Total Syntheses of Renieratene and Renierapurpurin*

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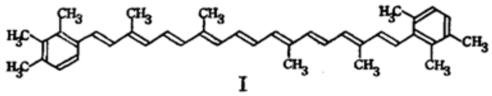
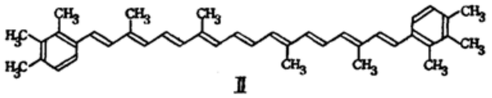
In the present paper are described the total syntheses of renieratene, I, and renierapurpurin, the chemical constitution of the latter having been hitherto unknown. By these works, therefore, the chemical constitution of renieratene has been established beyond doubt and the chemical constitution of renierapurpurin, II, has also been clearly established without any degradation studies.

The orange coloration of the sponge *Reniera japonica*, which is considered by zoologists to be identical with *Halichondria panicea*, a species of wide distribution, is mainly due to the presence of a complicated mixture of carotenoids. Fifteen different carotenoids have been isolated from the sponge in crystalline states[1]. The main pigments are, however, carotenoid hydrocarbons which are renieratene, isorenieratene (III), β-carotene and renierapurpurin. Among these pigments, the chemical constitution[2,3] of renieratene and isorenieratene



I



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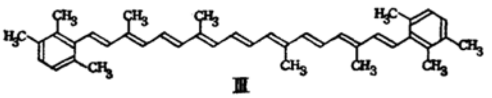

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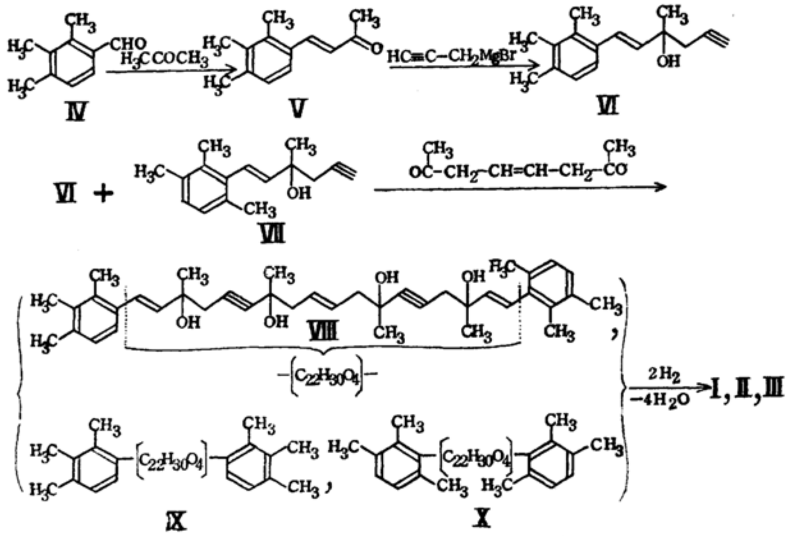

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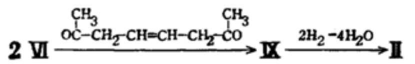
[*] Pigments of Marine Animals, Part XI. X of this series; T. Mukai, This Bulletin, 33, 1234 (1960).

[1] T. Tsumaki, M. Yamaguchi and T. Tsumaki, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), 75, 297 (1954); M. Yamaguchi, This Bulletin, 30, 111 (1957).

[2] M. Yamaguchi, This Bulletin, 31, 739 (1958).

[3] M. Yamaguchi, ibid., 31, 51 (1958).



$$2\ \mathrm{VI}\ \xrightarrow{\overset{\displaystyle CH_3}{\overset{|}{OC}}-CH_2-CH=CH-CH_2-\overset{\displaystyle CH_3}{\overset{|}{CO}}}\ \mathrm{IX}\ \xrightarrow{2H_2\ -4H_2O}\ \mathrm{II}$$

have been elucidated and the total synthesis of the latter has been carried out by the author[4] and later by M. C. Khosla and P. Karrer[5]. On the other hand, however, little progress has been made on the study of the chemical constitution of renierapurpurin because of the limited quantity of the pigment available. It has so far been known that renierapurpurin forms purple plates of m. p. 230°C, exhibits absorption maxima at 544, 504 and 475 mμ in carbon disulfide, and has the formula $C_{40}H_{48}$ (or $C_{40}H_{50}$)[1]. In regard to its constitution, it has been inferred from its absorption maxima and from an analogy to renieratene, etc., that if it contains two triemthylphenyl groups at both ends of the molecule as in renieratene and isorenieratene, the terminal groups should be ones having small steric hindrance between the polyene chain and annular methyl groups. For example 2, 3, 4-trimethylphenyl group satisfies the condition. However, no experiment has been carried out to draw any conclusion on the problem.

