TABLE II

NITROPHENYL[a] AND AMINOPHENYL[b] THIAZOLES

Thiazoles	M. p., °C.	Formula	Analyses for N, % Calcd.	Found
2-(*p*-Nitrophenyl)	147.5–148.5			
2-(*p*-Aminophenyl)	123–124	$C_9H_8N_2S$	15.99	16.02
2-(*p*-Nitrophenyl)-4-methyl	105.5–106.5			
2-(*p*-Aminophenyl)-4-methyl	112.5–113.5	$C_{10}H_{10}N_2S$	14.73	14.52
2-(*p*-Nitrophenyl)-4,5-dimethyl	169–169.5			
2-(*p*-Aminophenyl)-4,5-dimethyl	130.5–131.5	$C_{11}H_{12}N_2S$	13.72	13.62
2-(*p*-Nitrophenyl)-4-ethyl	79.5–80			
2-(*p*-Aminophenyl)-4-ethyl	106.5–107	$C_{11}H_{12}N_2S$	13.72	13.66
2-(*p*-Ethoxy-*m*-nitrophenyl)	107.3–108.3			
2-(*p*-Ethoxy-*m*-aminophenyl)	96.5–97.5	$C_{11}H_{12}ON_2S$	12.72	12.96
2-(*p*-Ethoxy-*m*-nitrophenyl)-4-methyl	130.5–132			
2-(*p*-Ethoxy-*m*-aminophenyl)-4-methyl	126–127	$C_{12}H_{14}ON_2S$	11.95	11.87
2-(*p*-Ethoxy-*m*-nitrophenyl)-4,5-dimethyl	140.2–141.2			
2-(*p*-Ethoxy-*m*-aminophenyl)-4,5-dimethyl	163.5–164.5	$C_{13}H_{16}ON_2S$	11.28	11.37
2-(*p*-Ethoxy-*m*-nitrophenyl)-4-ethyl	71–71.5			
2-(*p*-Ethoxy-*m*-aminophenyl)-4-ethyl	109–109.5	$C_{13}H_{16}ON_2S$	11.28	11.53

[a] The nitro compounds were all obtained in about 80% yields. They formed yellowish matted needles which were purified from dilute alcohol. [b] The amino compounds were white or slightly yellowish microcrystalline compounds or needles. They were obtained in yields of 60–80% and were purified from dilute alcohol, except in the case of 2-(*p*-aminophenyl)-4-methylthiazole when water was used.

of benzene and 0.1 g. of 2-(*p*-nitrophenyl)-4-chloromethylthiazole was refluxed for twelve hours. After evaporation of the solvent, the residue was treated with aqueous sodium bicarbonate and the base extracted with ether. The ether solution was dried and the hydrochloride precipitated with dry hydrogen chloride. The product was purified from a mixture of chloroform and carbon tetrachloride; colorless prisms, m. p. 202–204°.

Nitration of Thiobenzamide.—When thiobenzamide was nitrated according to the directions used for nitrating phenylthiazole, a colorless product was obtained, m. p. 89–90°. It proved to be 3,5-diphenyl-1,2,4-thiadiazol, a compound previously prepared by oxidizing thiobenzamide with alcoholic iodine[14] or ammonium persulfate.[15]

Summary

2-Aminophenyl oxazoles and 2 aminophenyl thiazoles have been prepared. They are local anesthetics.

(14) Hofmann, *Ber.*, **2**, 646 (1869); Hofmann and Gabriel, *ibid.*, **25**, 1578 (1892).

(15) Walther, *J. prakt. Chem.*, [2] **69**, 45 (1904).

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[CONTRIBUTION FROM THE DIVISION OF PLANT BIOLOGY, CARNEGIE INSTITUTION OF WASHINGTON]

Sources of *d*-Sorbitol

BY HAROLD H. STRAIN

A number of plant materials have been examined as possible sources of the rare sugar alcohol, *d*-sorbitol. This investigation was facilitated by the use of pyridine for the isolation of the crystalline sorbitol–pyridine compound from the mixture of substances extracted from leaves with ethanol.[1] Of those materials investigated thus far, the best sources for the isolation of sorbitol in quantity are fruits of *Pyrus*, *Sorbus*, *Photinia*, *Crataegus*, *Pyracantha*, and *Cotoneaster*. Since these species are widely distributed in the temperate zones, material for the isolation of sorbitol is readily available.

