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TRANSFORMATIONS OF GERANIOL IN AQUEOUS ACID SOLUTIONS

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Abstract—Geraniol decomposition in aqueous oxalic acid yields twenty-three identified products, most of which retain the oxidation level of geraniol and result from simple hydration and proton-transfer reactions. However, a large quantity of the reduced alcohol, citronellol, is formed along with cymenol, the oxidation product of α-terpineol, indicating that hydride ion transfer reactions play a major role in these terpene alcohol interconversions.

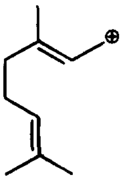
THE ACID-CATALYSED ALKYLATION of phenols with geraniol,[1] citral[2] and similar terpenes[3] has been the subject of a number of recent investigations connected with the synthesis of biologically-active phenolic terpenoids. The alkylations have commonly been effected in aprotic solvents with Lewis acids or strong, mineral acids, *e.g.* BF_3 in dioxane for the synthesis of tocopherols and geranyl and farnesyl analogs of the ubiquinones;[4, 5] *p*-toluenesulfonic acid in CH_2Cl_2 for the synthesis of cannabigerol and related marihuana constituents.[1] More recently it was reported[6] that *o*-isopentenyl phenols may be synthesized in good yields by condensation of γ,γ-dimethylallyl alcohol or 2-methyl-3-buten-2-ol with phenols in aqueous solutions of organic acids. Biogenetic-type syntheses of phenolic terpenoids by geranylation of phenols under similar aqueous conditions,[7] however, are complicated, not only by subsequent cyclizations of the initially formed C-geranyl phenols, but also by acid-catalysed intramolecular rearrangements and intermolecular oxidation-reduction reactions of the terpene alcohol. These latter transformations compete with phenolic condensation and account for up to 60% of the geraniol consumed in phenol-geraniol reaction mixtures.

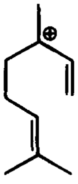
In connection with current studies on the synthesis of phenolic terpenoids we have extended earlier work on the identity of acid transformation products of geraniol. The reactions of this alcohol in aqueous solutions of organic acids does not appear to have been studied previously. However, it has been reported that under more vigorous conditions, *e.g.* with H_2SO_4 or BF_3, geraniol (XXII) may yield nerol, α-terpineol, dipentene, terpinolene, 2-cyclogeraniol, and linaloöl. Linaloöl, the allylic isomer of geraniol, has been reported to form 1,4-cineole, 1,8-cineole, and ocimene in addition to the above products.[8, 10–13]

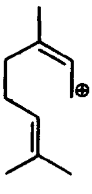
In this investigation geraniol was heated with aqueous solutions of oxalic acid (1–5%) for varying periods of time up to 8 hr, these conditions being similar to those used in typical phenol–geraniol condensations. After 2 hr in 1% aqueous oxalic acid, geraniol was completely converted into a mixture of 27 other compounds. These products were separated by gas chromatography and are tabulated in Table 1. In general they were identified on the basis of their mass spectra and standard retention times. Compounds giving rise to peaks 2, 13, 16 and 17 could not be identified with certainty by GLC-mass spectra; they were isolated by distillation and preparative gas chromatography and assigned structures IV,[14] VIII, IX and X on the basis of their 100 MHz NMR spectra in $CDCl_3$. The spectrum of myrcenol (VIII) previously synthesized[15] by alkaline hydrolysis of the acetate formed by addition of AcOH to myrcene, has not been reported. However, in accord with this structure, the NMR spectrum of peak 13 showed signals at δ1·14 (s, 6H, geminal dimethyl group), δ1·77 (s, 1H, OH), δ2·16 (t, 2H, J = 6·0 Hz, vinyl methylene), δ4·93 (s, 2H, terminal vinyl protons), δ4·98 (d, 1H, J = 10·0 Hz, terminal vinyl proton), δ5·14 (d, 1H, J = 17·0 Hz, terminal vinyl proton), δ6·27 (d–d, 1H, J = 10, 17 Hz). Mass spectrum: *m/e* 59 (100), 43 (66), 41 (47), 79 (38), 81 (33).

