(see above) was dissolved in benzene and the solution added slowly to an ethereal solution of diazomethane prepared from nitrosomethylurea (7.0 g.) and allowed to stand at 0° for sixteen hours. The solvent, together with the excess diazomethane, were removed under reduced pressure. The crude product (2.1 g.) was used directly in the following procedure.

**C.. Hydrolysis of 3,4,5-Trimethoxyphenyl Diazomethyl Ketone.**—The 3,4,5-trimethoxyphenyl diazomethyl ketone (2.1 g.) (see above) was hydrolyzed by heating at 70° for three hours with aqueous 2% sulfuric acid (100 cc.). The solution, after cooling, was extracted with chloroform, the chloroform solution dried and the solvent removed. The resulting product was recrystallized from ether: yield, 1.5 g., m. p. 77–78°.

*Anal.* Calcd. for $C_{11}H_{14}O_5$: $OCH_3$, 41.1. Found: $OCH_3$, 40.85.

**D. Reduction of 3,4,5-Trimethoxyphenyl Hydroxymethyl Ketone.**—3,4,5-Trimethoxyphenyl hydroxymethyl ketone (1.0 g.) was dissolved in ethanol (100 cc.) and hydrogenated over copper chromium oxide (0.5 g.) at 150–160° for one hour. The bomb contents were filtered, the filtrate concentrated under reduced pressure and the resulting yellow oil distilled at 220–240° (bath temperature) (0.02 mm.): yield, 0.8 g.

*Anal.* Calcd. for $C_{11}H_{16}O_4$: $OCH_3$, 43.8. Found: $OCH_3$, 43.5.

The $\alpha$-naphthyl urethan derivative of this oil melted at 131–133°.

**Acknowledgment.**—The authors wish to thank the National Research Council of Canada for the award of two studentships to one of them (J. M. P.) and also the Canadian Pulp and Paper Association for their kind financial assistance. The authors also wish to thank Dr. R. F. Patterson who so kindly assisted in the lengthy continuous fractionation procedures.

## Summary

1. Maple wood meal has been suspended in dioxane containing 3% sodium hydroxide and hydrogenated over Raney nickel catalyst using an initial pressure of 3000 lb./sq. in. and a temperature of 170° and complete conversion of the lignin portion of the wood into chloroform-soluble products has been effected.

2. From the reaction mixture three new lignin aromatic degradation products were isolated: 4-hydroxy-3-methoxyphenylethane, 4-hydroxy-3,5-dimethoxyphenylethane and 2-(4-hydroxy-3,5-dimethoxyphenyl)-ethanol in yields of 2.2, 15.4 and 6.2% (based on the Klason lignin content of the wood), respectively.

3. The syntheses of 4-hydroxy-3-methoxyphenylethane, 4-hydroxy-3,5-dimethoxyphenylethane and 2-(3,4,5-trimethoxyphenyl)-ethanol were accomplished.

4. The isolation of these lignin derivatives thus provides further confirmatory evidence for the essentially aromatic (alkylphenolic) nature of lignin; and for the belief that the lignin of hardwoods is composed of units of both the guaiacyl and syringyl types, compounds containing the latter type being the more readily isolated.

5. The isolation of 2-(4-hydroxy-3,5-dimethoxyphenyl)-ethanol as a lignin degradation product provides some evidence for a carbon–oxygen linkage through the $\beta$-carbon atom of the alkyl side chain.

MONTREAL, CANADA RECEIVED APRIL 10, 1947

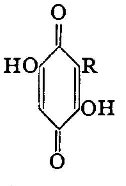
---

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

# Synthesis of Embelin, Rapanone and Related Quinones by Peroxide Alkylation[1]

BY LOUIS F. FIESER AND EARL M. CHAMBERLIN

Embelin, an orange pigment isolated from the berries of the Indian shrub *Embelia ribes*, is of interest because of early reports that the substance, like the fruit from which it is derived, possesses valuable properties as an anthelmintic agent, particularly against tapeworm.[2] Degradative studies of the substance led to varying conclusions[3]; then Hasan and Stedman[4] synthesized 2,5-dihydroxy-3-lauryl-1,4-benzoquinone (II) and an isomer and concluded from the results of their comparisons that embelin is identical with synthetic II. More recently Asano and Yamaguti[5] obtained analytical data pointing to a structure with one less methylene group. The latter investigators synthesized both II and the lower homolog I and found that both quinones have very nearly the same melting point as embelin and give no



