Studies on the Cooking Mechanism of Wood. XV[1]*. Mannich Reaction on Lignin Model Compounds and the Estimation of the Amount of the Simple Guaiacyl Nucleus in Thiolignin*

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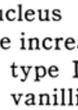
Introduction

Our knowledge on the side chain and nuclear structure of thiolignin is very unsatisfactory. The elucidation of this problem is of fundamental importance to find out a valuable utilization of thiolignin, which is now burned in order to recover sodium. According to the investigation of Richtzenhain[2], the yield of isohemipinic acid by permanganate oxidation of the methylated lignin preparations is higher in the case of thiolignin, than in the case of the lignin in wood or other lignin preparations. In order to explain this fact, it was assumed that a condensation of substances of carbohydrate origin occurred at the 5th position of the nucleus during the digestion, resulting in the increase of the frequency of the nucleus of type II. According to Csellak[3], the yield of vanillin from thiolignin by nitrobenzene oxidation is lower, when compared to that from the lignin in wood or the other types of lignin preparations. The yield of vanillin and syringaldehyde from Meadol by cupric oxide oxidation or oxidation with Fehling solution is also lower, when compared to that from lignosulphonic acid[4]. According to Leopold, model compounds having such nucleus as ((I) (R=H)), except those belonging to diphenyl methane type (III) or to pinoresinol type (IV), give vanillin in very high yield on oxidation with nitrobenzene[5]. The fact, that the yield of vanillin is lower in thiolignin in spite of its rather high content of phenolic hydroxyl group, suggests us, to together with the results of Richtzenhain, that thiolignin contains nuclei of type ((II) (R=H)) in rather high frequency.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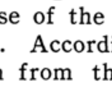
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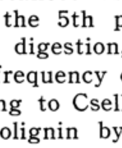
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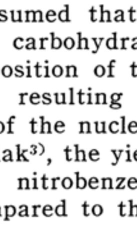
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As the yield of veratric acid and isohemipinic acid from the methylated lignin preparations by permanganate oxidation is supposed to be far from quantitative, and the yield of vanillin from thiolignin is expected to be very much influenced by the presence of carbonyl group[6] or of carboxyl group directly connected to benzene nucleus, it seems to be very interesting to estimate the frequency of the nucleus of type I (R=H) and II (R=H) by a quite different method. As will be stated later, Mannich reaction was used to differentiate both types of phenolic hydroxyl groups and the ratio of the amount of the phenolic hydroxyl groups belonging to these two types were found to be 25–40% and 75–60% respectively. If one can assume, according to Leopold[5], the ratio of (I) and (II) of the lignin in wood as 50 to 50%, one must probably admit the slight increase of (II) during the kraft cooking. It seems, however, incorrect to explain the low yield of vanillin from thiolignin by nitrobenzene oxidation by the increase of the condensed nucleus alone. It seems also to be important that thiolignin contains a carbon atom of higher oxidation stage directly connected to the nucleus, i. e. carbonyl group and carboxyl group, as was reported in the previous communication[1].

Estimation of the Amount of the Non-etherified Simple Guaiacyl Nucleus in Thiolignin

Mannich reaction on phenols, especially with dimethylamine, has been investigated rather much and the investigations done until 1942 are summarized by Blicke[7]. Among them, however, there is only guaiacol as phenols having a close connection to lignin, i. e. with guaiacyl nucleus. In general,

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[1] Part XIV, This Bulletin, 29, 254 (1956).

[2] H. Richtzenhain, *Svensk Papperstidn.*, 53, 644 (1950).

[3] W. Csellak, *Tappi.*, 34, 472 (1951).

[4] I. Pearl, *J. Am. Chem. Soc.*, 64, 1429 (1942).

[5] B. Leopold, *Svensk Kem. Tid.*, 64, 18 (1952).

[6] A. Wacek and K. Kratzl, *Cellulosechem.*, 20, 108 (1942), *Ber.*, 76, 891 (1943), *Ber.*, 77, 516 (1944).

[7] F. Blicke, "Organic Reactions", John Wiley & Sons, Inc., New York, Vol. I (1942), p. 303.

dimethylaminomethyl radical is introduced by Mannich reaction to ortho and para positions of the phenolic hydroxyl group.

