

1.214 at 0°. The polarimetric data are recorded in Table I and are plotted in Fig. 1.

TABLE I

DEGREE OF POLYMERIZATION OF POTATO STARCH (*c*, 4.84) AFTER HYDROLYSIS WITH HYDROCHLORIC ACID (37.5 G. HCl PER 100 CC. SOLN.) AT 0° FOR VARIOUS TIME INTERVALS

Time of hydrolysis, hrs. ^a	[α] _D ^b	Acetylated mercaptalated product from 2.42 g. starch, wt., g.		D. P. ^c by S content	Acetyl content (cc. 0.1 N NaOH)	
		%S	%S		Calcd.	Found
0	+203 ^{ob}
0.55	200	2.5	1.29	16.5
1.05	198	3.7	1.72	12.2
1.55	197	4.0	2.03	10.2	10.37	10.43
2.55	192	4.0	2.31	8.9	10.35	10.51
4.25	186	5.0	2.59	7.9
5.55	179	4.5	3.46	5.7	10.32	10.39
7.55	172	4.0	4.51	4.2	10.29	10.06
9.55	167	4.2	5.23	3.5
12.05	161	4.7	5.56	3.3
14.80	151	3.9	6.31	2.8	10.24	10.01
17.80	145	3.7	7.59	2.2
25.80	126	4.2	8.35	2.0	10.20	10.13

^a Initial time taken as time of addition of the acid to the starch. ^b By extrapolation. ^c Average degree of polymerization in glucose units, assuming complete acetylation.

Sulfur Analyses of Acetylated Mercaptalated Products.—The sulfur analyses were performed by the Parr bomb method, employing total samples of approximately 1 g., on a moisture-free basis, in the manner described previously.² In Table I are recorded the sulfur analytical data and the corresponding average degrees of polymerization calculated from them. The degree of polymerization (D. P.) may be calculated from the sulfur content by the equation

$$D. P. = 2 + \left[\frac{6412}{\%S + C_{12}H_{16}O_8} \right] - 2 \left[\frac{C_{14}H_{19}O_9 + C_2H_5S}{C_{12}H_{16}O_8} \right]$$

where $C_{14}H_{19}O_9$ is the molecular weight of the end structural units and $C_{12}H_{16}O_8$ is the molecular weight of the intervening units.

Summary

1. Potato starch has been hydrolyzed with a concentrated solution of hydrochloric acid at 0° in the presence of an excess of ethyl mercaptan. The resulting mercaptalated mixtures of hydrolyzed products were isolated as their acetates at various time intervals, during the first twenty-six hours of the hydrolysis.

2. Sulfur analytical data indicated that the average degree of polymerization of the mercaptalated products varied from 17 glucose units after one-half hour to 2 glucose units after twenty-six hours.

3. The course of the hydrolytic reaction (without mercaptalation) at 0° was followed by optical rotation measurements.

4. A graphic analysis of the data yields a value of 2.66×10^{-2} for the specific rate constant (hours⁻¹) of the rate of change of the degree of polymerization in concentrated hydrochloric acid at 0°.

5. By graphic analysis the value 20 ± 4 glucose units is obtained for the initial average degree of polymerization of the potato starch.

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The Action of Isobutylmagnesium Bromide on 3,4,5-Trimethoxybenzonitrile

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A recent communication by Suter and Weston² describes the preparation of some 5-alkylresorcinols. As work along similar lines has been under way for some time in this Laboratory, occasion is taken to present some of the results that are closely related to the studies of Suter and Weston. This work had for its object the preparation of 5-isoamylresorcinol³ in order that its properties

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(2) Suter and Weston, *THIS JOURNAL*, **61**, 232 (1939).

(3) Because the junior author has been assigned to new duties, the work was interrupted before its completion.

might be compared with those of 4-isoamylresorcinol⁴ and 2-isoamylresorcinol.⁵

4-Isoamylresorcinol was first prepared by Dohme⁴ in connection with his studies on the bactericidal action of 4-alkylresorcinols, and 2-isoamylresorcinol was first synthesized by Haller⁵ and shown to be identical with tetrahydrobutanol,⁶ a degradation product of rotenone.⁷

The reaction of 3,5-dimethoxybenzonitrile with

(4) Dohme, Cox and Miller, *THIS JOURNAL*, **48**, 1688 (1926).

