the above electrolysis the two products were separated by column chromatography and their identities were confirmed by comparison of their infrared spectra with those of authentic samples.

Electrolysis of Propionic and Acetic Acids.—A mixture of propionic acid (6.8 g.), acetic acid (20 g.), and sodium acetate (2.1 g.) was electrolyzed as above (0.3 amp.) for a period of 6 hr. All material boiling below 120° was distilled directly from the reaction mixture, and the distillate was examined by gas chromatography using three different column packings. Peak enhancement, using authentic ethyl acetate, confirmed the presence of this ester, which was calculated to have been formed in about 13% yield from the propionic acid precursor.

Electrolysis of 2,3,3-Triphenylpropanoic Acid. A. In Methanol.—2,3,3-Triphenylpropanoic acid[2] (685 mg.) in methanol (20 ml.) containing sodium (26 mg.) was electrolyzed as above for a period of 17 min., after which the crude product was recovered by solvent evaporation. The residue was dissolved in ether, and the solution was extracted with dilute aqueous sodium hydroxide. Ether extraction of the acidified aqueous layer afforded 290 mg. of unchanged acid. Evaporation of the original ether layer yielded 351 mg. of crude product. This was chromatographed on acid-washed alumina (grade III, benzene–hexane eluent) to provide 172 mg. of white solid, m.p. 67.5–68°, after recrystallization from dilute methanol. The sample gave no mixture melting point depression, and displayed an infrared spectrum identical with that of authentic methyl 1,2,2-triphenylethyl ether. The latter sample, m.p. 66.5–68°, was prepared by the methylation of 1,2,2-triphenylethanol, as described before,[28] using methyl iodide and silver oxide.

Anal. Calcd. for $C_{21}H_{20}O$: C, 87.46; H, 6.99. Found: C, 86.82; H, 6.87.

B. In Acetic Acid.—A mixture of 2,3,3-triphenylpropanoic acid (450 mg.) and sodium acetate (200 mg.) in acetic acid (20 ml.) was electrolyzed as described above (8 f./mole). The mixture was evaporated to dryness, dissolved in ether and extracted with ammonium hydroxide solution (discard). Evaporation of the ether solvent yielded 370 mg. of crude product which was chromatographed on acid-washed alumina (grade III, benzene–hexane eluent), affording 260 mg. of white solid. This was recrystallized from ethanol, m.p. 147–149°. The product showed no mixture melting point depression and had an infrared spectrum superimposible on that of authentic 1,2,2-triphenylethyl acetate, m.p. 155–156°.[29]

(29) W. A. Bonner and C. J. Collins, *J. Am. Chem. Soc.*, **75**, 5372 (1953).

Wheat Bran Phenols[1]

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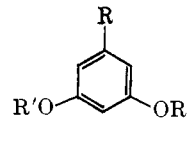
A mixture of 5-*n*-alkylresorcinols is found to be present in the nonsaponifiable fraction of wheat bran. The structures of two phenols are shown to be 5-*n*-nonadecylresorcinol and 5-*n*-heneicosylresorcinol by analysis and synthesis.

While much effort has been expended in the past on investigations of the chemical constitution of wheat, only little is known about the composition of the nonsaponifiable portion of wheat bran.[2] On undertaking an investigation of the latter and initially carrying out alumina chromatography, we encountered the presence of hydrocarbons, steroids, and a phenolic material. The unusual presence of a phenolic constituent, designated at first as substance A, in the nonsaponifiable fraction of a plant extract aroused our attention and led to a structure analysis which constitutes the major portion of this communication.

Early elemental analyses of crystalline substance A, m.p. 84–85°, pointed to a $C_{13}H_{24}O$ formula. Its infrared spectrum showed hydroxyl and aromatic absorption bands and its ultraviolet spectrum was characteristic of a phenolic compound. Its phenolic character was confirmed by the preparation of a crystalline methyl ether and acetate. The infrared spectrum of the ester revealed no hydroxyl peaks and only a 5.65-μ band in the carbonyl region. Inspection of the n.m.r. spectra of substance A and its two derivatives indicated the presence of aromatic hydrogens. The ratio (2:1) of the intensities of the O-methyl signal *vs.* the aromatic hydrogen signal in the methyl ether as well as the same ratio of the acetyl methyl signal *vs.* the aromatic hydrogen signal in the ester showed that A was a monoalkylated dihydric phenol of a $C_{26}H_{48}O$ formula. A positive mercuric nitrate test[3] suggested it was an alkylresorcinol. An n.m.r. analysis of the six dimethoxytoluenes (*vide infra*) and comparison of their spectra with the spectrum of the dimethyl ether of substance A established that A was a 5-alkylresorcinol.

The resistance of A to hydrogenation over palladium–charcoal and the absence of olefinic hydrogen signals in its n.m.r. spectrum indicated that the alkyl side chain was saturated. The n.m.r. signal of the side chain was composed of a benzylic two-proton multiplet at 2.33–2.75 p.p.m. (deuterioacetone solution with an internal tetramethylsilane standard), a broad methylene *ca.* 36-proton singlet at 1.32 p.p.m., and a methyl three-proton multiplet at 0.82–1.05 p.p.m. Thus substance A appeared to be 5-*n*-eicosylresorcinol (Ia).