As the phenolic hydroxyl groups of lignin belong mainly to type (I) and (II), it seems to be possible to estimate the amount of the former type with Mannich reaction, if it is confirmed by many model phenols that only those having the former nucleus react with formalin and dimethylamine under the condition of Mannich reaction. As will be stated later, experiments with model compounds revealed that 1) model compounds of type (I) give, without exception, Mannich base with substituent at 5th position in very high yield, 2) those of type (II) do not react, 3) carboxyl group having phenolic hydroxyl group in its para position is split off as carbon dioxide and dimethylaminomethyl group is introduced to the same position, 4) methylol group having phenolic hydroxyl group in its para position reacts with dimethylamine resulting in a formation of dimethylaminomethyl group at the same position, 5) other groups remain intact even when phenolic hydroxyl group exists in the para position, and 6) no reaction occurs when the phenolic hydroxyl group is etherified.

Since it is possible to estimate the amount of the carboxyl group, as reported previously¹⁾, and the benzyl alcoholic group can be sulphonated at neutral pH to the sulphonic acid group, a group which does not react under the condition of Mannich reaction, it seems possible to estimate the amount of the phenolic hydroxyl groups belonging to type (I) and (II) (R=H) by Mannich reaction with dimethylamine.

When treated with formaldehyde and dimethylamine, the N/OCH_3 values of the thiolignin, which was used in the previous communication¹⁾, increase along the curve I of Fig. 1. Saturation of the reaction is very good and about 0.35 atom nitrogen was introduced per methoxyl group after one to two days nitrogen content remaining constant even after prolonged reaction. Detailed analytical values are listed in the table.

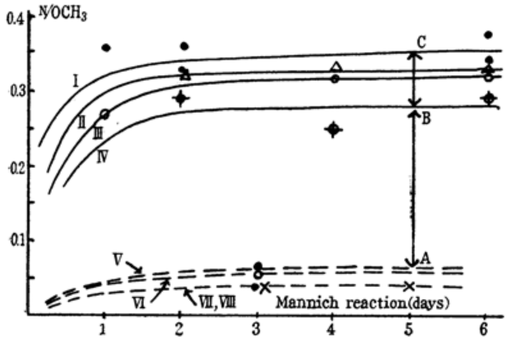


Fig. 1. N/OCH_3 values of thiolignin preparations after Mannich reaction with dimethylamine (D) or with piperidine (P).
I Thiolignin (D), II Raney-Ni (D), III $NaBH_4$ (D), IV Sulphonation (D), V CH_2N_2 (D), VI $NaBH_4$, CH_2N_2 (P), VII CH_2N_2 (P), VIII Dioxanelignin CH_2N_2 (P).

Analytical Values of the Thiolignin Treated with Mannich Reaction.
(Analyzed in perchlorate form)

Reaction (days)	0	1	2	6
C%	61.33	55.12	56.36	56.51
H%	5.64	5.44	6.21	6.24
MeO%	15.31	12.56	13.05	12.95
S%	2.42			
N%	0.0	2.02	1.91 2.10	2.02 2.22
N/MeO%	0.0	0.356	0.323 0.356	0.345 0.379

Curves II and III, which show the N/MeO values of the thiolignin reduced with Raney alloy or with sodium borohydride respectively, followed by the treatment with Mannich reaction, are almost the same as Curve I. Curve IV is for the thiolignin sulphonated at neutral pH. This curve is lower than the Curves I, II or III. The difference BC seems to be due to the sulphonation of benzyl alcoholic group with phenolic hydroxyl group in its para position.

When thiolignin is once methylated with diazomethane, nitrogen must not be introduced by Mannich reaction. Curve V is for thiolignin methylated with diazomethane. Curves VI, VII and VIII are the N/MeO values of the thiolignin, thiolignin reduced with sodium borohydride and of the dioxane lignin used in the preceeding communication, after treating them with Mannich reaction using piperidine instead of dimethylamine. AB, obtained by subtracting this, so to say, blank value from the N/MeO value for the sulphonated thiolignin, corresponds to the amount of the nitrogen introduced to the unsubstituted fifth position and to the first position by displacing the carboxyl group.