I, R = $-(CH_2)_{10}CH_3$
II, R = $-(CH_2)_{11}CH_3$
III, R = $-(CH_2)_{12}CH_3$

depression when mixed with the natural pigment. However, they observed that although the three hydroquinone tetraacetates likewise had very similar melting points, the derivative of II gave a definite, slight depression when mixed with the embelin derivative (Hasan and Stedman indeed reported a mixed melting point 1–2° below that of either component). We have not found in the Japanese paper any statement of a comparison of the derivatives of I and of embelin.

---

[1] Based largely upon the doctoral dissertation of Earl M. Chamberlin, May 6, 1946.

[2] Paranjpe and Gokhale, *Arch. intern. pharmacodyn.*, **42**, 212 (1932) [*C. A.*, **27**, 1400 (1933); E. Merck's *Jahresber.*, **20**, 33 (1906)].

[3] Heffter and Feuerstein, *Arch. Pharm.*, **238**, 15 (1900); Kaul, Ray and Dutt, *J. Indian Chem. Soc.*, **6**, 577 (1929); **8**, 231 (1931); Nargund and Bhide, *ibid.*, **8**, 237 (1931).

[4] Hasan and Stedman, *J. Chem. Soc.*, 2112 (1931).

[5] Asano and Yamaguti, *J. Pharm. Soc. Japan*, **60**, 105 (1940 [*C. A.*, **34**, 5069 (1940)].

Asano and Yamaguti[6] further characterized a pigment rapanone isolated (by Kawamura, 1937) from the bark and woody portion of *Rapanea maximowiczii* and assigned to it the structure II on the basis of degradation and synthesis. They synthesized III and the next higher homolog and showed that these quinones likewise give no melting point depressions when mixed with the natural pigment, but that a differentiation can again be made by comparison of the hydroquinone tetraacetates.

We have now synthesized the homologs I, II and III by causing the appropriate diacyl peroxide to decompose in an acetic acid solution containing 2,5-dihydroxybenzoquinone.[7] The yields were low and in the first instance the dialkyl derivative was isolated as a by-product, but small amounts of the pure pigments can be prepared readily by this method. Our comparison of natural embelin with the synthetic substances and their derivatives confirms the conclusion of Asano and Yamaguti[5] that embelin has the structure I (see table).

TABLE I

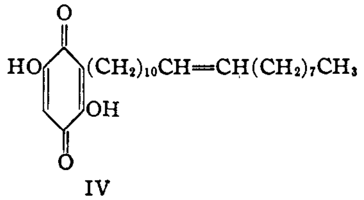
MELTING POINTS, °C.

| Substance | Hasan and Stedman | Asano and Yamaguti | Fieser and Chamberlin |
|---|---|---|---|
| | Quinones | | |
| Embelin | 143 | 142 | 142–143 |
| I | ... | 143–144 | 145–146 |
| II | 143 | 142 | 142–143 |
| Embelin + I | ... | 143–144 | ..... |
| Embelin + II | 143 | 142 | ..... |
| I + II | ... | ..... | 144–145 |
| | Hydroquinone Tetraacetates | | |
| Embelin | 121 | 123.5 | 125–126 |
| I | ... | 124 | 124.5–125.5 |
| II | 121 | 120 | 120–121 |
| Embelin + I | ... | ..... | 125–126 |
| Embelin + II | 119 | 118 | ..... |
| I + II | ... | ..... | 118–119 |

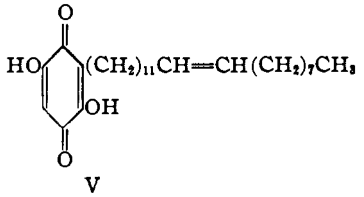
The depressions observed with mixtures of homologous hydroquinone tetraacetates are very evident to the experimenter even though they amount to only a degree or two.

