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BIOGENETIC-TYPE SYNTHESES OF ISOPRENOID AND DIISOPRENOID DERIVATIVES OF ORCINOL

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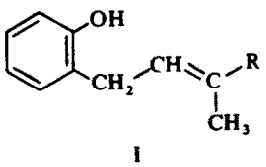
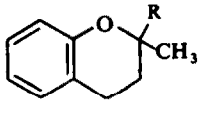
Abstract—The products formed by condensation of orcinol with 2-methyl-3-buten-2-ol, with geraniol, and with linaloöl in aqueous solutions of organic acids have been separated and identified. C-isoprenyl- and C-geranyl-orcinols are obtained as major products. Minor amounts of the corresponding hydrates, chromans, chroman hydrates, and hexahydroxanthene derivatives are also formed.

A WIDE variety of phenolic natural products contain isoprenoid (C_5) or polyisoprenoid residues.[1] Interest in the synthesis of these phenolic terpenoids, particularly those derived from 1,4-quinols and from 5-alkyl resorcinols (orcinol, olivetol), has increased with the recognition that many of these compounds are effective antibiotics, e.g. siccanin,[2,3] grifolin,[4] or possess other significant physiological properties, e.g. the tocopherols, ubiquinones,[5,6] and *Cannabis* constituents derived from geranylolivetol.[7,8]

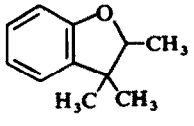
C-geranyl and C-farnesyl phenols have been prepared by reaction of geranyl or farnesyl bromide with the sodium salt of the phenol. Alkylation of sodium salts, however, invariably leads to complex mixtures containing both nuclear and oxygen substituted products. More recently, C-alkylation has been effected by the acid-catalyzed condensation of geraniol or farnesol with phenols in aprotic solvents in the presence of Lewis acids (BF_3)[6,7] or strong mineral acids such as *p*-toluenesulfonic acid.[9] The synthesis of *o*-isoprenylated phenols (I) by direct alkylation under strongly acidic conditions is often inefficient,[10] however, because of the predominance of subsequent cyclization reactions to yield chromans and coumarans of types II and III, respectively.



I



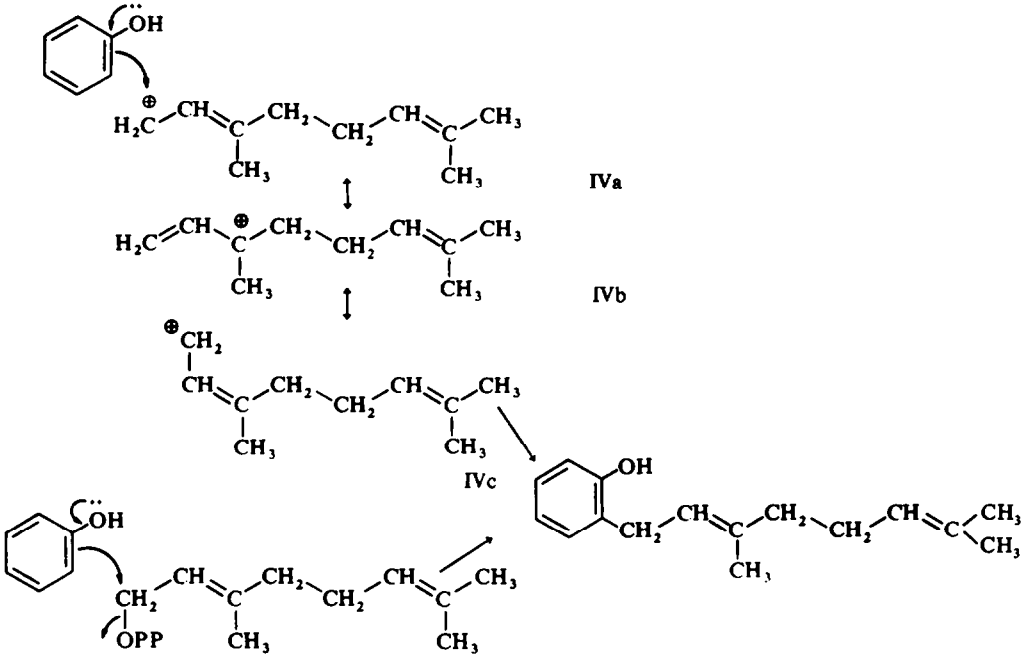
II



III

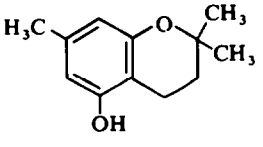
It has been suggested[1,11] that the biosynthetic origin of phenolic isoprenoids involves initial C-alkylation of a preformed phenol or its poly-β-ketonic precursor by an active

isoprenoid allylic alcohol derivative. For example, C-geranyl compounds may arise by nucleophilic attack of a phenol on the resonance stabilized cation IV or by an S_N2-type displacement of pyrophosphate from geranylpyrophosphate V. The C-isoprenylated phenol may then undergo further modification by subsequent hydration, oxidation, and cyclization reactions to yield the variety of structures found in natural systems.