Ia, R = $(CH_2)_{19}CH_3$; R′ = H
b, R = $(CH_2)_{18}CH_3$; R′ = Me
c, R = $(CH_2)_{20}CH_3$; R′ = Me
d, R = $(CH_2)_{18}CH_3$; R′ = H
e, R = $(CH_2)_{20}CH_3$; R′ = H
f, R = $(CH_2)_{16}CH_3$; R′ = Me
g, R = $(CH_2)_{22}CH_3$; R′ = Me
h, R = $(CH_2)_{24}CH_3$; R′ = Me

In view of the fact that all previously reported naturally occurring *n*-alkylphenols have been shown to possess side chains containing odd numbers of carbon atoms in agreement with biosynthetic arguments (*vide infra*), the structure Ia was anomalous. The first indication of the heterogeneity of substance A was the wide melting ranges of its diacetate and dimethyl ether. As a consequence the vapor phase chromato-

(1) This work was carried out under contracts with the U. S. Department of Agriculture and authorized by the Research and Marketing Act. The contracts were supervised by the Northern Utilization Research Branch and the Western Utilization Research and Development Division of the Agricultural Research Service.

(2) M. T. Ellis, *Biochem. J.*, **12**, 160 (1918); R. J. Anderson and F. P. Nabenhauer, *J. Am. Chem. Soc.*, **46**, 1717 (1924); M. Gažo and V. Špringer, *Pol'nohospodárstvo*, **7**, 807 (1960); *Chem. Abstr.*, **55**, 8694*b* (1961).

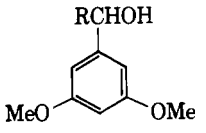
(3) A. Butenandt and F. H. Stodola, *Ann.*, **539**, 40 (1939).

TABLE I
CHEMICAL SHIFTS
(in parts per million, singlets unless otherwise noted)

Methoxy substitution	Aldehydes: Aromatic hydrogens	Aldehydes: Methoxy hydrogens	Aldehydes: Aldehyde hydrogens	Toluenes: Aromatic hydrogens	Toluenes: Methoxy hydrogens	Toluenes: Methyl hydrogens
2,3	7.05–7.50 multiplet	3.90, 3.98	10.40	6.58–7.05 multiplet	3.77, 3.80	2.26
2,4	6.35–6.58, 7.62–7.80 multiplets	3.83, 3.86	10.20	6.22–6.43, 6.83–7.08 multiplets	3.73, 3.75	2.14
2,5	6.80–7.35 multiplet	3.78, 3.87	10.47	6.68 broad singlet	3.72, 3.75	2.21
2,6	6.47–6.65, 7.28–7.58 multiplets	3.87, 3.87	10.47	6.35–6.53, 6.88–7.21 multiplets	3.77, 3.77	2.11
3,4	6.84–7.02, 7.32–7.52 multiplets	3.91, 3.94	9.80	6.69 broad singlet	3.79, 3.81	2.27
3,5	6.62–6.72, 6.92–7.02 multiplets	3.83, 3.83	9.87	6.37 broad singlet	3.77, 3.77	2.30

graphic behavior of the ether was investigated. It revealed the presence of five constituents of which the two with longest retention times and the one with the shortest were decidedly minor components. The presence of two major constituents (82% of the total), the previous analyses of substance A, and biosynthetic speculations made the possibility of these two chromatographic fractions representing resorcinol dimethyl ethers with C_{19} and C_{21} side chains (Ib and Ic, respectively) an attractive working hypothesis. Therefore, the synthesis of these compounds was undertaken.

Treatment of 3,5-dimethoxybenzaldehyde with *n*-octadecylmagnesium bromide as well as with *n*-eicosylmagnesium bromide led to the carbinols IIa and IIb, respectively, whose hydrogenolysis over palladium–charcoal yielded Ib and Ic, respectively. Conversion of Ib and Ic to their respective resorcinols, Id and Ie, was accomplished by heating in refluxing pyridine hydrochloride.



IIa, R = $(CH_2)_{17}CH_3$
b, R = $(CH_2)_{19}CH_3$

The two major components of the v.p.c. fractionation of A-dimethyl ether were isolated. The one with the shorter retention time proved to be identical in all respects with Ib and the one with the longer retention time was shown to be Ic. Repeated crystallization of A-dimethyl ether also afforded Ic. The three minor components of the vapor phase chromatogram were isolated in moderate states of purity but in exceedingly low yields. Their ultraviolet spectra were identical with those of Ib and Ic. A plot of retention times of the chromatographic fractions *vs.* homologous molecular formulas suggested that the three minor constituents possessed C_{17}, C_{23}, and C_{25} side chains (If, Ig, and Ih, respectively). Unfortunately insufficient quantities of these compounds prevented a rigorous proof of their structure.

As already indicated above, the structure analysis of the wheat bran phenols required an inspection of the n.m.r. spectra of dimethoxytoluene model compounds. Table I lists the n.m.r. signals of all six toluenes and the dimethoxybenzaldehydes from which the toluenes were derived. While the chemical shift (3.72–3.81 p.p.m.) of the methoxy hydrogens in the toluenes appears to be essentially independent of their position in the aromatic nucleus, the chemical shift of the methyl hydrogens varies with their relationship to the methoxy groups. Substitution in the *ortho* and *para* position leads to as much as a 0.2-p.p.m. upfield shift of the methyl hydrogen signal with respect to *meta* substitution. In the aldehyde series *ortho* substitution moves the aldehyde hydrogen signal 0.4–0.5 p.p.m. downfield, while *para* substitution shifts it 0.1–0.2 p.p.m. upfield.

The wheat bran phenols now take their place alongside a growing group of naturally occurring phenols of polyacetate biosynthetic origin[4] containing *meta*-oriented, long, unbranched, odd-numbered, and sometimes unsaturated carbon chains. Their closest structural relatives are the 5-*n*-alkylresorcinols of the Anacardium, Ginkgo, and Grevillea species.[5]

Experimental[6]

Nonsaponifiable Portion of Wheat Bran.—Wheat bran (22.7 kg.) was extracted in a Soxhlet apparatus with hexane for 24 hr.