As can be seem from the Fig. 2, the content of the phenolic hydroxyl group and the carboxyl group of the thiolignin used in these experiments are 0.4 and 0.18 per methoxyl group. Although it is unknown, how much of the carboxyl group has phenolic hydroxyl group in its para position, we may be allowed to assume, that about a half of the total carboxyl group has phenolic hydroxyl group in the para position, as the

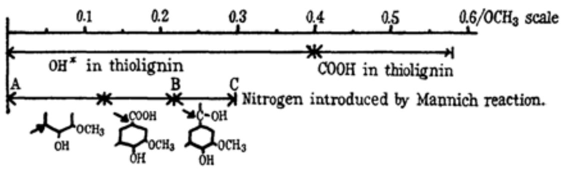
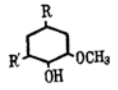


Fig. 2. Relation between the content of OH* and COOH groups thiolignin and the amount of nitrogen introduced by Mannich reaction.

thiolignin contains 0.4 phenolic hydroxyl group per methoxyl group, i. e. about one phenolic hydroxyl group per every two building units. If so, about one half of the total carboxyl group, i.e. 0.09 carboxyl group, may be displaced with dimethylaminomethyl group with Mannich reaction. Subtracting this amount from AB=0.22, the amount of the guaiacyl nucleus having no C–C bond at the fifth position may be obtained, the amount being calculated as 0.13 per methoxyl group. Admitting some uncertainty concerning the amount of the carboxyl group having free phenolic hydroxyl group in its para positon, it will be concluded that about 25–40% of the phenolic hydroxyl group of the thiolignin belongs to the simple guaiacol nucleus having no C–C bond at its fifth position.

Mannich Reaction on Lignin Model Compounds

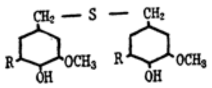
Vanillin gives 5-dimethylaminomethyl vanillin (V) almost quantitatively by Mannich reaction with dimethylamine after one day. With piperidine, 5-piperidinomethyl vanillin (VI) was obtained in good yield. The structure of (V) was confirmed by synthesizing from it 5-formylvanillin (VII). At first, we attempted to lead (V) to (VII) with Thesing's method[8], i. e. to convert (V) to its methiodide (VIII) and then to oxidize the methiodide with nitrobenzene and phenylhydroxylamine to (VII). Although the methiodide was obtained in very good yield, the subsequent oxidation was unsuccessful. Snyder's method[9] was then attempted and found to be successful. 5-dimethylaminomethyl vanillin was reacted with hexamine in acetic acid and the product was hydrolyzed with water. 5-formylvanillin was obatined in the yield of 20%, which gave 5-carboxyvanillin with silver oxide oxidation, according to Pearl[10]. 5-Formylvanillin has been synthesized, according to Pearl, by nitrobenzene oxidation of 5-propenylvanillin, but the method was not so simple. Our method seems to be very convenient to synthesize 5-formylvanillin.



R	R′
V $-CHO$	$-CH_2N(CH_3)_2$
VI $-CHO$	$-CHN(CH_2)_5$
VII $-CHO$	$-CHO$
VIII $-CHO$	$-CH_2N(CH_3)_3I$
IX $-COCH_3$	H
X $-COCH_2CH_3$	H
XI $-COCH_3$	$-CH_2N(CH_3)_2$
XII $-COCH_2CH_3$	$-CH_2N(CH_3)_2$
XIII $-CH_2CH_2CH_2$	H
XIV $-CH_2CH_2CH_2$	$-CH_2N(CH_3)_2$
XV $-CH_2SO_3\frac{1}{2}$ Ba	H
XVI $-CH_2SO_3\frac{1}{2}$ Ba	$-CH_2N(CH_3)_2$
XXI $-CH_2N(CH_3)_2$	$-OCH_3$
XXII $-CH_2N(CH_3)_2$	$-CH_2N(CH_3)_2$
XXIII $-CH_2OH$	$-CHN(CH_2)_5$
XXIV $-CHN(CH_2)_5$	$-CHN(CH_2)_5$

Acetovanillone (IX) and propiovanillone (X) gave 5-dimethylaminomethyl derivatives (XI) and (XII) respectively. Although it is known that some methylene group adjacent to carbonyl group reacts under some condition of Mannich reaction, Mannich base derived from acetovanillone (XI) was iodoform test positive (existence of -COMe) and Millon reaction negative (nonexistence of phenolic hydroxyl group with unsubstituted ortho position) and the Mannich base derived from propiovanillone (XII) was Millon reaction negative. As the iodoform tests of (V) and (XII) were negative and Millon reaction of (V) was negative and those of vanillyl sulphonic acid (XV) and guaiacol were positive, these color reactions seem to be effective for Mannich bases, too. The side chains of acetovanillone and propiovanillone may, therefore, remain intact during the Mannich reaction.