The syntheses were carried out according to Karrer's method[6]. 2, 3, 4-Trimethylbenzaldehyde (IV)[2] was condensed with acetone to give 2, 3, 4-trimethylbenzalacetone (V), which was converted into acetylenic alcohol VI by Grignard reaction. A mixture of this acetylenic alcohol and another acetylenic alcohol VII[4] was condensed with octene-2, 7-dione to give a mixture of three isomeric C_{40}-diynetetraols (VIII, IX and X). The mixture was partially hydrogenated and then dehydrated, and the chromatographic separations of the product gave renieratene (I), renierapurpurin (II) and isorenieratene (III) in pure states but in low yields. The identity of these pigments with the natural specimens was verified by mixed melting point determinations, mixed chromatographies, and IR- and UV-determinations.

Renierapurpurin was obtained in a better yield in another experiment starting from acetylenic alcohol VI.

Renierapurpurin is the third carotenoid that is proved to contain benzene rings, and the fact that three possible isomers derivable by combinations of 2, 3, 4-trimethylphenyl and 2, 3, 6-trimethylphenyl groups are all present in the sponge, may be considered to provide an important orientation of the biogenesis of this interesting group of carotenoids.

Furthermore these isomers afford a typical example of steric hindrance, the cause of which has been discussed in the previous paper[3]. The absorption maxima (the longest wavelength, in carbon disulfide solution) of renierapurpurin, renieratene and isorenieratene are at 544, 532 and 520 mμ, respectively[2]. The shifts of maxima (12 and 24 mμ) are proportional to the number of 2, 3, 6-trimethylphenyl group in their molecules.

Experimental

Solutions were evaporated under diminished pressure unless otherwise mentioned. Anhydrous sodium sulfate was employed for drying solutions.

4-(2, 3, 4-Trimethylphenyl)-3-buten-2-one (V).—It was prepared from 2, 3, 4-trimethylbenzaldehyde (IV, 22 g., b. p. 133~135°C/20 mmHg), in the way described in 4-(2, 3, 6-trimethylphenyl)-3-buten-2-one in the previous paper[4]. Colorless solid (17.2 g.), b. p. 125~130°C/3 mmHg. On recrystallization from petroleum benzine it formed thick plates of m. p. 70~71°C.

Found: C, 82.87; H, 8.74. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57%.

From the residue of the distillation, 1, 5-bis-(2, 3, 4-trimethylphenyl)-1, 4-pentadien-3-one (1.6 g.) was obtained in yellow plates when recrystallized from benzene-ethanol, m. p. 150°C.

Found: C, 86.69; H, 8.33. Calcd. for $C_{23}H_{26}O$: C, 86.74; H, 8.23%.

1-(2, 3, 4-Trimethylphenyl)-3-methyl-1-hexen-5-yn-3-ol (VI).—Operations of the experiment and the proportions of the reagents are similar to those of the synthesis of 1-(2, 3, 6-trimethylphenyl)-3-methyl-1-hexen-5-yn-3-ol in the previous paper[4]. From C_{13}-ketone (V, 13 g.), acetylenic alcohol (VI, 6.1 g.) was obtained as faint colored oil, b. p. 115~120°C (bath temperature)/0.05 mmHg.

Found: C, 84.41; H, 8.92. Calcd. for $C_{16}H_{20}O$: C, 84.16; H, 8.83%.

C_{40}-Diynetetraol Mixture (VIII, IX and X).—An ethereal solution (ca. 30 cc.) of ethylmagnesium bromide prepared from 3.9 g. of ethyl bromide, was added dropwise to a well-stirred mixture of the above acetylenic alcohol (VI, 2 g.), 1-(2, 3, 6-trimethylphenyl)-3-methyl-1-hexen-5-yn-3-ol (VII, 2 g.)[4], cuprous chloride (50 mg.) and dry ether (20 cc.) during one and a half hours, and the mixture was refluxed for an hour. A solution of 4-octene-2, 7-dione (840 mg.) in dry ether (20 cc.) was added dropwise during thirty minutes under stirring. After refluxing for one hour, the mixture was allowed to stand overnight, and decomposed with 1 N sulfuric acid under ice-cooling. The organic layer was extracted with ether and the ethereal solution was washed with dilute sulfuric acid, aqueous sodium hydrogen carbonate and water, dried and evaporated. The residue (4.8 g.) dissolved in benzene (20 cc.) was adsorbed on alumina (Merck, 80 g.) and the column was washed successively with benzene (100 cc., the eluate gave an oily residue 1.95 g.), with ether (60 cc., residue 0.8 g.) and with ether-methanol 10 : 1 (200 cc., residue 1.8 g.). The last fraction was the mixture

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4) M. Yamaguchi, ibid., 32, 1171 (1959).

5) M. C. Khosla and P. Karrer, *Helv. Chim. Acta*, 43, 453 (1960).

6) P. Karrer and C. H. Eugster, ibid., 33, 1172 (1950).

of three isomers of C_{40}-diynetetraol and formed a yellowish-colored glass-like mass.