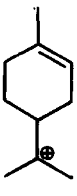
The compounds responsible for peaks 16 and 17 are geometric isomers and give essentially identical mass spectral cracking patterns (MW. 154), *m/e* 93 (100), 59 (99), 43 (79), 81 (65), 41 (60). The NMR spectrum of peak 17 showed a geminal dimethyl group at δ1·18 (s, 6H), a vinyl methyl group at δ1·72 (s, 3H), a terminal vinyl proton at δ4·83 (d, 1H, J = 10·0 Hz), a terminal vinyl proton at δ4·97 (d, 1H, J = 18 Hz), a vinyl proton at δ5·41 (t, 1H, J = 7·0 Hz), and a vinyl proton at δ6·24 (d–d, 1H, J = 10·0, 18·0 Hz). On the basis of this spectrum this compound is either *cis* or *trans* ocimol[17] (IX or X). The NMR spectrum of peak 16 is very similar to that of peak 17 except that the vinyl methyl group occurs as a singlet at δ1·75. Since it has been shown[16] that in nonsymmetrical trisubstituted double bonds a vinyl methyl group occurs at a lower field (approximately 7 Hz) in the *cis* relative to the *trans* isomer, peak[17] is considered to be *trans*-ocimol X and peak 16 the *cis* isomer IX.[17]

In aqueous acid solutions geraniol forms a cation which is a resonance stabilized hybrid of the canonical conformers Ia, Ib and Ic. Cyclization of the cation results in the formation of the carbonium ion II.