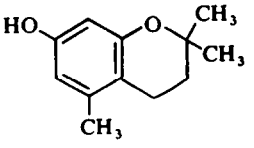


IVa IVb IVc V

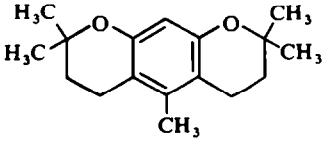
As previously mentioned, a number of important natural isoprenoids are derived from orcinol or other 5-alkyl resorcinols. The possible synthesis of these compounds in aqueous media, either by reaction with phosphate esters of allylic alcohols or by reaction with the cation, e.g. IV, formed from the protonated alcohol, is particularly attractive because of the relation of these reactions to the biogenetic proposals. The reactions of



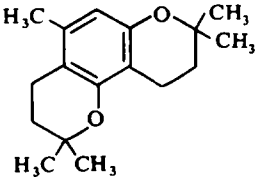
VI



VII



VIII

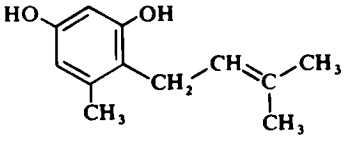


IX

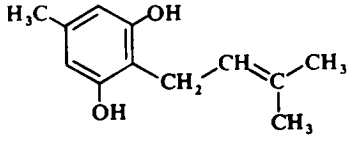
orcinol and other phenols with phosphate esters of γ,γ-dimethylallyl alcohol, geraniol, and farnesol were recently reported by Miller and Wood[12] to give chromans of type II, e.g. orcinol and γ,γ-dimethylallyl diphenyl phosphate gave the chromans VI and VII as oils and a benzodipyran of indefinite structure (VIII or IX). In this investigation we have examined the isoprenylation and geranylation of orcinol in aqueous acidic media in some detail. These studies extend earlier work[13] on the formation of *o*-isopentenylphenols and provide a basis for the synthesis of grifolin and its isomers, which is currently being undertaken in this laboratory.

Isoprenylation of orcinol. Treated with an equimolecular quantity of 2-methyl-3-buten-2-ol in dilute aqueous formic acid, orcinol gave an oily mixture from which a major product, m.p. 68–69°, readily crystallized in an overall yield of about 18%. The 100 MHz NMR spectrum of this compound in $CDCl_3$ showed the presence of two allylic Me groups as singlets at δ 1.70 and δ 1·77, a benzylic Me group as a singlet at δ 2·20, a methylene group as a doublet ($J = 6·5$ Hz) at δ 3·26, and a vinyl proton as a triplet ($J = 6·5$ Hz) at δ 5·10. These data and elemental analysis establish that the product is a noncyclized mono-isoprenylorcinol. Since the two aromatic protons appear as nonequivalent, meta coupled doublets ($J = 2$ Hz) at δ 6·19 and δ 6·24, the isoprenyl group is located between the phenolic OH and Me group of the orcinol nucleus. Structure X was further confirmed by the nuclear Overhauser effect (NOE) upon irradiation of the aromatic Me group. The high field aromatic proton at δ 6·24 increased in intensity, while that at δ 6·19 showed no change.

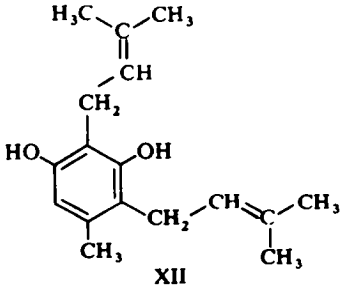
Gel filtration chromatography of the residue from the crystallization of X indicated the presence of twelve compounds. The four major components of this mixture were separated. The first of these readily crystallized (m.p. 79–80°) and its NMR spectrum showed the presence of an uncyclized dimethyl allyl group. Since the two aromatic protons occurred as a 2H singlet at δ 6·22, this product is the mono-isoprenyl orcinol XI



X



XI

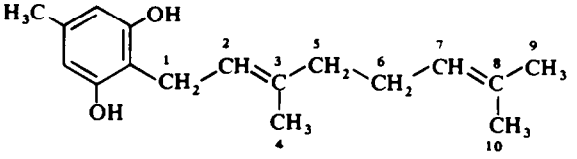


XII

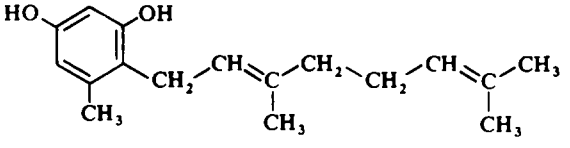
with the isoprenyl substituent between the two phenolic hydroxyls. The second chromatographic product was obtained as a homogeneous oil, whose NMR spectrum showed the presence of only one aromatic proton and two dimethylallyl groups. The methylene

groups of the two allyl units appeared as nonequivalent 2 H doublets at δ 3·32 and δ 3·46. Thus, this compound is assigned the unsymmetrical structure XII.

The two remaining major chromatographic products were chromans, apparently identical with the products VI and VII obtained in the phosphate reaction by Miller and Wood.[12] One of these chromans crystallized (m.p. 55–56°), and structures were assigned on the basis of NOE effects on their 100 MHz NMR spectrum. The spectrum of the crystalline chroman showed the *gem* dimethyl groups as a 6 H singlet at δ 1·32, two methylene groups as triplets (J = 7·0 Hz) at δ 1·79 and δ 2·62, and two aromatic protons as singlets at δ 6·15 and δ 6·23. This product is assigned structure VI. The isomeric oily chroman VII had a similar NMR spectrum, except that the two aromatic protons appeared as well-defined meta-coupled doublets at δ 6·14 and δ 6·24 (J = 2·0 Hz). The relative intensity of the doublet at δ 6·24 increased in a NOE experiment. In accord with these structural assignments the crystalline chroman VI gave an immediate intense blue color with Gibbs reagent. VII gave a brown color with this reagent.