(5) Haller, *ibid.*, **56**, 3032 (1933).

(6) Haller and LaForge, *ibid.*, **53**, 4460 (1931); **54**, 1988 (1932).

(7) LaForge, Haller and Smith, *Chem. Rev.*, **12**, 181 (1933).

isobutylmagnesium bromide according to the procedure described by Haller⁵ in his work on 2,6-dimethoxyphenyl isobutyl ketone was first studied. The yield of the resulting ketone was 45 to 50% based on the nitrile.

Several methods for the reduction of the ketone were investigated, with results similar to those described by Suter and Weston² in the reduction of their ketones.

Reduction with sodium and alcohol, as described by Asahina⁸ for the 3,4,5-trimethoxyphenyl alkyl ketone, yielded mixtures which were difficult to separate. When the ketone was shaken in an atmosphere of hydrogen with palladium charcoal as described by Hartung and Crossley,⁹ no hydrogen was absorbed and the unchanged starting material was recovered. The Clemmensen method likewise failed to yield a satisfactory reduction product.

Owing to the high cost of 3,5-dimethoxybenzonitrile, a study of the reaction between 3,4,5-trimethoxybenzonitrile and isobutylmagnesium bromide was undertaken, as it has been shown¹⁰ that the methoxyl group in the 4-position of trimethylpyrogallol derivatives can be replaced by hydrogen. The reaction of this nitrile and the Grignard reagent yielded, after hydrolysis, in addition to the expected 3,4,5-trimethoxyphenyl isobutyl ketone, two other products. One of these products is soluble in aqueous alkali and forms a semicarbazone, an oxime, and an acetyl and a benzoyl derivative. With ferric chloride in alcohol it gives a faint green color. On the basis of these reactions, analytical data, and the known reactivity of the methoxyl group in the 4-position of trimethylpyrogallol derivatives, it is suggested that the compound is 3,5-dimethoxy-4-hydroxyphenyl isobutyl ketone. The other compound forms a crystalline semicarbazone, possesses two methoxyl groups, and is insoluble in aqueous alkali. Analyses of the compound and of its semicarbazone indicate the empirical formula $C_{17}H_{26}O_3$. It is suggested that this compound possesses a butyl group in the 4-position of the benzene ring and that the compound is probably a 3,5-dimethoxybutylphenyl isobutyl ketone.

Several attempts were made to reduce the trimethoxyphenyl isobutyl ketone. In some cases a reduction was accomplished, but it could not be repeated and further studies are desirable.

(8) Asahina, *Ber.*, **69B**, 1643 (1936).

(9) Hartung and Crossley, *THIS JOURNAL*, **56**, 158 (1934).

(10) Houben, "Die Methoden der organischen Chemie," pt. 3, 1930, p. 179.

Experimental

3,5-Dimethoxybenzonitrile.—This compound was obtained on dehydration of the corresponding amide¹¹ with phosphorus pentoxide.

Five-tenths of a gram of 3,5-dimethoxybenzamide was mixed intimately with 0.4 g. of phosphorus pentoxide, and the mixture heated in a sand-bath. After the vigorous reaction had subsided, the mixture was treated with ice and water, filtered, thoroughly washed with water, and then dried. The product was recrystallized from 60% ethanol. It melted at 87–88°.

Anal. Calcd. for $C_9H_9NO_2$: N, 8.6. Found: N, 8.58.

In attempts to prepare the nitrile from the amide and phosphorus pentachloride according to the procedure of Kauffmann,¹² dehydration took place, but the product also contained chlorine.

A mixture of 0.4 g. of 3,5-dimethoxybenzamide and 0.65 g. of phosphorus pentachloride was heated in a sand-bath to initiate reaction. After the vigorous reaction had subsided and the mixture had cooled, ice and water were added. The reaction product was thoroughly washed with water and dried. After recrystallization from ethanol it melted at 124–125°.

Anal. Calcd. for $C_9H_9ClNO_2$: N, 7.1. Found: N, 7.18.

