fonamides or similar compounds which are solely bacteriostatic. Under these circumstances the MIC method for the determination of the activity seems preferable because it is less expensive and less time consuming than the kinetic method. Kinetic experiments, however, may give a better indication of the type of antibacterial action.

Acknowledgment.—The author is greatly indebted to Miss E. Wempe for biological activity determinations, to Miss H. Henke and Mr. W. Diller for physicochemical measurements, and to Dr. P. H. Doukas of Temple University, School of Pharmacy, Philadelphia, Pa. 19140, for assistence in the preparation of the manuscript.

Synthesis of Compounds Structurally Related to Poison Ivy Urushiol. 3.[1a-c] 3-*n*-Pentadecylcatechol and 3-*n*-Alkylcatechols of Varying Side-Chain Length

A. PETER KURTZ[1d] AND CHARLES R. DAWSON*

Department of Chemistry, Columbia University, New York, New York 10027

Received July 3, 1970

The allergenic components of poison ivy urushiol have the carbon skeleton of 3-*n*-pentadecylcatechol. An improved synthetic route to 3-*n*-pentadecylcatechol and related 3-*n*-alkylcatechols has been developed incorporating pyridinium chloride cleavage of the corresponding veratrole(s). The route has been shown to be of general utility through its application to the synthesis of a series of 3-*n*-alkylcatechols bearing saturated side chains of varying length: C_1, C_3, C_5, C_8, C_{11}, C_{15}, C_{17}, C_{19}. Biological evaluation of these compounds has demonstrated that antigenic specificity is sensitive to changes in side-chain length in the function of these agents as sensitizers and elicitors of delayed contact dermatitis.

Poison ivy urushiol, the dermatitis-producing principle of the poison ivy plant, is an oil composed of four 3-*n*-alkylcatechols, each having the C skeleton of 3-*n*-pentadecylcatechol (3-PDC, **1g**) and each varying in the degree of unsaturation of the alkyl side chain.[2] 3-PDC, the saturated component of the urushiol of poison ivy and many related plants,[3] is itself a compound increasingly in demand for diagnostic patch testing for Rhus hypersensitivity.[4] As part of a continuing systematic investigation into the structure–activity relationships involved in the function of 3-alkylcatechols as allergic agents,[1] an improved synthesis of 3-PDC has been developed and applied to the synthesis of its analogs having varying side-chain length.

Since poison ivy dermatitis, in the great majority of instances, is an allergic phenomenon (delayed contact hypersensitivity),[5] an interest in a possible antigenic specificity for side-chain length prompted the synthesis of a series of analogs of 3-*n*-pentadecylcatechol varying only in the length of the saturated side chain.[1,6] The structures of the alkylcatechols involved, and their synthesis precursors, are indicated and labeled as shown in Scheme I.

Chemistry.[7a]—Veratrole precursors to the alkylcatechols (**5b–5g, 5i**) were obtained routinely as described in the Experimental Section and outlined in Scheme I by direct hydrogenolysis[8] of the product of the reaction of the appropriate Grignard reagent with *o*-veratraldehyde (**3**). 3-Methylveratrole (**5a**) was obtained by direct hydrogenolysis of **3**, while 3-*n*-propylveratrole (**5b**) was obtained by purification of an available sample. Each veratrole was brought to a state of high purity by fractional distillation *in vacuo*. Data and physical properties[9] pertinent to these preparations are presented in Table I. Data for the preparation of 3-*n*-pentadecylveratrole (**5g**), precursor to the naturally occurring 3-PDC, are presented in Table I.

(1) (a) Previous paper in the series (2): J. S. Byck and C. R. Dawson, *J. Org. Chem.*, **33**, 2451 (1968); (b) accompanying paper (4): A. P. Kurtz and C. R. Dawson, *J. Med. Chem.*, **14**, 733 (1971), describes the synthesis of analogs varying in side-chain shape and flexibility; (c) taken from the Ph.D. Dissertation of A. P. Kurtz, Columbia University, 1968; these investigations were supported by Contract PH-43-64-76 with the Division of Biologics Standards of the National Institutes of Health; (d) National Institutes of Health Predoctoral Fellow, 1965–1968.

