Total Synthesis of Natural Acetylenic Analogues of Isorenieratene and Renieratene[1]

Tetsuji IKE,[2] Junji INANAGA, Akio NAKANO, Nobuhisa OKUKADO, and Masaru YAMAGUCHI

Department of Chemistry, Faculty of Science, Kyushu University, Higashi-ku, Fukuoka 812

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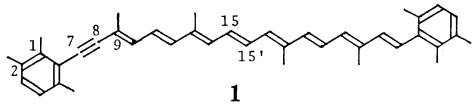
The total synthesis of two natural acetylenic aromatic carotenoids, 7,8-didehydroisorenieratene (**1**) and 7,8-didehydrorenieratene (**2**), was carried out. Although the condensations involving C_{15}-acetylenic ylids (derived from the phosphonium salts **7**, and **8**) as the intermediates gave only 9-*cis* isomers of **1** and **2**, low-temperature condensations of C_{25}-hexaene yield (derived from **19** and **28**) with C_{15}-acetylenic aldehyde (**12a**) led to all-*trans* **1** and **2**, which were identical with natural specimens.

It has recently been shown that two minor carotenoid constituents, mp 194—194.5 °C and mp 204—205 °C, isolated from a sea sponge "*Reniera japonica*" ("*Halichondria japonica*") have the acetylenic aromatic structures of **1** and **2**,[3] which correspond to those of the 7,8-didehydro derivatives of isorenieratene[4] and renieratene[5] respectively. The present work has been



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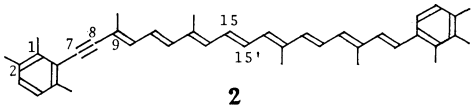

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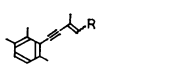
undertaken to verify these structures by synthesis. Analogous syntheses have already been done on several alicyclic acetylenic carotenoids by Weedon.[6] In the present work, a similar construction principle, $C_{15}+C_{10}\rightarrow C_{25}$, $C_{25}+C_{15}\rightarrow C_{40}$, has been used.

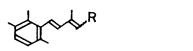
Results and Discussion

Synthesis of 7,8-Didehydroisorenieratene (1). The first synthesis, which led to the 9-*cis* isomer (**22**) of **1**, was started with 2,3,6-trimethylbenzoic acid,[7] which was converted into the acetylenic alcohol (**5**) through **3** and **4**. The treatment of **5** with triphenylphosphonium bromide gave a sole product, which was later proved to be the *cis* salt (**7**) by comparing its NMR spectrum with that of **8** to be described below. The condensation of the ylid from **7** with the C_{10}-dialdehyde

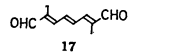
3 R:$COCH_3$
4 R:C≡CH
5 R:C≡CCCH=CH_2 (H_3C, OH)
6 R:C≡CCOCH_3



7 R:$CH_2\overset{+}{P}Ph_3\bar{B}r$(2-cis)
8 R:$CH_2\overset{+}{P}Ph_3\bar{B}r$(2-trans)
9a R:CO_2H(2-trans)
9b R:CO_2H(2-cis)
10a R:CH_2OH(2-trans)
10b R:CH_2OH(2-cis)
11a R:CH_2Br(2-trans)
11b R:CH_2Br(2-cis)
12a R:CHO(2-trans)
12b R:CHO(2-cis)



13a R:$CO_2C_2H_5$(2-trans)
13b R:$CO_2C_2H_5$(2-cis)
14a R:CO_2H(2-trans)
14b R:CO_2H(2-cis)
15 R:CH_2OH(2-trans)
16 R:$CH_2\overset{+}{P}Ph_3\bar{B}r$(2-trans)



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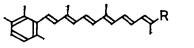
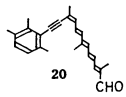


18 R:CHO
19 R:$CH_2\overset{+}{P}Ph_3\bar{B}r$



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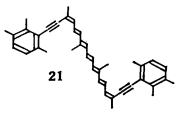

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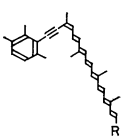
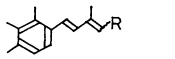
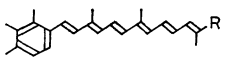


22 R:2,3,6-$(CH_3)_3C_6H_2$
23 R:2,3,4-$(CH_3)_3C_6H_2$



24a R:CO_2CH_3(2-trans)
24b R:CO_2CH_3(2-cis)
25 R:CH_2OH(2-trans)
26 R:$CH_2\overset{+}{P}Ph_3\bar{B}r$(2-trans)



