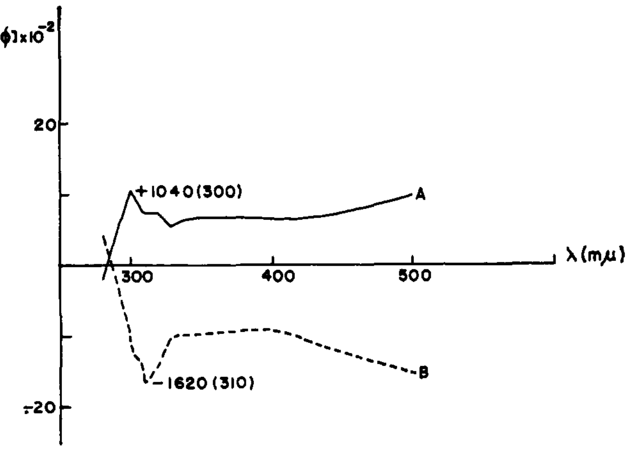

Fig. 1.–Optical rotatory dispersion curves of A, canarone (I); and B, keto alcohol V.

is the antipodal type (*−ve* Cotton effect, $a = -30$) compared to that shown by *trans*-9-methyl-1-decalone (VIII).[5] The molecular amplitude values, a, for compounds I and V are in better agreement with those reported[6] for *trans*-1-decalones from the eudesmanic group than from the eremophilane group. The ring fusion in canarone should therefore be *trans*, as shown in the formula of IX. Application of the octant rule[7] also points to a *trans* fusion of the ring.

The customary, β-equatorial configuration is assigned to the C-7 isopropyl side chain in analogy with other eudesmanic compounds. Canarone can therefore be represented by the stereoformula IX.

Experimental[8]

Isolation of Canarone (I).—From the petroleum ether (b.p. 60–80°) extract of the resin (7 kg.), pure ketone (1.8 g.) was isolated by column chromatography over alumina (grade II, 30-fold), followed by regeneration from its semicarbazone (oxalic acid, petroleum ether), b.p. 120–125° (bath) at 1 mm., $n^{28}\mathrm{D}$ 1.5020, $[\alpha]\mathrm{D}$ +34.78° (c 3.45), $d^{29}{}_{29}$ 0.9819; $\nu_{\max}^{\text{liq film}}$ 3080, 1700, 1640, 1420, 1360, 1375, 1225, 1260, 1183, 1160, and 890 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.00; H, 10.98.

The semicarbazone had m.p. 222–224°.

Anal. Calcd. for $C_{16}H_{27}N_3O$: N, 15.15. Found: N, 15.50.

Reduction of Canarone (I) and Dehydrogenation of Canarol (IV).—To a suspension of lithium aluminum hydride (0.9 g.) in dry ether (50 ml.) was added a solution of the ketone (1.03 g.) in dry ether (25 ml.). During addition, the temperature was maintained between 0 and 5° and the solution was then refluxed for 5 hr. The reaction mixture on decomposition in the usual way furnished the secondary alcohol canarol (IV), b.p. 110–115° (bath) at 0.2 mm., $n^{28}\mathrm{D}$ 1.5040, $[\alpha]\mathrm{D}$ +23.81° (c 1.26, ethanol).

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.04; H, 11.74. Found: C, 80.65; H, 11.58.

The secondary alcohol (0.4 g.) was heated with selenium (0.4 g.) at 280° for 7 hr. in a nitrogen atmosphere. The product obtained was filtered through alumina (grade I, 20 g.) and eluted with petroleum ether. The ultraviolet spectrum indicated more than 80% naphthalenic material. It was identified as eudalene (II) through its trinitrobenzene (TNB) derivative, m.p. and m.m.p. 110°, and through its infrared spectrum.

Quantitative Determination of Unsaturation.—Canarone (I, 30 mg.) was hydrogenated in methanol in the presence of palladium on charcoal (5%, 30 mg.); the absorption of hydrogen (3.5 ml., 24°, 710 mm.) amounted to one double bond; $\nu_{\max}^{\text{liq film}}$ 1704, 1420, 1383, and 1366 cm.$^{-1}$.

