inum oxide absorbed 1 mole of hydrogen in twenty-two hours. After removal of the alcohol under diminished pressure, the oily residue was crystallized by addition of ether; yield 3.6 g., m. p. 203–210°. After four crystallizations from ethyl acetate it had the m. p. 215–217° and $(\alpha)^{24}D$ −155.9° (methanol, *c*, 0.76).

Anal. Calcd. for $C_{22}H_{30}N_2O_2$: C, 74.6; H, 8.5; N, 7.9. Found: C, 74.2; H, 8.8; N, 7.8.

6-Piperidocodide.—A mixture of 10 g. of bromocodide and 10 g. of piperidine in an evacuated sealed tube was heated in the boiling water-bath for forty-five minutes. The product was dissolved in acid, precipitated with sodium carbonate, and extracted into ether. The residue from the ether was again put through this procedure to remove piperidine. The oily product (10 g.) was treated with 6 cc. of 60% perchloric acid and diluted with 75 cc. of water, warming into solution. When the solution cooled, oily material began to separate, and was brought just into solution with alcohol. After twelve hours, the solution had deposited 6.5 g. of crystalline diperchlorate, which was purified from water to constant rotation $(\alpha)^{23}D$ −113.4° (water, *c*, 0.44); m. p. 172–175°.

Anal. Calcd. for $C_{23}H_{32}Cl_2N_2O_{10}$: Cl, 12.5. Found: Cl, 12.1.

The perchlorate was converted to the base, extracted with ether, and the residue from the ether was washed with cold 30–60° ligroin. The base was sublimed four times in a high vacuum at 130° (to constant rotation); melting point, 75–80°, $(\alpha)^{25}D$ −233.9° (methanol, *c*, 0.87).

Anal. Calcd. for $C_{23}H_{30}N_2O_2$: C, 75.4; H, 8.2; N, 7.6. Found: C, 75.1; H, 8.2; N, 7.6.

The same base and perchlorate were obtained by treatment of 6-piperidomorphide with diazomethane, likewise by heating β-chlorocodide with piperidine for six hours at 130°. Hydrogenation of 6-piperidocodide resulted in absorption of 1 mole of hydrogen, but the product was a viscous liquid from which no crystalline derivatives could be prepared. A similar substance was obtained when dihydro-6-piperidomorphide was methylated with diazomethane.

Treatment of 50 g. of bromocodide with liquid ammonia at 50° for twenty-four hours resulted in recovery of 40 g. of unchanged material. No halogen-free product could be isolated.

Summary

The reaction of α-chloromorphide and α-chlorocodide with secondary amines or ammonia proceeds with a rearrangement such that the new basic groups appear at the 8-position. The morphine derivatives that are believed to have the halogen atom in the 8-position, as bromomorphide, bromocodide, and β-chlorocodide, react with a rearrangement in the reverse sense, to give 6-aminomorphide and 6-aminocodide derivatives. The introduction of basic groups into the morphine or codeine molecule results in a considerable diminution of physiological action, especially analgesic effect.

UNIVERSITY, VIRGINIA RECEIVED JUNE 12, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLI. The Detection, Isolation and Estimation of the Syringyl Radical in Plant Products[1]

BY M. J. HUNTER AND HAROLD HIBBERT

The syringyl group was first identified in natural products as a unit in the glucoside, syringin,[2] and later in the anthocyanidin, malvin chloride.[3] Although its presence in hard wood lignin occasionally had been inferred from indirect evidence of various kinds,[4] the first isolation of syringyl components from this source was accomplished in these Laboratories.[5] More recently, it was shown that the ethanolysis of hard woods gave much higher yields[6a] than previous methods, and α-ethoxypropiovanillone and α-ethoxypropiosyringone were successfully isolated in almost equal amounts.[6b] The far-reaching implications which the corresponding hydroxy compounds (I) and (II) have for the theory of lignin structure have already been discussed exhaustively,[6,7] and it will suffice to emphasize our view that hard wood lignin is a condensation product of the unit structures (I) and (II) in equal

(1) From a thesis submitted to the Faculty of Graduate Studies and Research, McGill University, by Melvin J. Hunter in partial fulfilment of the requirements for the Degree of Doctor of Philosophy, May, 1939.

(2) Vintilesco, *J. pharm. chim.*, [6] **24**, 529 (1906).