XIII



XIV

Geranylation of orcinol. Preliminary experiments indicated that reaction of geraniol with orcinol in aqueous formic acid solutions formed substantial quantities of cyclized products. However, cyclization was minimized by reaction in 1% aqueous oxalic acid. The phenolic reaction products thus obtained were separated by gel filtration into four main fractions, two of which were homogeneous and readily crystallized to give the isomeric C-geranyl orcinols XIII (m.p. 56·5–57·5°; 5·8% yield) and XIV (m.p. 43–44°; 18% yield).

In accord with structure XIII the 100 MHz NMR spectrum (Fig 1A) of the isomer, m.p. 56·5–57·5°, showed the allylic Me protons at C_9, C_{10} and C_4 as 3 H singlets at δ 1·59, 1·68 and 1·80, respectively. The C_5 and C_6 methylene groups appeared as a broad 4 H singlet at δ 2·06, while the C_1 methylene group occurs as a doublet (J = 7·0 Hz) at δ 3·38. The methine protons at C_2 and C_7 appear as triplets at δ 5·25 and δ 5·05, the latter overlapped by two phenolic OH proton signals at about δ 5·03. The two aromatic protons showed a 2 H singlet at δ 6·22, indicating location of the diisoprenoid unit between the two phenolic hydroxyls. The diisoprenoid group could be derived from either of the canonical forms IVa or IVc of the geranyl cation. The stereochemistry of the groups about the C_2—C_3 double bond, i.e. whether the diisoprenoid substituent is

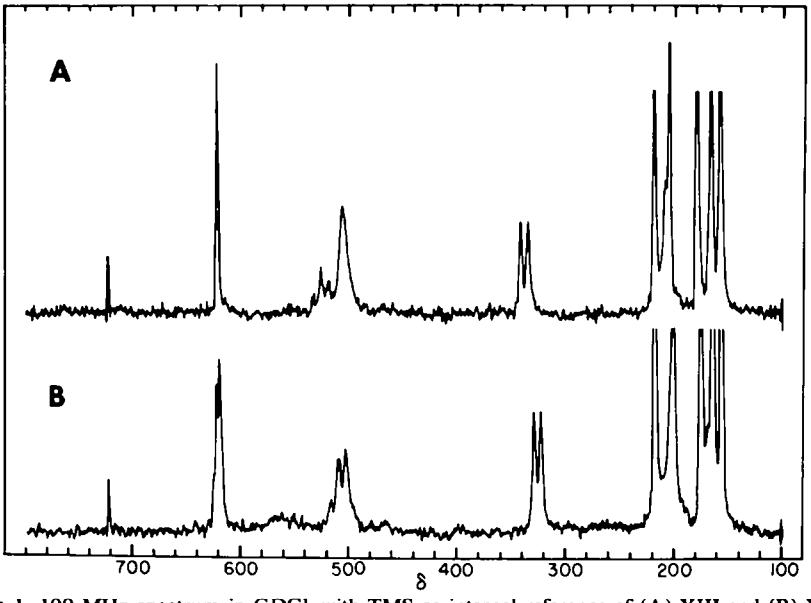
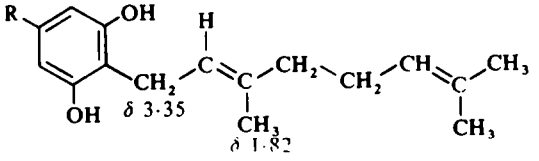
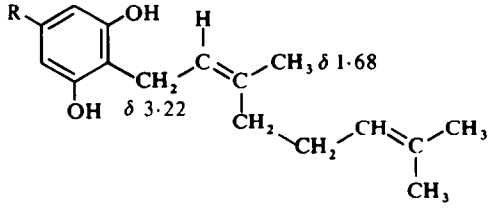


FIG 1. 100 MHz spectrum in $CDCl_3$ with TMS as internal reference of (A) XIII and (B) XIV.

geranyl or neryl, was established by the close similarity of the chemical shifts of the C_1 methylene group (δ 3·38) and Me group at C_4 (δ 1·80) with the chemical shifts[9] of corresponding methylene (δ 3·35) and Me group (δ 1·82) in geranyl-olivetol XV (cannabigerol). These chemical shifts differ markedly from those shown by neryl–olivetol XVI (C_1 methylene, δ 3·22; C_4 Me, δ 1·68) in which the C_1 methylene group is *trans* to the C_4 Me group.