Hydrogenation of Canarone (I) to Dihydrocanarol (VI).—Canarone (130 mg.) was hydrogenated in acetic acid (20 ml.) using platinum oxide (50 mg.) catalyst. The hydrogenation stopped after absorption corresponding to 2 moles of hydrogen. After removal of the catalyst, the filtrate afforded after the usual processing 90 mg. of dihydrocanarol (VI), b.p. 105–110° (bath) at 0.3 mm., $n^{28}\mathrm{D}$ 1.4940, $[\alpha]\mathrm{D}$ +8.43° (c 1.78); $\nu_{\max}^{\text{liq film}}$ 3450, 1380, and 1370 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{28}O$: C, 80.29; H, 12.56. Found: C, 80.52; H, 12.81.

Hydrogenation of Canarol (IV) to Dihydrocanarol. (VI)—A solution of canarol (100 mg.) in acetic acid (20 ml.) was hydrogenated over prereduced Adams' catalyst (50 mg.). The absorption corresponded to 1 mole of hydrogen. The infrared spectrum of the purified product was superimposable with the infrared spectrum of the product obtained by direct hydrogenation of canarone over Adams catalyst, and had identical properties.

Ozonolysis of Canarol (IV) to the Keto Alcohol (V).—Canarol (0.12 g.) in chloroform (10 ml.) was ozonized at −5° to completion. The chloroform was removed *in vacuo* and the ozonide was decomposed with water. The volatile component was identified as formaldehyde by its dimedone derivative, m.p. and m.m p. 189°. The trap water did not give a test for acetone. The nonvolatile product (60 mg.), purified by filtering through a short column of alumina (grade III), did not give a test for methyl ketone, b.p. 135° (6 mm.); $\nu_{\max}^{\text{liq film}}$ 3400, 1701, 1425, 1375, 1360, 1180, and 1065 cm.$^{-1}$.

Anal. Calcd for $C_{14}H_{24}O_2$: C, 75.04; H, 10.78. Found: C, 76.80; H, 10.6.

Due to the paucity of material a better analysis could not be obtained.

Grignard Reaction on Canarone (I) and Isolation of 4-Methyleudalene (VII) by Dehydrogenation.—The ketone (0.50 g.) in dry ether (20 ml.) was added dropwise to the solution of methyl magnesium iodide (prepared from 0.40 g. magnesium and 2.5 ml. of methyl iodide) in dry ether (50 ml.), and the reaction mixture was refluxed for 12 hr. The product was worked up in the usual way and the derived tertiary alcohol was separated from traces of unchanged ketone by chromatography. The crude tertiary alcohol (0.25 g.) was heated with selenium (0.3 g.) at 290° for 6 hr. The reaction product was extracted with ether and filtered through alumina (grade I, 10 g.). The ultraviolet spectrum of the dehydrogenated product indicated 90% naphthalenic product. It was identified as 1,4-dimethyl-7-isopropylnaphthalene (VII) by its TNB derivative, m.p. 102–103°, lit. m.p. 103–104°.[9]

Anal. Calcd. for $C_{15}H_{18}\cdot C_6H_3N_3O_6$. N, 10.21. Found: N, 10.3.

The parent hydrocarbon regenerated from its TNB complex gave a picrate, m.p. 112–113°, lit. m.p. 113–114°.[3]

Acknowledgment.—We are grateful to Professor W. Klyne of Westfield College, University of London, for optical rotatory dispersion measurements and helpful discussions.

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(5) C. Djerassi, R. Riniker, and B. Riniker, *J. Am. Chem. Soc.*, **78**, 6362 (1956).

(6) C. Djerassi and W. Klyne, *J. Chem. Soc.*, 4929 (1962).

(7) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p. 181.

(8) Melting points are uncorrected. Rotations were determined in chloroform solution unless otherwise stated. Infrared spectra were taken by H. Gopinath using a Perkin-Elmer Model 137b spectrophotometer. Ultraviolet spectra were measured in ethanol solution by Miss Prabhu with a DK-2 Beckman spectrophotometer. Analyses were carried out by Mr. Pansare and colleagues.