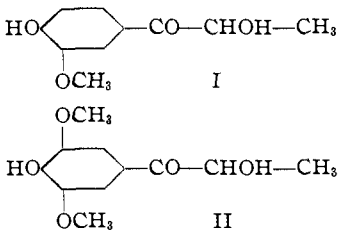
(3) (a) Karrer, *Helv. Chim. Acta*, **10**, 67, 79 (1927); **12**, 292 (1929); **15**, 507 (1932); (b) Robinson, *J. Chem. Soc.*, 25, 1687 (1931); 1647 (1932); 206 (1933).

(4) (a) Wacek, *Ber.*, **63**, 282, 2984 (1930); *Oesterr. Chemiker-Zeitung*, **36**, 84 (1933); (b) Freudenberg, Zocher and Dürr, *Ber.*, **62**, 1821 (1929); (c) Schorger, "The Chemistry of Cellulose and Wood," McGraw-Hill, London, 1926, p. 111; (d) Brauns and Hibbert, *Can. J. Research*, **13**, 28 (1935); (e) Freudenberg, Knopf and Haag, *Ber.*, **69**, 1415 (1936).

(5) (a) Hawkins, Wright and Hibbert, THIS JOURNAL, **59**, 2447 (1937); (b) Leger and Hibbert, *Can. J. Research*, **B16**, 151 (1938); THIS JOURNAL, **60**, 565 (1938); (c) Brickman, Pyle, McCarthy and Hibbert, *ibid.*, **61**, 868 (1939).

(6) (a) Cramer, Hunter and Hibbert, *ibid.*, **61**, 509 (1939); (b) Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939).

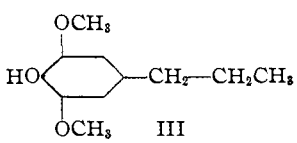
(7) Hibbert, *ibid.*, **61**, 725 (1939).



amounts, while in soft wood lignin the syringyl nucleus is lacking. Unpublished results[8] indicate that both the extracted lignins and the individual units give C_6–C–C–C derivatives, in practically quantitative yield, on hydrogenation at high pressure. The methoxyl content of spruce lignin, 15–17%, is in accord with that of α-hydroxypropiovanillone (I), 15.8%. An equimolecular mixture of (I) and (II) has a calculated value of 21.6%, in comparison with an observed methoxyl content of 20–21.5% for maple and other hard wood lignins.[4a,9] Ethanol lignin from maple wood[6b] contains 27–28% alkoxyl calculated as methoxyl. Of this, 10% is ethoxyl, equivalent to one ethoxyl group per molecular weight of 450 and identical with that of an equimolecular mixture of the ethoxy derivatives from (I) and (II). As a result of improvements in the separation of syringyl from guaiacyl derivatives, we are now able to show that 53% of the phenol fraction from ethanol maple lignin consists of α-ethoxypropiosyringone. All these observations support our view as to the nature of hard wood lignins. On the other hand, the presence of the very small amounts (a fraction of 1%) of syringyl derivatives reported in a soft wood lignin[10] (spruce) could not be confirmed, due possibly to the fact that less than 3–5% of syringyl in presence of 95–97% of guaiacyl derivatives cannot be detected by our method.

Separation of Syringyl and Guaiacyl Derivatives.—The recent discovery[6b] of the presence of both of these type substances in hard woods has necessitated the development of practical methods for their isolation and quantitative separation. In this communication[6b] a separation of syringyl from guaiacyl derivatives by formation of their *p*-nitrobenzoates was given, and, while this procedure served for the characterization of the former, the method was unsuitable, quantitatively, and the original compounds were difficult to reclaim. The following new method does away with these disadvantages. It rests on the discovery that addition of an anhydrous ethanol solution of potassium acetate to an ethanol solution of a mixture of guaiacyl and syringyl derivatives brings about precipitation of the latter in the form of a crystalline potassium salt, usually in high yield; the potassium salt of the guaiacyl-containing product is more soluble and remains in solution. The efficiency of the method when applied to a number of different syringyl compounds is shown in Table I.

