monium base gave ethyl trimesate (IX) whereas sodium ethoxide and (I) yielded ethyl 4-hydroxy-5-formylisophthalate (XIII).

4. Mechanisms are postulated for these transformations.

The Rearrangement of α,α'-Dibromoketones[1]

BY R. B. WAGNER AND JAMES A. MOORE

The conversion of an α,α'-dibromo-α-alkylketone to an unsaturated acid was first reported by Favorskii, who found that 1,3-dibromo-3-methyl-2-butanone, on treatment with alcoholic potassium hydroxide, gave β,β-dimethylacrylic acid in 60% yield.[2] This reaction has also been carried out with steroidal compounds, 17,21-dibromopregnan-3(β)-ol-20-one being converted to 17-pregnen-3(β)-ol-21-oic acid.[3]

A closely related rearrangement of α,β-dibromoketones to unsaturated esters has been observed in the pregnane series,[4] and has recently been extended to aliphatic compounds.[5] In this later work, it has been shown that α,β-dibromo-α-alkylketones, on treatment with sodium methylate, yield β,γ-unsaturated esters.

$$RCHBrC(CH_3)BrCOCH_3 \xrightarrow[\text{Ether}]{NaOCH_3}$$
$$RCH{=}C(CH_3)CH_2CO_2CH_3$$
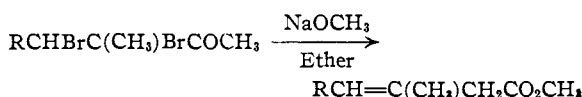
The purpose of the present work was to extend the Favorskii rearrangement beyond the first member of the series in order to test its generality, and to determine the extent and nature of secondary reactions, if any. Furthermore, an effort was made to obtain an insight into any common basis for these two similar rearrangements. Four α,α'-dibromoketones, namely, 1,3-dibromo-3-methyl-2-butanone, 1,3-dibromo-3-methyl-2-pentanone, 1-(bromoacetyl)-1-bromocyclohexane and 2,4-dibromo-2,5-dimethyl-3-hexanone have been prepared and subjected to the same basic conditions which were employed in the α,β-dibromoketone reactions. Since direct correlation of the two rearrangements was desired, three of these α,α'-dibromoketones have the same carbon skeleton as the compounds in the previously studied α,β-dibromoketone series. Thus, the two groups of compounds differ only in the position of one of the bromine atoms.

These α,α'-dibromoketones were prepared by direct bromination of the ketones (Table I). Since this method of formation is not entirely free of

complications, one of the dibromoketones was prepared by the following series of reactions, which leaves little doubt as to the structure of the product.
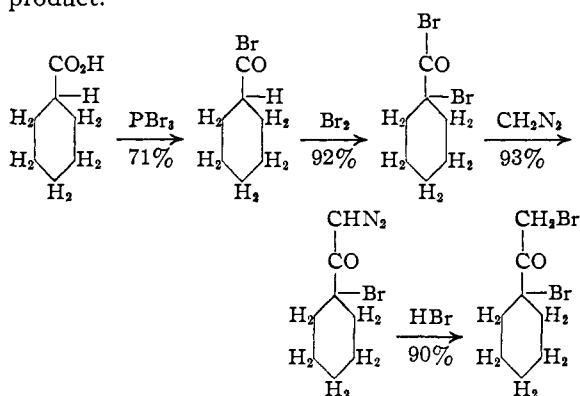
The compounds prepared by the two methods were identical in all respects, and this indicates that the direct dibromination proceeds as expected, viz.: $RR'CHCOCH_3 \xrightarrow{2Br_2} RR'CBr\text{-}COCH_2Br$.

The products formed when these dibromoketones were treated with sodium methylate in anhydrous ether, in every case, consisted solely of the methyl ester of an α,β-unsaturated acid. The nature of these esters and their properties are indicated in Table II. In all these reactions, heavy resins remained after the isolation of the methyl esters.

Comparing the results of these reactions with those from the α,β-dibromoketone series, it is seen that the esters obtained from either type of ketone possess the same carbon skeleton. In every case, however, α,α'-dibromoketones give rise to α,β-unsaturated esters, and α,β-dibromoketones to esters with β,γ-unsaturation. One further difference in the two rearrangements which might be noted is the fact that both geometrical isomers of 3-methyl-2-pentenoic ester were obtained in the present work, whereas only one of the isomers of the 3-methyl-3-pentenoic acid was obtained from the corresponding α,β-dibromoketone. That the reaction actually involves a carbon skeleton rearrangement at least in the case of. α,α'-dibromoketones is indicated by the formation of the isopropylideneacetic ester from dibromoisopropylisobutyl ketone.