Some two years after the synthetic work of this paper had been completed, one of us received from O. Fernandez of Madrid a supply of orange pigment melting at 141–142° that had been extracted from *Oxalis purpurata*, Jacq.[8] Analyses indicate the formula $C_{19}H_{30}O_4$, which is that of rapanone (III), and the color, solubilities, melting point, and formation of a hydroquinone tetraacetate, m. p. 116.5–117.5°, all suggested strongly that the substance is a member of the embelin–rapanone series. Mixtures of the pigment with the quinones I–III melted the same as the components or at intermediate temperatures, which definitely places the substance in this series. The hydroquinone tetraacetate did not depress the melting point of the derivative of synthetic III, whereas mixtures with the derivatives of I and II melted at 110.5–111.5° and 114–115.5°, respectively. From these observations we conclude that the pigment isolated from the Spanish plant is identical with rapanone, III.

The orange-red pigment maesaquinone[9] may be another member of the same or a related series, for it has been characterized as a dihydroxybenzoquinone with a $C_{20}$ side chain (or chains) with one double bond. Fieser and Gates[10] noted that the side chain may be a phytyl group, and as a test of this hypothesis we initially planned to try to synthesize 2,5-dihydroxy-3-dihydrophytyl-1,4-benzoquinone for comparison with dihydromaesaquinone. The required acid intermediate was prepared from dihydrophytol through the bromide and the nitrile and found to be a liquid at ordinary temperatures: $CH_3CH(CH_3)CH_2CH_2[CH_2CH(CH_3)CH_2CH_2]_3COOH$ (homophytanic acid). An acid of the same composition was isolated by Hiramoto as a product of the oxidation of dihydromaesaquinone and stated, without supporting evidence, to be heneicosanoic acid (m. p. 75–76°). Since the acid is a solid, the side chain of the saturated quinone can hardly be the dihydrophytyl group. If the side chain is normal, it is possible that maesaquinone is related to one of two known naturally occurring eicosenoic acids, namely, the $\Delta^{11}$-derivative found in the liquid seed wax of *Californica simmondsia;* hence the structure may be IV. The acid intermediate required for the synthesis of IV was prepared from oleyl alcohol by the steps indicated ($X = Br$ or $SO_2C_6H_4CH_3$-*p*)



IV



V

$$\underset{\text{VI}}{CH_3(CH_2)_7CH{=}CH(CH_2)_7CH_2X} \xrightarrow{\text{mal. ester}}$$

$$\underset{\text{VII}}{CH_3(CH_2)_7CH{=}CH(CH_2)_9COOH} \longrightarrow$$

---

[6] Asano and Yamaguti. *J. Pharm. Soc. Japan.* **60**, 585 (1940) [*C. A.*, **36**, 81 (1942)].

[7] Fieser and Oxford. THIS JOURNAL. **64**, 2060 (1942).

[8] Fernandez and Pizarroso. *Farm. nueva* (*Madrid*). **108**, 3 (1946).

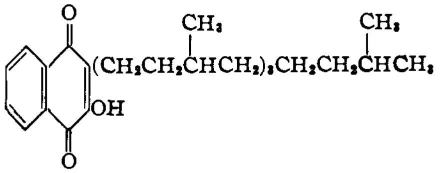
[9] Hiramoto, *Proc. Imp. Acad.* (*Tokyo*). **15**, 220 (1939).

[10] Fieser and Gates. THIS JOURNAL. **63**, 2948 (1941).

methyl ester $\longrightarrow$
VIII
$CH_3(CH_2)_7CH{=}CH(CH_2)_9CH_2OH \longrightarrow$
IX
bromide $\longrightarrow$ nitrile $\longrightarrow$
X XI
$CH_3(CH_2)_7CH{=}CH(CH_2)_{10}COOH$
XII

$\Delta^{12}$-Heneicosenoic acid (XII) was obtained as a crystalline solid melting at 56–57°. However, in a trial alkylation of 2,5-dihydroxybenzoquinone with the peroxide from erucic acid, the next higher homolog V was produced (along with the dialkyl derivative) with such difficulty and in so low yield (0.3%) that the synthesis of IV has not yet been attempted. The quinone V melts at 112.5–113.5°; maesaquinone melts at 122°.