The fact that 3,5-dimethoxy-4-hydroxyphenylpropane-1 (III) is not precipitated by potassium



acetate would seem to indicate that precipitability with this reagent apparently is limited to syringyl compounds having a carbonyl group in the para position. This is in harmony with the evidence presented by Lock,[11] indicating a direct relationship between the 1,4-hydroxycarbonyl groups in the benzene nucleus. The much lower value obtained with α-acetoxypropiosyringone (Table I, no. 5) is possibly the result of an intramolecular effect exerted between the acetate and the carbonyl groups.

The reaction appears to be a general one, although trinitrophenol, which contains a strongly acidic hydroxyl group, is also precipitated readily with potassium acetate under the same conditions. Apparently phenols with both ortho hydrogen atoms substituted, and also having a strongly negative group in the para position, are precipitated by potassium acetate in absolute ethanol.

The quantitative efficiency of the method is shown in Table II.

The actual process of separation may be varied greatly, depending on the nature of the products under investigation. Addition of one to three volumes of dry ether to the potassium acetate solution, in the case of the more difficultly precipitable syringyl derivatives, was found greatly to increase the yield of potassium salts. Other reagents such as dry ammonia, and potassium and sodium hydroxides in ethanol, were found effective in bringing about a practical separation

(8) Cooke, McCarthy and Hibbert, unpublished results.

(9) (a) Harris, THIS JOURNAL, **58**, 894 (1936); (b) Hibbert and Steeves, *ibid.*, **59**, 1768 (1937); (c) Freudenberg and Müller, *Ber.*, **71**, 1821 (1938).

(10) Freudenberg, Engler, Flickinger, Sobeck and Klinck, *ibid.*, **71** 1817 (1938).

(11) Lock, *ibid.*, **61**, 2245 (1928); *ibid.*, **62**, 1177 (1929).

TABLE I

PRECIPITATION OF SYRINGYL DERIVATIVE WITH POTASSIUM ACETATE IN ABSOLUTE ETHANOL SOLUTIONS

	Syringyl derivative	Weight used, g.	Potassium salt precipitated G.	%	OCH_3 (calcd. on wt. of potassium salt) Found, %	Calcd., %	Color of ppt.
1	α-Bromopropiosyringone	0.1000	0.1057	93.5	18.1	18.9	Lemon-yellow
2	Propiosyringone	.1000	.1042	91.8	24.4	25.0	Cream
3	α-Hydroxypropiosyringone	.1000	(a) .1250	107.4	23.7	23.6	Pale yellow
			(b) .1242				
4	Syringaldehyde	.1000	.0877	72.3	27.7	28.2	Peach
5	α-Acetoxypropiosyringone	.1000	.0480	42.7	21.6	20.3	Pale yellow
6	3,5-Dimethoxy-4-hydroxy-phenylpropane	.1000	.000	0.00	..	..	.....

TABLE II

QUANTITATIVE SEPARATION OF α-BROMOPROPIOSYRINGONE AND α-HYDROXYPROPIOVANILLONE BY USE OF POTASSIUM ACETATE IN ETHANOL SOLUTIONS

	Amounts in mixture α-Bromopropio-syringone, g.	α-Hydroxypro-piovanillone, g.	Precipitated potassium syringyl derivative G.	%
1	0.1000	0.1000	0.1058	93.5
2	.0500	.1000	.0525	92.2
3	.0250	.1000	.0214	73.3
4	.0000	.1000	.0000	0.0

in dilute solution in many cases, although they are not entirely specific, since most of the guaiacyl analogs are precipitated, to some extent, when *concentrated* ethanol solutions are used.

Sodium acetate, apparently because of its low solubility in ethanol, does not precipitate syringyl compounds, while ammonia, *in anhydrous ether*, precipitates both guaiacyl and syringyl compounds containing a carbonyl group in the para position to the hydroxyl group.

In Table III a survey of the conditions necessary for the qualitative precipitation of syringyl and guaiacyl derivatives is given.

The progressive order (1 to 5) in which the reagents are tabulated is that of their increasing relative value as precipitating media for phenolic derivatives. Thus compounds precipitated by reagent no. 1 will be precipitated more readily by each subsequent reagent, nos. 2, 3, 4 and 5, in the order named, and the conditions for separating a given mixture of syringyl and guaiacyl components will be determined by the relative ease with which they are precipitated in the form of their potassium or ammonium salts. Both potassium and ammonium derivatives of syringyl compounds separate in a microcrystalline form; the former on heating do not melt, while the latter do, with evolution of ammonia, over a wide range depending on the rate of temperature increase.