27 R:CHO
28 R:$CH_2\overset{+}{P}Ph_3\bar{B}r$

(**17**)[8] afforded the acetylenic aldehyde (**20**) as the major product (25% yield), besides 9,9′-di-*cis*-7,7′,8,8′-tetradehydroisorenieratene (**21**). The condensation of 2,3,6-trimethylbenzalacetone with ethoxycarbonylmethylenetriphenylphosphorane gave, after saponification, a mixture of the *trans* (**14a**) and the *cis* acid[9] (**14b**) (3 : 1), which were then separated by fractional crystallization. The *trans* acid (**14a**) was converted into the phosphonium bromide (**16**) *via* the corresponding alcohol (**15**). The Wittig reaction of the ylid of **16** with the C_{25}-acetylenic aldehyde (**20**) gave the 9-*cis*-didehydroisorenieratene (**22**) as reddish-orange needles in a 51% yield.

The pigment (**22**) thus obtained exhibited λ_{max} at wavelength locations about 8 nm shorter than those of **1**, and showed a distinct *cis*-peak at 356 nm (Fig. 1).

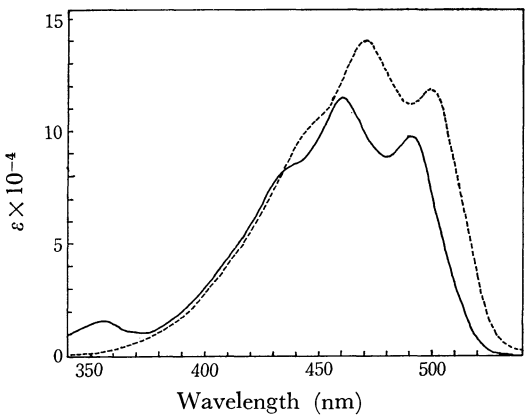


Fig. 1. Absorption spectra of **1** (natural, mp 194—194.5 °C, ----) and its 9-*cis* isomer (**22**, ——) in benzene.

On isomerization (iodine and light[10]), however, both the pigments gave the same absorption curve, which was essentially identical with that of **22**. This means that the 9-*cis* isomer (**22**) is the most stable one among the stereoisomers, including all-*trans* **1**, and that **22** is the major constituent of the equilibrium mixture, which is to be expected in view of the small steric

requirement of the triple bond.

B. C. L. Weedon reported that *trans*-[5-(4-hydroxy-2,2,6-trimethyl-6-cyclohexen-1-yl)-3-methyl-2-penten-4-ynyl]-triphenylphosphonium salt gave an all-*trans* Wittig condensation product when the reaction was conducted in the dark.[6b] In our second synthesis, therefore, *trans*-C_{15}-phosphonium salt (**8**) was prepared in the hope that its configuration would be retained during the condensation, thus leading to the predominant formation of **1**.

A mixture of the *trans* and the *cis* ester (1 : 3), prepared from **4** through **6**, was saponified and separated by fractional crystallization into the corresponding acids (**9a** and **9b**). In contrast to the fact that the base treatment of the ester mixture did not change the isomeric ratio, the *cis* acid seemed to be less stable than the *trans* isomer in an alkaline medium, and the former was converted into the latter by heating with an aqueous-methanolic potassium hydroxide solution. The *trans* acid (**9a**) was converted into the *trans* phosphonium salt (**8**) by the usual procedures. The condensation of the ylid from **8** with the all-*trans* C_{25}-aldehyde (**18**), prepared by the condensation of **16** with C_{10}-dialdehyde (**17**), proceeded smoothly under various reaction conditions, but the product was always predominantly the 9-*cis* isomer (**22**), even when the reaction was run in the dark. The isolation of the *trans* pigment (**1**) was practically impossible, though a very faint zone corresponding to **1** was observed on the chromatographic column.

In order to circumvent the lability of the 2-double bond in the ylid, a reversed combination of ylid and aldehyde was then undertaken. The *trans* C_{15}-aldehyde (**12a**), obtained by the manganese dioxide oxidation of **10a**, seemed to be stable, at least at room temperature, for several days. When **12a** was condensed with C_{25}-ylid (prepared from **19**) at room temperature, however, the predominant product was again **22**. When the reaction was run at a low temperature, on the other hand, the yield of the condensation product was very low, though the product contained a substantial amount of **1**, which could be purified and which was proved to be identical with a natural specimen in every respect.

