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Intramolecular Interaction between Hydroxyl Group and π-Electrons. XX.[1] Conformationally-fixed *o*-Vinylphenols

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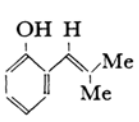
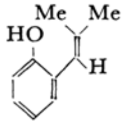
1, 2-Dihydro-5-hydroxy-8-methoxy-3-methylnaphthalene (III) was prepared, starting from 5, 8-dimethoxy-α-tetralone, via 8-hydroxy-5-methoxy-2-methyl-1-keto-1, 2, 3, 4-tetrahydronaphthalene. The O–H stretching absorptions (ν_{O-H}) and the ultraviolet absorptions of III, 1, 17 β-dihydroxy-4-methylestra-1, 3, 5(10), 9(11)-tetraene (IV), and the related naphthols were measured and compared with those of *o*-isobutenylphenol. IV showed a ν_{O-H} at 3532 cm^{-1} which is assigned to the hydroxyl group taking part in the strong interaction with the π-electrons on the ethylenic group; it corresponds well in its location to the lowest frequency band of *o*-isobutenylphenol. The previous assignment of this band to the conformer II with the double bond *syn* to the hydroxyl was thus confirmed. III showed only a symmetric band at 3618 cm^{-1}, which was assigned to the free ν_{O-H}, and could not be a model for the conformer with a ν_{O-H} at 3576 cm^{-1}, presumably because of the more planar structure for the overlap between the orbitals of the hydroxyl group and the ethylenic group.

In the foregoing paper,[1] the doublet O–H stretching absorption bands (ν_{O-H}) at 3576 and 3539 cm^{-1} of *o*-isobutenylphenol were assigned to the hydroxyl groups interacting with the π-electrons in conformations expressed approximately by I and II respectively. In an attempt to verify this tentative assignment, the model compounds conformationally fixed as in I and II have now been prepared and their ν_{O-H} absorptions examined. They are α-naphthol, 5-hydroxy-1, 2-dihydronaphthalene,[2] 1, 2-dihydro-5-hydroxy-8-methoxy 3-methylnaphthalene (III), and 1, 17-β-dihydroxy-4-methylestra-1, 3, 5(10), 9(11)-tetraene(IV)[3];

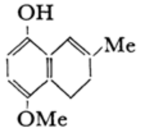


I

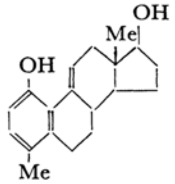


II

all are known compounds except III, whose preparation started from 5, 8-dimethoxy-α-tetralone and was analogous to the route to equilenin developed by Bachman et al.[4]