Ia

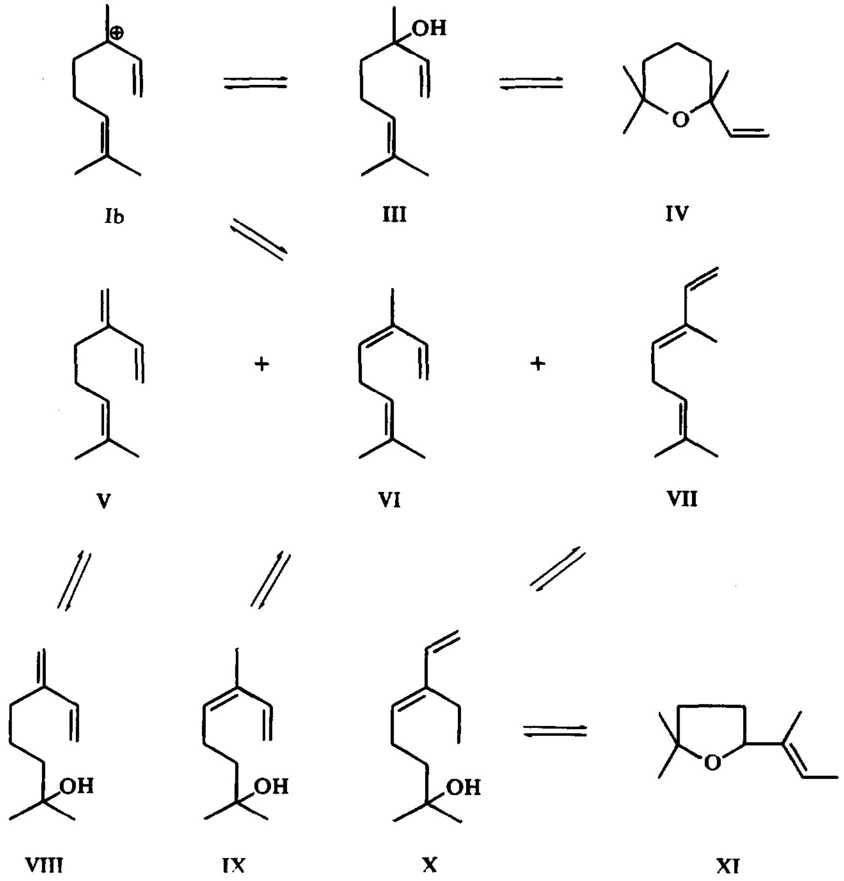

Ib


Ic


II

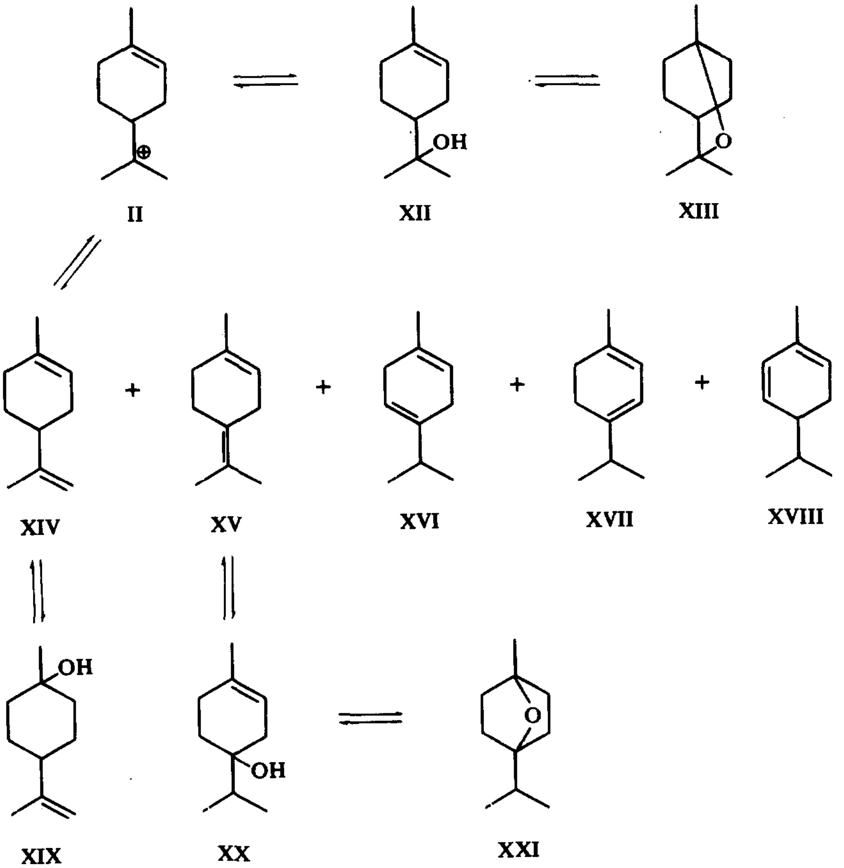
With the exception of citronellol, and a minor quantity (2%) of nerol, the terpenes formed from geraniol may be considered to be derived by subsequent well-recognized reactions (deprotonation, hydration) of the carbonium ion II (49% of total product) or the canonical form Ib of the geranyl cation (35% of the total product). Essentially, therefore, geraniol decomposition combines the decomposition reactions of both α-terpineol[18] and linaloöl.

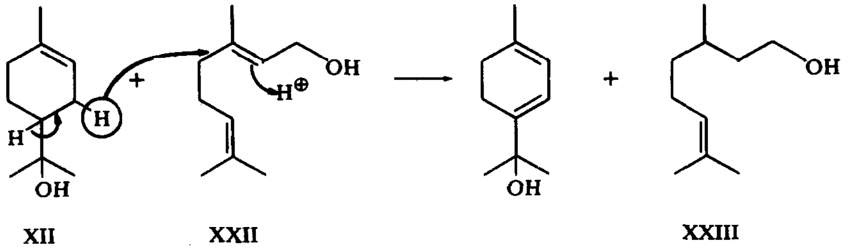
Thus, in aqueous oxalic acid Ib is hydrated to give linaloöl III, which cyclizes to IV. Also Ib is deprotonated to yield the hydrocarbons, myrcene V, *cis*- VI and *trans*-ocimene VII. Hydration of these hydrocarbons yields the corresponding alcohols VIII, IX, X and the ether XI.



In the aqueous medium, II is chiefly hydrated to yield α-terpineol XII (26%) and, subsequently, 1,8-cineole (XIII). Deprotonation of II gives the hydrocarbons limonene (XIV), terpinolene (XV), γ-terpinene (XVI), α-terpinene (XVII), and α-phellandrene (XVIII). Hydration of limonene and terpinolene yields the corresponding alcohols, β-terpineol (XIX) terpinen-4-ol (XX), and 1,4-cineole (XXI).

As indicated above, about 80% of the geraniol in aqueous oxalic acid solutions is converted into other terpenes at the same oxidation level by simple hydration and proton transfer reactions. However, the observation that geraniol (XXII) yields substantial quantities of the reduced alcohol, citronellol (XXIII), was entirely un-