Because of the interest in naphthoquinone antimalarials in this Laboratory, the intermediate homophytanic acid was utilized for the synthesis of 2-hydroxy-3-dihydrophytyl-1,4-naphthoquinone. The substance was isolated with difficulty by high vacuum distillation as a yellow oil; it possesses no antirespiratory activity.



XIII

Tests of synthetic embelin and rapanone for their effects on dog helminths kindly conducted at the American University at Beirut by Dr. D. A. Berberian and E. Rajm through the courtesy of Dr. S. E. Kerr were negative (method of M. C. Hall).[11]

## Experimental

### 1. 2,5-Dihydroxy-3-undecyl-1,4-benzoquinone (Embelin), I

**Peroxide.**—Redistilled lauric acid (44.1 g.) was heated with phosphorus trichloride (11 g.) at 50° for one hour, the upper layer was decanted, treated with a current of dry air to remove excess reagent, and the lauroyl chloride distilled; b.p. 138–142° (15 mm.), yield 45.9 g. (95%). A solution of 45 g. of the acid chloride in 100 cc. of 20–40° petroleum ether was added to a mixture of 100 cc. of petroleum ether, cracked ice, and 20 g. of sodium peroxide. The mixture was shaken vigorously for two minutes and then, after the addition of 15 g. more sodium peroxide and more ice, for ten minutes. The mixture was transferred to a separatory funnel, enough diethyl ether was added to keep the dilauroyl peroxide in solution, and the organic layer was separated, washed, dried, and the solvent removed in vacuum at room temperature. The yield of waxy white solid, dried over potassium hydroxide in vacuum, was 35.5 g. (85%).

**Alkylation.**—A suspension of 11.2 g. of 2,5-dihydroxybenzoquinone[12] and 35.5 g. of dilauroyl peroxide in 550 cc. of acetic acid was warmed to the point where gas began to be evolved (92°), maintained at that temperature for one-half hour and the solution allowed to stand overnight. A crystallizate that separated proved to be the dialkylated derivative (see below); the filtered solution was concentrated to a small volume in vacuum at steam-bath temperature. Some product separated during the evaporation and was collected after cooling and crystallized in turn from alcohol, benzene and acetic acid. **2,5-Dihydroxy-3-undecyl-1,4-benzoquinone** was thus obtained as glistening orange plates, m.p. 145–146°; yield 1.7 g. (7.2%).

*Anal.* Calcd. for $C_{18}H_{26}O_4$: C, 69.35; H, 9.19. Found: C, 69.53; H, 8.90.

The **hydroquinone tetraacetate** when recrystallized from alcohol melted at 124.5–125.5° (Asano and Yamaguti,[5] 124°).

*Anal.* Calcd. for $C_{25}H_{36}O_8$: C, 64.70; H, 7.77 Found: C, 64.36, H, 8.21.

**2,5-Dihydroxy-3,6-diundecyl-1,4-benzoquinone.**—The material that separated from the cooled alkylation mixture was crystallized from alcohol and found to contain unchanged dihydroxybenzoquinone. The dialkyl derivative could be extracted from the mixture with hot benzene, and it separated from the benzene filtrate as orange crystals. Recrystallization from alcohol gave glistening orange plates, m.p. 129–130°.

*Anal.* Calcd. for $C_{28}H_{48}O_4$: C, 74.95; H, 10.78. Found: C, 74.99; H, 10.84.

**Natural embelin** was obtained by extracting dried powdered berries of *Embelia Ribes* (22.4 g.) with ether in a Soxhlet apparatus and digesting the extracted product with petroleum ether. The residue (340 mg.) melted at 141–144.5°, and the material crystallized from absolute alcohol formed glistening orange plates, m.p. 142–143° (Heffter and Feuerstein,[3] 142°). The **hydroquinone tetraacetate**[13] melted at 125–126° (A. and Y.,[5] 123.5°). A mixture of the synthetic and natural tetraacetates showed no depression; m.p. 125–126°.