XV: R - C_5H_{11}



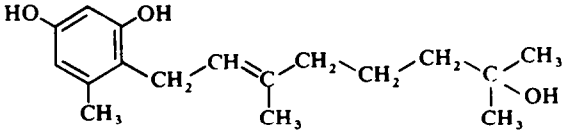
XVI: R = C_5H_{11}

The NMR spectrum (Fig 1B) of the major reaction product XIV is similar to that of XIII except that the two aromatic protons, as expected, appear as meta-coupled doublets at δ 6·19 and δ 6·23. The C_1 methylene group appears as a doublet at δ 3·26, and the C_4 Me as a singlet at δ 1·77. In the spectrum of X, the corresponding isoprenyl orcinol, the

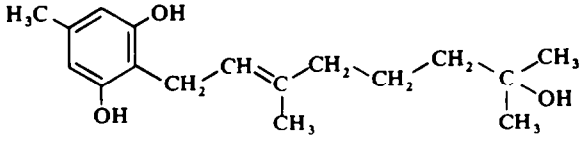
methylene group appears at δ 3·26 and the two allylic Me groups at δ 1·77 and δ 1·71. Following the observations of Bates *et al.*[14] on the chemical shifts of *cis* and *trans* allylic Me groups in phenolic substituted terpenoids, the Me group in X which appears downfield (at δ 1·77) is *cis* to the methylene group. Thus, in XIV the C_4 Me group (δ 1·77) is *cis* to the C_1 methylene group (δ 3·26) and the diisoprenoid unit is geranyl.

The remaining major fractions of the phenolic reaction mixture obtained in yields of about 18%, consisted of a mixture of nine separable minor products. Two of these proved to be hydrates of XIII and XIV, one was a hydrate of the neryl stereoisomer of XIII, one was the monogeranyl ether of orcinol, three were chromans of type II, and two were tricylic hexahydroxanthene derivatives.

One of the hydrated geranyl–orcinols was an oil, the other a crystalline solid (m.p. 110–112°). In the NMR spectrum of the oily hydrate the two aromatic protons appeared as a 2 H singlet, the C_1 methylene group as a doublet at δ 3·36, and the C_4 Me group as a singlet at δ 1·75. These data established that this product is derived from the geranyl–orcinol XIII. Hydration of the C_7–C_8 double bond of XIII to give structure XVII was indicated by the upfield shift of the C_9,C_{10} *gem*-dimethyl group to δ 1·19. The tertiary OH group at C_8 was not acetylated by acetic anhydride in cold pyridine. However, acetylation of the reaction product with isopropenyl acetate gave a triacetate in which the two aromatic acetoxyl groups appeared as a 6 H singlet at δ 2·27 and the tertiary acetoxyl as a 3 H singlet at δ 1·95. In accord with structure XVII the acetylation of the tertiary OH resulted in a 21 Hz deshielding of the *gem*-dimethyl group (from δ 1·19 to δ 1·40). The NMR spectra of the crystalline hydrate and its triacetate were similar to those of XVII and its triacetate, except that the aromatic protons appeared as meta-coupled doublets. This hydrate, therefore, is the corresponding isomer XVIII.

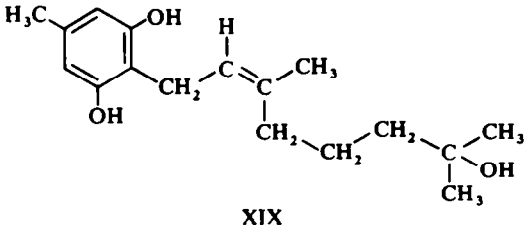


XVIII



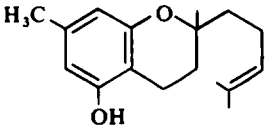
XVII

The hydrated neryl-orcinol XIX is unique in being the only isolated geraniol–orcinol reaction product in which the C_1 methylene group is *trans* to the C_4 Me group. The structural features present in this product were ascertained by spectral considerations similar to the above. The stereochemistry about the C_2—C_3 double bond was confirmed by the close identity of the chemical shifts of its C_1 methylene group (δ 3·22) and C_4 Me group (δ 1·69) with those[9] of the C_1 methylene (δ 3·22) and C_4 Me (δ 1·68) of neryl–olivetol XVI.

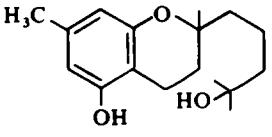


XIX

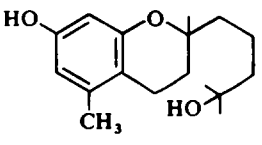
The three chromans isolated in this reaction were identified on the basis of their NMR spectra[15] and their color reactions with Gibbs reagent,[16] and were assigned structures XX, XXI and XXII. In accord with the structural assignments the oily chroman XX



XX



XXI

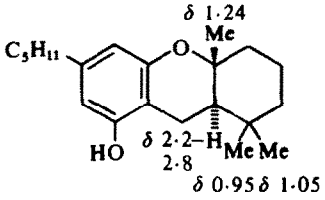


XXII

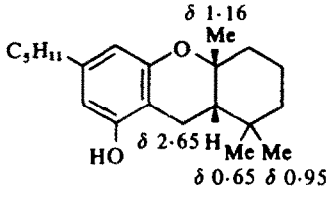
showed a vinylic proton at δ 5·21 and two allylic Me groups at δ 1·60 and δ 1·68. Hydration of XX to yield XXI resulted in an upfield shift of the *gem*-dimethyl group to δ 1·23. With Gibbs reagent XXI gave an immediate, intense blue color. In contrast to XXI, the crystalline isomer XXII did not give a positive Gibbs test.