(4) A. J. Birch and F. W. Donovan, *Australian J. Chem.*, **6**, 360 (1953), and references cited therein. In a letter of July 3, 1945 to Professor Roger Adams, Professor Marvin Carmack pointed to the Collie hypothesis as a possible route of biosynthesis of the natural 5-*n*-alkylresorcinols found among the depsides, in cashew nut oil, and as part of the skeleta of the marihuana principles. While these comments appear to represent the first modern expression of the polyacetate biosynthesis of certain phenolic natural products, they were never published.

(5) S. Furukawa, *Sci. Papers Inst. Phys. Chem. Res.* (Tokyo), **26**, 178 (1935); H. J. Backer and N. H. Haack, *Rec. trav. chim.*, **60**, 661 (1941); W. F. Symes and C. R. Dawson, *Nature*, **171**, 841 (1953); J. L. Occolowitz and A. S. Wright, *Australian J. Chem.*, **15**, 858 (1962).

(6) Melting points were determined on a Kofler hot stage and are uncorrected. Ultraviolet spectra were determined for ethanol solutions using a Cary recording spectrophotometer Model 14. Infrared spectra were measured using a Perkin-Elmer Infracord spectrophotometer Model 137 and, unless otherwise stated, were for Nujol mulls. N.m.r. spectra were obtained using a Varian A-60 spectrometer; the positions of the peaks were measured relative to tetramethylsilane as the internal reference; unless otherwise stated the solvent was deuteriochloroform. Gas phase chromatography (g.p.c.) was carried out using a F & M Model 500 programmed temperature gas chromatograph; all gas chromatograms were obtained using a 2-ft. column of 5% silicone gum rubber on Chromasorb P, with a carrier gas (helium) flow rate of 135 ml. per min. Thin layer chromatography (t.l.c.) was conducted using silica as the absorbant, 95:5 chloroform–ethyl acetate as the developing solvent, and iodine as the visualizing agent; R_f values reported are only reproducible to ±0.05. Optical rotations were determined using a Rudolph polarimeter Model 80. Microanalyses were preformed by Dr. A. Bernhardt, Mulheim, Germany. Wheat bran was supplied by Pillsbury Mills, Inc., Minneapolis 14, Minn. Unless otherwise stated, alumina was 80–200 mesh, as supplied by the Chicago Apparatus Co. Solvents were removed *in vacuo* on the steam bath.

The solvent was eliminated from the extract leaving a dark oil (785 g.). This oil was added to a mixture of 50% aqueous potassium hydroxide solution (1.5 l.) and 5% ethanolic pyrogallol (3.0 l.), and the mixture was boiled under reflux for 90 min. The cooled solution was diluted with water (27 l.), and extracted continuously with ether for 4 days. The ether extract (6 l.) was washed with two 1-l. portions of water and brine (1 l.), then dried over sodium sulfate. The solvent was removed from this dried extract, leaving a brown solid (87.0 g., 0.38% of wheat bran).

Chromatography of the Nonsaponifiable Portion of Wheat Bran.—The nonsaponifiable portion of wheat bran (87.0 g.) was chromatographed over a column of alumina (4.8 kg., 180 × 10 cm.), and five main fractions were obtained. Hexane eluted a colorless semisolid (2.7 g., 3.1%), the hydrocarbon fraction; 1:1 hexane–benzene eluted a yellow oil (4.0 g., 4.6%), the middle fraction; benzene eluted a colorless crystalline solid, m.p. 128–138° (13.1 g., 15.0%), the steroid fraction; 1:1 benzene–ether eluted a colorless crystalline solid, m.p. 81–84° (9.6 g., 11.0%), substance A; ether eluted a yellow oil (27.6 g., 31.6%), the end fraction.

Chromatography of the Hydrocarbon Fraction.—A portion of the hydrocarbon fraction (100 mg.) was chromatographed over a column of alumina (200 g., 30 × 5 cm.), and successive fractions (100 ml.) of eluate were examined. Fractions 8–15 (hexane) contained a colorless semisolid (total, 92 mg.) which could not be induced to crystallize. Its infrared and ultraviolet spectra indicated the absence of functional groups, but it gave a positive unsaturation test with tetranitromethane. G.p.c. examination of this fraction, programming the temperature from 125–300°, then keeping the temperature at 300°, revealed the presence of at least thirty-two constituents.

Chromatography of the Middle Fraction.—A portion of the middle fraction (2.14 g.) was chromatographed over a column of alumina (200 g., 30 × 5 cm.), and successive fractions (100 ml.) of eluate were examined. Fractions 3–11 (hexane) contained colorless semisolid hydrocarbon(s) (total, 0.14 g.). Fractions 18–25 (3:1 hexane–benzene) contained a colorless oil (total 0.18 g.); ultraviolet spectrum, no absorption above 220 mμ; infrared spectrum, $\mu_{max}^{CHCl_3}$ 5.85, 6.25. Fractions 34–43 (1:1 hexane–benzene) contained a colorless solid (total 0.09 g.), m.p. 55–66°; ultraviolet spectrum, λ_{max} 285 mμ; infrared spectrum, $\mu_{max}^{CHCl_3}$ 5.89 (m), 6.07 (s), 6.17 (s), 6.30 (m). Fractions 50–55 (1:3 hexane–benzene) and 56–66 (benzene) contained a colorless crystalline solid (total, 0.94 g.), m.p. 130–135° (β-sitosterol mixture). Fractions 74–86 (3:1 benzene–ether) contained a colorless solid (total, 0.14 g.), m.p. 71–78° (impure substance A).