Propylguaiacol (XIII) and vanillyl sulphonic acid (XV) gave also 5-dimethylaminomethyl derivatives (XIV) and (XVI) in good yield under the same condition. Divanillyl monosulphide (XVII) gave Mannich base (XVIII) with two dimethylaminomethyl groups at its two unsubstituted fifth positions.



XVII R=H
XVIII $R=CH_2N(CH_3)_2$

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[8] J. Thesing, *Ber.*, **87**, 507 (1954).
[9] H. Snyder, S. Swaminathan and H. Sims, *J. Am. Chem. Soc.*, **74**, 5110 (1952).
[10] I. Pearl, ibid., **74**, 4263 (1952).

Mannich base (XX) derived from dihydro-dehydro-diisoeugenol (XIX) could not be obtained in crystalline form, but the analytical values of the perchlorate, obtained as a glassy substance, revealed that one dimethylaminomethyl group was introduced to the substance. As can be seen from the Fig. 3,

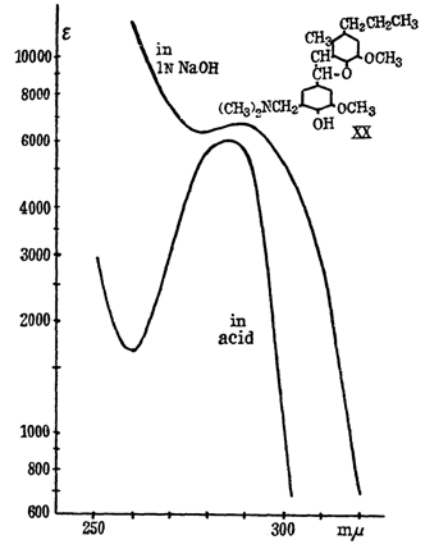
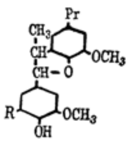


Fig. 3. UV-absorption spectra of the Mannich base obtained from Dihydro-dehydro-diisoengenol in acidic and alkaline media.

the UV-absorption spectrum of the Mannich base is very similar to that of the starting material and it is concluded, from the difference of its alkaline spectrum and acidic spectrum, that the base is a monovalent phenol. For that reason, it may be concluded, that the phenyl-coumaran structure remains intact during the reaction and the dimethylaminomethyl is introduced only to the unsubstituted fifth position.



XIX R=H

XX R=$CH_2N(CH_3)_2$

Syringic acid gave Mannich base (XXI) with simultaneous decarboxylation of the carboxyl group. This base was converted to syringaldehyde by the Snyder's method, which was mentioned before. The yield of the syringaldehyde was rather low, but if it is possible to increase the yield by changing the reaction condition, this method may provide a very convenient way to synthesize syringaldehyde from gallic acid.

Mannich reaction with dimethylamine on vanillyl alcohol gave, after one day, picrate of Mannich base melting at 164-5°, with dimethylamino groups both at the fifth position and at the position of the methylol group (XXII). With piperidine, only the fifth position reacted even after four days, the picrate having the m. p. 153-4° (XXIII) being obtained. The yield was good in both cases.

With dimethylamine, vanillic acid gave Mannich base (XXII) having the m. p. of the picrate 164-5° after six days, which was found to be the same with the picrate obtained from vanillyl alcohol. The reaction must, therefore, involve the substitution under replacement of the carboxyl group, as well as the substitution at the fifth position. After only one day a picrate having the m. p. 175.5-176.5° was obtaind. No structural formula having the same analytical values with this compound was however found.

Mannich reaction with piperidine on vanillic acid during four days gave mannich base (XXIV) with simultaneous decarboxylation and substitutions at the fifth position and the position of the carboxyl group, the m. p. of the picrate being 204.5-5.5°. Mannich reaction during one day gave this picrate and that having the m. p. 209-210°. No structural formula for the latter picrate corresponding to the analytical values was however found. The structure of this unknown picrate seems to be analogous with that having the m. p. 175.5-176.5° obtained with dimethylamine.