One of the two hexahydroxanthene derivatives was isolated as an oil, the other as a crystalline solid. The spectrum of the oily product showed the presence of three Me groups (singlets at δ 0·92, 1·01, 1·22), three methylene groups (multiplet, 6 H, δ 1·30–1·80) and a benzylic methylene group (multiplet at δ 2·20–2·84). Comparison of this spectrum with those of the *trans* XXIII and *cis* XXIV hexahydroxanthene derivatives, prepared from cannabigerol and neryl–olivetol,[9] indicates a *trans* ring junction and structure XXV for this compound. On the basis of its NMR spectrum the crystalline, isomeric product can be assigned the *trans* structure XXVI.

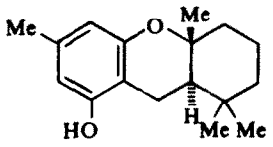
The hexahydroxanthene XXIII was synthesized by the action of 100% sulfuric acid on a solution of geranyl–olivetol in nitromethane. Mechoulam and Yagen[9] recently suggested that this bicyclization reaction, initiated by direct proton addition to the terminal double bond, may represent an organic model for related biochemical cyclizations. The formation of hexahydroxanthenes, in addition to the terminal hydrates and chromans, in the reaction of geraniol with orcinol under more mild conditions in aqueous media lends additional support to this proposal. The variety of phenolic diisoprenoids formed in aqueous media arise from proton addition to the C_2,C_3 double bond or the terminal C_7,C_8 double bond. The carbonium ion formed from the terminal



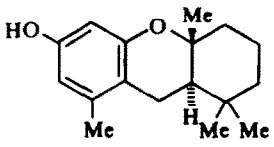
XXIII



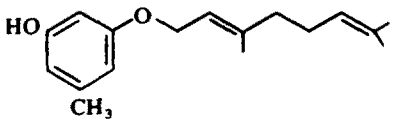
XXIV



XXV



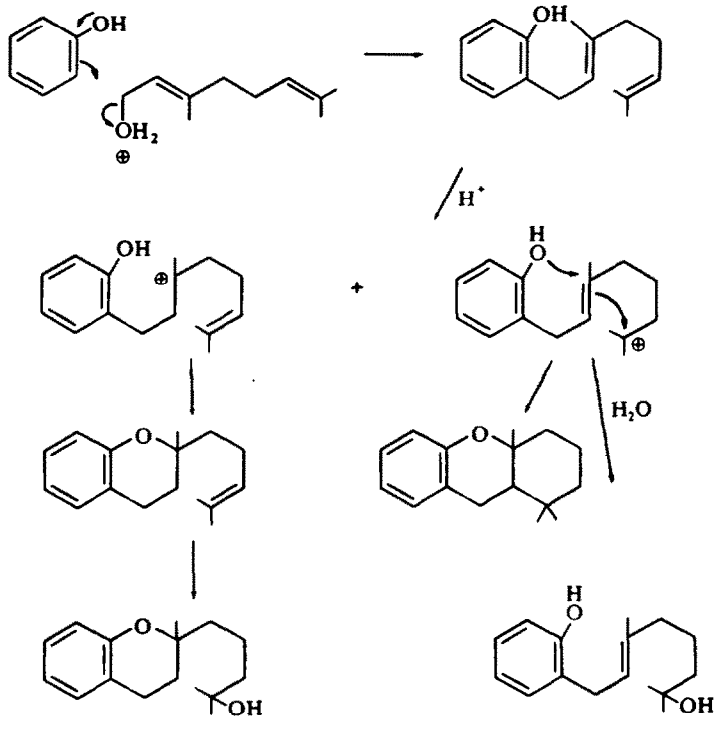
XXVI



XXVII

double bond may then undergo competitive hydration or intramolecular cyclization.

The experimental evidence does not indicate whether the initial orcinol–geraniol condensation involves an S_N1 or S_N2 reaction. However, since the condensation of



linaloöl with orcinol in aqueous acid solution yields essentially similar yields of the same products, these products seem to support the condensation reaction proceeding by nucleophilic attack of the phenol on the cation IV, the retention of the geranyl configuration in the phenolic products being due to the greater thermodynamic stability of this form compared to neryl.

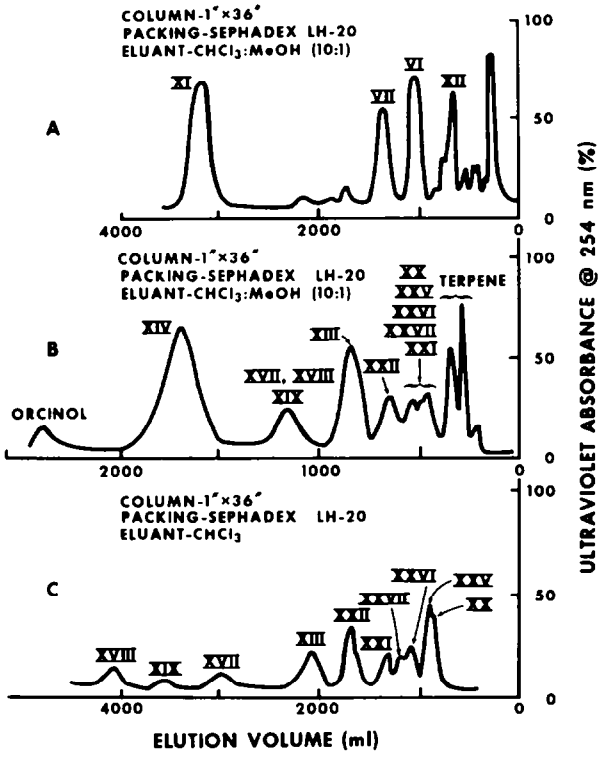


FIG 2. (A) Elution profile of orcinol–prenylation reaction; (B) and (C) elution profiles of orcinol–geraniol reaction products.

