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5-Hydroxy-*seco*-carotenoids from *Pittosporum tobira*

Takashi Maoka [a,*], Yasuhiro Fujiwara [b], Keiji Hashimoto [c], Naoshige Akimoto [d]

[a] *Research Institute for Production Development, 15 Shimogamo-morimoto-cho, Sakyo-ku, Kyoto 606-0805, Japan*
[b] *Kyoto Pharmaceutical University, 5 Nakauchi-cho, Misasagi, Yamashina-ku, Kyoto 607-8414, Japan*
[c] *Nagahama Institute of Bio-sciences and Technology, Tamura-cho, Nagahama, Shiga 526-0829, Japan*
[d] *Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida-shimoadachi-cho, Sakyo-ku, Kyoto 606-8501, Japan*

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Abstract

Three 5-hydroxy-*seco*-carotenoids were isolated from seeds of *Pittosporum tobira*. These structures were determined to be (3*S*,3′*S*,5′?)-3,3′-di(tetradecanoyloxy)-5′-hydroxy-5,6,5′,6′-*diseco*-β,β-carotene-5,6,6′-trione (**1**), (3*S*,5?,3′*S*,5′*R*,6′*S*,9′*Z*)-3-tetradecanoyloxy-5′,6′-epoxy-5,3′-dihydroxy-5′,6′-dihydro-5,6-*seco*-β,β-caroten-6-one (**2**), and (3*S*,5?,3′*S*,5′*R*,6′*R*)-3-tetradecanoyloxy-5,3′,5′-trihydroxy-6′,7′-didehydro-5′,6′-dihydro-5,6-*seco*-β,β-caroten-6-one (**3**) based on analysis of UV–vis, IR, FAB MS, and NMR spectroscopic data.

Keywords: *Pittosporum tobira*; Pittosporaceae; *seco*-Carotenoid; 5-Hydroxy *seco*-carotenoid; Structure determination

1. Introduction

More than 700 carotenoids have been isolated in nature (Britton et al., 2004). Some exhibit biological activities, such as anti-oxidative, anti-tumor, anti-carcinogenic, and immune enhancement activities (Krinsky et al., 2004). Since natural carotenoids have extensive structural variety (Britton et al., 2004), this prompted us to search for new carotenoids from various natural sources (Maoka et al., 2001, 2002, 2004, 2005).

Pittosporum tobira (Pittosporaceae) is a evergreen tree that grows on the southwestern Pacific coast of Japan. The seeds undergo a gradual color change from green to red in late autumn to winter. Previously, we reported the isolation and structural elucidation of novel carotenoids, pittosporumxanthins (carotenoid–tocopherol complexes) (Fujiwara and Maoka, 2001) and tobiraxanthins (esterified-*seco*-carotenoids, structures shown in Fig. 1) (Fujiwara et al., 2002), from the seeds of *P. tobira.* In the course of the studies on carotenoids in *P. tobira*, recently, three new 5-hydroxy-*seco*-carotenoids **1**, **2**, and **3** (Fig. 1) were isolated from the seeds of *P. tobira* as minor components. This paper reports the isolation and structural elucidation of these new carotenoids.

2. Results and discussion

The MeOH extract of the red-colored seeds (30 kg) of *P. tobira* was subjected to silica gel column chromatography using hexane, Et_2O, Me_2CO and MeOH as eluting solvents. Fractions of interest obtained in this way were applied to HPLC on ODS with $CHCl_3$-MeCN (1:4) as eluent to yield **1** (2 mg), **2** (1 mg), and **3** (3 mg), respectively.

Compound **3** showed absorption maxima at 457 and 481 nm. The molecular formula of **3** was determined to be $C_{54}H_{82}O_6$by high-resolution (HR) FABMS. The characteristic fragment ion at *m*/*z* 600 $[M-(C_{14}H_{28}O_2)]^+$ in the EIMS indicated the presence of a myristate moiety in **3**. The ^1H and ^{13}C NMR spectroscopic data, which were assigned by analysis of COSY, NOESY, HSQC, and HMBC experiments, were compiled in Tables 1 and 2, respectively. These data showed the presence of both carotenoid and saturated fatty acid moieties in **3**. The ^{13}C NMR

* Corresponding author. Tel.: +81 75 781 1107; fax: +81 75 791 7659.
E-mail address: maoka@mbox.kyoto-inet.or.jp (T. Maoka).