*Synthesis of 7,8-Didehydrorenieratene (**2**).* 9-*cis*-7,8-Didehydrorenieratene (**23**) was synthesized by a route analogous to that of the first synthesis of **1**. The absorption maxima of the isomer were about 8 nm shorter than those of natural **2**, but both the pigments gave the same absorption curve after isomerization. The all-*trans* **2** was also synthesized in a way corresponding to that used for all-*trans* **1**; it was identical with the natural specimen in every detail examined.

Experimental

All the Wittig condensations were carried out under an atmosphere of nitrogen. The phosphonium salts were dried under a vacuum for several hours just before use. Anhydrous sodium sulfate was used for drying the solutions. The melting or boiling points were uncorrected. Unless otherwise mentioned, the IR spectra were taken in potassium bromide pellets. The NMR spectra were taken in a deuterochloroform solution. Benzene solutions were used for the UV determination.

*2,3,6-Trimethylacetophenone (**3**).* It was prepared from 2,3,6-trimethylbenzoyl chloride (prepared from 2,3,6-trimethylbenzoic acid and thionyl chloride by heating at 60 °C for 12 hr; bp 80—81 °C/6 mmHg) and methyl magnesium iodide in a way similar to that reported for 2,4,6-trimethylacetophenone.[11] A colorless oil;[12] bp 99—101 °C/6 mmHg, IR (liquid film) 1690 cm^{-1}.

2,3,6-Trimethyl-α-chlorostyrene. The method for the synthesis of 2,4,6-trimethyl-α-chlorostyrene[13] was modified because of the very low yield of the product (less than 10%). To a mixture of **3** (30 g) and phosphorus pentachloride (50 g) in benzene (50 ml), we added a portion (10 ml) of a solution of collidine (25 g) in dry benzene (50 ml). After the mixture had been heated at 80 °C for 24 hr with occasional additions of the remainder of the collidine solution, it was cooled and poured into ice water. The organic layer was worked up in a usual way. A colorless liquid (21 g); bp 68—70 °C/5 mmHg; IR (liquid film) 1630, 888 cm^{-1}.

*2,3,6-Trimethylphenylacetylene (**4**).* 2,3,6-Trimethyl-α-chlorostyrene (18 g) was heated (160—180 °C) with sodium amide (12 g) in mineral oil (30 ml) for 3 hr, after which the crude product was fractionally distilled. A fragrant mobile liquid[12] (9.4 g); bp 54—55 °C/5 mmHg. IR (liquid film) 3295, 2090 cm^{-1}.

*3-Methyl-1-(2,3,6-trimethylphenyl)-4-penten-1-yn-3-ol (**5**).* The magnesium derivative was prepared from **4** (5.7 g), isopropyl magnesium bromide (0.04 mol), and a catalytic amount of cuprous chloride in ether (50 ml) in the usual way. A solution of methyl vinyl ketone (2.8 g) in dry ether (20 ml) was stirred into this over a period of 1 hr at room temperature. After refluxing for 3 hr, the reaction mixture was poured into cold water and treated with saturated aqueous ammonium chloride. The organic layer was then washed, dried, and distilled. A viscous oil[12] (3 g); bp 86—87 °C/0.024 mmHg; IR(liquid film) 3370, 2220, 925 cm^{-1}.

*[3-Methyl-5-(2,3,6-trimethylphenyl)-*cis*-2-penten-4-yn-1-yl]triphenylphosphonium Bromide (**7**).* A solution of **5** (1.09 g) and triphenylphosphonium bromide (1.71 g) in dichloromethane (25 ml) was stirred for 20 hr at room temperature. The subsequent evaporation of the solvent gave a solid, which was recrystallized from dichloromethane-ethyl acetate. Colorless needles[12] (2.4 g); mp 211—212 °C; NMR δ 1.97 (3H, d, J=6.0 Hz; 3-methyl).