(1) Presented at the Organic Division of the St. Louis Meeting of the American Chemical Society, September 6, 1948.
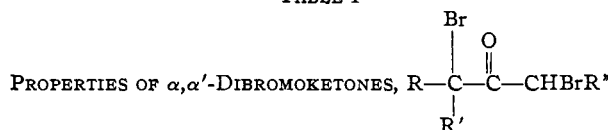
(2) Favorskii. J. prakt. Chem., [2] 88, 658 (1913).

(3) Marker. Crooks and Wagner. THIS JOURNAL. 64, 213, 817 (1942).

(4) Marker. Wagner and Wittbecker. ibid., 64, 2093 (1942).

(5) Wagner, ibid.. 71, 3214 (1949).

TABLE I

PROPERTIES OF α,α'-DIBROMOKETONES, $\overset{\displaystyle Br}{\underset{\displaystyle R'}{R-C-}}\overset{\displaystyle O}{\underset{}{C}}-CHBrR''$

R	Ketone R'	R″	Molecular formula	B. p. °C.	Mm.	M. p. °C.	$n^{20}D$	d^{20}	MD Calcd.	MD Obs.	Br Calcd.	Br (Stepan-off), % Found
CH₃	CH₃	H	C₅H₈OBr₂ᵃ	111	15	10–12	1.5178	1.812	40.9	39.8	65.7	66.0
CH₃	C₂H₅	H	C₆H₁₀OBr₂	57	1	...	1.5155	1.722	45.5	45.2	62.0	61.6
Cyclohexyl		H	C₈H₁₂OBr₂	...	..	19–20	1.5461	1.720	52.5	52.3	57.2	56.3
CH₃	CH₃	(CH₃)₂CH	C₆H₁₄OBr₂ᵇ	41	1	...	1.5002	1.530	54.7	55.0	55.9	55.4

ᵃ Reported[2] for 1,3-dibromo-3-methyl-2-butanone: b. p. 99° (18 mm.), m. p. 10°. ᵇ This compound was generously furnished by Mr. J. D. Newkirk.

TABLE II

PRODUCTS OBTAINED FROM REACTION: $RR'CBrCOCHBrR'' \xrightarrow{\text{NaOCH}_3} RR'C{=}CR''CO_2CH_3$

R	R'	R″	Yield, %	B. p. °C.	Mm.	$n^{20}D$	d^{20}	MD calcd.ᵃ	MD obs.
CH₃	CH₃	H	58	60	50ᵇ	1.4382	0.9424	31.10	31.80
CH₃	CH₂CH₂	H	29 cis	74	50	1.4420	0.9279	35.72	36.55
			22 trans	79	50	1.4446	0.9302	35.72	36.65
Cyclohexyl		H	46	78	5	1.4838ᶜ	1.003	42.76	43.97
CH₃	CH₃	CH(CH₃)₂	84	48	5	1.4389	0.9054	44.96	45.44

ᵃ No increment for exaltation due to conjugated system was used. ᵇ Reported[5] for methyl β,β-dimethylacrylate: b. p. 60° (50 mm.), $n^{20}D$ 1.4378, d^{20} 0.9425. ᶜ Auwers and Ellinger, Ann., 387, 200 (1912), report for methyl cyclohexylideneacetate: $n^{20}D$ 1.4829, d^{20} 0.999, MD 44.03.

Experimental[6]

Starting Materials.—(a) Methyl isopropyl ketone was prepared in 68% yield by the hydrolysis of trimethylethylene dibromide.[7]

(b) Methyl s-butyl ketone was prepared by adding a solution of 231 g. (0.79 mole) of potassium dichromate and 676 g. of sulfuric acid in 2.2 l. of water to a mixture of 231 g. of potassium dichromate in 1.7 l. of water and 480 g. (4.7 moles) of crude methyl s-butylcarbinol. The addition was carried out with stirring over a two-hour period with the temperature at 20–25°. After stirring for fifteen hours the reaction mixture was steam-distilled and 444 g. of organic material was obtained. After fractionation in a 1.8 × 53 cm. column with ³/₃₂ in. helices, 380 g. of methyl s-butyl ketone was obtained, b. p. 116.5° (734 mm.), $n^{20}D$ 1.4002, representing a yield of 81%.