(2) (a) W. F. Symes and C. R. Dawson, *J. Amer. Chem. Soc.*, **76**, 2959 (1954); (b) K. H. Markiewitz and C. R. Dawson, *J. Org. Chem.*, **30**, 1610 (1965).

(3) (a) G. A. Hill, V. Mattacotti, and W. D. Graham, *J. Amer. Chem. Soc.*, **56**, 2736 (1934); (b) R. Majima and J. Tahara, *Chem. Ber.*, **48**, 1606 (1915).

(4) (a) H. Keil, D. Wasserman, and C. R. Dawson, *J. Allergy*, **16**, 275 (1945); (b) H. Keil, D. Wasserman, and C. R. Dawson, U. S. Patent No. 2,451,955 (Oct 19, 1948); (c) A. M. Kligman, *Arch. Dermatol.*, **77**, 149 (1958); (d) R. Auerbach and H. Baer, *J. Allergy*, **35**, 201 (1964).

(5) A. J. Crowle, "Delayed Hypersensitivity in Health and Disease," C. T. Thomas, Springfield, Ill., 1962, Chapter IV.

(6) (a) Although the synthesis of a series of 3-*n*-alkylcatechols (C_5, mp 34–35°; C_8, mp 30–31°; C_7, solid at 5°; C_2, liquid; C_{15}, mp 57–59°; C_{17}, mp 59°) was reported in 1946 (see ref 6b), characterization data for the synthetic products was inconclusive by present standards and yield data for the preparations were conspicuously absent. See footnote *k* to Table II. (b) R. D. Haworth and D. Woodcock *J. Chem. Soc.*, 999 (1946).

(7) (a) A review of the literature[7b-7e] indicates that the least satisfactory step in the prior syntheses of 3-PDC and alkylcatechols has been the last step, *i.e.*, the conversion of the precursor veratrole to the catechol. Halogen acid sealed-tube cleavages give poor yields of product difficult to purify.[3a,7d] The optimum method of cleavage reported prior to the present study incorporates $AlCl_3$–chlorobenzene. This reagent system gives 3-PDC in about 75% yield[7c,7e] after distn and several recrystns of the crude product but is not practical for large scale preps. After experimentally investigating all of the routes previously reported, an exploratory study of pyridinium chloride (PyrCl)[7f] as cleavage reagent for 3-alkylveratroles was made. Use of a PyrCl cleavage procedure analogous to that given in the literature (procedure A) or the more convenient procedure (procedure B) given in the Experimental Section affords easily purifiable 3-alkylcatechols in high yields and is practical for large scale work. (b) H. J. Backer and N. H. Haack, *Recl. Trav. Chim. Pays-Bas*, **57**, 225 (1938); (c) H. Keil, D. Wasserman, and C. R. Dawson, *J. Amer. Chem. Soc.*, **68**, 534 (1946). (d) H. S. Mason, *ibid.*, **67**, 1538 (1945); (e) B. Loev and C. R. Dawson, *ibid.*, **78**, 4083 (1956); (f) this reagent had previously been used for the cleavage of unsubstituted mono- and diphenol ethers [V. Prey, *Chem. Ber.*, **74**, 1219 (1941); *ibid.*, **75**, 350 (1942)] and long-chain alkylresorcinol dimethyl ethers (E. Wenkert, E. M. Loeser, S. N. Mahapatra, F. Schenker, and E. M. Wilson, *J. Org. Chem.*, **29**, 435 (1964).

(8) The direct hydrogenolysis (**4** to **5**) is essentially quantitative yielding a stable distillable product free of degraded material often characteristic of routes employing prior carbinol dehydration.

(9) As described in detail elsewhere,[10] the boiling points of the veratroles, when adjusted to a common pressure, and the logarithms of the vpc retention times for the C_{11}–C_{19} members of the series form a linear plot when graphed *vs.* chain length.

(10) Details on these and other studies are presented in the Ph.D. Diserstation of A. P. Kurtz, Columbia University, New York, N. Y., 1968.