*2,7,11-Trimethyl-13-(2,3,6-trimethylphenyl)-2,4,6,8,*cis*-10-tridecapentaen-12-yn-1-al (**20**) and 9,9′-Di-*cis*-7,7′,8,8′-tetradehydroisorenieratene (**21**).* To a stirred suspension of **7** (0.432 g) in dry ether, we added an ethereal phenyl lithium solution (0.2 mol, 4 ml); the mixture was stirred for 1 hr at room temperature, and then a dichloromethane-ether mixture (2 : 1, 3 ml) was added. The resulting deep red solution of the ylid was added, drop by drop, to a solution of the C_{10}-dial[8] (**17**, 0.256 g) in dichloromethane (20 ml). The mixture was refluxed with stirring for 3 hr, poured into water, and extracted with ether. The extract was dried and evaporated. The reddish-brown residue was chromatographed on neutral alumina [Merck, deactivated by the addition of water (5%)] with a benzene-petroleum benzine mixture (1 : 19) as a developer; this gave two main zones; i) a reddish-orange zone (upper) and ii) a yellow zone (lower). The elute (benzene-methanol, 9 : 1) of i) gave a crude product (63 mg) on evaporation; this product was recrystallized from dichloromethane-methanol. Orange needles[12] (**20**); mp 129—130 °C; λ_{max} 421 nm ($\varepsilon=5.96\times10^4$); IR 1660, 1605 cm^{-1}; NMR δ 9.69 (1H, s; 1-proton).

The elute of ii) gave crude **21** (14 mg), which, on recrystal-

lization, gave red thick plates;[12] mp 174—175 °C; λ_{max} 462 nm ($\varepsilon=10.1\times10^4$); IR 2920, 1455, 1435, 1365, 970, 960, 800 cm^{-1}; NMR δ 1.96 (6H, s), 2.09 (6H, s), 2.25 (6H, s), 2.44 (12H, s), 5.9—6.9 (14H, m).

Ethyl 3-Methyl-5-(2,3,6-trimethylphenyl)-trans-*2*, trans-*4-pentadienoate (**13a**) and Its 2*-cis *Isomer (**13b**).* A mixture of 4-(2,3,6-trimethylphenyl)-3-buten-2-one[14] (3.3 g, bp 127—132 °C/6 mmHg) and ethoxycarbonylmethylenetriphenylphosphorane (7.0 g) was heated at 150 °C for 4 hr with stirring. After cooling, the mixture was extracted with petroleum ether. The extract was then distilled to give a mixture of *trans* and *cis* esters (**13a** : **13b**=3 : 1, NMR) as a colorless oil (3.4 g); bp 156—160 °C/1 mmHg.

3-Methyl-5-(2,3,6-trimethylphenyl)-trans-*2*, trans-*4-pentadienoic Acid (**14a**) and Its 2*-cis *Isomer (**14b**).* A mixture of the above esters (6.7 g) and a 40% aqueous potassium hydroxide solution (10 ml) was stirred at 110 °C for 4 hr, washed with ether, acidified, and extracted with ether. The extract was then dried and evaporated to give a white crystalline solid (5.7 g, *trans* : *cis*=3 : 1), which was separated by fractional crystallization from ethyl acetate. The *trans* acid[12] (**14a**): mp 170—172 °C[9]; IR 2940, 1670, 1600 cm^{-1}; NMR δ 5.85 (1H, s; 2-proton), 6.26 and 7.07 (2H, ABq, J=16.3 Hz; 4,5-protons).

Methyl ester (diazomethane), mp 42 °C.

The *cis* acid[12] (**14b**): mp 173—174 °C,[9] colorless needles; NMR δ 5.76 (1H, broad s; 2-proton), 7.01 and 7.76 (2H, ABq, J=16.7 Hz; 4,5-protons).

*3-Methyl-5-(2,3,6-trimethylphenyl)-2,4-pentadien-1-ol (**15**).* To a cold (0 °C) suspension of lithium aluminium hydride (93.7 mg) in dry ether (15 ml), we added a solution of the methyl ester of **14a** (547 mg) in ether (5 ml) over a 15-min period, after which the mixture was stirred for 20 min at room temperature. After working-up in the usual way, the product was distilled to give an oil (**15**, 387 mg); bp 140—145 °C/0.9 mmHg; NMR δ 4.32(2H, d, J=6.9 Hz; 1,1-protons). This oil was employed for the next step without further purification.

*[3-Methyl-5-(2,3,6-trimethylphenyl)-2,4-pentadien-1-yl]triphenylphosphonium Bromide (**16**).* A mixture of **15** (232 mg), triphenylphosphonium bromide (377 mg), and dichloromethane (3 ml) was stirred at room temperature for 48 hr. The solvent was then removed, and the residue was washed with dry ether. A glass-like white solid (540 mg); NMR δ 4.83 (2H, dd, J=8.0, J=14.2 Hz; 1,1-protons).