EXPERIMENTAL

NMR spectra were recorded on a modified Varian HA-100 spectrometer as 5–10% W/V solns in $CDCl_3$ with TMS as an internal standard. TLC R_f values were determined on silica plates with benzene–EtOH (9 : 1, V/V) as solvent. The low yields of many of the minor components in this investigation necessitated high resolution mass spectral elemental analysis in lieu of normal elemental analysis.

Reaction of 2-methyl-3-buten-2-ol with orcinol. 2-Methyl-3-buten-2-ol (8·6 g) was added dropwise during 15 min to a stirred soln of orcinol (14·2 g) in warm (80°) water (25 ml) containing formic acid (10 ml). The mixture was allowed to come to room temp during the addition. Stirring was continued for 1 hr after which water (200 ml) and low boiling light petroleum (30 ml) were added. The oily product partially crystallized on cooling. Recrystallized from CCl_4 and from benzene–light petroleum, X separated as colorless, glistening plates, m.p. 68–69° (3·40 g), R_f 0·58. (Found: C, 74·6; H, 8·30. Calc. for $C_{12}H_{16}O_2$: C, 74·9; H, 8·39%); NMR spectrum: 3 H, δ 1·70, m; 3 H, δ 1·77, s; 2 H, δ 3·26, d, J = 6·5 Hz; 1 H, δ 5·10, t, J = 6·5 Hz; 1 H, δ 6·19, d, J = 2 Hz; 1 H, δ 6·24, d, J = 2 Hz.

Filtrates from the crystallization of X were concentrated to an oil, which was dissolved in chloroform (50% soln), applied to Sephadex LH-20 column (1" × 36"), and eluted with chloroform. The elution profile,

obtained by monitoring the elute at 254 nm, is shown in Fig 2A. The major components VI, VII, XI, and XII were separated by evaporation of the appropriate fractions.

XII was obtained as a chromatographically homogeneous oil, R_f 0·37, NMR: 6 H, δ 1·89, s, 6 H, δ 1·98, s; 3 H, δ 2·21, s; 2 H, δ 3·32, d, J = 6·5 Hz; 2 H, δ 3·46, d, J = 6·5 Hz; 2 H, 4·9–5·4, m; 1 H, δ 6·30, s. VI crystallized from low boiling light petroleum as slightly yellow needles, m.p. 55–56°, R_f 0·85; NMR: 6 H, δ 1·32, s; 2 H, δ 1·79, t, J = 7 Hz; 3 H, 2·20, s; 2 H, δ 2·62, t, J = 7 Hz; 1 H, δ 6·15, s; 1 H, δ 6·23, s. Mol. wt. required for $C_{12}H_{16}O_2$ 192·1150; obs. 192·1179. VII was obtained as an oil, R_f 0·75, NMR: 6 H, δ 1·23, s; 2 H, δ 1·79, t, J = 7 Hz; 3 H, δ 2·14, s; 2 H, δ 2·52, t, J = 7 Hz; 1 H, δ 6·14, d, J = 2 Hz; 1 H, δ 6·24, d, J = 2 Hz. Mol. wt. required for $C_{12}H_{16}O_2$ 119·1150; obs. 119·1241. XI crystallized from low boiling light petroleum to yield colorless needles, m.p. 79–80°, R_f 0·69. (Found: C, 74·9; H, 8·30. Calc. for $C_{12}H_{16}O_2$: C, 74·9; H, 8·39%); NMR: 3 H, δ 1·74, m; 3 H, δ 1·80, s; 3 H, δ 2·19, s; 2 H, δ 3·36, d, J = 7 Hz; 1 H, δ 5·25, t, J = 7 Hz; 2 H, δ 6·22, s.

Reaction of geraniol with orcinol. Geraniol (15·4 g) was added in portions during 10 min to a stirred soln of orcinol (28·4 g) in 1% aqueous oxalic acid (300 ml) at 80°. After 1 hr the mixture was cooled and extracted with chloroform. The dried chloroform extract (Na_2SO_4) was evaporated to an oil. A 50% chloroform soln of this oil was applied in 2·0 ml portions to a Sephadex LH-20 chromatographic column and eluted with $CHCl_3$–MeOH (10 : 1, V/V). The elution profile, obtained by monitoring at 254 mn, is shown in Fig 2B. Fractions containing the major components XIII and XIV were separated and evaporated to oils.

XIII crystallized on standing. Recrystallization from low boiling light petroleum gave XIII as fine, colorless needles, m.p. 56·5–57·5°, R_f 0·63. (Found: C, 78·4; H, 9·26. Calc. for $C_{17}H_{24}O_2$: C, 78·4; H, 9·29%); NMR: 3 H, δ 1·59, s; 3 H, δ 1·68, s; 3 H, δ 1·80, s; 4 H, δ 2·06, broad s; 3 H, δ 2·20, s; 2 H, δ 3·38, d, J = 7 Hz; 3 H, δ 4·9–5·1, m; 1 H, δ 5·25, t, J = 7 Hz; 2 H, δ 6·22, s.