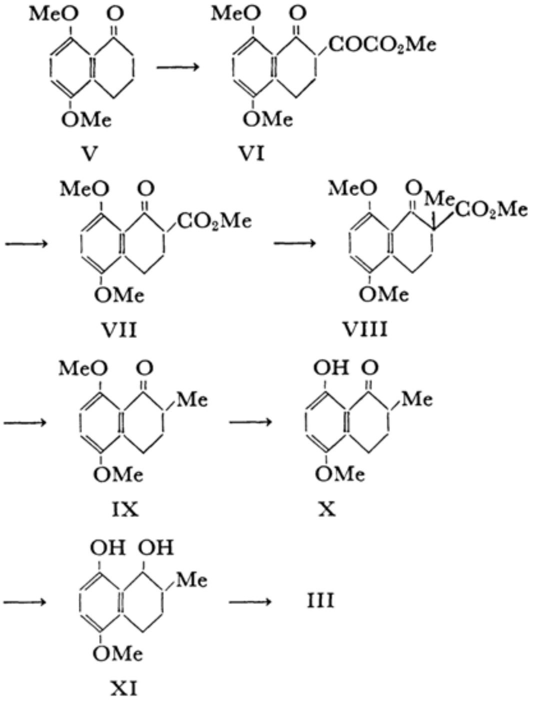


III

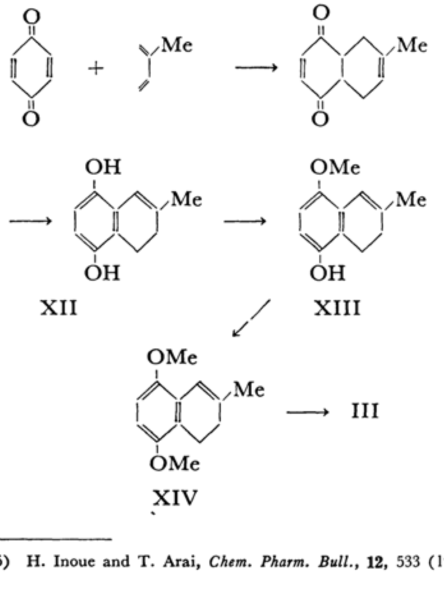


IV

The α-tetralone (V) was condensed with methyl oxalate by the action of sodium methoxide under nitrogen, and the methoxalyl derivative (VI) was heated in order to effect decarbonylation and to give the 2-methoxycarbonyl derivative (VII) of the α-tetralone. The sodio-derivative of the latter was methylated with methyl iodide. Saponification, followed by decarboxylation, gave 5, 8-dimethoxy-2-methyl-α-tetralone (IX). Gentle refluxing with constant boiling hydroiodic acid demethylated the 8-methoxyl group preferentially. The hydroxy-ketone (X) was reduced to the corresponding diol (XI) with lithium aluminum hydride. Refluxing with acetic anhydride, followed by saponification, gave III with a m. p. of 92—93°C.



The Diels-Alder reaction between toluquinone and isoprene has been shown to afford 3, 4-dihydro-5, 8-dihydroxy-2, 7-dimethylnaphthalene after acid-catalyzed rearrangement.[5] The diol (XII) similarly obtained from the reaction between benzoquinone and isoprene was dissolved in aqueous sodium hydroxide and partially methylated with dimethyl sulfate. Through chromatography on alumina, a fraction of a mono-methyl ether was obtained. Recrystallization gave pure mono-methyl ether, which was different from III. Since further methylation afforded the common dimethyl ether (XIV), the latter mono-methyl ether must be the 5-methoxy-8-hydroxy isomer (XIII).



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[1] Part XIX: M. Ōki and H. Iwamura, This Bulletin, **39**, 470 (1966).

[2] J. F. Eastham and D. R. Larkin, *J. Am. Chem. Soc.*, **80**, 2887 (1958).

[3] The sample was generously offered by Professor R. M. Dodson of the University of Minnesota, to whom the authors' thanks are due.

[4] W. E. Bachman, W. Cole and A. L. Wilds, *J. Am. Chem. Soc.*, **62**, 824 (1940).

[5] H. Inoue and T. Arai, *Chem. Pharm. Bull.*, **12**, 533 (1964).

Experimental

Spectral Measurements.—Those were carried out as described previously.1)

Materials.

Methyl 5, 8-Dimethoxy-1-keto-1, 2, 3, 4-tetrahydronaphthalene-2-glyoxalate (VI).—In 100 ml. of anhydrous methanol was dissolved 9.2 g. of sodium and the excess methanol was evaporated to dryness at 100°C under diminished pressure. To the white solid were added 47.2 g. of dimethyl oxalate and 200 ml. of dry benzene. The mixture was refluxed under dry nitrogen for half an hour in order to dissolve the solid. To the cooled solution was added 41.2 g. (0.2 mol.) of 5, 8-dimethoxy-α-tetralone (V)6) dissolved in 300 ml. of benzene. After it had stood for four hours at room temperature with occasional shaking, the mixture was hydrolyzed with 500 ml. of water. The aqueous layer was then drawn off, the benzene layer was extracted twice with 100 ml. of a 5% sodium hydroxide solution, and the combined aqueous solution was carefully acidified with dilute hydrochloric acid. The yellow crystalline deposit was collected and recrystallized from methanol to give 50.5 g. of the glyoxalate (VI), m. p. 108—109°C, corresponding to a yield of 95%.

Found: C, 61.83; H, 5.63. Calcd. for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52%.

Methyl 5, 8-Dimethoxy-1-keto-1, 2, 3, 4-tetrahydro-2-naphthoate (VII).—The methyl glyoxalate (VI) (26.7 g.) was mixed with 20g. of 200 mesh glass powder in a Claisen flask, and the mixture was carefully heated under diminished pressure. A vigorous evolution of carbon monoxide commenced at about 160°C. After half an hour at 180°C, the evolution of the gas stopped and, as the pressure inside the flask dropped, refluxing took place. The temperature of the oil bath was then raised to 240°C and an oil boiled at 180—190°C under ca. 3 mmHg was collected. The viscous oil was dissolved in benzene and recrystallized to give colorless prisms (20.5 g.; yield, 85%), m. p. 86°C.

Found: C, 63.54; H, 6.28. Calcd. for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10%.