(c) Methyl cyclohexyl ketone was prepared by the oxidation of methylcyclohexylcarbinol in the manner described above. After fractionation, methyl cyclohexyl ketone, b. p. 67° (12 mm.), $n^{20}D$ 1.4514, was obtained in a yield of 85%.

(d) Cyclohexanecarboxylic acid was prepared by carbonation of cyclohexylmagnesium chloride.[8] A yield of 82.5% was obtained in a 5-mole reaction; the fractionated acid had m. p. 29–30°, b. p. 131° (20 mm.).

Preparation of Dibromoketones.—The ketone was placed in a three-necked flask equipped with a sealed stirrer, dropping funnel and gas outlet tube, and cooled in a salt-ice mixture. To the ketone, at a temperature of −5 to 5°, was added the theoretical quantity of bromine, dropwise over a two to three hour period. In most of the reactions, the quantity of ketone was one or two moles. After addition of the bromine was complete, a stream of nitrogen or carbon dioxide was passed through the reaction mixture until all of the hydrogen bromide was swept out.

In all except one case, the crude dibromoketones were distilled rapidly in Claisen flask, and the distillate then

(6) All melting points and boiling points are uncorrected.

(7) Whitmore, Evers and Rothrock, Org. Syntheses, Coll. Vol. II, 408 (1943).

(8) Gilman and Kirby, ibid., Coll. Vol. I, 364 (1941).

fractionated in a 1.8 × 65 cm. column packed with ¹/₄ in. helices. The dibromoethyl cyclohexyl ketone could not be distilled, even at a pressure of 4 mm., but the crude material crystallized on standing at 0°, and was then purified by washing with cold pentane. The physical properties of these compounds are summarized in Table I.

Synthesis of 1-(Bromoacetyl)-1-bromocyclohexane via the α-Bromocyclohexyl Diazomethyl Ketone.—(a) Cyclohexanecarbonyl Bromide.—Cyclohexanecarboxylic acid (4 moles) was treated with phosphorus tribromide (1.33 moles) and allowed to warm to 30° and stand for forty-two hours. The upper layer of acid bromide was decanted into a Claisen flask and rapidly distilled. The main fraction of this distillate was then fractionated in a 1.8 × 65 cm. column packed with 0.25 in. helices, and 530 g. of material was obtained, b. p. 111° (40 mm.), $n^{20}D$ 1.5012, in a yield of 69%.

Anal. Calcd. for C₇H₁₁OBr: neut. eq., 191. Found: neut. eq., 189.2.

(b) α-Bromocyclohexanecarbonyl Bromide.—In a 1-l. three-necked flask, equipped with a sealed stirrer, dropping funnel and condenser, was placed 382 g. (2 moles) of cyclohexanecarbonyl bromide and 3 g. of red phosphorus. Bromine, 440 g. (2.75 moles), was added dropwise over a four-hour period. The reaction was heated and illuminated by two 200-watt incandescent bulbs; the bromine refluxed steadily. After an additional sixteen-hour period of stirring and illumination, excess bromine and hydrogen bromide were removed from the reaction mixture by a stream of nitrogen, and the residue was then fractionated in a 1.8 × 65 cm. column packed with 0.25 in. helices. The bromoacid bromide obtained amounted to 502 g. (93% yield), b. p. 125° (20 mm.), $n^{20}D$ 1.5429.

Anal. Calcd. for C₇H₁₀OBr₂: Br, 59.2. Found: Br (Stepanoff), 59.9.

A small portion of this compound was allowed to stand for five days with cold water. The heavy oil crystallized after this time, and the material was filtered and dried, m. p. 56–59°. The melting point of α-bromocyclohexanecarboxylic acid is reported to be 61°.[9]

(9) v. Braun, Ber., 67B, 218 (1934).

(c) **α-Bromocyclohexyl Diazomethyl Ketone.**—To a vigorously stirred solution of 0.29 mole of diazomethane in 410 cc. of ether was added 31.8 g. (0.118 mole) of α-bromo-cyclohexanecarbonyl bromide in 50 ml. of anhydrous ether. The temperature was kept below 0° by means of a salt-ice-bath. After standing at 0° for fifteen hours, the ether and excess diazomethane were evaporated *in vacuo*, and the residual yellow oil was clarified by filtration through Celite. This material crystallized completely on standing at 0°, and the diazoketone was purified by partially melting, filtering and washing with pentane. Three crops of golden needles obtained in this way amounted to 21 g. (93% yield), m. p. 13–16°, n^{20}D 1.56.