Experimental

Mannich Reaction on Vanillin with Dimethylamine.—A mixture of vanillin (18.3 g.), 25% dimethylamine (64.8 ml.) and 30% formaldehyde (30 ml.) was set aside overnight, concentrated repeatedly in order to expel dimethylamine by adding water and then concentrated nearly to dryness. The separated yellowish-colored crystal was recrystallized from normal butanol. Product from the first recrystallization gave correct m.p. 138-139°, 15 g.

Anal. Found: C, 63.28; H, 7.14. Calcd. for $C_{11}H_{15}O_3N$ (V): C, 63.14; H, 7.23%.

The yield of the melting point pure picrate, obtained by adding picric acid to the reaction mixture obtained in the same reaction condition as above, was 95%, m.p. of the picrate 190.5-192°.

Anal. Found: C, 46.5; H, 4.18; N, 13.0; MeO, 7.32. Calcd. for $C_{17}H_{18}O_{10}N_4$ (picrate of V): C, 46.6; H, 4.12; N, 12.8; MeO, 7.08%.

Perchlorate, m.p. 207-208°.

Anal. Found: C, 42.81; H, 5.11; N, 4.47; Cl, 11.52. Calcd. for $C_{11}H_{16}O_7ClN$ (perchlorate of V): C, 42.8; H, 5.18 N, 4.53; Cl, 11.3%.

Mannich Reaction on Vanillin with Piperidine.—Vanillin (18.3 g.), acetic acid (200 ml.), piperidine (30 ml.) and 30% formalin (30 ml.) were mixed and allowed to stand at room temperature overnight. Acetic acid was distilled off in vacuo, sulphuric acid (20 g.) diluted with water added, and the acetic acid was expelled as completely as possible. An appropriate amount of a dilute sodium hydroxide solution was added to make piperidine and the reaction product free, and the mixture was concentrated. The separated reaction product, which is contaminated by inorganic salt, was filtered, extracted with hot benzene, the benzene solution dried, and the product was crystallized from the benzene solution by adding ligroin and keeping in a refrigerator. After reprecipitation from its benzene solution by ligroin, the slightly brownish-colored 5-piperidinomethyl vanillin melted at 127–128.5°, 16.2 g.

Anal. Found: C, 67.30; H, 7.50. Calcd. for $C_{14}H_{20}O_3N$ (VI): C, 67.44; H, 7.68%.

Perchlorate, m.p. 212–213.5°C.

Anal. Found: C, 48.26; H, 5.58; N, 4.02; Cl 10.15; MeO, 9.28. Calcd. for $C_{14}H_{20}O_7NCl$ (perchlorate of VI): C, 48.2; H, 5.73; N, 4.02; Cl 10.0; MeO, 8.94%.

Picrate, m.p. 163–164°.

Anal. Found: C, 50.2; H, 4.60; N, 11.7. Calcd. for $C_{20}H_{22}O_{10}N_4$ (picrate of VI): C, 50.2; H, 4.60; N, 11.7%.

5-Dimethylaminomethyl Vanillin Methiodide.—5-Dimethylaminomethyl vanillin was shaken with methyl iodide, set aside over-night, petroleum ether added and the product was filtered. The iodide, m.p. 188–192° decomp., which was obtained nearly quantitatively, was dissolved in ethanol, which contained a little water, precipitated with ether, the m.p. being raised to 200–201° (decomp.).

Anal. Found: C, 40.97; H, 5.04; N, 3.76. Calcd. for $C_{12}H_{18}O_3NI$ (VIII): C, 41.0; H, 5.12; N, 3.99%.

Synthesis of 5-Formylvanillin from 5-Dimethylaminomethyl Vanillin.—A mixture of 5-dimethylaminomethyl vanillin (4.3 g.), hexamethylenetetramine (3.0 g.) and acetic acid (13 ml.) was boiled for five minutes, poured into water (130 ml.) and extracted repeatedly with ether. The etherial extract was shaken with dil. NaOH and the alkaline extract was acidified with dil. acid and kept in a refrigerator overnight. The separated crystal (0.8 g.), which melted at 115–118°, was filtered and recrystallized from xylol-ligroin, the m.p. being raised to 120–122° after one recrystallization

Anal. Found: C, 60.0; H, 4.35. Calcd. for $C_9H_8O_4$ (VII): C, 60.0; H, 4.4%.