Examination of the leaves of pear, peach, apple, apricot, cherry, and Toyon trees has also revealed the presence of small quantities of sorbitol. It thus appears that sorbitol may play the same role in the metabolism of plants of the genus *Rosacae* that sugar alcohols play in the metabolism of some marine algae.[2]

Since fruits of the *Rosacae*, such as cherries, peaches, pears, apples, etc., are consumed in large quantities by man, sorbitol must be a significant constituent of the human diet. The ready conversion of sorbitol into reducing sugars in the animal body[3] suggests that many fruits may be

(1) Strain, THIS JOURNAL, **56**, 1756 (1934).

(2) Haas and Hill, *Biochem. J.*, **26**, 987 (1932); Hassid, THIS JOURNAL, **55**, 4163 (1933); Hassid, *Plant Physiology*, **8**, 480 (1933).

(3) Embden and Griesbach, *Z. physiol. Chem.*, **91**, 251 (1914).

much richer in sugar-yielding substances than is indicated by the common methods of analysis which do not include the non-reducing sugar alcohols.[4]

Sorbitol is now prepared commercially by hydrogenation of glucose and is sold in the form of a sirup containing about 50% of the reduction products. Pure sorbitol is isolated readily from the sirup by the use of pyridine for crystallization of the residue obtained by evaporation of the water at reduced pressure.

Experimental

Isolation of *d*-Sorbitol–Pyridine Compound.—Plant material which had been freshly dried at 60° was steeped with about five times its weight of ethanol (85%) for twenty-four hours. The ethanol extract was separated from the plant material by decantation, and the residue was re-extracted with two additional portions of ethanol. The ethanol extracts were combined and evaporated to dryness at reduced pressure. The residue thus obtained was extracted with about three times its weight of pyridine at 100°. The pyridine extract, separated from insoluble gum by decantation, was cooled and placed in the refrigerator overnight. If crystals had not formed, very small crystals of the sorbitol–pyridine compound were added to the mixture which was again permitted to stand in the refrigerator for several days. When crystals of the sorbitol–pyridine compound had formed, these were separated from the solution by filtration, washed with a little cold pyridine and dried over sulfuric acid in a vacuum. The mother liquors were used to re-extract the residue which had not been dissolved by the hot pyridine. In this way two or three crops of the sorbitol–pyridine compound were obtained from each product which contained this sugar alcohol. The several crops of the sorbitol–pyridine compound, which usually contained only very small quantities of reducing sugars, were combined and weighed.

The plant materials examined for sorbitol are listed in the following table. The sorbitol content of the undried material, calculated from the weight of the sorbitol–pyridine compound which was crystallized, does not represent an accurate assay of the sorbitol contained in the products examined.