### 2. 2,5-Dihydroxy-3-dodecyl-1,4-benzoquinone, II

Tridecylic acid was prepared by a known method[14] as follows. Technical lauryl alcohol was distilled through a Widmer column and a fraction boiling at 168–175° (43 mm.) converted according to Kamm and Marvel[15] into the bromide, b.p. 178–180° (48 mm.), in 91% yield. The nitrile (76% yield) boiled at 153–158° (12 mm.), and the acid (97% yield) boiled at 155–160° (3 mm.) and melted at 44.5–45.5°; the melting point is the same as that reported for tridecylic acid prepared by another synthesis.[16] The conversion to the acid chloride (97%) and the crystalline peroxide (65%) was conducted as in the first section, as was the alkylation of 2,5-dihydroxy-1,4-benzoquinone (2 g.). A precipitate separated from the reaction mixture but was removed and not investigated; the filtrate in the course of several days deposited orange crystals of **2,5-dihydroxy-3-dodecyl-1,4-benzoquinone**. Recrystallized from acetic acid, the substance melted at 142–143° (A. and Y.,[5] 142°). The **hydroquinone tetraacetate** melted at 120–121° (A. and Y.,[5] 120°).

*Anal.* Calcd. for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 70.31; H, 9.24.

### 3. 2,5-Dihydroxy-3-tridecyl-1,4-benzoquinone (Rapanone), III

**Synthesis.**—By the procedures described above myristic acid was converted into the chloride (97%) and the

---

[11] Fieser, Leffler and co-workers, papers submitted for publication.

[12] Prepared most conveniently by the procedure of R. G. Jones and Shonle, THIS JOURNAL, 67, 1034 (1945).

[13] In conducting the reductive acetylation of this and other members of the series with zinc dust, acetic anhydride and triethylamine in the ordinary way, I observed the formation of persistent specks of a sparingly soluble purple substance; the formation of this substance can be avoided by warming the quinone with acetic anhydride and triethylamine until the initially red solution becomes yellow and then adding the zinc dust.—L. F. F.

[14] Ruzicka, M. Stoll and Schinz, *Helv. Chim. Acta*, 11, 685 (1928).

[15] Kamm and Marvel, "Organic Syntheses," Coll. Vol. I, 2nd ed., 29 (1941).

[16] Levine, *J. Biol. Chem.*, 23, 71 (1915).

peroxide (crystalline solid, 42%) and the latter (6 g.) used for the alkylation of 2,5-dihydroxybenzoquinone (1.7 g.). The material that precipitated from the reaction mixture was recrystallized in turn from methanol, benzene and 95% alcohol and obtained as glistening golden-orange plates, m.p. 141-142° (A. and Y.,[6] 139-140°). The hydroquinone **tetraacetate** melted at 116-117° (A. and Y.,[6] 118°).

From *Oxalis Purpurata*, **Jacq.**—The material as supplied by O. Fernandez was in the form of orange crystals melting at 141-142°. Three further crystallizations from toluene gave lustrous orange plates of the same melting point.

*Anal.* Calcd. for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 71.07, 70.86; H, 9.64, 9.43.

A mixture of this substance with the synthetic rapanone described above melted at 141-142°; a mixture with synthetic embelin melted at an intermediate temperature: 142-144°.

The **hydroquinone tetraacetate** formed small colorless needles, m.p. 116.5-117.5°.

*Anal.* Calcd. for $C_{27}H_{40}O_8$: C, 65.83; H, 8.19. Found: C, 66.13; H, 8.33.

A mixture of this substance and the corresponding derivative of synthetic rapanone melted at 116-117°; the melt readily solidified and remelted at the same temperature.