Application of the above methods to the distilled phenol fraction obtained in the ethanolysis of maple wood[6b] showed that 53% consisted of α-ethoxypropiosyringone.

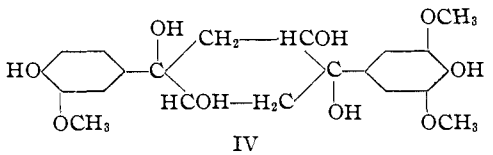
While these results are in harmony with the assumption of the presence of a mixed dimeric

TABLE III

QUALITATIVE PRECIPITATION OF SYRINGYL AND GUAIACYL DERIVATIVES

Derivative	(1) AcOK (ethanol soln.)	(2) AcOK (ethanol + ether soln.)	(3) NH_3 (ethanol soln.)	(4) NH_3 (ether soln.)	(5) KOH (ethanol soln.)
α-Hydroxypropiosyringone	Pptn. is approx. complete	.....	.....	.....	.....
α-Bromopropiosyringone	Pptn. is approx. complete	.....	.....	.....	.....
Syringoylacetaldehyde	Pptn. is approx. complete	.....	.....	.....	.....
Propiosyringone	Partial pptn.	Pptn. is approximately complete		.....	.....
Syringaldehyde	Partial pptn. (45%)	Pptn. is approx. complete	Pptn. is approx. complete	.....	.....
α-Acetoxypropiosyringone	Partial pptn.	Pptn. 80% complete	Pptn. is approx. complete	.....	.....
α-Ethoxypropiosyringone	No pptn.	No pptn.	No pptn.	Partial pptn.	Pptn. is approx. complete
3,5-Dimethoxy-4-hydroxy-phenyl propane	No pptn.	No pptn.	No pptn.	No pptn.	Pptn. is approx. complete
Pyrogallol 1,3-dimethyl ether	No pptn.	No pptn.	Partial pptn.	Pptn. is approx. complete	
α-Hydroxypropiovanillone	No pptn.	No pptn.	No pptn.	Pptn. is approx. complete	
α-Bromopropiovanillone	No pptn.	No pptn.	Partial pptn.	Pptn. is approx. complete	Partial pptn.
Vanillin	No pptn.	No pptn.			

lignin building unit in hard woods of type IV derived from one mole each of α-hydroxypropiovanillone and α-hydroxypropiosyringone, it should be emphasized that up to the present no experimental evidence has been obtained of its actual existence.



IV

Experimental

Quantitative Precipitation of Syringyl Derivatives.—The syringyl compound (0.1000 g.) is dissolved in 2 cc. of absolute ethanol and then a saturated solution (3 cc.) of anhydrous potassium acetate in absolute ethanol (3 cc.) added. The potassium salt generally separates out very rapidly as a microcrystalline product, the color varying in shade from colorless to deep orange. After standing at room temperature (25°) for thirty minutes, the mixture is filtered, washed with absolute ethanol (5 cc.) and dry ether (5 cc.) and dried for one hour at 100° (760 mm.) before weighing. Prior to analysis the precipitate is dried over phosphorus pentoxide at 56° (14 mm.). The results are given in Table I.

Quantitative Separation of Guaiacyl and Syringyl Derivatives.—To the mixture in anhydrous ethanol (2 cc.) of 0.1000 g. of the guaiacyl derivative and varying quantities of the syringyl product, as indicated, was added a saturated anhydrous ethanol solution of potassium acetate (3 cc.), and the precipitated potassium salt of the syringyl derivative filtered, washed and weighed. The results are shown in Table II.

Separation of the Syringyl and Guaiacyl Components in the Phenol Fraction Obtained in the Ethanolysis of Maple Wood.[6b]—The distilled phenol fraction (9.6 g.) was added to a solution of anhydrous potassium acetate (10 g.) dissolved in absolute ethanol (75 cc.) and the mixture well shaken. To this was added dry ether (175 cc.) and the yellow precipitate filtered, washed with ethanol, then with ether and dried (wt. 4.7 g.). The filtrate was shaken with 500 cc. of water and the aqueous layer then extracted thoroughly with benzene. The combined ether and benzene solutions were then concentrated and the residual oil distilled as usual under reduced pressure. The total distillate (4.96 g.) was dissolved in 40 cc. of *anhydrous ethanol* and dry ammonia gas passed into the solution for a few minutes. The yellow crystalline ammonium salt (1.1 g.) was filtered off, washed with ethanol and ether and dried under reduced pressure at room temperature. Both the ammonium and potassium salts when treated with an equivalent of *p*-nitrobenzoyl chloride in dry pyridine yielded the *p*-nitrobenzoate of α-ethoxypropiosyringone.[6b] The combined weights of the two crystalline fractions are equivalent to 5.07 g. of α-ethoxypropiosyringone or 53% of the original mixed phenol fraction.

