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The Synthesis of Methoxylated Aromatic Carotenoids

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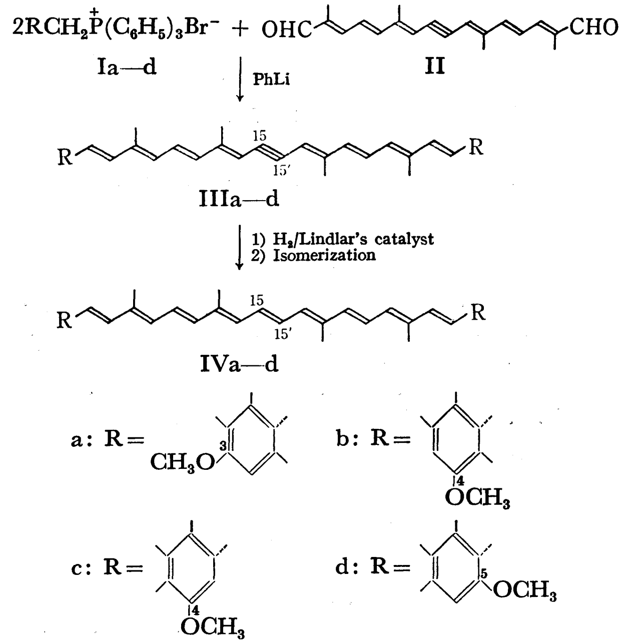
Synopsis. Four methoxylated aromatic carotenoid derivatives (IVa—d) were prepared by the condensations of the ylids derived from the phosphonium salts (Ia—d) with didehydrocrocetindial (II) followed by partial hydrogenation of the acetylenic bond.

Since aromatic carotenoid hydrocarbons had been isolated from a sea sponge "*Reniera japonica*",[1] the natural occurrence of aromatic carotenoids with oxygen functions such as hydroxyl or methoxy groups on their aryl end-groups has been expected. In fact, phenolic carotenoids were isolated from "*Streptmyces mediolani*" in 1969,[2] but the presence of pigments containing methoxylated aryl end-groups has not so far been reported. In this paper, the synthesis and characterization of 3,3′- and 4,4′-dimethoxyisorenieratene (IVa and IVb), 4,4′- and 5,5′-dimethoxyrenierapurpurin (IVc and IVd), and their 15,15′-didehydro compounds (IIIa—d) will be described.

Syntheses were carried out according to the $C_{10}+C_{20}+C_{10}$ building principle.[3] Wittig reactions of didehydrocrocetindial (II) with the appropriate methoxylated trimethylbenzylidenetriphenylphosphoranes prepared from the corresponding phosphonium salts (Ia—d) gave 15,15′-didehydro compounds (IIIa—d), which were then converted to all-*trans* pigments (IVa—d) by partial hydrogenation and isomerization during purification under diffused light.



The structures and configurations of IVa—d were ascertained by analytical and spectral studies, as is shown in Tables 1 and 2. The facts that IVa—d exhibited the highest UV $\lambda_{\max}$, with a wavelength 21—23 nm longer and with a higher intensity than those of the corresponding 15,15′-didehydro compounds (IIIa—d), and that IVa—d did not show any *cis*-peak in their UV spectra evidently suggest that IVa—d has the all-*trans* configuration.[4] This was also supported by the IR spectra of IVa—d, which showed a sharp singlet at 962—965 cm^{-1} due to CH out-of-plane deformation vibrations.[5]

When the highest $\lambda_{\max}$ of IVa—d were compared with those of the parent non-substituted compounds, isorenieratene[1b] [IV, R=2,3,6-$(CH_3)_3C_6H_2$-, $\lambda_{\max}$, 466 nm (C_6H_6)] and renierapurpurin[1c] [IV, R=2,3,4-$(CH_3)_3C_6H_2$-, $\lambda_{\max}$, 486 nm (C_6H_6)], the bathochromic effect of methoxy groups was observed only in IVa, in which the substituents are located at *para* positions to the polyene chain. The IVd and IVb pigments, which contain methoxy groups at positions *ortho* or *meta* to the chain respectively, absorbed at a wavelength location 3—4 nm lower than the corresponding parent compounds. This apparently shows that the chromophore systems of these pigments are more distorted than those of the corresponding parent compounds because of the steric interference between the polyene chain

Table 1. Melting points, yields, elemental analyses, UV, and IR data of IIIa—d and IVa—d

Compound	Mp (°C)	Yield (%)	Found		Highest $\lambda_{\max}^{C_6H_6}$ nm (log ε)	IR (cm^{-1})	
			C(%)	H(%)		Ar–OCH_3	–CH=CH–
IIIa	199	57[a]	85.32	8.53[b]	448 (4.95)	1121	962
IIIb	198—200	69	86.10	8.64[b]	441 (4.91)	1120	960
IIIc	242	74	85.95	8.85[b]	464 (4.94)	1120	960
IIId	235—236	64	85.43	8.67[b]	459 (5.04)	1120	962
IVa	227—230	57	85.55	9.09[c]	469 (5.07)	1122	965
IVb	231	66	85.19	9.12[c]	463 (5.09)	1121	965
IVc	216—218	51	85.32	8.83[c]	486 (5.08)	1123	963
IVd	225—228	64	85.27	8.87[c]	482 (5.08)	1120	962

a) Yields for IIIa—d were calculated based on didehydrocrocetindial. b) Calcd for $C_{42}H_{50}O_2$: C, 85.96; H, 8.59%. c) Calcd for $C_{42}H_{52}O_2$: C, 85.67; H, 8.90%.