Chromatography of the Steroid Fraction.—A portion of the steroid fraction (5.80 g.) was chromatographed over a column of alumina (330 g., 50 × 5 cm.), and successive fractions (200 ml.) of the eluate were examined. Fractions 4–11 (hexane) contained a colorless oil (total 0.06 g.); fractions 22–26 (benzene) and 27–41 (9:1 benzene–ether) contained colorless crystalline materials (total 4.42 g.) whose melting points rose steadily from 128–131° (fraction 22) to 135–138° (fraction 41) and whose optical rotations (chloroform) varied steadily from $[\alpha]^{28}D$ +5° (fraction 22) to −30° (fraction 41).

β-Sitosterol has m.p. 139–140°, $[\alpha]D$ −36° (chloroform).

Substance A.—Repeated crystallization from hexane afforded substance A as silvery flakes, m.p. 84–85°. This material showed the following properties: t.l.c., R_f 0.20; $[\alpha]^{22}D$ 0° (*c* 1.02% in ethanol); ultraviolet spectrum, λ_{max} 275, 281.5 mμ; infrared spectrum, μ_{max} 3.05 (s, hydroxyl), 6.15 (m), 6.25 (s, aromatic ring); n.m.r. spectrum (deuterioacetone), 3-proton multiplet between 0.82 and 1.05 p.p.m. (C–CH_3), *ca.* 36-proton broad singlet at 1.32 p.p.m. (–$(CH_2)_{ca\ 18}$–), 2-proton multiplet between 2.33 and 2.75 p.p.m. (benzylic protons), 3-proton broad singlet at 6.23 p.p.m. (aromatic protons), and 2 singlets, total 2 protons, at 3.17 and 7.97 p.p.m. (hydroxylic protons, *vide infra* for orcinol); a ferric chloride test in ethanol was negative; a mercuric nitrate test for resorcinols was positive.[3]

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96; O, 7.90; 1C–CH_3, 4.20. Calcd. for $C_{25}H_{44}O_2$: C, 79.73; H, 11.78; O, 8.49; 1C–CH_3, 4.51. Found: C, 80.05; H, 11.87; H, 7.79; C–CH_3, 2.50.

A-Dimethyl Ether.—A (1.30 g.) and dimethyl sulfate (6.1 g.) were added to a mixture of dry acetone (100 ml.) and anhydrous potassium carbonate (36 g.), and the mixture was boiled under gentle reflux for 50 hr. The mixture was cooled and filtered, and the solvent was eliminated from the filtrate, leaving a pale yellow solid (1.39 g.). T.l.c. showed a single spot (R_f 0.94). This material was crystallized from hexane (3 ml.) giving colorless crystals (1.10 g.), m.p. 43–50°; ultraviolet spectrum, λ_{max} 273, 280 mμ; infrared spectrum, no hydroxyl absorption; n.m r. spectrum, 3-proton multiplet between 0.82 and 1.05 p.p.m. (C–CH_3), *ca.* 40-proton broad singlet at 1.28 p.p.m. (–$(CH_2)_{ca\ 20}$–), 2-proton multiplet between 2.30 and 2.80 p.p.m. (benzylic protons), 6-proton singlet at 3.78 p.p.m. (aromatic methoxys), 3-proton broad singlet at 6.38 p.p.m. (aromatic protons).

Anal. Calcd. for $C_{29}H_{52}O_2$: C, 80.49; H, 12.11; O, 7.40. Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96; O, 7.91. Found: C, 80.54; H, 11.93; O, 7.42.

A-Dimethyl ether (839 mg.) was recrystallized five times from hexane, giving colorless crystals (62 mg.), m.p. 61–63°. A mixture melting point with Ic was 61–63°; the ultraviolet and infrared spectra were identical with those of Ic; the n.m.r. spectrum was identical with that of Ic, except that the broad singlet at 1.28 p.p.m. contained *ca.* 41 protons.

Anal. Calcd. for $C_{29}H_{52}O_2$: C, 80.49; H, 12.11; O, 7.40. Found: C, 80.70; H, 12.14; O, 7.28.

A-Diacetate.—A (402 mg.) was dissolved in a mixture of pyridine (5 ml.) and acetic anhydride (10 ml.), and this solution was stirred and heated (steam bath) for 3 hr. The solution was cooled, then poured into ice–water (20 ml.), and extracted with four 50-ml. portions of hexane. The hexane extract was washed with water (50 ml.) and brine (50 ml.), then dried over sodium sulfate. The solvent was eliminated from the dried extract, leaving a colorless solid (454 mg.). T.l.c. showed a single spot (R_f 0.80). This material was recrystallized four times from ethanol, giving colorless needles (238 mg.), m.p. 60–66°; t.l.c., R_f 0.80; ultraviolet spectrum, λ_{max} 261 mμ; infrared spectrum, no hydroxyl absorption, μ_{max} 5.65 (s, phenol acetate); n.m.r. spectrum, 3-proton multiplet between 0.78 and 1.05 p.p.m. (C–CH_3), *ca.* 38-proton broad singlet at 1.28 p.p.m. (–$(CH_2)_{ca\ 19}$–), 6-proton singlet at 2.26 p.p.m. (phenolic acetates), 2-proton multiplet between 2.40 and 2.85 p.p.m. (benzylic protons), 3-proton broad singlet at 6.83 p.p.m. (aromatic protons).

Anal. Calcd. for $C_{31}H_{52}O_4$: C, 76.18; H, 10.72; O, 13.10. Calcd. for $C_{29}H_{48}O_4$: C, 75.60; H, 10.50; O, 13.89. Found: C, 76.37; H, 10.46; O, 13.12.