9-cis-*7,8-Didehydroisorenieratene (**22**).* To a solution of the ylid of **16** (65 mg), prepared in a way similar to that described in **20**, we added a solution of **20** (10.4 mg) in dry dichloromethane (7 ml). After refluxing for 4 hr, the reaction mixture was treated in the usual way and the product was chromatographed on alumina (containing 5% water) from a benzene-petroleum benzine (1 : 9) solution. The residue (8 mg, 51%) of the elute of the main orange zone gave, on recrystallization from dichloromethane-methanol, reddish-orange needles[12] (**22**); mp 173 °C; λ_{max} 491.5, 462 ($\varepsilon=11.6\times10^4$), (435), 356 nm; IR 3040, 2920, 1590, 1560, 1460, 1440, 1380, 1368, 1035, 1000, 965, 960, 810, 795 cm^{-1}; NMR δ 1.96 (6H, s), 2.08 (6H, s), 2.28 (12H, s), 2.48 (6H, s), 6.1—7.2 (16H, m).

Both **22** and the natural pigment (mp 194—194.5 °C) were isomerized with iodine under diffused daylight in benzene for 1 hr.[10] They gave the same UV curves, with maxima at 490.5, 462, (435), and 357 nm.

4-(2,3,6-Trimethylphenyl)-3-butyn-2-ol. Acetaldehyde (3.0 g) was treated at 0 °C with a solution of the Grignard reagent prepared from **4** (4.0 g, 28 mmol), isopropyl magnesium bromide (30 mmol), and a catalytic amount of cuprous chloride in ether (40 ml). After working-up in the usual manner, the distillation of the product gave colorless crystals[12] (3.3 g); bp 125 °C/1 mmHg, mp 42—44 °C.

*4-(2,3,6-Trimethylphenyl)-3-butyn-2-one (**6**).* A mixture of the above acetylenic alcohol (13 g) and active manganese dioxide[15] (50 g) in dry dichloromethane (100 ml) was stirred overnight at room temperature, after which the reaction mixture was filtered through celite. The evaporation residue (12.5 g) of the filtrate was purified by sublimation; mp 39—40 °C.[12]

3-Methyl-5-(2,3,6-trimethylphenyl)-trans-*2-penten-4-ynoic Acid (**9a**) and Its 2*-cis *Isomer (**9b**).* The condensation reaction and the separation of isomeric acid after hydrolysis were carried out in a manner similar to those used for **13a**, **13b**, **14a**, and **14b**. The ratio of the *trans* and *cis* esters in the mixture was 1 : 3 (NMR). The *trans* acid[12] (**9a**): mp 158—159 °C, colorless prisms; IR 2190, 1680, 1600 cm^{-1}; NMR δ 6.18(1H, q, J=1.6 Hz; 2-proton). Methyl ester (diazomethane); mp 45—46 °C.

The *cis* acid[12] (**9b**): mp 163.5—165.5 °C, white needles; NMR δ 6.03 (1H, q, J=1.5 Hz; 2-proton). Methyl ester (diazomethane); mp 67—68 °C.

*Isomerization of **9b**.* A mixture of the *cis* acid (**9b**, 400 mg), potassium hydroxide (5 g), methanol (2.5 ml), and water (2.5 ml) was stirred at 80 °C for 2 days. After the methanol had been removed, the reddish-brown solution was washed with ether and then acidified with aqueous hydrochloric acid to give a solid (200 mg), which was proved to be the *trans* acid (**9a**) from its NMR spectrum. No *cis* acid was recovered.

3-Methyl-5-(2,3,6-trimethylphenyl)-trans-*2-penten-4-yn-1-ol (**10a**) and Its 2*-cis *Isomer (**10b**).* To a cold (0 °C) suspension of aluminium hydride, prepared from lithium aluminium hydride (11.4 mg) and aluminium chloride (13.3 mg) in dry ether (5 ml), we added a solution of the methyl ester of **9a** (48.4 mg) in ether (5 ml); the mixture was then stirred for 1 hr at room temperature. The reaction mixture was then worked-up in the usual way. A colorless oil (**10a**, 33.3 mg); IR (liquid film) 3350, 2190, 1625 cm^{-1}; NMR δ 6.08 (1H, qt, J=1.7 Hz, J=6.8 Hz; 2-proton). This oil was used for the next step without purification, since the distillation of the alcohol caused a partial isomerization to the *cis* isomer.