TABLE I

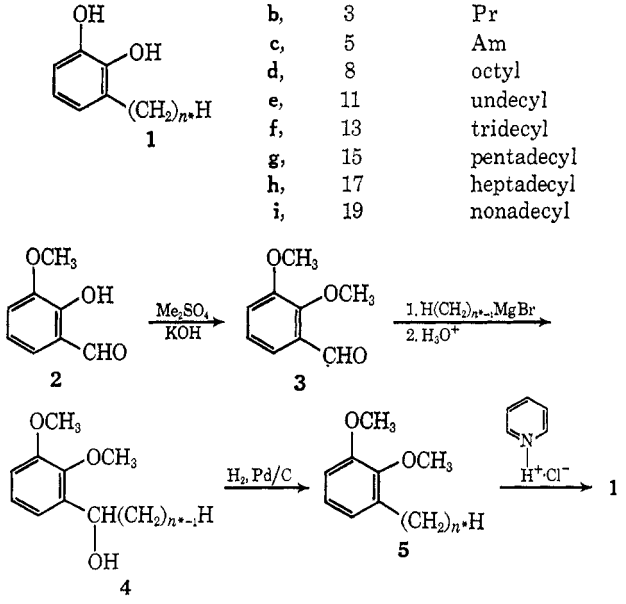
3-*n*-ALKYLVERATROLES (5) FROM *o*-VERATRALDEHYDE (3)

Compd	Chain[a] length	Crude carbinol (4)[b] bp (mm) or mp, °C	5 % yield[c]	3-*n*-Alkylveratroles (5) bp (mm) or mp, °C	Contamination[d] Total, %	Contamination[d] Isomers or homologs, %
5a	1		86[e]	200–202 (76)	0.5	<0.1
5b	3[f]			85–86 (1.3)	0.3	<0.1
5c	5	189–191 (5)	78	145–149 (8–10)	0.7	<0.1
5d	8	155–156 (0.4)	73	144–146 (1–2)	0.3	<0.1
5e	11	160 (0.4)	80	154–156 (0.4)	1.6	<0.5
5f	13	39.5–40.5[g]	83	161–164 (0.2)	5.3	<0.2
5g	15	48–50[g]	78	193–97 (0.4) 36.2–36.7[h]	2.0	<0.5
5i	19	Solid wax	70	235–238 (0.7) 48–50[i]	1.9	<0.5

[a] Number of CH_2 groups in the 3-*n*-alkyl side chain (total C length). [b] Compounds **4c**, **4d**, and **4e** were distilled *in vacuo;* since **4e** partially dehydrated on distn, no attempt was made to distill higher mol wt carbinols. [c] Per cent yield of 3-*n*-alkylveratrole (**5**) from **3**; purity defined in table under heading Contamination. [d] Vpc, SE-30, 160–225°: sensitivity of detection of contaminant 3-*n*-alkylveratroles of other chain-lengths or 4-alkylveratroles[12] = <0.1% in chromatograms of the C_1–C_{13} veratroles and <0.5% in chromatograms of the C_{15} and C_{19} veratroles. Isomers or homologs contamination figures in the table are either these sensitivity limits or peaks found in actual chromatograms having retention times suitable for known possible isomer or homolog contaminants. Total contamination = peaks corresponding in retention time to possible contaminant isomers or homologs plus peaks of anomalous retention times.[10] [e] Yield of direct hydrogenolysis of **3**. [f] This sample had been prepared by related methods in our laboratory by previous workers; its identity was confirmed by mp of the derivative catechol (**1b**): 72.5–73.0°; lit. mp 70–72° (J. R. A. Pollack and R. Stevens, Ed., "Dictionary of Organic Compounds," 4th ed, Oxford University Press, New York, N. Y., 1965). [g] Recryst from hexane. [h] Mp after spinning-band distn; lit.[3a] mp 36.0–37.0°. [i] Mp after recryst from hexane; lit. mp 45.5–47.0° [B. Loev and C. R. Dawson, *J. Amer. Chem. Soc.*, **78**, 1180 (1956)].