Synthesis of 3,5-Dimethoxy-4-hydroxyphenylpropane-1.—This derivative was prepared by Mauthner[12] by a molecular rearrangement of the allyl ether of pyrogallol 1,3-dimethyl ether followed by hydrogenation of the acetate of the resulting phenol with a palladium catalyst. The material used in these experiments was prepared by a Clemmensen[13] reduction of propiosyringone[6b] obtained by demethylating 3,4,5-trimethoxypropiophenone with concentrated sulfuric acid.

From 2.0 g. of propiosyringone there was obtained 0.9 g. of product. Distillation of this gave a colorless, mobile oil (0.50 g., 26.6%) which solidified at −5 to 0°; b. p. 123–126° (0.004 mm.), 279–281° (749 mm.); reported by Mauthner[12] 285° (760 mm.). The product could not be purified further.

Anal. Calcd. for $C_9H_{10}O(OCH_3)_2$: OCH_3, 31.6. Found: OCH_3, 30.3.

Synthesis of α-Hydroxypropiosyringone.—The method used was similar to that developed by Robinson[14] for an analogous compound.

α-Acetoxypropiosyringone[6b] (12.5 g.) was dissolved in boiling anhydrous methanol (120 cc.) and mixed with a warm methanol solution of potassium hydroxide (12.0 g.). There was a vigorous reaction, the solution darkened and in a few seconds a yellow crystalline material was precipitated. After filtration, washing first with methanol, then with ether, it was dried in a vacuum desiccator; yield, 12.0 g. (98% calculated as potassium salt of α-hydroxypropiosyringone).

This potassium salt (11.1 g.) was dissolved in a dilute acetic acid solution (50 cc. of water and 7.2 cc. of glacial acetic acid), the solution inoculated with crystals of α-hydroxypropiosyringone and allowed to stand at room temperature for twenty-four hours, the crystalline product removed by filtration, the filtrate carefully extracted with chloroform and the chloroform solution dried with anhydrous sodium sulfate and concentrated, under reduced pressure, to a thick sirup. To this was added the previous crystalline material and the combined product dissolved in a minimum amount of hot benzene. After filtration and cooling, 8.6 g. of crystalline precipitate (90%) was obtained. Three recrystallizations from benzene gave a pure white product in the form of square-shaped crystals, m. p. 126–127°.

Anal. Calcd. for $C_9H_8O_3(OCH_3)_2$: C, 58.4; H, 6.20; OCH_3, 27.4. Found: C, 58.3; H, 6.38; OCH_3, 27.1.

The authors desire to express to the Dow Chemical Company their best thanks for the assistance rendered in the form of a Scholarship granted to one of them (M. J. H.).

Summary

1. A simple method for the quantitative separation of syringyl from guaiacyl derivatives is given.

2. A characteristic difference between hard and soft woods is shown to consist in the presence in the lignin derived from the former of an equal amount of guaiacyl and syringyl analogs;

(12) Mauthner, *J. prakt. Chem.*, **102**, 36 (1921).

(13) (a) Clemmensen, *Ber.*, **46**, 1837 (1913); (b) Hurd and Fowler, THIS JOURNAL, **61**, 252 (1939).

(14) Robinson, *J. Chem. Soc.*, 2701 (1931).

in the latter only the corresponding guaiacyl components are present.

3. It is suggested that in hard woods the lignin building unit may be a mixed dimer, derived, for example, from one mole each of α-hydroxypropiovanillone and α-hydroxypropiosyringone.