XIV also crystallized on standing. On repeated recrystallization from low boiling light petroleum it separated as glistening, colorless needles, m.p. 43–44°, R_f 0·54. (Found: C, 73·5, H, 9·31. Calc. for $C_{17}H_{24}O_2$. H_2O: C, 73·4; H, 9·41%); NMR: 3 H, δ 1·58, s; 3 H, δ 1·66, s; 3 H, δ 1·77, s; 4 H, δ 2·02, broad s; 3 H, δ 2·19, s; 2 H, δ 3·26, d, J = 6·5 Hz; 2 H, δ 4·90–5·10, broad m; 1 H, δ 5·60–5·80, br.s; 1 H, δ 5·09, t, J = 6·5 Hz; 1 H, δ 6·19, d, J = 2 Hz; 1 H, δ 6·23, d, J = 2 Hz.

After crystallization of XIII and XIV residual phenolic fractions were combined and concentrated to an oil. A 50% chloroform soln of this oil was rechromatographed on an LH-20 Sephadex column with chloroform as eluent. The elution profile showing the separation of compounds, XVII, XVIII, XIX, XX, XXI, XXII, XXV, XXVI, and XXVII is indicated in Fig 2C.

XVII was obtained as an oil, R_f 0·37, NMR: 6 H, δ 1·19, s; H, δ 1·30–1·58, m; 3 H, δ 1·75, s; 1 H, δ 1·65, br.s; 2 H, δ 1·86–2·08, m; 3 H, δ 2·15, s; 2 H, δ 3·36, d, J = 7 Hz; 1 H, δ 5·22, t, J = 7 Hz; 2 H, δ 6·19, s. Mol. wt. required for $C_{17}H_{26}O_3$ 278·1890; obs. 278·1858. Acetylation of XVII with Ac_2O in pyridine gave a noncrystalline diacetate, NMR: 6H, δ 1·20, s; 4H, δ 1·30–1·53, m; 3 H, δ 1·71, s; 1H, δ 1·65, br.s; 2H, δ 1·86–2·08, m; 6H, δ 2·27, s; 3 H, δ 2·31, s; 2 H, δ 3·27, d, J = 7 Hz; 1 H, δ 5·17, t, J = 7 Hz; 2 H, δ 6·75, s. Acetylation of XVII with isopropenyl acetate containing 1% *p*-toluenesulfonic acid gave a triacetate, NMR: 6 H, δ 1·40, s; 2 H, δ 1·20–1·45, m; 4 H, δ 1·55–1·78, m; 3 H, δ 1·75, s; 3 H, δ 1·95, s; 2 H, δ 1·80–2·08, m; 3 H, δ 2·27, s; 3 H, δ 2·28, s; 3 H, δ 2·31, s; 2 H, δ 3·27, d, J = 7 Hz; 1 H, δ 5·17, t, J = 7 Hz; 2 H, δ 6·75, s. Mass spectrum of XVII triacetate shows no m^+ at m/e 404. Analysis of m^+—CH_3COOH (m/e 344) requires for $C_{21}H_{28}O_2$ 344·1985; obs. 344·1916.

XVIII crystallized from low boiling light petroleum as granular, colorless crystals, m.p. 110–112°, R_f 0·19, NMR: 6 H, δ 1·20, s; 4 H, δ 1·35–1·60, m; 3 H, δ 1·78, s; 1 H, δ 1·70, br.s; 2 H, δ 1·88–2·14, m; 3 H, δ 2·23, s; 2 H, δ 3·28, d, J = 6·5 Hz; 1 H, δ 5·12, t, J = 6·5 Hz; 1 H, δ 6·20, d, J = 2 Hz; 1 H, δ 6·26, d, J = 2 Hz. Acetylation with Ac_2O and pyridine gave an oily diacetate, NMR: 6 H, δ 1·20, s; 4 H, δ 1·35–1·60, m; 3 H, δ 1·73, s; 1 H, δ 1·70, br.s; 2 H, δ 1·85–2·10, m; 3 H, δ 2·26, s; 3 H, δ 2·28, s; 3 H, δ 2·30, s; 2 H, δ 3·21, d, J = 6·5 Hz; 1 H, δ 4·98, t, J = 6·5 Hz; 1 H, δ 6·77, d, J = 2 Hz; 1 H, δ 6·81, d, J = 2 Hz. Acetylation with isopropenyl acetate gave a noncrystalline triacetate, NMR: 6 H, δ 1·40, s; 2 H, δ 1·20–1·45, m; 4 H, δ 1·35–1·65, m; 3 H, δ 1·73, s; 2 H, δ 1·85–2·10, m; 3 H, δ 1·96, s; 3 H, δ 2·26, s; 3 H, δ 2·28, s; 3 H, δ 2·30, s; 2 H, δ 3·21, d, J = 6·5 Hz; 1 H, δ 4·98, t, J = 6·5 Hz; 1 H, δ 6·71, d, J = 2 Hz; 1 H, δ 6·81, d, J = 2 Hz. Mass spectrum of XVIII triacetate shows no m^+ at m/e 404. Analysis of m^+—CH_3COOH (m/e 344) requires for $C_{21}H_{28}O_4$ 344·1985; obs. 344·1930.