5-Formylvanillin thus obtained gave 5-carboxyvanillic acid, m.p. 176–177°, by silver oxide oxidation according to Pearl[10].

Anal. Found: C, 50.66; H, 3.85. Calcd. for $C_9H_8O_6$: C, 50.9; H, 3.8%.

Mannich Reaction on Acetovanillone with Dimethylamine.—One gram of acetovanillone was dissolved in 25% dimethylamine (8 ml.), and 35% formalin (4 ml.) was added and the mixture was kept at room temperature overnight. Water was added and the picrate was precipitated by adding an alcoholic solution of picric acid. 3.3 g. of crude picrate, m.p. 166–170°, thus obtained, was recrystallized from 70% alcohol to give 2.0 g. of the pure picrate melting at 175–176°, yield 73.5%.

Anal. Found: C, 48.17; H, 4.63; N, 12.1. Calcd. or $C_{18}H_{20}O_{10}N_4$ (picrate of XI): C, 47.8; H, 4.43; N, 12.4%.

Mannich Reaction on Propioguaiacone with Dimethylamine.—Propioguaiacone (1 g.), synthesized according to Nakazawa[11], was dissolved in 25% dimethylamine (4 ml.), and 35% formalin (2 ml.) was added and the mixture was kept at room temp. overnight. Water was added and the picrate was precipitated by adding an alcoholic solution of picric acid. 3.3 g. of crude picrate, m.p. 155–157°, thus obtained, was recrystallized from 70% alcohol to give 2.2 g. of pure picrate melting at 160.5–161.5°, yield 85%.

Anal. Found: C, 49.33; H, 4.99; N, 11.8. Calcd. for $C_{19}H_{22}O_{10}N_4$ (picrate of XII): C, 49.0; H, 4.72; N, 12.0%.

Mannich Reaction on Cörulignol with Dimethylamine.—Cörulignol (XIII) (1 g.) was dissolved in 25% dimethylamine (4 ml.), and 35% formalin (2 ml.) was added and the mixture was kept at room temperature overnight. Water was added and the solution was acidified with dilute hydrochloric acid and extracted with ether. An alcoholic solution of picric acid was added in excess to the aqueous solution and the picrate, which separated as an oil was rubbed with a little amount of toluene to give 2.5 g. of crude picrate, m.p. 116–119°. 2.0 g. of the pure picrate was obtained from propyl alcohol, m.p. 120–121° yield, 74%.

Anal. Found: C, 50.7; H, 5.44; N, 12.6. Calcd. for $C_{19}H_{24}O_9N_4$ (picrate of XIV): C, 50.5; H, 5.31; N, 12.4%.

Mannich Reaction on Vanillyl Sulphonic Acid with Dimethylamine.—Barium salt of vanillyl sulphonic acid (0.5 g.) was dissolved in a mixture of 25% dimethylamine (2 ml.) and 35% formalin (1 ml.), and the mixture was kept at room temperature overnight, poured into alcohol and the precipitated barium salt was washed well with alcohol and analyzed.

Anal. Found: C, 37.40; H, 5.02; N, 3.87; S, 9.6; Ba, 20.7, Calcd. for $C_{11}H_{16}\ O_5NS\ \frac{1}{2}\ Ba$ (XVI): C, 38.55; H, 4.67; N, 4.08; S, 9.32; Ba, 19.9%.

Mannich Reaction on Divanillyl Monosulphide (XVII) with Dimethylamine.—Divanillyl monosulphide synthesized previously[12] (1.0 g.) was dissolved in a mixture of 25% dimethylamine (8 ml.) and 35% formalin (4 ml.), and kept at room temperature for four days. The solution was diluted with water, acidified with dilute hydrochloric acid and the separated starting material (0.3 g.) was recovered by filtration. Alcoholic solution of picric acid was added to the filtrate, and the picrate precipitated as an oil was washed with water and crystallized with alcohol to give 1.4 g. of pure picrate, melting at 179–180°.