4. A method for the synthesis of α-hydroxypropiosyringone (possibly a building unit of hard wood lignins) is described.

MONTREAL, CANADA RECEIVED MAY 18, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLII. The Isolation of a Bisulfite Soluble "Extracted Lignin"

BY WILLIAM H. STEEVES[1] AND HAROLD HIBBERT

The fact that "extracted lignins," isolated for example by the use of acids and of organic solvents in presence of a catalyst (hydrochloric acid, etc.), are insoluble on heating with bisulfite solution points to their having undergone deep-seated changes in structure during their isolation, since "protolignin" as present in the wood is readily bisulfite soluble.

In a recent investigation[2] it was shown that an acetylated oak lignin isolated by the acetylation procedure developed by Suida and Titsch[3] (use of a mixture of acetic anhydride, glacial acetic acid and a small amount of concentrated sulfuric acid) gave, on deacetylation, and for the first time, an extracted lignin completely soluble in hot bisulfite solution at 110°. As shown in another communication[4] the oak lignin sulfonic acid thus formed, on heating with alkali, gave a mixture of vanillin and syringaldehyde in approximately equal amounts.

Under the same conditions of acetylation, the reactive sugar, fructose,[5] and its dehydration product, hydroxymethylfurfural,[6] yield crystalline acetates and no appreciable amounts of acetylated lignin-like materials.

These results thus serve to indicate that lignin is not formed during isolation from carbohydrate material as postulated by Hilpert.[7]

This method of lignin isolation, through acetylation, evidently gives a relatively unchanged, and only slightly polymerized, form of "protolignin." This recently has been confirmed by the partial reconversion of an acetylated lignin, isolated in this manner, to simple lignin building units by treatment with hydrogen chloride and ethanol.[8]

More recently it has been shown that after deacetylation the recovered oak lignin can also be depolymerized in the same manner.[9]

Experimental

Extraction with Alkali.—The procedure followed was that used by Suida and Titsch.[3] Alcohol–benzene and hot water extracted red oak meal (600 g.) was stirred for forty-eight hours at room temperature with 12 liters of 5% sodium hydroxide solution. The wood meal was then removed by filtration, washed with water at 60°, and the extraction repeated in an identical manner three times to ensure complete removal of soluble hemicelluloses. An atmosphere of nitrogen was maintained during the alkali treatments. The extracted wood meal was finally washed with distilled water, 1% acetic acid, water and methyl alcohol, in the order named, and dried (50° at 15 mm.). The pale yellow residual wood meal represented about 80% of the original wood.

Anal. Found: methoxyl, 6.8; lignin, 31.0; cellulose, 66.6; pentosan, 13.3.

Acetylation of the Extracted Wood Meal and Isolation of Acetylated Oak Lignin.—The dried, alkali-extracted oak wood meal (50 g.) was acetylated with a mixture of acetic anhydride (450 g.), glacial acetic acid (250 g.), and concentrated sulfuric acid (3.5 g.), the reaction being carried out in a bronze Werner–Pfleiderer mixer provided with a water cooling system. The temperature was allowed to rise gradually from 15 to 30°, as follows: two and one-half hours at 15°, one-half hour at 15–20°, two hours at 20–25°, and two hours at 25–30°. The highly viscous, dark brown solution was allowed to stand overnight in an atmosphere of nitrogen without stirring. It was then poured into 2 liters of a vigorously stirred 20% sodium acetate solution. The resulting solid, acetylated product

(1) From the thesis of William H. Steeves submitted to McGill University in partial fulfilment of the requirements for the Degree of Doctor of Philosophy, May, 1936. (Previous paper, THIS JOURNAL, **59**, 1768 (1937).)

(2) Steeves, Ph.D. Thesis, McGill University, 1936; Hibbert and Steeves, THIS JOURNAL, **59**, 1768 (1937).

(3) Suida, Hermann and Titsch, *Monatsh.*, **54**, 700 (1929).

(4) Hawkins, Wright and Hibbert, THIS JOURNAL, **59**, 2447 (1937).

(5) Hudson and Brauns, *ibid.*, **37**, 1283 (1915).

(6) Blanksma, *Chem.-Ztg.*, **2**, 1220 (1909).

(7) Hilpert and Hellwage, *Cellulosechemie*, **17**, 25 (1936).

(8) Peniston, McCarthy and Hibbert, THIS JOURNAL, **61**, 530 (1939).

(9) Peniston, McCarthy and Hibbert, unpublished results.