(9) G. S. K. Rao and S. Dev, *J. Indian Chem. Soc.*, **33**, 561 (1956).

Reactions of Derivatives of 2-Formyl-1-tetralone

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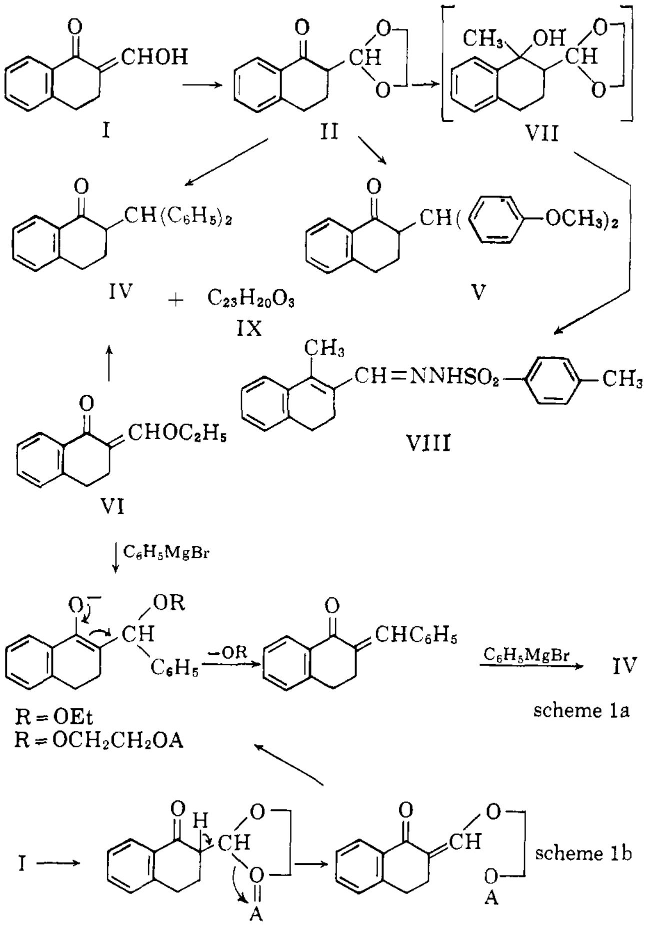
In the course of the preparation of 1-substituted 3,4-dihydronaphthalenes, we had occasion to investigate the reaction of the acetal II with phenylmagnesium bromide.

The reaction of 2-formyl-1-tetralone[1] with 1 equiv. of ethylene glycol afforded this acetal in excellent yield. The absence of a low-field aldehyde proton band, in the n.m.r. spectrum of this compound, serves to confirm the structure. When the acetal was allowed to react with phenylmagnesium bromide in tetrahydrofuran there was obtained in 62% yield a product, m.p. 144–146.5°, which still showed carbonyl absorption in the infrared (1685 cm.$^{-1}$), as well as a small amount of a higher melting ketone (164–165°), IX. The n.m.r. spectrum of the low-melting compound quickly revealed that this was not the product of reaction of II at the 1-carbonyl[2]; there was no band present at low field as would be required by an aldehyde and the integral indicated the presence of fourteen rather than the expected nine aromatic protons. These findings, and the splitting pattern can be accommodated by structure IV. The melting point of this product is in good agreement with that reported for this ketone in the literature.[3] The structure of IX is still unknown: analytical and physical data indicate this to be a diphenyldihydroxy derivative of a tetralone.