The *cis* alcohol (**10b**) was also obtained from the corresponding *cis* ester as a solid[12]: mp 73—75 °C; NMR δ 5.90(1H, qt, J=1.2 Hz, J=6.8 Hz; 2-proton).

3-Methyl-5-(2,3,6-trimethylphenyl)-trans-*2-penten-4-yn-1-yl Bromide (**11a**) and Its 2*-cis *Isomer (**11b**).* To a solution of **10a** (33.3 mg) in ether (6 ml) containing a catalytic amount of pyridine, we added phosphorus tribromide (25 mg), after which the mixture was stirred for 1 hr at room temperature. The reaction mixture was washed with a 5% aqueous sodium hydroxide solution and water, dried, and evaporated to give a viscous oil (32.3 mg); IR (liquid film) 2190, 1450, 1195, 800 cm^{-1}; NMR δ 6.66 (1H, qt, J=1.4 Hz, J=8.6 Hz; 2-proton). It was used for the next step without purification, since distillation caused partial isomerization.

The *cis* bromide (**11b**) was also obtained from **10b** as a viscous oil;[12] bp 80 °C (bath)/5—6 mmHg; NMR δ 5.97 (1H, qt, J=2.0 Hz, J=8.0 Hz).

[3-Methyl-5-(2,3,6-trimethylphenyl)-trans-*2-penten-4-yn-1-yl]triphenylphosphonium Bromide (**8**).* To a solution of **11a** (22.4 mg) in ether (2 ml), we added triphenylphosphine (21.3 mg), after which the mixture was stirred for 14 hr at room temperature. The precipitate was recrystallized from dichloromethane-carbon tetrachloride to give the *trans* salt

(**8**, 25.1 mg); mp 196—199 °C (decomp.); NMR δ 1.65 (3H, d, J=4.4 Hz; 3-methyl).

*2,7,11-Trimethyl-13-(2,3,6-trimethylphenyl)trideca-2,4,6,8,10,12-hexaen-1-al (**18**).* The operations were similar to those described in **20**. The condensation of **16** (540 mg) with the C_{10}-dial (**17**, 450 mg) gave all-*trans* C_{25}-aldehyde (**18**, 8 mg) as reddish-orange needles;[12] mp 126 °C; λ_{max} 426 nm (ε=6.90×10^4); IR 2920, 1655, 1610, 1595, 1550, 1355, 1210, 1185, 970, 960, 810 cm^{-1}; NMR δ 9.52(1H, s; 1-proton).

A mixture of **13a** and **13b** (1.082 g) gave a mixture of *cis* and *trans* **18** (197 mg) in a similar way. This was isomerized by iodine and light in benzene for 3 hr and purified by alumina chromatography and recrystallization to give a further amount of *trans* **18** (134 mg).

*Wittig Reaction of **18** with the Ylid from **8**.* 1) The condensation was carried out in a way similar to that used for the synthesis of **22**. Starting with **8** (58 mg), the main product (6.2 mg) was obtained as reddish-orange needles; it was completely identical with **22**. The elute of the faint orange zone, which moved just above the main orange zone of **22**, gave λ_{max} 500, 470, and 442 nm, values which were very similar to those of **1**,[3] but the amount was too small to be worked out further.

The following three experiments also gave the *cis* pigment (**22**) almost exclusively:

2) Base, sodium methylsulfinylmethide: solvent, benzene–DMSO(1 : 11): 1 hr at room temperature and 2 hr at 35—45 °C.

3) Base, sodium methoxide: solvent, methanol–pyridine (5 : 2): 1 hr at room temperature and 2 hr at 35—45 °C.

4) Base, sodium methoxide: solvent, methanol: 20 hr at room temperature in the dark.[6b]

2,7,11-Trimethyl-13-(2,3,6-trimethylphenyl)-2,4,6,8,10,12-tridecahexaen-1-ol. To a cold (0 °C) suspension of aluminium hydride prepared from lithium aluminium hydride (38 mg) and aluminium chloride (42 mg) in dry ether (30 ml), we added a solution of **18** (116 mg) in dry benzene (10 ml), and the subsequent mixture was stirred for 30 min. The mixture was then treated in the usual way to give a canary yellow solid (114 mg); mp 106—107 °C; λ_{max} 404, 387, 366 nm; IR 3400, 1080, 970 cm^{-1}; NMR δ 4.09 (2H, s; 1,1-protons).