SCHEME I

1	*n**	3-*n*-alkylcatechol
a,	1	Me
b,	3	Pr
c,	5	Am
d,	8	octyl
e,	11	undecyl
f,	13	tridecyl
g,	15	pentadecyl
h,	17	heptadecyl
i,	19	nonadecyl



*n**, number of C atoms in 3-*n*-alkyl side chain.

Employing either a variation of the published procedure[7f] or the more convenient procedure described in the Experimental Section, pyridinium chloride (PyrCl) was used to convert the alkylveratroles to alkylcatechols (**1a–1g**, **1i**) in high yields. All catechols were brought to high purity by distillation *in vacuo* and/or recrystallization. Data for all of the 8 synthetic 3-*n*-alkylcatechols and a purified sample of 3-*n*-heptadecylcatechol (hydrogenated laccol)[11] are presented in Table II. The data for 3-PDC (**1g**) are given in Table II. The purity and structure of each member of the series was established by microanalysis, vapor phase chromatography (homologous purity was previously established by vpc examination of each veratrole relative to figures for known mixtures of homologs and isomers), constancy of physical properties on repeated purification, and spectral analysis.

As described elsewhere, the present synthetic scheme has been shown to be applicable to the synthesis of 4-*n*-alkylcatechols,[12] ring-methylated 3-*n*-pentadecylcatechols,[1a,13] and 3-alkylcatechols bearing side chains branched at the 1′ or 2′ positions.[1b]

While the melting points of the C_8–C_{19} 3-*n*-alkylcatechols follow a nearly linear pattern when plotted against side-chain length (increasing intermolecular lipophilic attractions), the melting points of the C_1 to C_8 catechols follow an irregular pattern when plotted against side-chain length. These data suggest that complex intra- and intermolecular interaction changes occur with initial side-chain length increase from 1 to 8 CH_2 units. Such changes may control, in part, the antigenic specificity and skin permeability of these compounds as poison ivy allergens. Further, as determined by Baer and coworkers[14a] in an examination of each of the C_1–C_{15} alkylcatechols, the per cent total catechol which is water-soluble in H_2O–isooctane equilibration varies from about 93% for unsubstituted catechol to less than 1% for 3-PDC.

Biological Results.—The entire series of unbranched 3-alkylcatechols has been systematically evaluated[15] for activity as sensitizers and elicitors[16] of poison ivy

(11) R. Majima, *Chem. Ber.*, **55**, 191 (1922).

(12) From 3,4-dimethoxybenzaldehyde. Vpc and spectral data for 4-*n*-tridecylcatechol, mp 86.7–88.0°, 4-*n*-pentadecylcatechol, mp 93.0–93.5° (lit.[7e] mp 92.3–93.0°), and the corresponding precursor veratroles, were used in the present study as reference standards.

(13) J. S. Byck and C. R. Dawson, *J. Org. Chem.*, **32**, 1084 (1967).

(14) (a) H. Baer, R. C. Watkins, A. P. Kurtz, J. S. Byck, and C. R. Dawson, *J. Immunol.*, **99**, 365 (1967); (b) *ibid.*, **99**, 370 (1967); (c) H. Baer, C. R. Dawson, J. S. Byck, and A. P. Kurtz, *ibid.*, **104**, 178 (1970); (d) H. Baer, C. R. Dawson, and A. P. Kurtz, *ibid.*, **101**, 1243 (1968).

(15) Biol evaluation of the compds herein described was carried out by Dr. Harold Baer and associates of the Division of Biologics Standards of the National Institutes of Health, Bethesda, Md.