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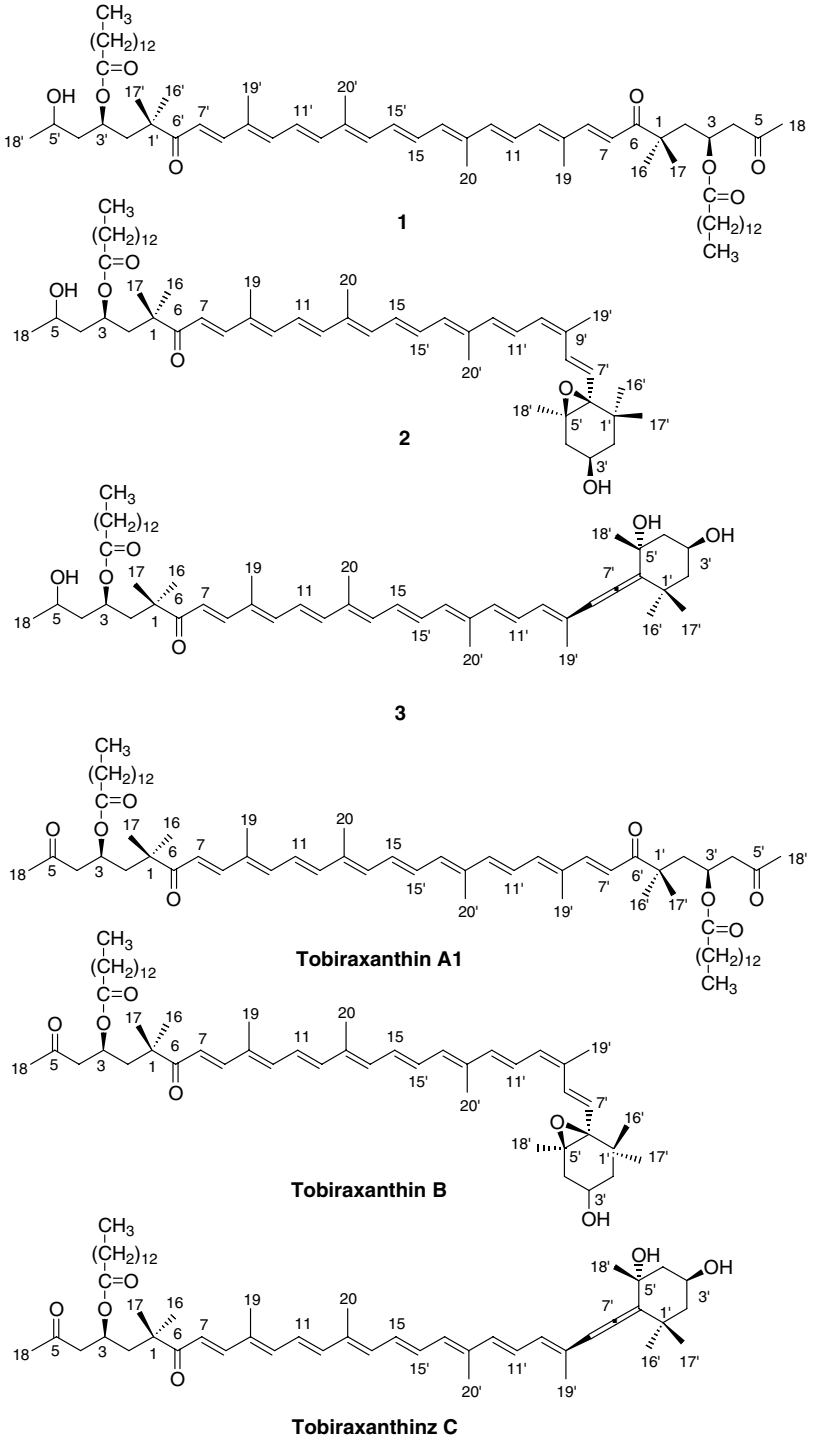