*[2,7,11-Trimethyl-13-(2,3,6-trimethylphenyl)-2,4,6,8,10,12-tridecahexaen-1-yl]triphenylphosphonium Bromide (**19**).* A mixture of the above C_{25}-alcohol (14 mg), triphenylphosphonium bromide (14 mg), and dry dichloromethane (10 ml) was stirred at room temperature for 72 hr under nitrogen in the dark. After the removal of the solvent, the resulting solid (**19**) was dried under a vacuum.

*3-Methyl-5-(2,3,6-trimethylphenyl)-*trans*-2-penten-4-yn-1-al (**12a**) and Its 2-*cis* Isomer (**12b**).* A mixture of **10a** (214 mg), active manganese dioxide[15] (2 g), and dry dichloromethane (10 ml) was stirred at 0 °C for 1 hr, after which the reaction mixture was filtered quickly. The filtrate was then evaporated to dryness at 0 °C to give a solid (214 mg); mp 67 (sinter)—77 °C; λ_{max} 337, 327 nm; IR 2180, 1660, 1595, 853 cm^{-1}; NMR δ 6.32 (1H, qd, J=1.2 Hz, J=8.0 Hz; 2-proton), 10.8 (1H, d, J=8.0 Hz; 1-proton). This was stored in a refrigerator under nitrogen and used without further purification. On sublimation at 60 °C, most of the aldehyde changed into its *cis* isomer (**12b**). In solution in deuterochloroform for NMR measurement, it also changed completely into the *cis* isomer within 12 hr. In the crystalline state, however, it seemed to be stable for more than a week at room temperature.

The *cis* aldehyde (**12b**) was obtained from **10b** and purified by sublimation: mp 89—91 °C;[12] λ_{max} 323 nm; NMR δ 6.19(1H, qd, J=1.6 Hz, J=8.1 Hz; 2-proton), 10.20 (1H, d, J=8.1 Hz; 1-proton).

*7,8-Didehydroisorenieratene (**1**).* A solution of the ylid was prepared from **19** (60 mg) in a way similar to that described in **20**. A solution of **12a** (30 mg) in dichloromethane (2 ml) was added to this on cooling at −78 °C. The mixture was stirred at −78 °C for 3 hr, then at −20 °C for 20 hr, at 0 °C for 4 hr, and at room temperature for 1 hr. Cold water was added to the deep red mixture. The product was extracted with ether, washed with water, dried, and evaporated below 40 °C. The dark red residue was chromatographed on alumina (5% water) with a benzene–petroleum benzine (1 : 9) mixture, thus giving two main zones: a reddish-orange zone (upper) and an orange zone (lower). The upper zone gave, after rechromatography on alumina, crude **1**, which was then recrystallized three times from a dichloromethane–methanol mixture. Red needles (**1**, 0.3 mg, 1% based on the C_{25}-alcohol); mp 196 °C, undepressed by admixture with a natural specimen. A mixed chromatography of the synthetic and the natural pigment showed no separation. The spectral properties (UV, NMR, and mass) were also identical with those reported previously.[3]

In an experiment carried out at room temperature, the product was essentially **22**. A very small amount of **1** was also observed on the column.

All the 2,3,4-trimethylphenyl derivatives necessary for the synthesis of **2** or its *cis* isomer (**23**) were prepared in essentially the same manners as were used for the corresponding compounds described in the syntheses of **1** or **22**.

*Methyl 3-Methyl-5-(2,3,4-trimethylphenyl)-*trans*-2,*trans*-4-pentadienoate (**24a**) and Its 2-*cis* Isomer (**24b**).* 4-(2,3,4-Trimethylphenyl)-3-buten-2-one[16] (4.5 g) was condensed with ethoxycarbonylmethylenetriphenylphosphorane to give a mixture of 2-*trans* and 2-*cis* isomers of the ethyl ester (1 : 1) (6.2 g, bp 100 °C (bath)/5 mmHg). The ester mixture was then saponified, and the acids (5.5 g) were separated by fractional crystallization.

The *trans* acid[12] (mp 214—215 °C) was treated with diazomethane to give the methyl ester (**24a**). Colorless prisms;[12] mp 84—86 °C; bp 80 °C (bath)/4—5 mmHg; IR 1710 cm^{-1}; NMR δ 5.87 (1H, s; 2-proton).