Anal. Calcd. for $C_8H_{11}OBrN_2$: N, 12.56. Found: N, 12.35.

(d) **1-(Bromoacetyl)-1-bromocyclohexane.**—To a solution of 3 g. of the α-bromocyclohexyl diazomethyl ketone in 10 cc. of absolute ether was added 18 cc. of 0.75 N ethereal hydrogen bromide. After gas evolution had ceased, the ether was evaporated, and the residue was allowed to stand in the ice-box until crystallization occurred. This material, after trituration with cold pentane, was filtered and dried, m. p. 19–20°, n^{20}D 1.5460.

In order to obtain a direct comparison of this dibromo ketone with the product obtained from the direct bromination of methyl cyclohexyl ketone, a sample of each was converted to the pyridinium salt. The dibromoketone, 0.3 g., was dissolved in 2.5 cc. of anhydrous pyridine and the solution was allowed to stand at room temperature. In twenty minutes, white crystals began to separate from the reaction mixture. This salt was filtered and washed with ether until free of pyridine; m. p. and mixed m. p. 114–117°.

Anal. Calcd. for $C_{13}H_{17}ONBr_2$: Br, 44.0. Found: Br (Stepanoff), 44.0.

Reaction of Dibromoketones with Sodium Methylate.—Preliminary experiments indicated that the amount of resinous product was decreased and the yield of ester somewhat improved when the sodium methylate was added to the dibromoketone rather than the more conventional reverse manner. A standard procedure was used in all of these reactions.

A 2-l. three-necked flask was equipped with a mercury-sealed stirrer, thermometer and a 5-l. separatory funnel. The funnel was equipped with a mercury-sealed stirrer and a wide-bore stopcock. A solution of 1 mole of the dibromoketone in 250 cc. of absolute ether was placed in the flask and cooled with a salt-ice bath. In the separatory funnel was placed 111.5 g. (2 moles) of sodium methylate (95% assay, from Mathieson Alkali Works) suspended in 500 cc. of ether. The slurry of sodium methylate was added in small portions over a 4-hour period, with the reaction temperature at 0–5°. After stirring for an additional thirty minutes, an aliquot of the reaction mixture was titrated with standard acid and it was found that less than 4% of the sodium methylate remained. The reaction mixture was processed immediately as previously described.[5] Further data on these reactions are summarized in Table II.

Identification of Unsaturated Esters.[10] (a) **Methyl β,β-Dimethylacrylate.**—In addition to comparison of physical properties with literature values, a sample of the ester was converted to the anilide of dimethylacrylic acid, m. p. and mixed 130–131°.

(b) **Methyl 3-Methyl-2-pentenoate—Low Boiling Isomer (cis).**—Saponification of the ester yielded methanol, identified as the 3,5-dinitrobenzoate, m. p. and mixed m. p. 106–107°. The acid obtained from the saponification was crystallized from ether, m. p. 22–24°. As discussed below, an authentic sample of this acid for comparison could not be obtained. A sample of the ester was oxidized with hot neutral permanganate, and steam distillation of the mixture yielded methyl ethyl ketone,

identified as the 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 112–114°. The ester was recovered unchanged from an attempted ozonolysis.

The *p*-toluide prepared from this ester was obtained as white needles from ethyl acetate, m. p. 78–79°.

Anal. Calcd. for $C_{13}H_{17}ON$: N, 6.89. Found: N, 6.90.

An amide was obtained as glistening plates from benzene-pentane, m. p. 81–82°.

Anal. Calcd. for $C_6H_{11}ON$: N, 12.38. Found: N, 12.13.

(c) **High Boiling Isomer (trans).**—This ester upon saponification yielded methanol and an acid which crystallized from aqueous methanol as needles, m. p. and mixed m. p. with an authentic sample of *trans*-3-methyl-2-pentenoic acid 46–47°. Methyl ethyl ketone was obtained from the oxidation of this ester, and characterized in the manner stated above.

The *p*-toluide was obtained as needles from ethyl acetate, m. p. and mixed m. p. with the *p*-toluide of *trans*-3-methyl-2-pentenoic acid 77.5–78.5°.