Methyl 5, 8-Dimethoxy-1-keto-2-methyl-1, 2, 3, 4-tetrahydro-2-naphthoate (VIII).—To 23 g. of sodium dissolved in 500 ml. of anhydrous methanol was added 23.9 g. of VII dissolved in 200 ml. of benzene. After this mixture had been refluxed for fifteen minutes on a water bath, 50 ml. of methyl iodide was added over a five-minute period. Another 50 ml. of methyl iodide was added after an exothermic reaction had ceased, and the mixture was refluxed for an hour. After neutralization with acetic acid, the solvents were evaporated nearly to completion, and the residue was treated with 500 ml. of benzene and 300 ml. of water. The organic layer was washed with 5% sodium hydroxide and then with water, and dried over sodium sulfate. After the solvent had then been evaporated, the residue was crystallized from carbon tetrachloride (yield, 20 g.; 80%) m. p., 63—63.5°C.

Found: C, 64.92; H, 6.73. Calcd. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52%.

5, 8-Dimethoxy-2-methyl-1-keto-1, 2, 3, 4-tetrahydronaphthalene (IX).—A mixture of 100 ml. of 45% aqueous potassium hydroxide and 300 ml. of methanol was mixed with 30 g. of VIII, refluxed on a water bath for two hours, and diluted with water in order to collect the resulting solid. Recrystallization from methanol gave colorless prisms, m. p. 69°C.

Found: C, 70.99; H, 7.46. Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32%.

8-Hydroxy-5-methoxy-2-methyl-1-keto-1, 2, 3, 4-tetrahydronaphthalene (X).—IX (20 g.) was heated under reflux with 200 ml. of 52% hydroiodic acid for 2 hr. The mixture was then diluted with water, and the product was triturated with a 20% aqueous sodium hydroxide solution to give the insoluble sodium salt, which was collected and washed with aqueous alkali and then with water. The residue was then suspended in 50 ml. of water and acidified with 1 N hydrochloric acid. The oil was extracted with ether, and the solution was dried over anhydrous sodium sulfate. After evaporation, the residue was crystallized from methanol to give pale yellow needles (yield, 16 g.; 85.4%), m. p. 46.5—47°C.

Found: C, 69.93; H, 6.84. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84%.

The NMR spectra7) of 5% $CDCl_3$ solution consisted of the following signals; 1.26 ($C_{(2)}'$-Me, doublet), 1.8—3.1 (aliphatic, multiplet), 3.81 (O'Me), 6.70, 6.85, 7.01 and 7.16 (the AB quartet of the aromatic protons), and 11.99 (chelated OH).

1, 8-Dihydroxy-5-methoxy-2-methyl-1, 2, 3, 4-tetrahydronaphthalene (XI).—To a slurry of 4 g. of lithium aluminum hydride in 100 ml. of ether was added, drop by drop, a solution of 10.3 g. of the hydroxyketone (X) in 70 ml. of ether. After the reaction had subsided, the mixture was refluxed for an hour. The excess reagent was decomposed with ethyl acetate and then treated with 2 N sulfuric acid. The combined ether extracts were washed with 1 N sodium bicarbonate and dried over anhydrous potassium carbonate. The solvent was evaporated, and the residue was recrystallized from carbon tetrachloride to give needles, m. p. 125°C (yield, 9.5 g.; 91.3%).

Found: C, 68.91; H, 8.02. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%.

1, 2-Dihydro-5-hydroxy-8-methoxy-3-methylnaphthalene (III).—A solution of 5 g. of the above diol (XI) in 50 ml. of acetic anhydride was refluxed for an hour. When, after the solvent had been evaporated, the dehydrated acetate was distilled under diminished pressure, a fraction boiling at 120—130°C/1.5 mmHg was collected. The distillate was dissolved in 50 ml. of 5% ethanolic sodium ethoxide, and the mixture was refluxed for thirty minutes. The volume of the solvent was reduced to half, and the residue was diluted with water. The solution was treated with a small portion of active charcoal and filtered while hot. The filtrate was acidified and the product crystallized from carbon tetrachloride to give needles, m. p., 92—93°C; the yield was 2.8 g. (61.3%).

Found: C, 75.78; H, 7.66. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42%.

1, 2-Dihydro-5, 8-dihydroxy-3-methylnaphthalene (XII).—A solution of 12 g. of *p*-benzoquinone and 7 g.

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6) M. Crawford and V. R. Supaneka, *J. Chem. Soc.*, **1960**, 1985.