Attempted Reduction of A.—A (201 mg.) was dissolved in ethanol (150 ml.) and was subjected to hydrogenation at 50° and 40 p.s.i. in the presence of 10% palladium on charcoal (20 mg.). After 4 hr. the mixture was filtered through Celite to remove the catalyst, and the solvent was removed from the filtrate leaving a colorless solid (192 mg.). This material was crystallized from hexane, and the resulting crystals (167 mg.) were shown to be identical with A (melting point, mixture melting point, infrared spectrum, t.l.c.).

3,5-Dimethoxybenzyl Alcohol.—3,5-Dimethoxybenzoic acid (25.0 g., R_f 0.04) was dissolved in warm, dry tetrahydrofuran (400 ml.), and this warm solution was added continuously over 90 min. to a gently refluxing suspension of lithium aluminum hydride (10 g.) in tetrahydrofuran (100 ml.). When the addition was complete the mixture was boiled under gentle reflux for 4 hr., then cooled (ice–water bath). The excess hydride and the complex were decomposed by cautious addition of ethyl acetate (60 ml.), water (60 ml.), and 2 *N* aqueous hydrochloric acid (100 ml.). The volume of the resulting suspension was reduced to 150 ml. (rotatory evaporator, bath temperature of 40°), diluted by addition of water (200 ml.), and extracted with six 500-ml. portions of ether. The ether extract was washed with water (1 l.), 2 *N* aqueous sodium hydroxide (1 l.), water (1 l.), and brine (1 l.), then dried over sodium sulfate. The solvent was eliminated from this dried extract, leaving a colorless solid (22.9 g.), which was crystallized from hexane, giving 3,5-dimethoxybenzyl alcohol as needles (21.8 g., 94%), m.p. 46.5–47° (lit.[7], m.p. 47–48°); t.l.c., R_f 0.14; infrared spectrum, μ_{max} 2.95 (m, hydroxyl), no carbonyl absorption; n.m.r. spectrum, 1-proton broad singlet at 2.25 p.p.m. (hydroxyl proton), 6-proton singlet at 3.77 p.p.m. (aromatic methoxys), 2-proton broad singlet at 4.61 p.p.m. (benzylic protons), 3-proton, 5-line multiplet between 6.30 and 6.60 p.p.m. (aromatic protons).

3,5-Dimethoxybenzaldehyde.—Freshly prepared "active" manganese dioxide[8] (201 g.) was added to a solution of 3,5-di-

(7) R. Adams, S. MacKenzie, Jr., and S. Loewe, *J. Am. Chem. Soc.*, **70**, 664 (1948).

(8) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J. Chem. Soc.*, 1094 (1952).

methoxybenzyl alcohol (17.8 g.) in dry, ethanol-free chloroform (2 l.), and the mixture was stirred in an atmosphere of nitrogen for 24 hr. at room temperature. The mixture was filtered, and the residue was washed with six 500-ml. portions of boiling chloroform. The solvent was eliminated from the combined filtrate and washings, leaving a colorless crystalline solid (13.9 g.), m.p. 43–45°. This was crystallized from pentane, giving 3,5-dimethoxybenzaldehyde as prisms (12.8 g., 72%), m.p. 45–45.5° (lit.[9] m.p. 48°); t.l.c., R_f 0.57; infrared spectrum, no hydroxyl absorption, μ_{max} 5.93 (s, aldehyde carbonyl); n.m.r. spectrum, 6-proton singlet at 3.83 p.p.m. (aromatic methoxys), 1-proton, 2-line multiplet between 6.60 and 6.75 p.p.m., and a 2-proton, 2-line multiplet between 6.92 and 7.05 p.p.m., (aromatic protons), 1-proton singlet at 9.87 p.p.m. (aldehydic protons).

***n*-Eicosyl Bromide.**—1-Eicosanol (19.1 g.) was powdered and added to concentrated sulfuric acid (7 g.) and 48% aqueous hydrobromic acid (22 g.), and this solution was stirred and heated at 140° (bath temperature) for 5 hr. The resulting dark solution was cooled, diluted by the addition of water (30 ml.), and extracted with two 80-ml. portions of ether. The ether extract was washed with water (50 ml.), two 50-ml. portions of saturated aqueous sodium bicarbonate, water (50 ml.), and brine (50 ml.), then dried over sodium sulfate. The solvent was eliminated from the dried extract, leaving a very dark brown solid (23.4 g.). This was dissolved in hexane (150 ml.), and this solution was applied to a column of alumina (Guilini, neutral, activity I, 200 g., 18 × 3.8 cm.). Hexane (1 l.) eluted *n*-eicosyl bromide as a colorless solid (18.7 g., 82%), m.p. 33–34°, lit.[10] 30–31°; t.l.c., R_f 0.87; infrared spectrum, no hydroxyl absorption. G.p.c. showed that this material was 90% pure (retention time for *n*-eicosyl bromide, 3.4 min. with a column temperature of 250°).

***n*-Octadecyl Bromide.**—The commercially available *n*-octadecyl bromide was a very pale yellow semisolid. A 20.0-g. sample was dissolved in hexane (100 ml.) and this solution was applied to a column of alumina (Guilini, neutral, activity I, 200 g., 18 × 3.8 cm.). Hexane (600 ml.) eluted the bromide as a colorless solid (18.7 g.), m.p. 26–27°, lit.[11] m.p. 25.5–26°; t.l.c., R_f 0.87; infrared spectrum, no hydroxyl absorption. G.p.c. showed that this material was 87% pure (retention time for *n*-octadecyl bromide, 4.7 min. with a column temperature of 215°).