SORBITOL CONTENT OF VARIOUS NATURAL MATERIALS

Plant[a]	Part	Sorbitol, %	
Aesculus californicus	Fruit	0.0	
Arbutus unedo	Fruit	.0	
Berberis stenophylla	Fruit	.0	
Citrus Aurantium	Fruit	.0	
Celastrus scandens	Fruit	.0	
Cotoneaster frigida	Fruit	2.7	
Cotoneaster horizontalis	Fruit	2.1	
Cotoneaster microphylla	Fruit	3.6	
Cotoneaster pannosa	Fruit	5.1	
Crataegus monogyna	Fruit	4.7	
Crataegus oxyacantha	Fruit	7.6	
Eriobotrya japonica	Fruit	0.2	
Eschscholtzia californica	Petals	.0	
Juglans californica	Leaves	.0	
Photinia arbutifolia[b]	Leaves	0.89	0.93
Photinia arbutifolia	Small green fruits	1.7	
Physalis Alkekengi	Fruits	0.0	
Prunus Armeniaca	Leaves	.4	
Prunus avium	Leaves	.2	
Prunus Persica	Leaves	.6	
Pyrus communis[b]	Leaves	1.2	
Pyrus communis	Small green fruits	2.4	
Pyrus communis	Large green fruits	1.9	
Pyrus communis	Ripened fruits	2.3	
Pyrus Malus	Leaves	0.45	
Pyracantha angustifolia	Fruit	4.7	
Pyracantha crenulata	Fruit	3.3	
Rhamnus californica	Fruit	0.0	
Rosa gymnocarpa	Fruit	0.0	
Sorbus aucuparia	Fruit	10.4	9.6
Sorbus sitchensis	Fruit	6.1	
Symphoricarpos albus	Fruit	0.0	
Umbellularia californica	Leaves	.0	
Umbellularia californica	Flowers	.0	

[a] The plants were identified by reference to Jepson, "Manual of the Flowering Plants of California," Berkeley, 1925, and to Bailey, "Manual of Cultivated Plants," New York, 1925. [b] The sorbitol–pyridine compound isolated from the leaves of the pear and the Toyon was converted into triformal-sorbitol.[1] This product was identical with triformal-*d*-sorbitol prepared from glucose with respect to melting point and optical rotation.

Sorbitol from Cider.—Tutin[5] has suggested that cider may be used as a source of sorbitol and has recommended that the sorbitol be isolated as the hexaacetate and reconverted into the free sorbitol by hydrolysis in the presence of acid. The formation of the hexaacetate involves the use of expensive reagents, and experience has shown that the yields of sorbitol recovered from the hexaacetate are small. Consequently, attempts were made to isolate the sorbitol from fermented cider by the use of pyridine. The cider which was used contained small quantities of sorbitol and this was isolated very readily.

Cider (1800 ml.) was pressed from pippin apples which had been in cold storage for some time. The cider was fermented with yeast, filtered through charcoal and siliceous earth and evaporated to dryness at reduced pressure. The residue (70 g.) was extracted with pyridine (200 ml.) at 100°. The pyridine was decanted and cooled in the refrigerator for several days. It was separated from the sorbitol–pyridine crystals which formed and used to re-extract the residue obtained from the cider. From this extract cooled in the refrigerator, a second crop of sorbitol–pyridine crystals was obtained. The sorbitol–pyridine crystals were washed with cold pyridine and dried over concentrated sulfuric acid in vacuum; weight of sorbitol–pyridine compound, 7.5 g. Triformal-sorbitol prepared from the pyridine compound was identical with triformal-sorbitol prepared from glucose. A 7.0-g. portion of the sorbitol–pyridine compound was exposed to the air of the laboratory for seven days. It had then lost 2.0 g. and did not contain detectable quantities of pyridine. The pyridine-free sorbitol melted at 90°.

Crystalline Sorbitol–Pyridine Compound from Technical Sorbitol.—Technical sorbitol in the form of a sirup containing 50% sorbitol and 1% formalin (as preservative) was obtained through the courtesy of E. I. du Pont de Nemours and Company. Two hundred grams of the sirup was evaporated to dryness at reduced pressure. The resi-

(4) Martin, *Plant Physiology*, **11**, 139 (1936).

(5) Tutin, *Biochem. J.*, **19**, 416 (1925).

due (102 g.) was dissolved in pyridine (300 ml.) and the solution was cooled and placed in the refrigerator overnight. The crystals which separated were collected on a filter and redissolved in pyridine (300 ml.). This solution was filtered in order to remove slightly soluble polymerization products of formaldehyde which had separated. It was cooled and placed in the refrigerator. After twenty-four hours, the crystals which had formed were isolated by filtration and dried in vacuum over concentrated sulfuric acid for two days; weight of the sorbitol–pyridine compound, 106.3 g.; melting point 90°. When this compound was mixed with pure sorbitol–pyridine, the melting point of the mixture was 90°. The sorbitol–pyridine compound was converted into the triformal derivative which proved to be identical with triformal-*d*-sorbitol prepared from glucose.[1]

Summary

The fruits of several species of the family *Rosacae* are convenient sources of sorbitol. Small quantities of sorbitol have been isolated from the leaves of some of these plants. Sorbitol extracted from a variety of plant materials with alcohol is crystallized readily from pyridine.