Indirect confirmation of the structure of IV comes from the reaction of II with anisylmagnesium bromide. In this case, the yield of product was 82%. The n.m.r. spectrum of this ketone is quite similar to that of IV with the addition of the methoxyl protons. The presence of six of the latter rather than the three which would be expected from the "normal" reaction serves to confirm the addition of 2 moles of the reagent. It is of interest in connection with the mechanism of this reaction that the enol ether VI also affords IV with phenylmagnesium bromide, albeit in lower yield. The latter can be rationalized by a 1,4-addition of the reagent to the enol, loss of ethoxide, and again a 1,4-addition (scheme 1a). If it is assumed that the acetal is opened by a Lewis acid component of the Grignard mixture (*e.g.*, $MgBr_2$),[4] an intermediate is at hand which is in effect equivalent to the enol ether. The reaction may then follow a path such as scheme 1b. It is of interest in this connection that the addition of a Grignard reagent to an acetal to afford the ether has been reported.[5]



The reaction of the acetal II with methylmagnesium bromide on the other hand proceeds in a normal manner. The product VII was not isolated as such, but was dehydrated and hydrolyzed in a single step, and the aldehyde was characterized as its *p*-toluenesulfonylhydrazone.

Finally, in order to further characterize V, the compound was treated under ether cleaving conditions with 48% hydrobromic acid in acetic acid. Unexpectedly, the only product which could be isolated from the reaction mixture was α-tetralone. The fact that treatment of IV under the same conditions leads to recovery of better than 50% of starting material leads to the inference that the free phenol may be involved in this unusual scission.

Experimental[6]

2-Formyl-1-tetralone, 2-Ethylene Acetal (II).—A mixture of 18.4 g. of 2-formyl-1-tetralone, 6.6 g. of ethylene glycol, and 0.10 g. of *p*-toluenesulfonic acid in 200 ml. of benzene was heated at reflux with vigorous stirring under a Dean–Stark trap until no more water was evolved (2 hr.). The solution was allowed to cool, washed with aqueous sodium bicarbonate and water, and the solvent was removed *in vacuo*. The residue, a yellow crystalline solid, was recrystallized twice from cyclohexane to afford 20.15 g. of the acetal II, m.p. 61–63.5°. The analytical sample melted at 63.5–65°.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.46. Found: C, 71.37; H, 6.17.

2-Diphenylmethyl-1-tetralone (IV). A. From 2-Ethoxymethylene-1-tetralone (VI).—A solution of 15.08 g. (0.078 mole) of the enol ether in 150 ml. of ether was added to an ice-cooled solution of phenylmagnesium bromide prepared from 13.5 g. (0.086 mole) of bromobenzene, 2.10 g. of magnesium, and 130 ml. of ether. The mixture was stirred overnight at room temperature, and then ice and 70 ml. of 2.5 *N* hydrochloric acid were added. The organic layer was separated, washed with water, and evaporated to dryness. The residual oil was taken up in 100 ml. of methanol, 5 ml. of 2.5 *N* hydrochloric acid was added, and the mixture was stirred at room temperature. The crystalline solid which separated (6.20 g., m.p. 132–140°) was collected on a filter and recrystallized once from methanol and then from aqueous acetone to afford 4.9 g. of IV, m.p. 144–146.5°, lit.[3] m.p. 147–148°. The infrared (ν_{max} 1685 cm.$^{-1}$) and n.m.r. (14 protons above δ 7.0; doublet at 4.7; multiplets at 3.4, 2.97, and *ca.* 1.9) spectra are in full accord with the structure.

B. From 2-Formyl-1-tetralone, 2-Ethylene Acetal (II).—To an ice-cooled solution of 0.073 mole of phenylmagnesium bromide in 150 ml. of tetrahydrofuran there was added 5.0 g. of the acetal

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[1] W. S. Johnson, J. M. Anderson, and W. E. Shelburg, *J. Am. Chem. Soc.*, **67**, 1745 (1945).

[2] The absence of hydroxyl absorption and presence of carbonyl absorption in the infrared spectrum of the product led us first to suppose that loss of acetal and dehydration had occurred during the work-up.

[3] W. D. Garden and F. D. Gunstone, *J. Chem. Soc.*, 2650 (1952).

[4] R. E. Dessey and G. S. Handler, *J. Am. Chem. Soc.*, **80**, 5824 (1958).

[5] E. Späth, *Monatsh.*, **35**, 319 (1914).

[6] The author is indebted to the Upjohn Physical and Analytical Chemistry Department for analyses, ultraviolet, infrared, and n.m.r. spectra. All melting points are uncorrected and were determined on a Thomas–Hoover capillary melting point apparatus. N.m.r. spectra were determined in deuteriochloroform on a Varian A-60 instrument.