α-(3,5-Dimethoxyphenyl)-*n*-heneicosanol (IIb).—In a 100-ml. two-necked flask fitted with a dropping funnel and condenser, and containing a magnetic stirring bar, were placed dry magnesium turnings (1.16 g., 0.048 g.-atom), and these were covered with absolute ether (20 ml.). A few drops of a solution of *n*-eicosyl bromide (16.71 g., 0.046 mole) in absolute ether (30 ml.) were added, and, other less drastic methods having failed, the reaction was initiated by the addition of 2 small drops of methyl iodide. The rate of reaction was slow, and the mixture was heated under gentle reflux with rapid stirring while the remainder of the solution of *n*-eicosyl bromide was added dropwise over a period of 1 hr. Heating and stirring were continued for a further 5 hr. to complete formation of the Grignard reagent.

The heating bath was removed and an ice–water bath substituted. A solution of 3,5-dimethoxybenzaldehyde (6.15 g., 0.037 mole) in absolute ether (15 ml.) was added dropwise over a period of 45 min. to the rapidly stirred Grignard suspension. When this addition was complete, the heating bath was reintroduced, and the stirred mixture was boiled under gentle reflux for 4 hr. to complete the reaction. Excess magnesium was removed from the cooled reaction mixture by filtration, and the complex salt present in the filtrate was decomposed by the portionwise addition of powdered ice. Thereafter the mixture was extracted with two 50-ml. portions of 2 *N* aqueous sulfuric acid, washed with saturated aqueous sodium bicarbonate solution (30 ml.), water (30 ml.), and brine (30 ml.), then dried over sodium sulfate. The solvent was eliminated from this dried solution, leaving a pale yellow solid (17.90 g.), which was crystallized from hexane (400 ml.) giving IIb as colorless crystals (13.96 g., 85%), m.p. 75–75.5°; t.l.c., R_f 0.39; ultraviolet spectrum, λ_{max} 274 mμ (ε 1900), 280 (1930); infrared spectrum, μ_{max} 3.05 (m, hydroxyl), no carbonyl absorption; n.m.r. spectrum, 3-proton multiplet between 0.78 and 1.05 p.p.m. (C–CH_3), *ca.* 40-proton broad singlet at 1.27 p.p.m. (–$(CH_2)_{ca\ 20}$–), 1-proton broad singlet at 2.03 p.p.m. (hydroxylic proton), 6-proton singlet at 3.77 p.p.m. (aromatic methoxys), 1-proton multiplet between 4.40 and 4.75 p.p.m. (benzylic proton), 3-proton, 5-line multiplet between 6.25 and 6.55 p.p.m. (aromatic protons). Recrystallization of a sample for elemental analysis did not raise the melting point.

Anal. Calcd. for $C_{29}H_{52}O_3$: C, 77.62; H, 11.68; O, 10.70. Found: C, 77.58; H, 11.61; O, 10.81.

α-(3,5-Dimethoxyphenyl)-*n*-nonadecanol (IIa).—This preparation was identical with that described above except that *n*-octadecyl bromide (15.43 g., 0.046 mole) was used. This procedure afforded IIa as colorless crystals (12.08 g., 77%), m.p. 71–71.5°; t.l.c., R_f 0.38; ultraviolet spectrum, λ_{max} 274 mμ (ε 1860), 280 (1880); infrared spectrum, μ_{max} 3.04 (m, hydroxyl), no carbonyl absorption; n.m.r. spectrum, identical with that of IIb, except that the broad singlet at 1.27 p.p.m. contained *ca.* 37 protons. Recrystallization of a sample for elemental analysis did not raise the melting point.

Anal. Calcd. for $C_{27}H_{48}O_3$: C, 77.09; H, 11.50; O, 11.41. Found: C, 77.23; H, 11.40; O, 11.16.

5-*n*-Heneicosylresorcinol Dimethyl Ether (Ic).—IIb (12.68 g.) was dissolved in warm ethyl acetate (200 ml.) containing concentrated sulfuric acid (10 drops), and the mixture was subjected to hydrogenation at 55° and 40 p.s.i. in the presence of 10% palladium on charcoal (1.27 g.). After 4 hr. the mixture was filtered through Celite to remove the catalyst, and the volume of the filtrate was reduced to 80 ml. (rotatory evaporator, bath temperature 40°). The concentrate was kept at 0° for 1 hr., and the resulting precipitate was collected, giving Ic as colorless crystals (11.70 g., 96%), m.p. 62–64°; t.l.c., R_f 0.94; ultraviolet spectrum, λ_{max} 273 mμ (ε 1590), 280 (1610); infrared spectrum, no hydroxyl absorption; n.m.r. spectrum, 3-proton multiplet between 0.75 and 1.05 p.p.m. (C–CH_3), *ca.* 40-proton broad singlet at 1.28 p.p.m. (–$(CH_2)_{ca\ 20}$–), 2-proton multiplet between 2.33 and 2.75 p.p.m. (benzylic protons), 6-proton singlet at 3.76 p.p.m. (aromatic methoxys), 3-proton broad singlet at 6.33 p.p.m. (aromatic protons). Recrystallization of a sample for elemental analysis gave fine needles, m.p. 63.5–64.5°.

Anal. Calcd. for $C_{29}H_{52}O_2$: C, 80.49; H, 12.11; O, 7.40. Found: C, 80.41; H, 12.05; O, 7.49.

5-*n*-Nonadecylresorcinol Dimethyl Ether (Ib).—This preparation was similar to that described before. Hydrogenolysis of IIa (9.86 g.) afforded Ib as colorless crystals (8.93 g., 94%), m.p. 55–57°; t.l.c., R_f, 0.94; ultraviolet spectrum, λ_{max} 273 mμ (ε 1550), 280 (1570); infrared spectrum, no hydroxyl absorption; n.m.r. spectrum, identical with that of Ic, except that the broad singlet at 1.28 p.p.m. contained *ca.* 36 protons. Recrystallization of a sample for elemental analysis gave fine needles, m.p. 56.5–57.5°.

