methoxyl, 20.95. Found: 20.7.

2,3-Dimethylmethyl-*l*-arabinomethyloside.—The mixed alpha- and beta-glycosides from the Pacsu reaction (4.77 g.), after one recrystallization from chloroform and petroleum ether, were methylated with 45 g. of methyl sulfate, 52 cc. of sodium hydroxide (56%), 16 cc. of carbon tetrachloride, and 2 cc. of water according to the directions of West and Holden[17] for the methylation of glucose. On distillation there was obtained 2.5 g. of a light, mobile liquid of pungent, mint-like odor. It reduced Benedict's solution only after boiling with acid; b. p. 60–65° (6 mm.).

Anal. Calcd. for $C_5H_7O(OCH_3)_3$: methoxyl, 52.85. Found: 53.4.

2,3-Dimethyl-*l*-arabinomethylose.—2,3-Dimethylmethyl-*l*-arabinomethyloside (4 g.) was heated for two hours on the boiling water-bath with 20 cc. of sulfuric acid (2%). The solution was neutralized with barium carbonate, filtered and extracted with 100 cc. of chloroform in three portions. After drying over Drierite, the chloroform was distilled off at ordinary pressure. The remaining yellow liquid was distilled, and gave a colorless, odorless, mobile liquid which readily reduced Benedict's solution; b. p. 97–99° (6 mm.), $[\alpha]_D^{24°}$ −43.8° (α −2.00°; 0.457 g. in 10.00 cc. of U. S. P. chloroform, 1-dm. tube).

Anal. Calcd. for $C_5H_7O_2(OCH_3)_2$: methoxyl, 38.3. Found: 37.6.

Oxidation of Dimethyl-*l*-arabinomethylose.—Two grams of dimethyl-*l*-arabinomethylose was oxidized with 20 cc. of nitric acid (*d* 1.2)[18] and the resulting acid-free sirup esterified with methyl alcohol containing 3% of hydrochloric acid. The resulting dimethyl ester of dimethoxy-*l*(+)-succinic acid was not distilled. After removal of hydrochloric acid with barium carbonate, the methyl alcohol was evaporated *in vacuo*, the remaining barium chloride removed by dissolving the residue in ether and filtering, and the resulting sirup, after evaporation, dissolved in 20 cc. of methyl alcohol. This solution was then saturated with dry ammonia and allowed to stand. After thirty-six hours there had crystallized 0.7 g. of dimethoxy-*l*(+)-succinic diamide;[19] long needles, m. p. 270°, dec. 284°; $[\alpha]_D^{30°}$ +91°, *c*, 0.46, H_2O.

Summary

1. The first methyltetroside, alpha-methyl-*l*-arabinomethyloside, has been prepared, characterized and the furanoside structure proved.

2. The sugar has been removed from its reaction mixture as the ethyl mercaptal following a suggestion of Emil Fischer.[20]

3. The yield of *l*-arabinomethylose from calcium rhamnonate by hydrogen peroxide degradation has been increased from 6.1 to 18%.

(16) C. S. Hudson, THIS JOURNAL, **31**, 66 (1909).
(17) E. S. West and R. F. Holden, *ibid.*, **56**, 930 (1934).
(18) E. L. Hirst and A. K. Macbeth, *J. Chem. Soc.*, 22–26 (1926).
(19) E. L. Hirst, *ibid.*, 350 (1926).
(20) E. Fischer, *Ber.*, **27**, 673 (1894).

COLUMBUS, OHIO RECEIVED NOVEMBER 13, 1934

[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACOLOGY, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE]

The Fries Reaction with α-Naphthol Esters[1,2]

BY R. W. STOUGHTON

The Fries rearrangement of naphthyl esters offers a means of preparation of the hydroxynaphthyl ketones which can be reduced to alkylnaphthols. Lederer[3] has investigated the low temperature rearrangement of a few α-naphthyl esters in nitrobenzene solution and found that the principal product is the *p*-hydroxy ketone. As the *o*-ketones were desired, a study of the reaction to higher temperatures was made. Previously, only the acetate[4] has been studied in this manner but now the series has been extended through the valerate.

It was found that when a fatty acid ester of α-naphthol is heated with aluminum chloride under optimum conditions there is found 50–60% of the *o*- and 5–10% of the *p*-hydroxy ketone. The relative proportions of these isomers are similar to those obtained from a phenol substituted in the ortho and meta positions rather than from

(1) Presented before the Organic Division of the American Chemical Society at the Cleveland, Ohio, Meeting, September, 1934.
(2) The funds for carrying out this work were given by the International Health Division of the Rockefeller Foundation.
(3) Lederer, *J. prakt. Chem.*, **135**, 49 (1932).
(4) Fries, *Ber.*, **54**, 709 (1921).