Compound XIX was obtained as an oil, R_f 0·37, NMR: 6 H, δ 1·16, s; 4 H, δ 1·20–1·48, m; 1 H, δ 1·58, br.s; 3 H, δ 1·69, s; 2 H, δ 1·70–1·98, m; 3 H, δ 2·14, s; 2 H, δ 3·22, d, J = 6·5 Hz; 1 H, δ 5·06, t, J = 6·5 Hz; 2 H, δ 6·19, s. Acetylation with Ac_2O in pyridine yields a noncrystalline diacetate, NMR: H, δ

1·15, s; 4 H, δ 1·20–1·50, m; 3 H, δ 1·65, s; 2 H, δ 1·78–2·00, m; 6 H, δ 2·27, s; 3 H, δ 2·31, s; 2 H, δ 3·13, d, J = 6·5 Hz; 1 H, δ 5·01, t, J = 6·5 Hz; 2 H, δ 6·75, s. Acetylation with isopropenyl acetate yields a noncrystalline triacetate. Triacetate NMR: 6 H, δ 1·40, s; 4 H, δ 1·50–1·80, m; 3 H, δ 1·65, s; 2 H, δ 1·80–2·08, m; 3 H, δ 1·95, s; 6 H, δ 2·27, s; 3 H, δ 2·31, s; 2 H, δ 3·13, d, J = 6·5 Hz; 1 H, δ 5·01, t, J = 605 Hz; 2 H, δ 6·75, s.

Compound XX was obtained as an oil, R_f 0·65; NMR: 3 H, δ 1·29, s; 3 H, δ 1·60, s; 3 H, δ 1·68, s; 4 H, δ 1·40–1·75; 2 H, δ 1·79, t, J = 6·5 Hz; 3 H, δ 2·19, s; 2 H, δ 2·62, t, J = 6·5 Hz; 1 H, δ 5·08, t, J = 6·5; 1 H, δ 6·16, s; 1 H, δ 6·23, s. Mol. wt. required for $C_{17}H_{24}O_2$ 260·1775; obs. 260·1719.

Compound XXI was obtained as an oil, R_f 0·43; NMR: 6 H, δ 1·22, s; 3 H, δ 1·25, s; 6 H, δ 1·27–1·60, m; 2 H, δ 1·76, t, J = 7 Hz; 3 H, δ 2·18, s; 2 H, δ 2·59, t, J = 7 Hz; 1 H, δ 6·14, s; 1 H, δ 6·23, s. Mol. wt. required for $C_{17}H_{26}O_3$ 278·1880; obs. 278·1845.

Compound XXII crystallized from low boiling light petroleum to yield fine colorless needles, m.p. 130–131°, R_f 0·42. NMR: 6 H, δ 1·22, s; 3 H, δ 1·25, s; 6 H, δ 1·35–1·68, m; 2 H, δ 1·78, t, J = 7 Hz; 3 H, δ 2·13, s; 2 H, δ 2·50, t, J = 7 Hz; 1 H, δ 6·14, d, J = 2 Hz; 1 H, δ 6·23, d, J = 2 Hz. Mol. wt. required for $C_{17}H_{26}O_3$ 278·1880; obs. 278·1903.

Compound XXV was obtained as an oil, R_f 0·66. NMR: 3 H, δ 0·92, s; 3 H, δ 1·01, s; 3 H, δ 1·22, s; 6 H, δ 1·30–1·80, m; 1 H, δ 1·84–2·05, m; 3 H, δ 2·19, s; 2 H, δ 2·20–2·83, m; 1 H, δ 5·50–5·80, br.s; 1 H, δ 6·16, s; 1 H, δ 6·23, s. Mol. wt. required for $C_{17}H_{24}O_2$ 260·1775; obs. 260·1743.

Compound XXVI was obtained as an oil which crystallized from low boiling light petroleum to yield fine colorless crystals, m.p. 165–169°. R_f 0·66. NMR: 3 H, δ 0·92, s; 3 H, δ 1·01, s; 3 H, δ 1·18, s; 6 H, δ 1·38–1·82, m; 1 H, δ 1·80–2·00, m; 3 H, δ 2·18, s; 2 H, δ 2·04–2·65, m; 1 H, δ 4·68, br.s; 1 H, δ 6·12, d, J = 2 Hz; 1 H, δ 6·21, d, J = 2 Hz. Mol. wt. required for $C_{17}H_{24}O_2$ 260·1775; obs. 260·1791.

Compound XXVII was obtained as an oil, R_f 0·55. NMR: 3 H, δ 1·55, s; 3 H, δ 1·63, s; 3 H, δ 1·66, s; 4 H, δ 1·90–2·16, m; 3 H, δ 2·22, s; 2 H, δ 4·42, d, J = 6 Hz; 1 H, δ 5·05, m; 1 H, δ 5·44, tr, J = 6 Hz; 3 H, δ 6·15–6·30, m. Mol. wt. required for $C_{17}H_{24}O_2$ 260·1775; obs. 260·1727.

Reaction of linaloöl with orcinol. Purified linaloöl (94%) was reacted with orcinol under conditions identical to the geraniol–orcinol reaction. Reaction products were separated on a Sephadex LH-20 column as previously described and yields were approximated by gravimetric analysis. Components and yields were: XIII (6%), XIV (18·5%); XVII, XVIII, XIX (2·7%); XX, XXI, XXII, XXV, XXVI, XXVII (8·8%).

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