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96; O, 7.91. Found: C, 79.93; H, 12.02; O, 7.91.

Anhydrous Pyridine Hydrochloride.—Dry hydrogen chloride was bubbled through a rapidly stirred solution of dry pyridine (60 g.) in absolute ether (500 ml.) contained in a cooled (ice–water bath) flask. After 3 hr. the gas flow was stopped and most of the solvent was decanted, the remainder being pumped off *in vacuo* at room temperature, leaving colorless crystals of pyridine hydrochloride (84 g., 96%), m.p. 143–144°. This salt was very hygroscopic and was stored *in vacuo* over concentrated sulfuric acid.

5-*n*-Heneicosylresorcinol (Ie).—Ic (4.65 g.) was mixed with anhydrous pyridine hydrochloride (37.5 g.) in a 100-ml. flask fitted with a short air condenser. This mixture was heated in an atmosphere of nitrogen until the pyridine hydrochloride refluxed freely (bath temperature, 265°). (Preliminary experiments had established that with a bath temperature of 220° no reaction occurred although orcinol dimethyl ether was efficiently demethylated under these conditions.) The mixture was maintained at this elevated temperature for 8 hr., then the flask was allowed to cool. The solidified contents were removed and shaken with a mixture of 2 *N* aqueous sodium hydroxide solution (500 ml.) and ether (1 l.). The pale yellow ether layer was combined with the three 1-l. portions of further ether extracts of the red basic aqueous layer, and the resulting ether solution was washed with two 1-l. portions of 2 *N* aqueous hydrochloric acid to remove pyridine, then with water (1 l.), and brine (1 l.), then dried over sodium sulfate. The solvent was eliminated from this dried solution, leaving a solid neutral material (3.87 g.), which was crystallized from hexane (75 ml.) giving a fawn ma-

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terial (3.15 g.), m.p. 98–100°, t.l.c. of which revealed only 1 spot (R_f 0.20). This material was distilled at 1 μ and 160° (bath temperature) using a cold-finger sublimator, giving colorless material (2.54 g.), m.p. 99.5–100.5°, which was crystallized from hexane, giving Ie as plates (2.34 g., 54%), m.p. 99.5–100.5°; t.l.c., R_f 0.20; ultraviolet spectrum, λ_{max} 275 mμ (ϵ 1740), 281.5 (1730); infrared spectrum, identical with that of A; n.m.r. spectrum (deuterioacetone), identical with that of A, except that the broad singlet at 1.32 p.p.m. contained *ca.* 35 protons, and the 2 peaks, total of 2 (hydroxyl) protons, appeared at 2.97 and 7.97 p.p.m.; a ferric chloride test in ethanol was negative; a mercuric nitrate test for resorcinols was positive.

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96; O, 7.90; 1C–CH_3, 4.20. Found: C, 80.01; H, 12.06; O, 7.99; C–CH_3, 2.94.

5-*n*-Nonadecylresorcinol (Id).—The demethylation of Ib was carried out in a manner very similar to that described above for Ic. Heating a mixture of Ib (3.81 g.) and anhydrous pyridine hydrochloride (31.0 g.) at 265° (bath temperature) for 8 hr., followed by the above work-up, gave a solid neutral material (3.21 g.), which was crystallized from hexane (45 ml.) giving fawn material (2.68 g.), m.p. 94–96°, t.l.c. of which revealed only 1 spot (R_f 0.20). This material was distilled at 1 μ and 160° (bath temperature) using a cold-finger sublimator, giving colorless material (2.19 g.), m.p. 96.5–97.5°, which was crystallized from hexane, giving Id as plates (2.03 g., 57%), m.p. 96.5–97.5°; t.l.c., R_f 0.20; ultraviolet spectrum, λ_{max} 275 mμ (ϵ 1780), 281.5 (1740); infrared spectrum, identical with that of A in the 2.5–12-μ region, very slight differences from that of A in the 12–15-μ region; n.m.r. spectrum (deuterioacetone), identical with that of A, except that the broad singlet at 1.32 p.p.m. contained *ca.* 31 protons, and the 2 peaks, total of 2 (hydroxyl) protons, appeared at 3.05 and 7.97 p.p.m.; a ferric chloride test in ethanol was negative; a mercuric nitrate test for resorcinols was positive.

Anal. Calcd. for $C_{25}H_{44}O_2$: C, 79.73; H, 11.78; O, 8.49; 1C–CH_3, 4.51. Found: C, 79.71; H, 11.76; O, 8.48; C–CH_3, 2.94.

Methylation of Ie.—Ie (150 mg.) and dimethyl sulfate (0.8 g.) were added to a mixture of dry acetone (10 ml.) and anhydrous potassium carbonate (4 g.) and the mixture was boiled under gentle reflux for 48 hr. The mixture was cooled and filtered, and the solvent was eliminated from the filtrate, leaving a pale yellow solid (161 mg.). This material was crystallized from hexane (1 ml.) and the resulting colorless crystals (112 mg.) were shown to be identical with Ic (melting point, mixture melting point, infrared spectrum, t.l.c.). This confirmed that no rearrangement of the side chain of Ic had occurred during its demethylation.

Methylation of Id.—The methylation of Id (148 mg.) was conducted exactly as described above for Ie and furnished a pale yellow solid (160 mg.). This material was crystallized from hexane (1 ml.) and the resulting colorless crystals (92 mg.) were shown to be identical with Ib (melting point, mixture melting point, infrared spectrum, t.l.c.). This confirmed that no rearrangement of the side chain of Ib had occurred during its demethylation.