### 4. Experiments with Unsaturated Acids

**Alkylation of 2,5-Dihydroxybenzoquinone with Dierucoyl Peroxide.**—A mixture of 10.9 g. of erucic acid and 8.3 g. of purified thionyl chloride was allowed to stand overnight and then heated on the steam-bath for one-half hour. The excess reagent was removed by evaporation in vacuum with dry benzene and the erucoyl chloride was then distilled by the "unobstructed path" technique of Hickman[17] at a bath temperature of 180-190° (0.08 mm.); the yield of colorless product was 9.4 g. (81%). The peroxide was prepared from 8 g. of the acid chloride as in the other instances but was not isolated from the ether-petroleum ether solution: titration of an aliquot indicated a yield of 56% of peroxide. The solution was then run slowly into a solution at 65° of 0.89 g. of the benzoquinone in 70 cc. of acetic acid and at the rate of evaporation of the low-boiling solvents. The reaction mixture was then refluxed for one-half hour and allowed to stand overnight, when an orange precipitate containing the disubstituted product had separated (see below). The mother liquor was evaporated in vacuum and the residue extracted with petroleum ether. The extract was evaporated in a stream of dry air to a point where a small amount of oily dark solid separated and this was removed by centrifugation. After considerable further processing, the clarified petroleum ether solution, when cooled in Dry Ice, yielded a solid product, and this on spontaneous evaporation of an acetone solution afforded orange crystals of **2,5-dihydroxy-3-($\Delta^{12}$-heneicosenyl)-1,4-benzoquinone** (V), m.p. 109-114°. When recrystallized from alcohol-water and from absolute alcohol the substance was obtained in glistening orange plates, m.p. 112.5-113.5°; the yield was only 8 mg. (0.3%).

*Anal.* Calcd. for $C_{27}H_{44}O_4$: C, 74.95; H, 10.25. Found: C, 74.98; H, 10.39.

Purification of the less soluble reaction product that separated from the reaction mixture by repeated slow evaporation of a petroleum ether solution afforded 15 mg. (0.6%) of **2,5-dihydroxy-3,5-di-($\Delta^{12}$-heneicosenyl)-1,4-benzoquinone**, m.p. 84-85°.

*Anal.* Calcd. for $C_{48}H_{84}O_4$: C, 79.38; H, 11.80. Found: C, 79.43; H, 11.85.

### $\Delta^{12}$-Heneicosenoic Acid, XII

Oleyl alcohol was prepared according to Reid and Cockerille[18] except that methyl oleate was employed for reduction with sodium and butyl alcohol; the yield from 1333 g. of methyl oleate, b.p. 140-145° (0.3 mm.) of twice distilled, colorless oleyl alcohol, b.p. 132-142° (0.2 mm.) was 804 g. (67%).

The preparation of **oleyl bromide** by the method of Deatherage and Olcott[19] proved tedious because of the troublesome emulsions encountered, and in batches of 1 mole each the yield was never better than 43% of colorless, fractionated product, b. p. 175-178° (0.6 mm.).

**Oleyl *p*-toluenesulfonate** was investigated as a possible alternate intermediate and was obtained readily by the method of Tabern and Volwiler[20] by interaction of the alcohol and acid chloride in pyridine and benzene; the crude product was obtained in 94% yield as an oil that failed to crystallize and that decomposed on attempted distillation, but it could be employed satisfactorily in place of the bromide in the malonic acid synthesis.

**Methyl $\Delta^{11}$-eicosenoate** (VIII) was the next intermediate isolated in a pure form. Oleylmalonic ester proved to be undistillable at 0.1 mm. but on saponification afforded a solid dibasic acid; this was decarboxylated at 160-180° and the product esterified with methanol and sulfuric acid. After an initial rough distillation, the ester was fractionated through a Vigreux column and obtained as a colorless liquid boiling at 164-174 (0.02 mm.). The yield from 100.8 g. of oleyl bromide was 52 g. (53.5%), which represents an over-all yield from oleyl alcohol of 23%. The over-all yield from 588 g. of oleyl alcohol through the tosylate was 189 g. (26%).

*Anal.* Calcd. for $C_{21}H_{40}O_2$: C, 77.72; H, 12.42. Found: C, 77.76; H, 12.27.

A sample of free **$\Delta^{11}$-eicosenoic acid** (VII) obtained by hydrolysis of the ester, purified through the lead salt, and crystallized from acetone melted at 49-51° (Bodenstein,[21] m.p. 50°).

**Butyl $\Delta^{11}$-eicosenate** was prepared from 20 g. of the acid, 300 cc. of *n*-butyl alcohol and 4 g. of acetyl chloride at room temperature.[22] After six days the ester was recovered and distilled, b.p. 190-193° at 0.7 mm. (11.5 g.).

*Anal.* Calcd. for $C_{24}H_{46}O_2$: C, 78.62; H, 12.65. Found: C, 78.70; H, 12.80.