II in 100 ml. of tetrahydrofuran. Following 18 hr. of heating under reflux, the mixture was worked up in the same manner as above. The solid product was chromatographed over Florisil (elution with 5% acetone in ligroin) to afford 4.42 g. of crude IV followed by 1.68 g. of a higher melting compound. The former was recrystallized twice from cyclohexane to give 2.88 g. of the ketone IV, m.m.p. (with IV from VI) 146–148°.

The by-product IX was recrystallized from aqueous acetone to a constant melting point of 164–165°, ν_{max} 3375 and 1680 cm.$^{-1}$, λ_{max} 251 (ϵ 10,300) and 290 mμ (1280).

Anal. Calcd. for $C_{23}H_{30}O_3$: C, 80.21; H, 5.85. Found: C, 79.93, 80.63; H, 6.09, 6.21.

1-Methyl-3,4-dihydronaphthalene-3-carboxaldehyde, *p*-Toluenesulfonylhydrazone (VIII).—A solution of 17.84 g. of the acetal II in 400 ml. of tetrahydrofuran was added over 30 min. to an ice-cooled solution of 425 ml. of 2 *M* methylmagnesium bromide in benzene–tetrahydrofuran. Following 18 hr. of heating under reflux, the mixture was again cooled in ice and decomposed with 15 ml. of water followed by 250 ml. of saturated aqueous ammonium chloride. The organic layer was separated and washed with water and brine; the solvent was removed *in vacuo.* There remained 18.59 g. of viscous oil whose infrared spectrum shows no absorption in the carbonyl region.

A solution of 4.0 g. of VII, used as obtained above, and 10 ml. of 2.5 *N* hydrochloric acid in 100 ml. of acetone was stirred for 1 hr. at room temperature and then 1 hr. under reflux. The bulk of the solvent was removed on a rotary evaporator, the residue was dissolved in ether, and the solution was washed with water, sodium bicarbonate, and brine. The solvent was removed *in vacuo* to afford 2.80 g. of the crude aldehyde, ν_{max} 2750 and 1650 cm.$^{-1}$

The crude aldehyde in 50 ml. of ethanol was heated in the presence of 3.0 g. of *p*-toluenesulfonylhydrazine for 6 hr. The solution was allowed to cool and diluted with water. A gum came out which slowly solidified on scratching. This was recrystallized three times from methanol to afford 1.41 g. of the hydrazone VIII, m.p. 156–158° dec.

Anal. Calcd. for $C_{19}H_{20}N_2O_2S$: C, 67.04; H, 5.92; N, 8.23. Found: C, 66.62; H, 6.18; N, 8.28.

2-Di(*p*-methoxyphenyl)methyl-1-tetralone (V).—A solution of 10.0 g. of the acetal II in 200 ml. of tetrahydrofuran was added to an ice-cooled solution of the Grignard reagent prepared from 27.6 g. of *p*-bromoanisole and 5.6 g. of magnesium in 300 ml. of tetrahydrofuran. The reaction was run and the reaction mixture was worked up as above. The crude product was chromatographed over Florisil (elution with 3% acetone in ligroin); the combined crystalline fractions were recrystallized from ligroin to afford 11.13 g. of V, m.p. 105–108°.

A small sample was recrystallized from acetone–ligroin to give V, m.p. 103.5–105°; n.m.r., 12 protons above δ 6.5, doublet at 4.6, singlet 3.75, multiplets at 3.38, 2.95, and 2.0.

Anal. Calcd. for $C_{25}H_{24}O_3$: C, 80.62; H, 6.50. Found: C, 80.09; H, 6.60.

Reaction of 2-Di(*p*-methoxyphenyl)methyl-1-tetralone with Hydrobromic Acid.—A mixture of 2.0 g. of the ketone V and 60 ml. each of 48% aqueous hydrobromic acid and acetic acid was heated overnight at reflux. The volume was reduced to 70 ml. *in vacuo* and then the mixture was diluted with water and extracted with ether. The extracts were washed with aqueous sodium bicarbonate and brine and taken to dryness. The residual oil was chromatographed over Florisil (elution with 3% acetone in ligroin) to afford 0.37 g. (47%) of an oil whose infrared spectrum is identical with that of α-tetralone. The 2,4-dinitrophenylhydrazone of the oil melted at 258° dec., m.m.p. (with authentic α-tetralone 2,4-dinitrophenylhydrazone) 259° dec.