The *cis* acid,[12] mp 183—186 °C. Methyl ester (**24b**): mp 57—59 °C; NMR δ 5.71 (1H, broad s; 2-proton).

*3-Methyl-5-(2,3,4-trimethylphenyl)-2,4-pentadien-1-ol (**25**).* Aluminium hydride reduction of **24a** (531 mg) gave the *trans* alcohol (**25**) (442 mg); mp 56.5—58.5 °C; IR 3370, 1625 cm^{-1}.

*[3-Methyl-5-(2,3,4-trimethylphenyl)-2,4-pentadien-1-yl]triphenylphosphonium Bromide (**26**).* This was obtained from **25** (442 mg) and triphenylphosphonium bromide (700 mg): a glassy solid (900 mg); NMR (90 Mc) δ 4.86 (2H, dd, J=8.5 Hz, J=16.0 Hz; 1,1-protons).

*9-cis-7,8-Didehydrorenieratene (**23**).* The condensation of the ylid from **26** (630 mg) with **20** (10 mg) gave **23** as deep red needles (6.9 mg); mp 170.5 °C; λ_{max} 503.5, 472.5 (ε=11.0×10^4), (445), 369, (353) nm; IR 3030, 2915, 1477, 1460, 1440, 1361, 960, 800 cm^{-1}; NMR δ 1.95(6H, s), 2.05 (6H, s), 2.25 (12H, s), 2.45 (6H, broad s), 6.20—7.50 (16H, m). Mass (*m/e*) 526 (M), 434, 420, 393, 328, 133. Found: C, 90.27[17]; H, 8.87%. Calcd for $C_{40}H_{46}$: C, 91.20; H, 8.80%. The natural pigment (**2**) (mp 204—205 °C) and **23** were isomerized with iodine and light in benzene for 1 hr. Both the isomerized solutions gave the same UV curve, with maxima at 501, 470.5, (444), 370, and (354) nm. From the lower part of the chromatogram, a pigment which melted at 164—164.5 °C was obtained besides **23**; red needles [λ_{max} 498, 467, (439), 372, (354) nm]. It was considered to be

9,11′-di-*cis*-7,8-didehydrorenieratene from the mode of its formation.

*2,7,11-Trimethyl-13-(2,3,4-trimethylphenyl)-2,4,6,8,10,12-tridecahexaen-1-al (**27**).* The condensation of **26** (1 g) and the C_{10}-dial (**17**, 900 mg) gave **27** as red needles (23 mg); mp 161—162 °C; λ_{max} 444 nm ($\varepsilon=6.9\times10^4$); IR 3050, 2925, 1665, 1615, 1540, 1190, 970, 965 cm^{-1}; NMR δ 9.46 (1H, s; 1-proton). Mass (m/e) 346(M), 278, 262, 219, 210, 133, 29. Found: C, 85.86[17]; H, 8.69%. Calcd for $C_{25}H_{30}O$: C, 86.65; H, 8.73%.

From the reaction mixture, the 8-*cis* isomer of **27** was also obtained as red needles; mp 141—142 °C; λ_{max} 440 nm.

*[2,7,11-Trimethyl-13-(2,3,4-trimethylphenyl)-2,4,6,8,10,12-tridecahexaen-1-yl]triphenylphosphonium Bromide (**28**).* The aluminium hydride reduction of **27** (46.8 mg) gave the corresponding alcohol as a canary-yellow solid (46 mg). The crude alcohol [mp 116—126 °C; λ_{max} 432, 409, 389 nm; IR 3350, 1025, 1015, 965 cm^{-1}] (23 mg) was converted into the phosphonium salt (**28**) with triphenylphosphonium bromide (23 mg); this crude salt was used without purification.

*7,8-Didehydrorenieratene (**2**).* The condensation of the ylid of **28** (44 mg) with **12a** (20 mg) was carried out under a low temperature in the way described in the recipe for **1**. The crude product was chromatographed on 5% aqueous alumina with a benzene-petroleum benzine (1 : 4) mixture. After rechromatography and recrystallization (dichloromethane-methanol), **2** was obtained as purplish-red needles (0.05 mg); mp 205—206 °C, undepressed by admixture with a natural specimen. A mixed chromatography of the synthetic and the natural pigment showed no separation. The spectral properties (UV and mass) also agreed with those reported previously.[3]

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