Table 2. NMR data of IIIa—d and IVa—d

Compound	Chemical shifts of methyl protons[a] (δ in ppm; $CDCl_3$)					
	C-9,9′-	C-13,13′-	Aryl-			Methoxy-
IIIa	2.08 (2)[b]	2.14 (2)	2.14 (2)[c]	2.23 (2)	2.29 (2)	3.81 (2)
IIIb	2.09 (2)	2.11 (2)	2.15 (4)	2.27 (2)		3.80 (2)
IIIc	2.07 (2)	2.11 (2)	2.18 (2)	2.20 (2)	2.25 (2)	3.85 (2)
IIId	2.09 (2)	2.13 (2)	2.16 (2)	2.30 (4)		3.80 (2)
IVa	2.09 (2)	2.00 (2)	2.17 (2)	2.24 (2)	2.32 (2)	3.82 (2)
IVb	2.08 (2)	1.98 (2)	2.16 (4)	2.27 (2)		3.81 (2)
IVc	2.08 (2)	2.00 (2)	2.19 (2)	2.21 (2)	2.26 (2)	3.86 (2)
IVd	2.07 (2)	1.98 (2)	2.16 (2)	2.29 (4)		3.80 (2)

a) Besides the methyl signals described here, the NMR spectra of IIIa—d showed a singlet at δ 5.75—5.76 ppm assignable to 14,14′-protons and a complex multiplet in the region of δ 6.10—7.00 ppm due to the other olefinic and aromatic protons, but the spectra of IVa—d exhibited only a complex multiplet in the δ 6.10—7.00 ppm region due to all olefinic and aromatic protons. b) Values in parenthesis show number of methyl groups. c) The signal was overlapped with that of C-13, 13′-methyls.

and the newly-introduced substituents or because of the increase in the steric effect of 5,5′-standing methyl groups by the buttressing effect of 4,4′-standing methoxy groups. However, the methoxy groups at positions *meta* to the chain in IVc caused no appreciable change in the absorption maximum.

Experimental

All the melting points are uncorrected. The UV spectra were taken with a Hitachi EPS-3T spectrometer. The IR spectra were recorded from KBr pellets, using a Hitachi 215 infrared spectrometer. The NMR spectra were measured with a Hitachi R-22 spectrometer at 90 MHz, using tetramethylsilane as the internal standard.

Preparations of Methoxytrimethylbenzyltriphenylphosphonium Bromides (Ia—d). These were prepared from the corresponding benzyl alcohols[6] according to the method described by Cooper *et al.*[7] Ia, colorless prisms, mp 225 °C. Found: C, 68.82; H, 6.18%. Calcd for $C_{29}H_{30}BrOP$: C, 68.91; H, 5.98%. Ib, colorless prisms, mp 240 °C. Found: C, 68.56; H, 6.08%. Ic, colorless prisms, mp 229—230 °C. Found: C, 68.79; H, 5.88%. Id, colorless prisms, mp 249 °C. Found: C, 68.92; H, 6.22%.

Preparations of 15,15′-Didehydro Compounds (IIIa—d). A typical example is as follows: to a stirred suspension of phosphonium bromide (Ia, 1.5 g) in absolute ether (30 ml), was added an ethereal solution of phenyllithium (*ca.* 1 M, 5 ml) over a 5 min period under an atmosphere of nitrogen. The mixture was then stirred for 1 hr at room temperature, and methylene chloride (0.3 ml) was added to decompose the excess of phenyllithium. After 10 min, a solution of didehydrocrocetindial (II, 250 mg) in methylene chloride (15 ml) was added, and the mixture was stirred under reflux for 5 hr. The mixture was then diluted with methanol (70 ml) and allowed to stand overnight in an ice-box. The precipitate was subsequently collected; several recrystallizations from a mixture of methylene chloride and ethanol gave IIIa (280 mg) as orange prisms. The yields, melting points, elemental analyses, and UV, IR, and NMR spectral data of IIIa—d are given in Tables 1 and 2.

*Preparations of All-*trans *Carotenoids (IVa—d).* A typical example is as follows: IIIa (30 mg) was dissolved in toluene (45 ml) and hydrogenated at 25 °C in the presence of the Lindlar catalyst[8] (65 mg) and quinoline (0.3 ml) until a 1.2-molar equivalent of hydrogen (1.4 ml) was consumed. The catalyst was filtered and washed with benzene. The combined filtrate was concentrated under reduced pressure, petroleum benzine (20 ml) was added to the residue, and the mixture was allowed to stand overnight in an ice-box. The crystallized product was collected, and several recrystallizations from a mixture of chloroform and ethanol gave IVa (17 mg) as purple crystals. The yields, melting points, elemental analyses, and UV, IR, and NMR spectral data of IVa—d are given in Tables 1 and 2.

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