3,5-Dimethoxyphenyl Isobutyl Ketone.—A Grignard reagent was prepared in the usual manner from 2.4 g. (0.1 mole) of magnesium suspended in 40 cc. of ether and 13.0 g. (0.095 mole) of isobutyl bromide dissolved in 25 cc. of ether. To this ether solution was added, in the course of five minutes and with constant stirring, 3.2 g. (0.02 mole) of 3,5-dimethoxybenzonitrile dissolved in 50 cc. of ether. The reaction mixture was then refluxed for one hour, cooled, and poured into ice and concentrated hydrochloric acid. The aqueous solution, after separation from the ether solution, was extracted twice with ether, placed in an open beaker, and heated on the steam-bath to remove the dissolved ether. Finally the solution was boiled vigorously under reflux for one hour. The separated oil was extracted from the cooled solution with ether; the ether extract was washed with water and dried over sodium sulfate. The oil remaining after the ether had been removed was distilled. It boiled at 143–145° (2.0 mm.). The yield was 3.6 g. When treated with semicarbazide hydrochloride and sodium acetate, according to the procedure described by Shriner and Turner,¹³ 3.6 g. of the oil yielded 4.0 g. of a crystalline semicarbazone. The product after recrystallization from ethanol melted at 195–196°.

Anal. Calcd. for $C_{14}H_{21}N_3O_3$: C, 60.21; H, 7.53. Found: C, 59.86; H, 7.70.

3,4,5-Trimethoxybenzonitrile.—Gallic acid was methylated with dimethyl sulfate according to the directions in "Organic Syntheses."¹⁴ The methylated acid on treatment with thionyl chloride yielded the acid chloride, which was converted to the amide¹⁵ by treatment with concen-

(11) Mauthner, *J. prakt. Chem.*, **87**, 403 (1913).

(12) Kauffmann, *Ann.*, **344**, 30 (1906).

(13) Shriner and Turner, *THIS JOURNAL*, **52**, 1267 (1930).

(14) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, 1932, p. 522.

(15) Harding, *J. Chem. Soc.*, **99**, 1585 (1911).

trated aqueous ammonia. The amide, on being heated in benzene solution with phosphorus pentachloride, yielded the nitrile.¹⁶

Reaction of 3,4,5-Trimethoxybenzonitrile with Isobutylmagnesium Bromide.—To the Grignard reagent prepared from 34.2 g. (0.25 mole) of isobutyl bromide in 65 cc. of ether and 6.07 g. (0.25 mole) of magnesium turnings suspended in 200 cc. of dry ether was added, in the course of twenty minutes and with constant stirring, 19.3 g. (0.1 mole) of 3,4,5-trimethoxybenzonitrile dissolved in 200 cc. of dry toluene. The reaction mixture was then heated in an oil-bath and the ether removed by distillation, toluene being added gradually to maintain the original volume.¹⁷ After all of the ether had been replaced with toluene, the mixture was refluxed for three hours with constant stirring. The reaction mixture was then poured onto ice containing 30 cc. of concentrated hydrochloric acid. The aqueous layer, after separation of the toluene, was washed twice with ether, placed in an open beaker, and heated on the steam-bath until all the dissolved ether was removed. It was then boiled for two hours under reflux and cooled, and the oil that separated was removed by extraction with ether. The combined ether extracts were washed with 5% sodium hydroxide and with water, and then dried over sodium sulfate. The oil (A) remaining after removal of the ether was distilled under reduced pressure. It boiled at 147–150° (1 mm.). The yield was 6.5 g. Analysis indicated the compound to be trimethoxyphenyl isobutyl ketone.

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.66; H, 7.93; OCH_3 (3), 36.9. Found: C, 66.43; H, 7.88; OCH_3 , 36.4.

A crystalline semicarbazone was obtained readily when 0.5 g. of the distilled oil (A) in 5 cc. of ethanol was treated with 2 cc. of pyridine and 0.5 g. of semicarbazide hydrochloride dissolved in a small quantity of hot water. The yield was 0.6 g. The product, after crystallization from ethanol, melted at 205°.

Anal. Calcd. for $C_{14}H_{22}N_3O_4$: C, 58.3; H, 7.44; OCH_3 (3), 30.1. Found: C, 58.45; H, 7.81; OCH_3 , 30.0.