$\Delta^{11}$-Eicosenyl alcohol (IX) was prepared by reduction of 188 g. of methyl $\Delta^{11}$-eicosenate with sodium (66 g.) and *n*-butyl alcohol (1200 cc.) in the usual manner; the yield was 77.3 g. (45%); b.p. 134-146° (0.1 mm.), m.p. 25-26°.

*Anal.* Calcd. for $C_{20}H_{40}O$: C, 81.01; H, 13.60. Found: C, 80.88, 81.23; H, 13.89, 13.73.

**$\Delta^{12}$-Heneicosenoic Acid (XII) A. Through the Bromide.**—$\Delta^{11}$-Eicosenyl bromide was obtained by the action of phosphorus tribromide on the alcohol (50 g.) and distilled: b.p. 175-180° (0.7 mm.), yield 27.7 g. (46%). The product was refluxed for thirty hours in 300 cc. of alcohol with 10.7 g. of potassium cyanide dissolved in the minimum amount of water; 120 cc. of 50% sodium hydroxide was then added and refluxing continued for twelve hours. The bulk of the alcohol was distilled, the mixture diluted with water and the white curd of soap collected. The soap was digested with hot acetone and heated with hydrochloric acid until a clear oily layer formed, and the free acid was taken up in ether and the solution clarified with charcoal and evaporated. The residue (dried in vacuum) was a white crystalline solid, m.p. 56-57°; yield 5.5 g. (22% from the bromide, 10% from the alcohol).

**B. Through the Tosylate.**—The crude tosylate (15.2 g.) from 10 g. of $\Delta^{11}$-eicosenyl alcohol was converted through the nitrile to the acid exactly as in (a) and afforded 5.0 g. of crude acid (46% from the alcohol).

For purification, boiling solutions of 5 g. of the crude acid and 3.5 g. of lead acetate trihydrate, each in 25 cc. of alcohol, were mixed and the lead salt that crystallized was recrystallized from 70 cc. of alcohol and then shaken with

---

[17] Hickman, *Chem. Rev.*, **34**, 51 (1944).

[18] Reid and co-workers, "Organic Syntheses," Coll. Vol. II, 468 (1943).

[19] Deatherage and Olcott, THIS JOURNAL, **61**, 630 (1939).

[20] Tabern and Volwiler, *ibid.*, **56**, 1139 (1934).

[21] Bodenstein, *Ber.*, **27**, 3403 (1894).

[22] Method of Freudenberg, *ibid.*, **74**, 100 (1941).

ether and dilute sulfuric acid. The acid recovered from the ether layer on recrystallization from acetone afforded 0.2 g. of pure acid, m.p. 56–57°.

*Anal.* Calcd. for $C_{21}H_{40}O_2$: C, 77.72; H, 12.43; mol. wt., 324. Found: C, 77.54; H, 12.61; neut. equiv., 322.

### 5. 2-Hydroxy-3-dihydrophytyl-1,4-naphthoquinone, XIII

**Dihydrophytyl Bromide.**—Commercial phytol was shaken with catalyst and redistilled and the product (101 g.) was hydrogenated[23] in absolute alcohol (200 cc.) in the presence of Adams catalyst (0.5 g.) and gave 101 g. of dihydrophytol, b.p. 157–159° (0.8 mm.). This was converted to the bromide with phosphorus tribromide (92 g.) in carbon tetrachloride (30 cc.) according to Deatherage and Olcott[19] and the product extracted with ligroin. The solution was washed with saturated calcium chloride solution and with 30% methanol, dried and evaporated, and the bromide distilled. The yield of colorless liquid, b.p. 154–156° (0.1 mm.), was 68.3 g. (55%).

*Anal.* Calcd. for $C_{20}H_{41}Br$: C, 66.46; H, 11.43. Found: C, 66.67; H, 11.52.

**Homophytanic Acid (4,8,12,16-Tetramethylheptadecanoic Acid).**—Dihydrophytyl bromide (68g.) was refluxed with 15.5 g. of potassium cyanide in 625 cc. of alcohol for twenty-four hours, a solution of 25 g of sodium hydroxide in 200 cc. of alcohol was added and refluxing continued for another thirty hours. The solution was concentrated to a small volume on the steam-bath, acidified and extracted with ether. For purification, the crude acid (58 g.) was converted to the acid chloride with thionyl chloride (44 g.) and the product refluxed with methanol (500 cc.); the methyl **ester** when twice distilled was a colorless liquid (44.5 g.), b.p. 145–147° (0.1 mm.).