Fig. 1. Structures of compounds **1**, **2**, **3**, tobiraxanthin A1, B, and C.

spectroscopic signals of **3** were almost similar to those of tobiraxanthin C (Fujiwara et al., 2002), except for the presence of an oxymethine carbon signal at δ 63.0 instead of the carbonyl carbon resonance at δ 205.6 (C-5). Furthermore, compared with tobiraxanthin C, the ^{1}H resonance at δ 3.41 in **3** was attributed to a hydroxy group and that at δ 3.55 to a free oxymethine functional group. These data suggested that **3** was a 5-hydroxy derivative of tobiraxanthin C. The partial structure of the 3-esterified 3,5-dihydroxy-5,6-*seco*-β-end group (C-1 to C-6 including methyl groups at C-16, 17 and 18) was confirmed by COSY, NOESY and HMBC experiments as shown in Fig. 2. The remaining structural moiety (C-7 to C-1′ including methyl groups at C-19, 20, 16′, 17′, 18′, 19′ and 20′) was also confirmed by 2D NMR experiments (Fig. 2), and by comparison of NMR spectroscopic data with those of neoxanthin (Engl-

Table 1
^{1}H NMR spectroscopic data for **1**, **2** and **3** in $CDCl_3$

Position	Compound		
	1[a]	**2**[a]	**3**[b]
	δ mult. (*J*, Hz)	δ mult. (*J*, Hz)	δ mult. (*J*, Hz)
Carotenoid moiety			
H-2	1.80 *dd* (14.5, 3.0)	1.66 *dd* (15.0, 2.0)	1.66 *dd* (15.0, 2.0)
	2.12 *dd* (14.9, 9.5)	2.23 *dd* (15.0, 10.5)	2.23 *dd* (15.0, 10.5)
H-3	5.24 *m*	5.12 *m*	5.12 *m*
H-4	2.71 *dd* (15.5, 5.5)	1.52 *m*	1.52 *m*
	2.59 *dd* (15.5, 7.5)	1.57 *m*	1.57 *m*
H-5	–	3.55 *m*	3.55*m*
H-7	6.50 *d* (15.0)	6.50 *d* (15.0)	6.50 *d* (15.0)
H-8	7.37 *d* (15.0)	7.37 *d* (15.0)	7.37 *d* (15.0)
H-10	6.55 *d* (11.5)	6.55 *d* (11.5)	6.55 *d* (11.5)
H-11	6.65 *dd* (15.0, 11.5)	6.63 *dd* (15.0, 11.5)	6.63 *dd* (15.0, 11.5)
H-12	6.52 *d* (15.0)	6.57 *d* (15.0)	6.57 *d* (15.0)
H-14	6.35 *d* (10.0)	6.35 *d* (10.0)	6.35 *d* (10.0)
H-15	6.69 *m*	6.69 *m*	6.69 *m*
CH_3-16	1.19 *s*	1.16 *s*	1.16 *s*
CH_3-17	1.20 *s*	1.17 *s*	1.17 *s*
CH_3-18	2.14 *s*	1.15 *d* (6.5)	1.15 *d* (6.5)
CH_3-19	1.98 *s*	1.98 *s*	1.98 *s*
CH_3-20	1.98 *s*	1.98 *s*	1.98 *s*
H-2′	1.66 *dd* (15.0, 2.0)	1.27 *dd* (14.5, 10.0)	~1.34
	2.23 *dd* (15.0, 10.5)	1.65 *ddd* (14.5, 3.5, 1.5)	~1.95
H-3′	5.12 *m*	3.92 *m*	4.32 *m*
H-4′	1.52 *m*	1.65 *dd* (14.5, 9.0)	~1.41
	1.57 *m*	2.41 *ddd* (14.5, 5.0, 1.5)	2.26 *ddd* (13.5, 4.0, 2.0)
H-5′	3.55 *m*	–	–
H-7′	6.50 *d* (15.0)	5.95 *d* (11.5)	–
H-8′	7.37 *d* (15.0)	6.84 *d* (15.5)	6.03 *s*
H-10′	6.55 *d* (11.5)	6.08 *d* (11.5)	6.12 *d* (11.5)
H-11′	6.63 *dd* (15.0, 11.5)	6.80 *d* (15.5, 11.5)	6.58 *d* (15.5, 11.5)
H-12′	6.57 *d* (15.0)	6.30 *d* (15.5)	6.35 *d* (15.5)
H-14′	6.35 *d* (10.0)	6.25 *d* (10.0)	6.26 *d* (10.0)
H-15′	6.69 *m*	6.67 *m*	6.67 *m*
CH_3-16′	1.16 *s*	1.01 *s*	1.33 *s*
CH_3-17′	1.17 *s*	1.17 *s*	1.07 *s*
CH_3-18′	1.15 *d* (6.5)	1.22 *s*	1.35 *s*
CH_3-19′	1.98 *s*	1.94 *s*	1.81 *s*
CH_3-20′	1.98 *s*	1.98 *s*	1.98 *s*
OH	3.41 *br s* (OH-5′)	3.41 *br s* (OH-5)	3.41 *br s* (OH-5)
Fatty acid moiety			
CO–CH_2	2.17 t (7.5)	2.17 t (7.5)	2.17 t (7.5)
$(CH_2)_{10}$	~1.25 *m*	~1.25 *m*	~1.25 *m*
CH_3	0.88 t (6.5)	0.88 t (6.5)	0.88 t (6.5)