(16) Direct primary toxicity: potency as elicitor of delayed dermatitis on an animal not previously exposed to the compd or related compds; activity as homologous elicitor: potency as an elicitor of delayed dermatitis on an animal previously sensitized with the same compound; cross-reactivity:

TABLE II

3-*n*-ALKYLCATECHOLS (1)

Compd	Chain[a] length	% yield[b] from 3	% yield[b] from 5	Bp (mm), °C[c]	Crude[d] mp, °C	Pure[e,f] mp, °C	Purified by[g]	Formula[f]
1a	1	63[h]	(A) 73	132–136 (8–9)	63–66	65.5–67.5[i]	D, R	$C_7H_8O_2$
1b	3		(A) 98		66–72	72.5–73.0[j]	S, R	$C_9H_{12}O_2$
1c	5	71	(A) 91	123–125 (0.2)	35–38	40.4–42.2[k]	D, R	$C_{11}H_{16}O_2$
1d	8	60	(A) 82	160–164 (0.6)	31–33	38.2–39.2[k]	D, R	$C_{14}H_{22}O_2$
1e	11	70	(A) 88	160–163 (0.3)	44–48	48.5–49.7	D, R	$C_{17}H_{28}O_2$
1f	13	71	(B) 86		52–54	55.5–56.2	R	$C_{19}H_{32}O_2$
1g	15	65	(B) 83[l]		54–58	59.2–60.0[m]	R, S	$C_{21}H_{36}O_2$
1h	17[n]				60–63	63.5–65.0[n]	S	$C_{23}H_{40}O_2$
1i	19	56	(B) 79		64–67	68.0–69.0	R, S	$C_{25}H_{44}O_2$

[a] Number of CH_2 groups in the 3-*n*-alkyl side chain (total C length). [b] Per cent yield from **3** or **5**; calcn based on wts obtd on distn or after first recrystn (crude mp's). Comparison of crude mp and pure mp data gives an indication of purity of the crude samples. A and B refer to the procedures used for the cleavage reaction (see Experimental Section). [c] Data only available where product distd. [d] Mp after distn or first recryst. [e] Mp of pure product for elemental and spectral analysis and biol evaluation. [f] All catechol samples were analyzed for C and H; found values were correct to ±0.4%. [g] Methods of purification: D = distn; R = recryst from hexane; S = sublimation at 10^{-5} mm. [h] Material losses occurred due to the volatility of the veratrole. [i] Lit. mp 68° (C. A. Hoogman, Ed., "Handbook of Chemistry and Physics," 41st ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1960). [j] Lit. mp 70–72° (J. R. A. Pollock and R. Stevens, Ed., "Dictionary of Organic Compounds," 4th ed, Oxford University Press, New York, N. Y., 1965). [k] Mp's recorded in ref 6b: C_5, 34–35°; C_8, liquid. The difference between these reported physical properties and the physical properties for the present fully characterized materials suggests that the materials reported in ref 6b were grossly contaminated by synthetic precursors, principally, incompletely cleaved veratroles. [l] Several trials using procedure A gave comparable yields. [m] Lit.[7c] mp 59–60°. [n] A crude sample of tetrahydrolaccol, known[11] to have the structure: 3-*n*-heptadecylcatechol, was purified by repeated sublimation; characterized by nmr, vpc, mp, and elemental anal.; lit.[11] mp 63°.

dermatitis. Details on these studies have been reported in full detail in the immunologic literature.[14] As was anticipated on the basis of the increasing lipophilicity of the longer-chained compounds (which may facilitate skin and/or cell permeability) the direct primary toxicity and activity as homologous elicitors[16] increased regularly with increasing chain length to reach optimum activity at C_{11}. TD_{50}'s, or the skin dose at which half the experimental animals (previously untreated guinea pigs) would give an erythema, varied uniformly with increasing chain length from >1 μmole for unsubstituted catechol and the C_1 and C_3 catechols to ≤0.01 μmole for catechols with chain length greater than 13 CH_2 units.[14a] The activity of each compound as a homologous elicitor,[14b] *i.e.*, ability to elicit a delayed allergic response on an animal previously given a sensitization treatment with the same compound, increased regularly with increasing chain length from C_0 (geometric mean homologous reacting skin dose = 3.2 μmoles) to C_{11} (GM = 0.0018 μmole); activity as homologous elicitor was fairly uniform for the C_{11}–C_{19} compounds (range of GM = 0.047–0.0018) and variations within this range did not follow an intelligible pattern. The most active homologous elicitor was the C_{11} catechol. The naturally occurring 3-PDC had homologous GM = 0.011 μ mole.