Anal. Calcd. for $C_{13}H_{17}ON$: N, 6.89. Found: N, 6.85.

The amide which was prepared from the acid crystallized as white plates from benzene-pentane, m. p. and mixed m. p. with the amide of *trans*-3-methyl-2-pentenoic acid 97–98°.

Anal. Calcd. for $C_6H_{11}ON$: N, 12.38. Found: N, 12.22.

A mixed m. p. of this amide with that from the low-boiling ester was 64–66°, or a depression of 18°. The amides of *cis*- and *trans*-3-methyl-2-pentenoic acid have been reported to have m. p. 116° and 99°, respectively.[11] These derivatives were obtained by partial hydrolysis of the isomeric nitriles. Since the melting point of the "cis" amide from this work does not agree with the recorded value, both of the amides obtained from the rearrangement products were subjected to neutral permanganate oxidation, and both yielded methyl ethyl ketone, identified in the usual way. It is thus established that no structural changes occurred during saponification, conversion to the acid chloride or ammonolysis.

(d) **Methyl Cyclohexylideneacetate.**—The physical properties are in good agreement with values reported in the literature. A sample of the ester was saponified to give methyl alcohol and an acid, m. p. and mixed m. p. with cyclohexylideneacetic acid 89–91°.

(e) **Methyl Isopropylisopropylideneacetate.**—A small portion of the ester was saponified and methanol was identified. In order to characterize the acid fraction, 0.1 mole of the ester was refluxed with 6 g. of sodium hydroxide in aqueous alcohol for eight hours. After removing the alcohol and acidifying the solution, a solid acid was obtained which was recrystallized from aqueous methanol to yield long white needles, m. p. 61–63°.

Anal. Calcd. for $C_8H_{14}O$: neut. eq., 142. Found: neut. eq., 144.7.

For oxidation, a sample of the ester was treated with magnesium permanganate, and steam distillation yielded acetone, identified as the 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 124–125°.

A *p*-toluide prepared from this ester was obtained as white needles from aqueous methanol, m. p. 145–146°.

Anal. Calcd. for $C_{15}H_{21}ON$: C, 77.88; H, 9.15. Found: C, 77.86; H, 9.50.

In order to convert the unsaturated ester to diisopropylacetic acid for comparison, 15.6 g. (0.1 mole) of the ester in 150 cc. of ether containing one drop of hydrochloric acid was shaken for fifteen hours with 15 g. of 5% palladium-barium sulfate catalyst in a hydrogen atmosphere at 45 pounds pressure. The theoretical quantity of hydrogen was absorbed. (Attempted reductions using platinum oxide and Raney nickel catalysts were unsuccessful.) After removing the solvent, the hydrogenation product

(10) All derivatives were prepared according to the procedures described by Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 3rd ed., 1948.

(11) Bruylants, *Bull. sci. acad. roy. Belg.*, **17**, 1008 (1931).

was distilled in an 8-in. helix-packed column. The product had the following physical properties: b. p. 40–41° (5 mm.), n^{20}D 1.4153, d^{20} 0.8786, MD$_{obs}$. 45.21 (MD$_{calcd}$. 45.43).

This ester yielded an anilide which crystallized from aqueous methanol as long white needles, m. p. and mixed m. p. with diisopropylacetanilide[12] 147–148°.

Anal. Calcd. for $C_{14}H_{19}ON$: N, 6.44. Found: N, 6.64.

Preparation of Isomeric 3-Methyl-2-pentenoic Acids by Method of Kon and Linstead.—Both geometrical isomers of 3-methyl-2-pentenoic acid have been reported[13] and in order to obtain authentic samples of these acids, the preparation from 3-methyl-3-hydroxypentanoic acid was repeated. The unsaturated acids obtained by dehydration with anhydrous hydrogen chloride were partially esterified to remove the β,γ-isomers,[14] and the mixed α,β-acids were obtained.

After redistilling the 3-methyl-2-pentenoic acids, the *cis* and *trans* isomers were separated by fractional crystallization. Four crops of solid were removed from the mixture at successively lower temperatures, and this material proved to be the *trans* isomer, m. p. 46–48°. After long standing, the mother liquor deposited a solid acid, m. p. 13–14°, n^{20}D 1.4651, d^{20} 0.9851. These values are all in excellent agreement with those reported by the previous workers for these acids.[13]

(12) The diisopropylacetanilide used for comparison was prepared by Mr. A. Sacks (dec.) from diisopropyl cyanoacetate.