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[11] K. Nakazawa, *J. Pharm. Soc. Japan*, **74**, 836 (1954).

[12] H. Mikawa, This Bulletin, **27**, 50 (1954).

0.3 g. of the melting point pure picrate was recovered from the mother liquor, total yield 1.7 g.

Anal. Found: C, 46.63; H, 4.69. Calcd. for $C_{34}H_{36}O_{18}SN_{10}$ (picrate of XVIII): C, 46.5, H, 4.35%.

Mannich Reaction on Dihydro-dehydro-diisoeugenol (XIX) with Dimethylamine.—Dihydro-dehydro-diisoeugenol (0.2 g.) was dissolved in a mixture of 25% dimethylamine (0.4 ml.), 35% formalin (0.2 ml.) and 70% alcohol (1 ml.) and kept at room temperature overnight. On adding water to the solution, white precipitate separated, and this dissolved completely when dilute hydrochloric acid was added. Perchlorate was separated by perchloric acid, which did not crystallize.

Anal. Found: C, 57.99; H, 7.14; N, 3.06. Calcd. for $C_{23}H_{31}O_4N \cdot HClO_4$ (perchlorate of XX): C, 56.9; H, 6.59; N, 2.88%.

Mannich Reaction on Syringic Acid with Dimethylamine.—Syringic acid (1.5 g.) was dissolved in a mixture of 25% dimethylamine (6 ml.) and 35% formalin (3 ml.), was kept for four days at room temperature, diluted with water (100 ml.), and acidified with 2N hydrochloric acid; then an alcoholic solution of picric acid was added. The alcohol was distilled off in vacuo, and the separated picrate was filtered and washed with water. The crude picrate (3.2 g.) was recrystallized from aqueous alcohol to give 2.0 g. of melting point pure picrate, yield 60%.

Anal. Found: C, 46.55; H, 4.56; N, 12.60. Calcd. for $C_{17}H_{20}O_{10}N_4$ (picrate of XXI): C, 46.36; H, 4.58; N, 12.72%.

Syringaldehyde from 5-Dimethylaminomethyl-1, 3-Dimethylpyrogallol (XXI).—One gram of the picrate was dissolved in 50% aqueous acetone, passed through a column of an ion exchange resin IR 400 in bicarbonate form, acetone and water were distilled off in vacuo and the free base thus obtained was dissolved in the mixture of acetic acid (1.5 ml.) and hexamethylenetetramine (0.32 g.). The mixture was heated in an oil bath (115°) for five minutes, water was added and the mixture was extracted with ether. From the ether extract 50 mg. of melting point pure syringaldehyde was obtained by sublimation, yield 13%.

Mannich Reaction on Vanillyl Alcohol with Dimethylamine.—A mixture of vanillyl alcohol (1 g.), 25% dimethylamine (12 ml.) and 35% formalin (6 ml.) was kept at room temperature overnight, diluted with water, acidified and the picrate was precipitated with an alcoholic solution of picric acid. The precipitate was washed with water and recrystallized from aqueous alcohol to give 0.9 g. of pure dipicrate, melting at 164–165°.

Anal. Found: C, 42.26; H, 4.47; N, 16.2, 16.0. Calcd. for $C_{25}H_{29}O_{16}N_8$ (picrate of XXII): C, 42.1; H, 4.16; N, 16.1%.

Mannich Reaction on Vanillyl Alcohol with Piperidine.—Vanillyl alcohol (0.5 g.) was dissolved in a mixture of piperidine (0.8 ml.), 35% formalin (1 ml.) and alcohol (2 ml.), and the solution was kept at room temperature for four days, diluted with water, and acidified with dilute hydrochloric acid; alcoholic solution of picric acid was added and concentrated in vacuo. The separated crystalline picrate was recrystallized from aqueous alcohol to give 1.0 g. of pure picrate melting at 153–154°.

Anal. Found: C, 49.60; H, 5.12; N, 11.60. Calcd. for $C_{20}H_{24}O_{10}N_4$ (picrate of XXIII): C, 50.0; H, 5.0; N, 11.65%.