Reaction of 2-Diphenylmethyl-1-tetralone with Hydrobromic Acid.—Two grams of the ketone was treated exactly as above in 60 ml. each of 48% hydrobromic acid and acetic acid. The mixture was diluted with water and extracted with methylene chloride-ether. The oily solid which remained when the extracts were taken to dryness was crystallized twice from cyclohexane to afford 1.06 g. of the ketone, m.p. 141–144°.

Acknowledgment.—The author is indebted to Dr. Philip F. Beal, III, of these laboratories for valuable discussions concerning the n.m.r. spectra of these compounds.

A Synthesis of Polyhydroxy-2,6-diaryl-4-pyrones

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In a previous contribution[1] we have shown that when diethyl acetonedicarboxylate reacts with certain phenols in the presence of trifluoroacetic acid in a mole to mole ratio, ethyl coumarinacetates are formed. However, when the mole ratio is changed to two of the phenol to one of the ester, a polyhydroxy-2,6-diaryl-4-pyrone is produced as shown in the formula below. This reaction provides a one-step general process for the preparation of hydroxydiarylpyrones in acid media, a possibility not available by the method of Soliman and Kholy[2] or other earlier procedures.[3]

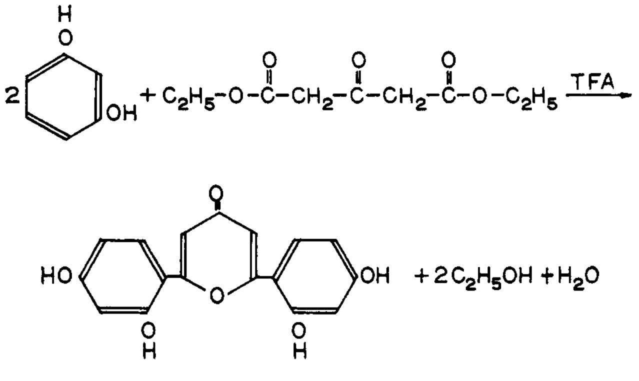

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Table I lists the compounds synthesized along with some pertinent physical data. Table II gives the *p*-nitrobenzoate esters of the members of the series and enumerates some of the spectral characteristics of the compounds. The fluorescence of some of the members of the series is of particular interest because three of them, compounds I, II, and IV, are much more fluorescent than quinine sulfate.

Compound I was selected as a model of the series to be subjected to alkaline degradation as proof of the proposed structures. Degradation in 30% potassium hydroxide[4] produced 2,4-dihydroxybenzoic acid, m.p. 208–210° dec., identical with an authentic sample.

Experimental[5]

Preparation of Members of I–VI Series.—A mixture consisting of 0.2 mole of the phenol, 0.1 mole of diethyl acetonedicarboxylate, and 30 ml. of trifluoroacetic acid was refluxed in the hood for 18 hr. The resulting solutions were diluted with about 150 ml. of water and chilled. The precipitates were filtered and dried in air. The analytical samples were obtained in most cases by recrystallizing the crude compound twice from boiling heptane;

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[1] L. L. Woods and J. Sapp, *J. Chem. Eng. Data*, **8**, 235 (1963).

[2] G. Soliman and I. E. Kholy, *J. Chem. Soc.*, 1755 (1954).

[3] R. C. Elderfield, "Heterocyclic Compounds," Vol. 1, John Wiley and Sons, New York, N. Y., 1952, p. 370.

[4] T. A. Geissman, "The Chemistry of Flavonoid Compounds," Macmillan and Co., New York, N. Y., 1962.

[5] Analyses were performed by Dr. Carl Tiedcke, Teaneck, N. J. All melting points were taken on a Fisher-Johns melting point block.