7) Determined at 60 Mc./sec. on a model A-60 spectrometer (Varian Associates, Palo Alto, Calif., U. S. A.) at the normal operating temperature (36.5°C) and reported in units of δ in p.p.m., from the signal of TMS used as the internal standard.

of isoprene in 50 ml. of acetic acid was kept at room temperature for 24 hr. The solid was then collected on a Buchner funnel and washed several times with water. To a suspension of the crude adduct in 50 ml. of chloroform, 20 ml. of concentrated hydrochloric acid was added, and the mixture was heated under reflux for 12 hr. The solid mass was filtered when it had cooled, washed several times with chloroform, and finally recrystallized from chloroform-acetone to give needles, m. p. 175°C.

Found: C, 75.10; H, 6.99. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86%.

1, 2-Dihydro-8-hydroxy-5-methoxy-3-methylnaphthalene (XIII).—To a solution of 8.8 g. of the diol (XII) in 200 ml. of 10% aqueous sodium hydroxide was added, drop by drop, 7 g. of dimethyl sulfate with cooling and shaking. The dark solution was washed twice with ether, and the aqueous layer was acidified with dilute hydrochloric acid. The heavy oil was dissolved in ether, and the ether solution was dried over anhydrous sodium sulfate. After the solvent had evaporated, the residue was dissolved in benzene-petroleum ether (b. p. —60°C) (1 : 1 in volume) and chromatographed on alumina. Following a fraction of an oil, a series of fractions was obtained and found to be homogeneous. The residue obtained after the evaporation of the solvent was recrystallized from carbon tetrachloride to give needles (1.2 g.; 12%), m. p. 124.5—125°C.

Found: C, 76.01: H, 7.34. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42%.

The ethereal layer yielded a small amount of a dimethyl ether which was identical with the specimen whose preparation is described below.

1, 2-Dihydro-5, 8-dimethoxy-3-methylnaphthalene (XIV).—To a solution of 3.8 g. of III in 50 ml. of 10% aqueous sodium hydroxide, 3 g. of dimethyl sulfate was added; the mixture was then shaken for ten minutes. The oil was extracted in ether, and the ether solution was dried over anhydrous potassium carbonate. The residue obtained after the evaporation of the solvent was recrystallized from petroleum ether to give needles (3.8 g.; 93%), m. p. 66°C.

Found: C, 76.56; H, 8.10. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90%.

Results and Discussion

In Fig. 1 are shown the apparent ν_{O-H} absorptions of III and IV, while in Table I all of the ν_{O-H} data concerned are collected.

The band at the highest frequency of IV is due to the secondary alcoholic hydroxyl group at the 17-position of the steroid skeleton; it is outside the present discussion. Judging from its location, the absorption maximum at 3606 cm^{-1} can be assigned to the free ν_{O-H} of the phenolic hydroxyl group.[1,8] The lowest-frequency band, at 3532 cm^{-1}, may consequently be assigned to the phenolic hydroxyl group interacting with π-electrons on the ethylenic group. Compared with the interacting ν_{O-H}'s of *o*-isobutenylphenol, the location of the last band of IV corresponds well to the lower one at 3539 cm^{1-} of *o*-isobutenylphenol; therefore, it may be concluded that this band should be assigned to the hydroxyl group in conformation II. The Dreiding model of IV suggests that the angle between the benzene ring and the plane made by the ethylenic linkage is ca. 10°. Table II lists the ultraviolet absorption maxima of these *o*-vinylphenol derivatives. The K-band in *n*-hexane of IV is shifted to the red side by 20 mμ from that of *o*-isobutenylphenol, and it is even comparable to those of the more planar *o*-vinylphenol and *o*-(*trans*-propenyl)phenol.[1] Although a part of the effect may be attributed to the auxochromic effect in IV of the additional alkyl groups attached to the chromophore, the UV data indicate that the benzene ring and the ethylenic group in IV are mutually more co-planar than those of *o*-isobutenylphenol. It is not yet clear why this molecule shows a strong interaction despite its near co-planarity, but it is interesting to note that the compound IV and *o*-isobutenylphenol show essentially the same ν_{O-H} values at the lower frequencies. It is possible that the ν_{O-H} in conformation II is rather insensitive to the angle between the benzen ring and the plane of the ethylenic group.