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Ketene Acetals. II. Bromoketene Diethylacetal. Observations on the Reactivity of Bromo- and Iodoethoxyacetal[1]

BY FREDERICK BEYERSTEDT AND S. M. MCELVAIN

The preparation of tetraethoxyethylene (IV) was the original object of this work. That compound is of particular interest on account of its alleged dissociation into the divalent carbon compound, carbon monoxide acetal. The latter substance is reported to have been isolated[2] in small yields from the reaction of sodium ethoxide with ethyl diethoxyacetate and in much larger yields from ethyl formate through the following series of reactions

$$HCOOC_2H_5 + NaOC_2H_5 \longrightarrow$$

$$C_2H_5OH + C(ONa)OEt \xrightarrow{POCl_3}$$

$$C(Cl)OC_2H_5 \xrightarrow{NaOC_2H_5} C(OC_2H_5)_2$$

Unsuccessful attempts to repeat the latter procedure have been reported[3] in the literature. The recent preparation of ketene diethylacetal[4] from iodoacetal and the demonstration that it had not been described previously would seem to invalidate the former procedure. In fact, it is doubtful if such an acetal, which is really an ether of the enolic form of an ester, has ever been prepared simply by the action of sodium ethoxide on the ester.

It seemed desirable, therefore, to undertake the preparation of tetraethoxyethylene (diethoxyketene diethylacetal) (IV) by a method related to that by which the ketene diethylacetal was obtained. The reactions involved in the projected synthesis were

$$BrCH_2CH(OC_2H_5)_2 \xrightarrow{Br_2} \underset{I}{Br_2CHCH(OC_2H_5)_2} \xrightarrow{KOC_2H_5}$$

$$\underset{II}{(C_2H_5O)_2CHCH(OC_2H_5)_2} \xrightarrow{Br_2}$$

$$\underset{III}{(C_2H_5O)_2CBrCH(OC_2H_5)_2} \longrightarrow \underset{IV}{(C_2H_5O)_2C{=}C(OC_2H_5)_2}$$

This synthesis failed at the transformation of dibromoacetal (I) to glyoxal tetraethylacetal[5] (II). The dibromoacetal (I) after fifteen hours of heating at 150° with an excess of saturated alcoholic solution of potassium ethoxide gave an incomplete reaction, as judged from the amount of precipitated potassium bromide. The product isolated still contained bromine and it was necessary to heat it for an additional ten hours at 150° to render it halogen-free. After these periods of heating the only products which could be isolated were small amounts of glyoxal and traces of the glyoxal tetraethylacetal. After several experiments it was found that one of the halogens of dibromoacetal was removed quite easily by the potassium ethoxide, but that the second one came out only with the greatest difficulty. Pinner[5] records a similar observation on the dichloroacetal.

The replacement of a single bromine of dibromoacetal by the ethoxyl group to form bromo-

(1) This work was supported in part by a grant from the Wisconsin Alumni Research Foundation.

(2) Scheibler, *Ber.*, **59**, 1022 (1926).

(3) Arbusow, *ibid.*, **64**, 698 (1931); Wood and Bergstrom, THIS JOURNAL, **55**, 3314 (1933); *cf.* also Adickes, *Ber.*, **60**, 272 (1927); **63**, 3012 (1930).

(4) Beyerstedt and McElvain, THIS JOURNAL, **58**, 529 (1936).

(5) The preparation of this acetal in very low yields from glyoxal has been described by Harris and Temme [*Ber.*, **40**, 171 (1907)] and from dichloroacetal by Pinner [*ibid.*, **5**, 151 (1872)].