s: singlet, *d*: doublet, *t*: triplet, *m*: multiplet.
br s: broad singlet.
[a] Recorded at 300 MHz.
[b] Recorded at 500 MHz.

Table 2
^{13}C NMR spectroscopic data for **3** (125 MHz, $CDCl_3$)

Position	δ mult.	Position	δ mult.
C-1	45.8 *s*	C-1′	35.8 *s*
C-2	45.1 *t*	C-2′	49.8 *t*
C-3	68.6 *d*	C-3′	64.3 *d*
C-4	45.8 *t*	C-4′	49.5 *t*
C-5	63.0 *d*	C-5′	73.0 *s*
C-6	202.4 *s*	C-6′	117.7 *s*
C-7	118.9 *d*	C-7′	202.8 *s*
C-8	147.0 *d*	C-8′	103.2 *d*
C-9	131.6 *s*	C-9′	132.3 *s*
C-10	140.5 *d*	C-10′	128.4 *d*
C-11	124.0 *d*	C-11′	125.4 *d*
C-12	141.9 *d*	C-12′	137.1 *d*
C-13	135.2 *s*	C-13′	137,5 *s*
C-14	135.8 *d*	C-14′	135.9 *d*
C-15	129.9 *d*	C-15′	128.7 *d*
C-16	23.2 *q*	C-16′	29.3 *q*
C-17	26.6 *q*	C-17′	32.1 *q*
C-18	22.6 *q*	C-18′	31.4*q*
C-19	12.9 *q*	C-19′	14.1 *q*
C-20	12.9 *q*	C-20′	14.1 *q*

The fatty acid moiety : 175.2 *s*, 33.9 *t*, 32.8 *t*, 31.9 *t*, 29.7 *t*, 29.6, *t*, 29.3 *t*, 28.6 *t*, 27.2 *t*, 24.7 *t*, 22.7 *t*, 14.2 *q*.
s: singlet, *d*: doublet, *t*: triplet, *q*: quartet.