Cross-reactivity[16] studies[14b] demonstrated that the alkyl side chain is an antigenic determinant of remarkable specificity; cross-reactivity was found to be dependent on chain length, the greatest degree of cross-reactivity occurring among those catechols whose side chains were closest in length.

Recent studies on the immunochemistry of immune tolerance involving this series of compounds[14c] has confirmed earlier data pointing to immunologic specificity for side-chain length in poison ivy reactivity. While subcutaneous pretreatment with long-chain alkylcatechols had a toleragenic effect in inhibiting subsequent sensitization with 3-PDC, such pretreatments with short-chained catechols were nearly ineffective.

Biological studies on this series of compounds together with a series having branching and cyclic side-chains (see companion paper) have shown[14c,d] the immune phenomena of poison ivy dermatitis to be sensitive not only to side-chain length but also side-chain shape.

potency as an elicitor of delayed dermatitis on an animal previously sensitized with a closely related compound.

Experimental Section[10]

Ir spectra were recorded on a Perkin-Elmer Infracord, Model 137, using approx 10% solns in either CCl_4 or $CHCl_3$. The nmr spectra were recorded using a Varian A-60 or A60A instrument and employing 20–50% solns in CCl_4 with a drop of TMS as internal standard. Mass spectra were recorded by Miss Vinka Parmakovich of the Dept of Chemistry, Columbia University, New York, N. Y., using a Perkin-Elmer/Hitachi RMU-6d instrument. Elemental microanalyses were performed by Microtech Laboratories, Skokie, Ill., and were within ±0.4% of the theoretical values. The vpc chromatograms were measured using an F&M flame ionization detector gas chromatograph, Model 609. Melting points were measured on a Thomas-Hoover mp apparatus (stirring silicone bath) and are corrected. Boiling points are uncorrected and approximate due to pressure variations and incomplete thermometer equilibrations during vacuum distns. Spinning-band distns were accomplished using a Nester-Faust 45 cm SB column and, in general, 4:1 reflux:cut ratio. The spinning band was made of stainless steel.

o-Veratraldehyde (3).—After recrystn of technical grade material[17] to mp 43–45° (lit.[18] mp 45.5°), *o*-vanillin (**2**) was methylated by a modification of the procedure of Barger and Silberschmidt.[19] From 364 g of **2**, 353 g of **3** was obtained: 89% yield; mp 50–51.5° (from 95% EtOH, lit.[20] mp 51°). The ir spectrum was identical with that of an authentic sample (Eastern Chemical Co.) and was distinctly different from the ir spectrum of 3,4-dimethoxybenzaldehyde (Eastman, mp 42–43°).

3-*N*-Alkylveratroles (5b–5g, 5i) *via* 3-*n*-(1′-Hydroxy)alkylveratroles (4c–4g, 4i).—Grignard reagents were prepd from the appropriate *n*-alkyl bromides,[21] treated with **3**, and worked-up in the conventional manner. Following removal of long-chain

(17) Gallard-Schlesinger Manufacturing Co., Carle Place, N. Y.

(18) C. R. Hoogman, Ed., "Handbook of Chemistry and Physics," 41st ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1960.

(19) G. Barger and R. Silberschmidt, *J. Chem. Soc.*, 2919 (1928).

(20) K. W. Merz and J. Fink, *Arch. Pharm. (Weinheim)*, **289**, 347 (1956).

(21) Eastman Organic Chemicals, Rochester, N. Y.

hydrocarbon coupling products by the procedure of Loev[22] and purification by vacuum distn in the case of the C_5, C_8, and C_{11} carbinols,[23] the resultant oils (waxy solids) were pressure hydrogenated. Ir and nmr spectral data for the crude carbinols **4c–4g**, **4i**, supported assigned structures.

Each carbinol (**4**) in EtOAc (2 ml/g of carbinol) contg 1 drop of concd H_2SO_4/10 ml of solvent and 1 g of 10% Pd/C per 30 g of carbinol was pressure hydrogenated at 3.5–4.2 kg/cm² for 24 hr at 70°,[24] worked-up in the conventional manner, and purified by distn *in vacuo* (Vigreux column).