Mannich Reaction on Vanillic Acid with Dimethylamine.—Vanillic acid (1.1 g.) was dissolved in a mixture of 25% dimethylamine (4 ml.) and 35% formalin (2 ml.), and kept at room temperature for six days. The solution was poured into 10 ml. of water and acidified with dil. hydrochloric acid. Alcoholic solution of picric acid was added and the alcohol was evaporated in vacuo. The separated picrate was recrystallized from aqueous alcohol, m.p. 165.5–167°. No melting point depression was observed on admixture with the picrate XXII, m.p. 164–166°, obtained from vanyllyl alcohol. Marked melting point depression was observed, however, on admixture with the picrate, m.p. 175.5–176.5°, which was obtained by Mannich reaction on vanillic acid during only one day. Yield 2.7 g.

The crude picrate obtained at the same reaction conditions but after only one day gave a picrate, m.p. 175.5–176.5°, after recrystallization from dilute alcohol. From the mother liquor 0.2 g. of the same substance was further recovered. Total 0.95 g. No other substances were obtained. (Found: C, 45.21; H, 4.48; N, 11.73%). No structural formula corresponding to these analytical values was found.

Mannich Reaction on Vanillic Acid with Piperidine.—Vanillic acid (1.1 g.) was dissolved in a mixture of piperidine (1.7 ml.), 35% formalin (2 ml.), water (3.3 ml.) and alcohol (4 ml.), and kept at room temperature overnight, poured into water and an alcoholic solution of picric acid was added. On recrystallization of the crude picrate from dilute alcohol, two different picrates having m.p. 204.5–205.5° and 209–210° were obtained. The former one, 1 g., which is comparatively sparingly soluble needles, was analyzed as follows.

Anal. Found: C, 47.5; H, 4.57; N, 14.1. Calcd. for $C_{31}H_{36}O_{16}N_8$ (picrate of XXIV): C, 47.9; H, 4.64; N, 14.4%.

The latter picrate, 1 g., which is comparatively easily soluble, showed the following analytical values, but no structural formula having these values were found

(Found: C, 43.11, 43.88, 43.72; H, 3.51, 3.49, 3.74; N, 13.65, 12.83; MeO, 4.5%).

This picrate with unknown structure disappeared when the Mannich reaction was performed four days at the same condition, picrate having the m.p. 204.5–205.5°, XXIV, being the only product obtained. Yield, 1.6 g.

Mannich Reaction on Thiolignins.—Various thiolignin preparations used in this communication are the same with those prepared in the previous communication[1]. When dimethylamine was used, 0.5 g. of lignin was dissolved almost completely in a mixture of 25% dimethylamine (4 ml.) and 35% formalin (2 ml.), and set aside at room temperature. When piperidine was used, 0.2 g. of lignin was dissolved in 2 ml. of piperidine solution (a mixture of piperidine (5 ml.), 35% formalin (6 ml.) and alcohol (12 ml.)), and the solution was kept at room temperature. After the reaction, the solution was poured into an excess of 2N hydrochloric acid, and the coagulated lignin was filtered and washed with water. The lignin was then dissolved in a little amount of acetone, poured into a dilute solution of perchloric acid and the precipitated lignin was filtered and washed with perchloric acid. The precipitate was redissolved in acetone and reprecipitated with perchloric acid in the same manner. After the lignin was washed well with perchloric acid, it was washed with water, ether-alcohol 1 : 1, ether and then with petroleumether.

Summary

Mannich reactions on many lignin model compounds revealed that 1) model compounds of type (I) give without exception Mannich base with substituent at fifth position in very high yield, 2) those of type (II) do not react, 3) carboxyl group having phenolic hydroxyl group to its para position is split off as carbon dioxide and dimethylaminomethyl group is introduced to the same position, 4) methylol group having phenolic hydroxyl group to its para position reacts with dimethylamine resulting in the formation of dimethylaminomethyl group at the same position, 5) other groups remain intact even when phenolic hydroxyl group exists in para position, and 6) no reaction occurs when the phenolic hydroxyl group is etherified.

By applying the Mannich reaction with dimethylamine on thiolignin, it has been concluded that about 25–40% of the phenolic hydroxyl group of thiolignin belongs to the simple guaiacol nucleus of type (I) having no C–C bond at its fifth position, admitting some uncertainty concerning the amount of carboxyl group having free phenolic hydroxyl group in its para position.

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