5-*n*-Heneicosylresorcinol Diacetate.—Ie (200 mg.) was acetylated in exactly the same way as described for A above. Regular work-up afforded a very pale yellow crystalline solid (227 mg.), t.l.c. of which showed 1 spot (R_f 0.80). This material was crystallized twice from ethanol, giving colorless plates (176 mg.), 72.5–73°; t.l.c., R_f 0.80; ultraviolet spectrum, λ_{max} 261.5 mμ (ϵ 305); infrared spectrum, no hydroxyl absorption, μ_{max} 5.64 (s, phenol acetate); n.m.r. spectrum, identical with that of A-diacetate, except that the broad singlet at 1.28 p.p.m. contained *ca.* 36 protons.

Anal. Calcd. for $C_{31}H_{52}O_4$: C, 76.18; H, 10.72; O, 13.10. Found: C, 76.27; H, 10.45; O, 13.10.

5-*n*-Nonadecylresorcinol Diacetate.—Id (199 mg.) was acetylated in exactly the same way as described for A above. Standard work-up afforded a very pale yellow crystalline solid (227 mg.), t.l.c. of which showed only 1 spot (R_f 0.80). This material was crystallized twice from ethanol, giving colorless needles (163 mg.), m.p. 67.5–68°; t.l.c., R_f 0.80; ultraviolet spectrum, λ_{max} 261 mμ (ϵ 291); infrared spectrum, no hydroxyl absorption, μ_{max} 5.65 (s, phenol acetate); n.m.r. spectrum, identical with that of A-diacetate except that the broad singlet at 1.28 p.p.m. contained *ca.* 32 protons.

Anal. Calcd. for $C_{29}H_{48}O_4$: C, 75.60; H, 10.50; O, 13.89. Found: C, 75.83; H, 10.31; O, 14.01.

Gas Phase Chromatography of A-Dimethyl Ether, Ib, and Ic.—Since the methylation of A was essentially quantitative, any method which reveals the number and relative amounts of the components in this dimethyl ether also reflects the number and relative amounts of the components in A. G.p.c. (with the column maintained at 300°) of the reaction product from the methylation of A revealed the presence of five constituents, whose retention times and per cent of total area were as follows: (i) 2.5 min., 4%; (ii) 4.2 min., 34%; (iii) 7.2 min., 48%; (iv) 11.0 min., 9%; (v) 16.8 min., 5%. Under the same conditions Ib had the same retention time as ii, and Ic had the same retention time as iii. When successive retention times were plotted against equal increments on the other coordinate axis the points fell on a smooth curve, suggesting that i, iv, and v were similar to Ib and Ic with side chains $-C_{17}H_{35}$, $-C_{23}H_{47}$, $-C_{25}H_{51}$, respectively.

The gas chromatograph was used as a preparative instrument. Because of the small capacity of the column, 3 mg. was the largest amount of sample which could be injected at a time. In this way 60 mg. of A-dimethyl ether was separated into five fractions, each of which was rechromatographed leading finally to five components of varying degrees of homogeneity (the numbering corresponds to that used above): (i) <1 mg. of a colorless solid, m.p. 50–52°, 95% purity (g.p.c.), ultraviolet spectrum, λ_{max} 273 and 280 mμ; (ii) 10 mg. of a colorless solid, m.p. 57–58.5°, 98% purity (g.p.c.), identified as Ib by mixture melting point and infrared spectrum; (iii) 14 mg. of a colorless solid, m.p. 63–64°, 98% purity (g.p.c.), identified as Ic by mixture melting point and infrared spectrum; (iv) 2 mg. of a colorless solid, m.p. 66–69°, 90% purity (g.p.c.), ultraviolet spectrum, λ_{max} 273 and 280 mμ; (v) <1 mg. of a colorless solid, m.p. 69–72°, 92% purity (g.p.c.), ultraviolet spectrum, λ_{max} 273 and 280 mμ.

Orcinol.—Commercial orcinol (pink, m.p. 106–108°) was sublimed at 1 μ and 100° (bath temperature), and the colorless sublimate was crystallized from benzene, giving needles, m.p. 107.5–108.5°; t.l.c., R_f 0.07; ultraviolet spectrum, λ_{max} 275 mμ (ϵ 1680), 281.5 (1660); infrared spectrum, μ_{max} 3.05 (s, hydroxyl); n.m.r. spectrum (deuterioacetone), 3-proton singlet at 2.18 p.p.m. (aromatic C–CH_3), 3-proton broad singlet at 6.25 p.p.m. (aromatic protons), and two singlets, approximate total 2 protons, one singlet at 8.10 p.p.m., independent of concentration, intensity increasing with increasing concentration, the other singlet appearing between 2 and 5 p.p.m., dependent on concentration (high-field position at low concentration), intensity decreasing with increasing concentration (hydroxylic protons).

2,3-, 2,4-, 2,5-, 2,6-, 3,4-, and 3,5-Dimethoxytoluenes.—The above toluenes were prepared by reduction and hydrogenolysis of the corresponding aldehydes. The aldehyde (1.00 g.) was dissolved in ethanol (100 ml.) containing concentrated hydrochloric acid (5 drops), and the mixture was subjected to hydrogenation at room temperature and 40 p.s.i. in the presence of 30% palladium on charcoal (0.10 g.). After 2 hr. the mixture was filtered through Celite to remove the catalyst, and the solvent eliminated from the filtrate leaving a residue which was distilled *in vacuo* to give the toluene. The yields are given in Table II.

TABLE II

YIELDS OF DIMETHOXYTOLUENES

Dimethoxytoluene	B.p. (bath temp, at 0.5 mm.), °C.	Yield, g.
2,3	90	0.84
2,4	85	0.83
2,5	90	0.86
2,6	110	0.83
3,4	90	0.85
3,5	90	0.88

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