Similar hydrogenation of *o*-veratraldehyde (**3**) afforded 3-methylveratrole (**5b**).

Physical properties, yield data, and purity analysis (vpc) for the 3-*n*-alkylveratroles are presented in Table I. Ir and nmr spectral data for **5b–5g** and **5i** supported structure and purity; spectra were nearly identical except for increase in bands corresponding to CH_2 units in all spectra concomitant with increased chain length.

3-*n*-Alkylcatechols (1a–1i).—The C_1–C_{11} 3-*n*-alkylveratroles (**5a–5e**) were cleaved to the corresponding catechols with preprepared refluxing pyridinium chloride (PyrCl) according to the technique of Wenkert[7f] (procedure A.) After an exploratory study carried out concurrent with these cleavages, the shorter reaction time and technical convenience of preparing the cleavage reagent *in situ* recommended use of the following improved technique (procedure B) for cleavage of the C_{13}, C_{15}, and C_{19} veratroles.

Procedure B.—A mixt of alkylveratrole and dry pyridine (2.0 moles per 0.1 mole of veratrole) was brought to pyridine reflux (water condenser only) while stirring under N_2. With the pyridine at reflux, passage of HCl gas instead of N_2 was begun. After a period of up to 2 hr (depending on the scale of the reaction being run) the internal temp of the mixt was observed to rise sharply and the refluxing of pyridine to stop. These phenomena indicated that the formation of PyrCl was complete. Continued heating brought the reaction to the reflux temp (air and water condensers) of PyrCl (218°).[25] The mixt was stirred at reflux for 4 hr, a slow flow of HCl through the reacting mixt being maintained. At the end of the reaction period, N_2 flow was substituted for HCl flow, and the reaction mixt was cooled and worked up according to the Wenkert procedure.[7f]

3-*n*-Heptadecylcatechol was obtd through purification of a sample of tetrahydrolaccol.[11]

Resulting crude oils or solids were purified by distn *in vacuo*, recrystn from hexane, or both, as necessary (see Table II). Data for the 3-*n*-alkylcatechols are given in the table. Ir, nmr, and mass spectral data for **1a–1i** supported structure and purity and were similar except as required for changes with chain length. The nmr spectrum of 3-PDC (**1g**) is representative: 3.43 (s, 3 H, arom), 3.5–4.5 (broad s, 2 H, OH), 7.49 (t, 2 H, benzylic), 8.74 (broad s, CH_2), 8.9–9.1 (t, terminal Me); signals τ 8.5–9.3 integrated for 29 H.

High-gain vpc chromatograms of each of the 3-*n*-alkylcatechols (under column conditions used for alkylveratroles; see footnote *e* to Table I) showed impurities in the range of 0.5–1.0% nearly all of which were materials of extremely low retention times and none of which corresponded to known retention time homologs or methylated analogs.

(22) B. Loev and C. R. Dawson, *J. Amer. Chem. Soc.*, **78**, 1180 (1956).

(23) Distillation of the higher mol wt carbinols was inefficient due to dehydration *in situ* and concomitant degradation–polymerization of the resulting olefins.

(24) On exploratory study of the hydrogenolysis of 3-*n*-(1′-hydroxy)pentadecylveratrole, it was found that milder conditions, *e.g.*, room temp and 2.1 kg/cm² gave complete hydrogenolysis, albeit somewhat more slowly. The conditions outlined in the text were used as standard procedure to insure completion of the desired reaction.

(25) For the complete cleavage of the longer-chained veratroles it was found necessary to run the cleavage at a temp not significantly less than the full reflux temp of PyrCl. To assure complete PyrCl reflux at 218°, it was sometimes found necessary to remove the water condenser momentarily at the beginning of the reaction in order to allow the escape of low-boiling materials. When such materials had been vented (the refluxing PyrCl could be seen to climb the walls of the air-condenser) the water-cooled condenser was replaced and the reflux temp stabilized. It was found important not to overheat the mixt once PyrCl reflux had been achieved. Overheating causes the PyrCl to reflux into the water-cooled condenser where it solidifies and fouls the vent glassware.