Found: C, 79.91; H, 8.80. Calcd. for $C_{40}H_{52}O_4$: C, 80.50; H, 8.78%.

Renieratene (I), Renierapurpurin (II) and Isorenieratene (III).—A solution of the above tetraol mixture (1.5 g.) in ethyl acetate (40 cc.) was filtered through a column of active charcoal (0.3 g.) and shaken with palladium-barium sulfate catalyst (1%, 50 mg.) in an atmosphere of hydrogen. Occasional additions of the small amount of catalyst were necessary until 2 mol. of hydrogen (ca. 116 cc., 9°C/760 mmHg) was absorbed. The catalyst was filtered and the solution was evaporated to glassy residue. A boiling solution of toluene-*p*-sulfonic acid (180 mg., dehydrated by melting in vacuo) in toluene (30 cc.) was added at a time to a boiling solution of the above residue in toluene (40 cc.) and the mixture was boiled for ca. eighty seconds. The greenish brown solution was, as soon as possible, poured into a mixture of a saturated aqueous solution of sodium hydrogen carbonate (300 cc.) and petroleum ether (200 cc.). The petroleum ether solution was then washed once with water and thrice with 90% methanol, dried and evaporated. The reddish-brown residue was dissolved in petroleum ether and chromatographed on alumina (4×20 cm.), giving the following zone: i) dark brown zone (most strongly adsorbed), ii) a broad zone, its color changing from red to orange, iii) an orange brown zone, and iv) faint yellow. The residue of the zone ii) was boiled several times with methanol, and the insoluble residue was rechromatographed on alumina giving the following main zones; a) purplish red (uppermost), b) red and c) orange. The pigment of the zone b) was further purified by rechromatography. The residue of the eluate of each zone was boiled with methanol. The insoluble parts were treated with petroleum ether and ethanol, and each pigment which separated out, was recrystallized several times from suitable solvents. The zone a) gave glistening purple plates (2.4 mg.) of renierapurpurin (from chloroform-ethanol), m. p. 229~230°C, its identity with natural pigment being confirmed by mixed melting point, 229~230°C, by mixed chromatography, and by IR- and UV-spectra (Fig. 1 and Fig. 2). The zone b) gave purplish red fine needles (1.4 mg.) of renieratene (from benzene-ethanol), m. p. 184~185°C, the identity with natural pigment being confirmed by mixed melting point, 184~185°C, by mixed chromatography, and by IR- and UV-spectra. The zone c) gave purplish red find needles (2.0 mg.) of isorenieratene (from benzene-ethanol), m. p. 199~200°C, the identity with natural pigment being confirmed by mixed melting point, 199~200°C, by mixed chromatography, and by UV-spectrum.

Because of the small yields of these pigments, no elementary analysis was carried out.

C_{40}-Diynetetraol (IX).—It was synthesized from acetylenic alcohol (VI, 3 g.) in the way described above. It formed a faint yellow glass-like mass (1.6 g.).

Found: C, 80.12; H, 8.81. Calcd. for $C_{40}H_{52}O_4$: C, 80.50; H, 8.78%.

Renierapurpurin (II).—Tetraol (IX, 1.5 g.) was partially hydrogenated and then dehydrated in the way described above. While petroleum benzine solution of the dehydration product was washed, a part of the pigment was crystallized out, which was filtered off (43 mg.). The mother liquor was chromatographed on alumina from a benzene solution, giving three main zones; i) pink, ii) red and iii) orange. From the zone i), 25 mg. of the pigment was obtained, which was combined with the crystals separated during washing. Several recrystallizations from chloroform-ethanol gave pure renierapurpurin (38 mg.), m. p. 230°C.

Found: C, 90.76; H, 8.99. Calcd. for $C_{40}H_{48}$: C, 90.85; H, 9.15%.

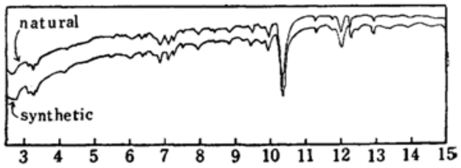

Fig. 1. Infrared spectra of renierapurpurin (KBr disk).

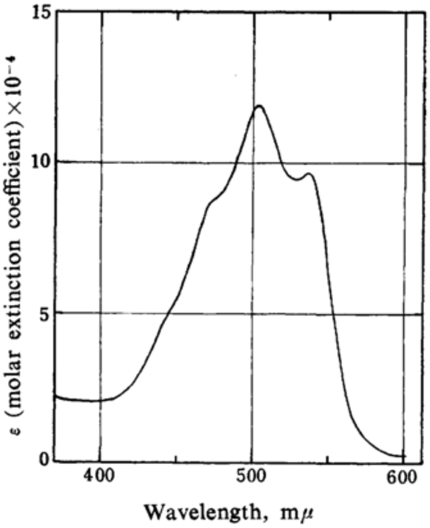

Fig. 2. Absorption curve of renierapurpurin (carbon disulfide).

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