⊕
OH
O
II
XII
XIII
+
XIV
XV
XVI
XVII
XVIII
OH
OH
O
XIX
XX
XXI


H
H
OH
+
OH
H⊕
+
OH
OH
XII
XXII
XXIII

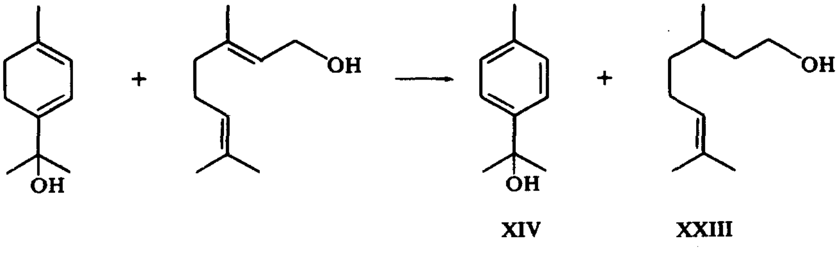

+
OH
OH
+
OH
OH
XIV
XXIII

TABLE 1. DECOMPOSITION OF GERANIOL IN AQ. OXALIC ACID

Peak No.	Product	%
1	Limonene(XIV)	0·21
2	2,6,6-Trimethyl-2-vinyl tetrandropyran(IV)	8·58
3	Myrcene(V)	1·28
4	α-Tepinene(XVII)	0·75
5	Tepinen-4-ol(XX)	0·75
6	α-Terpinene(XVI)	0·1
7	Terpinen-4-ol	0·1
8	1,4- and 1,8-Cineole(XXI), (XIII)	5·68
9	Ocimenes (VI), (VII) and (XI)	6·54
10	α-Phellandrene (XVII)	2·1
11	Terpinolene (XV)	3·75
12	Linaloöl (III)	3·86
13	Myrcenol (VIII)	2·46
14	Unknown	0·42
15	β-Terpineol (XIX)	0·75
16	*Cis*-ocimol (IX)	5·15
17	*Trans*-ocimol (X)	5·90
18	Unknown (MW. 154)	0·53
19	Unknown (MW. 154)	0·32
20	Unknown (MW. 154)	1·71
21	α-Terpineol (XII)	26·28
22	Cymenol (XXIV)	2·68
23	Unknown (MW. 154)	1·07
24	Citronellol (XXIII)	16·30
25	Unknown (MW. 154)	1·39
26	Unknown (MW. 154)	0·1
27	Nerol	2·03
	Unknown % 5·54	
	Known 95·25	

expected, the amount of citronellol formed (16%) indicating that reduction of geraniol is both a facile and favored reaction pathway in aqueous acid media. Furthermore, cymenol (XXIV), the oxidation product of α-terpineol, and *p*-cymene the oxidation product of γ-terpinene (XVI) and isomeric hydrocarbons, are also formed in the geraniol decomposition. The formation of trace amount of *p*-cymene and other oxidation products has been reported in lemon oil,[19] citral,[20] and α-terpineol[18] decomposition. The origin of these oxidation products—whether they are formed by aerial oxidation or disproportionation reactions— has not been clearly established. The identification of citronellol as a major product, however, indicates that the oxidation products are almost certainly formed in acidic media by intermolecular hydride ion transfer reactions, chiefly from α-terpineol to geraniol.

Heating geraniol in 1% aqueous oxalic acid for longer periods of time or using more concentrated acid solutions gave the same product distribution with minor quantitative differences. Under similar conditions linaloöl decomposed to give essentially the same products as geraniol except that a higher relative concentration of the tetrahydropyran (IV) was obtained.

EXPERIMENTAL

Acid decomposition of geraniol

Commercial geraniol was purified by distillation at 10 mm pressure through a two foot spinning band column. The distillate consisted of a mixture of geraniol (95%) and nerol (5%). A mixture of the purified geraniol (5 g) and 1% aq. oxalic acid (100 ml) was heated under reflux for two hr, cooled, and extracted with ether (2 × 100 ml.). The ether extract was washed with water (3 × 100 ml), dried ($MgSO_4$), and evaporated to yield a yellow oil (4·8 g). The oily product was separated into its components by gas chromatography on a 980 ft × 0·03 in. (i.d.) open tubular column coated with OV-101 silicone oil. The initial temperature was 100° and a program rate of approximately 1°/min was maintained until 180° was reached.

The components emerging from the gas chromatograph were directed over a single stage, membrane-type molecular separator[21] which was held at 135°. A quadrupole mass spectrometer (EAI model 300) was connected to the high vacuum side of the separator to obtain mass spectral cracking patterns of the individual compounds as they diffused through the molecular separator. Mass spectral charts were obtained from a recording oscillograph and these compared with the cracking pattern of known compounds to make the structural assignments shown in Table 1.

Isolation of peaks 2, 13, 16 *and* 17

Components 2, 13, 16 and 17 were isolated by distillation on a 2 ft. spinning band column at 10 mm pressure. The final purification was effected by prep GC on a 30 ft. × ½ in. SF-96(50) silicone oil column which was held at 150°.

Reference to a company or product does not imply approval or recommendation of the product by the U.S. Department of Agriculture to the exclusion of others that may be suitable.

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