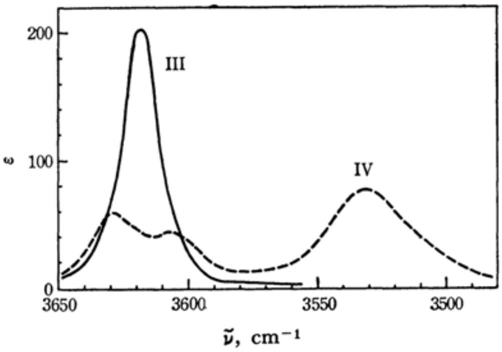

Fig. 1. ν_{O-H} absorptions of 1, 2-dihydro-5-hydroxy-8-methoxy-3-methylnaphthalene (III) and 1, 17β-dihydroxy-4-methylestra-1, 3, 5(10), 9(11)-tetraene (IV).

The ν_{O-H}'s of 5-hydroxy-1, 2-dihydronaphthalene and III are, contrary to the expectation, singlets, like those of α-naphthol and XIII. The apparently unusually high ν_{O-H} of III and XIII is due to the electronic effect of the methoxyl substitution.[8] No absorption of any degree indicative of the presence of intramolecular interaction between the hydroxyl group and the π-electrons was detected. It is not unreasonable to assume, however, that there is no interaction in α-naphthol and XIII, since there is no π-electron available for the interaction in the latter, and since in the former the hydroxyl group must point to the node of the π-orbitals. The Dreiding models of 5-hydroxy-1, 2-dihydronaphthalene and III suggest that the angle between the benzene

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[8] K. U. Ingold and D. R. Taylor, *Can. J. Chem.*, **39**, 471 (1961).

TABLE I. ν_{O-H} ABSORPTIONS OF *o*-VINYLPHENOLS

	ν_{max} cm^{-1}	$\Delta\nu^{a}_{1/2}$ cm^{-1}	$A\times10^{-4}$ $l.mol^{-1}\,cm^{-2}$	$\Delta\nu_{max}$ cm^{-1}
o-Isobutenylphenol	3609.8	14.6	0.12	33.7
	3576.1	37.0	0.40	70.5
	3539.3	26.8	0.81	
α-Naphthol	3609.2	18.3	1.46	0
5-Hydroxy-1,2-dihydronaphthalene	3613.2	17.8	1.42	0
III	3618.5	16.1	1.23	0
IV	3606.1	—	—	74.4
	3531.7	38.4	1.05	
XIII	3618.2	17.4	1.18	0

TABLE II. ULTRAVIOLET ABSORPTIONS OF *o*-VINYLPHENOLS

	Solvent	K-band mμ (log ε)	B-band mμ (log ε)
o-Isobutenylphenol	H	235.0 (3.79)	282.0 (3.41)
	A	242.0 (3.96)	287.5 (3.57)
5-Hydroxy-1,2-dihydronaphthalene	H	—	—
	A	267.0 (3.83)	298.0 (3.45), 308 (3.41)
III	H	267 (s), 273.5 (3.96) 285 (s)	317 (3.68), 330 (s)
	A	266 (s), 272.0 (3.97) 283 (s)	320 (3.72)
IV	H	255.5 (—)	302 (—)
	A	249 (s), 257.5 (4.01) 265 (s)	301 (3.49), 310 (s)
XIII	H	264.5 (s), 273.5 (4.05)	317 (3.78)
	A	264.5 (s), 274 (4.08)	319 (3.75)

H; *n*-Hexane; A; 95% Ethanol; s; shoulder

ring and the plane made by the ethylenic group is ca. 25°. Since there is no interaction even in III, in which the proton-accepting power of the ethylenic group is enriched by methyl substitution, it may be concluded that III does not reflect the conformation I of *o*-isobutenylphenol, but that the dihedral angle made by the plane of the ethylenic group and the plane of the benzene ring must be much larger than that in III in order to have interaction with the hydroxyl group.

The effects of conformations, including the dihedral angles made by the benzene ring and the ethylenic linkage and the relative location of the double bond, remain to be fully explored. However, one possible reason for the poor interaction in the compound III may be that two *p*-orbitals are available for the interaction in conformation II, while only one is available in conformation I. The former is expected to be the preferable interacting form, on analogy with the benzene-silver ion complex.[9,10]

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9) W. von Doering, M. Saunders, H. G. Boyton, H. W. Earhart, E. F. Wadley, W. R. Edwards and G. Laber, *Tetrahedron*, **4**, 178 (1958).

10) M. Ōki and H. Iwamura, This Bulletin, **32**, 1135 (1959).