(13) Kon, Linstead and Wright, *J. Chem. Soc.*, 602 (1934), report for the *trans* acid, m. p. 48–49°; for the *cis* acid, m. p. 12°, n^{20}D 1.4650, d^{20} 0.9830.

(14) The *cis*- and *trans*-3-methyl-3-pentenoic esters were obtained from this fraction in the prescribed manner (for details see ref. (5)).

Both of these acids were converted to the *p-toluides*. The *trans* acid yielded a very clean derivative, which was readily crystallized to a constant m. p. of 78°. The *cis* acid was converted to a *p*-toluide by two methods. In the first method the acid chloride was prepared using thionyl chloride, and the resulting material was treated with *p*-toluidine. In the second procedure, the acid was converted to the methyl ester by means of diazomethane, and the ester was treated with *p*-toluido-magnesium bromide. From both of these reactions a product was obtained which after repeated crystallizations from different solvents had m. p. 61–63°. It is to be noted that this value corresponds with the melting point of the mixed *p*-toluides obtained from the rearrangement products of dibromomethyl s-butyl ketone. Thus the *cis* acid and its *p*-toluide melt considerably lower than the corresponding products from the rearrangement and are evidently contaminated with the *trans* isomer.

Summary

1. The Favorskii rearrangement has been applied to four α,α'-dibromo-α-alkyl ketones, and has been found to be a general reaction.

2. Under identical rearrangement conditions, α,α'-dibromoketones yield α,β-unsaturated esters, whereas α,β-dibromoketones yield β,γ-unsaturated esters.

3. The geometrical isomers of 3-methyl-2-pentenoic acid have been definitely characterized, and their properties and derivatives are described.

Investigations on Lignin and Lignification. I. Studies on Softwood Lignin[1]

BY WALTER J. SCHUBERT AND F. F. NORD

Much of the difficulty involved in determining the constitution of lignin can be attributed to the fact that, until relatively recent times, no method was known by which lignin could be isolated in an unchanged form. Whatever procedure was employed, a preparation was obtained which was no longer identical with lignin as it exists in nature.[1a]

The solution to the problem of isolating lignin in a chemically unchanged form therefore requires an approach that avoids high temperatures and employs neutral, chemically inert solvents.[2] Brauns' extraction of Native Lignin from black spruce,[3a] western hemlock[3b] and aspen[3c] with 95% ethyl alcohol at room temperature seems to have met these requirements. However, the failure

(1) Presented at the Wood Symposium of the National Research Council and the Office of Naval Research, Washington, D. C., June, 1949, and before the Division of Cellulose Chemistry of the Am. Chem. Soc., Atlantic City, N. J., September, 1949.

(1a) M. Phillips, in Wise's "Wood Chemistry," Reinhold Publishing Corp., New York, N. Y., 1944, p. 272.

(2) W. J. Wald, P. F. Ritchie and C. B. Purves, THIS JOURNAL, **69**, 1371 (1947).

(3) (a) F. E. Brauns, *ibid.*, **61**, 2120 (1939); (b) F. E. Brauns, *J. Org. Chem.*, **10**, 211 (1945); (c) M. A. Buchanan, F. E. Brauns and R. L. Leaf, Jr., THIS JOURNAL, **71**, 1297 (1949).

of approximately 97% of the lignin present to be so extracted[3a] suggests that either this native lignin is not identical with the bulk of the lignin of the wood, or that the residual lignin is associated (either chemically or physically) with the cellulose of wood.

Prior to Brauns' isolation of native lignin, however, a preparation very similar in character to his lignin was obtained by extraction with ethyl alcohol of Norwegian spruce wood which had been rotted by the "dry rot," *Merulius lacrymans*.[4] Thus, these two findings suggested the possibility of utilizing cellulolytic enzyme systems as a convenient method for obtaining larger amounts of native lignin from wood.[5]

It is generally assumed that there are two different types of wood decay brought about by fungi, namely, the "brown" and the "white" rots. In the former, preferential attack is made on the carbohydrate components of the wood, and the lignin remains unaffected, with the decaying residue turning brown in color. In the second type,

(4) E. C. Barton-Wright and J. G. Boswell, *Biochem. J.*, **25**, 494 (1931).

(5) F. F. Nord and J. C. Vitucci, *Adv. in Enzymol.*, **8**, 253 (1948).