The alkali-soluble fraction (B) obtained on extraction of the ether solution was acidified with dilute sulfuric acid and the separated product removed by extraction with ether. The ethereal solution was washed with water and dried with sodium sulfate. On removal of the ether a colorless crystalline product was obtained. The yield was 6.0 g. When recrystallized from 50% ethanol, it melted at 94°. Analyses indicate it to be a dimethoxyhydroxyphenyl isobutyl ketone.

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.54; H, 7.56; OCH_3 (2), 26.05. Found: C, 66.04; H, 7.80; OCH_3 , 26.09.

A crystalline semicarbazone was obtained readily when the product (B) was treated with semicarbazide hydrochloride as described above for the trimethoxyphenyl isobutyl ketone. After recrystallization it melted at 162.5°.

Anal. Calcd. for $C_{14}H_{21}N_3O_4$: C, 56.9; H, 7.12; OCH_3 (2), 21.0. Found: C, 57.75; H, 7.67; OCH_3 , 21.2.

(16) Harding, *J. Chem. Soc.*, **105**, 2790 (1914).

(17) When the reaction was carried out in ether only, in which the nitrile is slightly soluble, about two-thirds of the starting material was recovered unchanged.

With hydroxylamine the alkali-soluble product yielded an oxime. A solution of 1.2 g. of the oil (B), 0.35 g. of hydroxylamine hydrochloride, and 0.45 g. of anhydrous sodium acetate in 10 cc. of absolute ethanol was refluxed for two hours. The solution was filtered and concentrated to a small volume, and water was added. The separated product was filtered and dried. The yield was 1.0 g. After recrystallization from dilute ethanol it melted at 110°.

Anal. Calcd. for $C_{13}H_{19}NO_4$: OCH_3 (2), 24.5. Found: OCH_3 , 24.4.

Fraction B with benzoyl chloride yielded a benzoyl derivative.

One gram of the oil (B), 1 g. of benzoyl chloride, and 1 cc. of pyridine in 7 cc. of benzene were heated in a boiling water-bath for one hour. To the cooled reaction mixture dilute hydrochloric acid was added and the solution was extracted with ether. The ether-benzene solution was washed with dilute sodium carbonate solution, with water, and then dried over anhydrous sodium sulfate. After removal of the solvent the remaining product crystallized readily. It was recrystallized from methanol. The yield was 1 g. It melted at 111°.

Anal. Calcd. for $C_{20}H_{26}O_5$: OCH_3 (2), 18.15. Found: OCH_3 , 18.0.

The toluene solution obtained after separation of the aqueous acid solution was washed with water, dried over sodium sulfate, and the toluene removed by distillation. The residue was distilled and 2.0 g. of an oil that boiled at 140–145° (1 mm.) was obtained. It yielded 0.2 g. of alkali-soluble material on treatment in ether solution with 5% sodium hydroxide. The alkali-insoluble fraction distilled at 128–130° (0.35 mm.).

Anal. Calcd. for $C_{17}H_{26}O_3$: C, 73.4; H, 9.35; OCH_3 (2), 22.3. Found: C, 72.8; H, 9.14; OCH_3 , 23.0.

When treated in ethanol with semicarbazide hydrochloride and pyridine, the oil yielded a crystalline semicarbazone. When recrystallized from methyl alcohol it melted at 184°.

Anal. Calcd. for $C_{18}H_{26}O_3N_3$: C, 64.5; H, 8.66; OCH_3 (2), 18.5. Found: C, 64.53; H, 8.82; OCH_3 , 18.5.

Summary

Reaction of 3,5-dimethoxybenzonitrile and isobutylmagnesium bromide yields 3,5-dimethoxyphenyl isobutyl ketone.

Interaction of 3,4,5-trimethoxybenzonitrile and isobutylmagnesium bromide yields, in addition to the expected 3,4,5-trimethoxyphenyl isobutyl ketone, two other products. The one has the empirical formula $C_{14}H_{20}O_4$, is soluble in alkali, and forms both carbonyl and hydroxyl derivatives. It is probably 3,5-dimethoxy-4-hydroxyphenyl isobutyl ketone. The other product has the empirical formula $C_{17}H_{26}O_3$, is insoluble in alkali, and forms a semicarbazone. It is suggested that the compound is probably a 3,5-dimethoxy-4-butylphenyl isobutyl ketone.

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