*Anal.* Calcd. for $C_{22}H_{42}O_2$: C, 77.58; H, 13.02. Found: C, 77.90; H, 13.17.

A solution of the pure ester (44.5 g.) in 300 cc. of methanol was refluxed with 35 g. of potassium hydroxide in 200 cc. of 45% methanol for sixteen hours and the solution was concentrated on the steam-bath to the point of frothing, acidified and diluted. Extraction with ether and distillation afforded 35.2 g. (57% from the bromide) of acid as a clear liquid b.p. 184–188° (1.2 mm.).

*Anal.* Calcd. for $C_{21}H_{42}O_2$: C, 77.24; H, 12.96. Found: C, 77.48; H, 13.04.

**Peroxide.**—The acid (10 g.) was converted to the acid chloride with purified thionyl chloride and the excess reagent removed by evaporation in vacuum with benzene. Distillation by the Hickman technique[17] gave 9.9 g. (93%) of the acid chloride, b.p. 150–155° (0.08 mm.). The acid chloride was treated with sodium peroxide, petroleum ether and ice, as above, and the peroxide collected in dried petroleum ether solution and titrated: yield 60%.

**Alkylation.**—The alkylation was conducted by running the solution of the peroxide into a solution of hydroxynaphthoquinone in acetic acid maintained at 65°. In one experiment the peroxide from 24 g. of acid chloride was caused to react with 3.6 g. of hydroxynaphthoquinone and the material recovered by evaporation of the acetic acid solution in vacuum and the residue was digested with several portions of 70–90° ligroin. The combined extract was cooled in Dry Ice, filtered from hydroxynaphthoquinone and evaporated. The residue was a reddish oil weighing 15.8 g. This was then processed by a procedure used with success for the isolation of vitamin $K_1$,[24] namely, by extraction of the hydroquinone from petroleum ether with Claisen alkali and oxidation with silver oxide. A small amount (50 mg.) of a viscous red oil was obtained of composition not far from that of the expected product (C, 78.38; H, 11.55).

In a second experiment the crude material resulting from the alkylation of 1 g. of hydroxynaphthoquinone was distilled in high vacuum. At a pressure of $5 \times 10^{-5}$ mm., 2.63 g. of light yellow oil distilled at a bath temperature of 100°, and then 0.63 g. (24%) of a dark reddish oil distilled at 140–150° that appeared to be substantially pure **2-hydroxy-3-dihydrophytyl-1,4-naphthoquinone**. The substance did not crystallize when an acetone solution was chilled in Dry Ice, but the oil itself solidified in the ice box to waxy orange plates that melted at room temperature.

*Anal.* Calcd. for $C_{30}H_{46}O_3$: C, 79.24; H, 10.20. Found: C, 79.52; H, 10.54.

The **hydroquinone triacetate** was obtained by crystallization from alcohol as a waxy white solid melting at 79–80°.

*Anal.* Calcd. for $C_{36}H_{54}O_6$: C, 74.19; H, 9.34. Found: C, 74.40; H, 9.54.

## Summary

1. The peroxide alkylation reaction has been applied to the synthesis of the 3-undecyl (I), 3-dodecyl (II) and 3-tridecyl (III) derivatives of 2,5-dihydroxy-1,4-benzoquinone. A comparison with natural embelin confirms the structure I assigned to the pigment by Asano and Yamaguti.

2. A pigment isolated by Fernandez from a plant in Spain has been found identical with synthetic rapanone, III.

3. A structure is suggested for maesaquinone on the basis of certain model experiments.

4. The synthesis of 2-hydroxy-3-dihydrophytyl-1,4-naphthoquinone is described.

CAMBRIDGE, MASSACHUSETTS RECEIVED MAY 23, 1947

---

[23] Willstätter and A. Stoll. "Untersuchungen über Chlorophyll." 312 (1913).

[24] Fieser, THIS JOURNAL, 61, 3467 (1939).