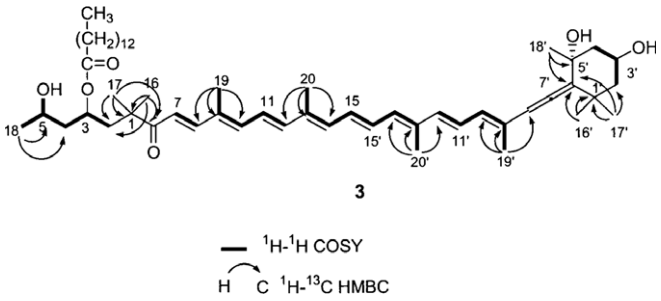

Fig. 2. Summary of the ^{1}H NMR experiments for the compound **3.**

ert, 1995). The *E* geometry of the polyene part was confirmed by analysis of the NOESY spectroscopic data. Thus, structure **3** was determined to be 3-tetradecanoyloxy-5,3′,5′-trihydroxy-6′,7′-didehydro-5′,6′-dihydro-5,6-*seco*-β,β-caroten-6-one. The CD spectrum of **3** was almost the same as that of tobiraxanthin C. From analysis of the CD spectral data and of the biosynthetic consideration described later, the (3*S*, 5?, 3′*S*, 5′*R*,6′*R*) chirality was tentatively postulated although the chirality at C-5 has not been established.

Compound **1** showed absorption maxima at 440, 468, and 500 nm, indicating the presence of a β-carotenone type chromophore (Yokoyama and White, 1968; Britton, 1995). The molecular formula of **1** was determined to be $C_{68}H_{110}O_8$by high-resolution (HR) FABMS. The characteristic fragments ions of *m*/*z* 826 $[M-(C_{14}H_{28}O_2)]^+$ and *m*/*z* 598 $[M-2(C_{14}H_{28}O_2)]^+$ in the EIMS indicated the presence of a dimyristate moiety in **1**. The ^{1}H NMR spectroscopic assignments (Table 1), which were assigned by ^{1}H-^{1}H COSY, NOESY, and decoupling experiments, also indicated the presence of carotenoid and saturated fatty acid moieties in **1**. The ^{1}H signals of H-2′ to H-20′ were identical to H-2 to H-20 moiety of compound **3** described above. The ^{1}H signals of the remaining structural moiety (H-2 to H-20) were identical to those of tobiraxanthin A1

(Fujiwara et al., 2002). The *E* geometry of the polyene part was also confirmed by analysis of the NOESY spectroscopic data. Therefore, structure **1** was determined to be 3,3′-di(tetradecanoyloxy)-5′-hydroxy-5,6,5′,6′-*diseco*-β,β-carotene -5,6,6′-trione. The CD spectra of **1** showed almost the same Cotton effects as that of tobiraxanthin A1, possessing a (3*S*, 3′*S*) chirality (Fujiwara et al., 2002). From the CD spectral data and biosynthetic considerations (Fig. 3), the (3*S*,3′*S*,5′?) chirality was tentatively proposed, although the chirality at C-5 could not be determined.

Compound **2** showed absorption maxima at 455 and 479 nm. The molecular formula of **2** was determined to be $C_{54}H_{82}O_6$by HRFABMS. The characteristic fragment ion of EIMS at *m*/*z* 600 $[M-(C_{14}H_{28}O_2)]^+$ indicated the presence of a myristyl group. The ^1H chemical shifts and spin coupling constants of H-2 to H-20, including the myristate moiety, were identical to those of **3**. On the other hand, the ^1H signals of the remaining part (H-2′ to H-20′) were identical to those of (9*Z*)-violaxanthin (Englert, 1995), which were also confirmed by COSY and NOESY experiments. Thus, the structure of **2** was determined to be 3-tetradecanoyloxy-5,3′,5′-trihydroxy-6′,7′-didehydro-5′,6′-dihydro-5,6- *seco*-β,β-caroten-6-one. The CD spectrum of **3** was almost the same as that of tobiraxanthin C. From analysis of the CD spectral data and biosynthetic considerations described later, the (3*S*,5?,3′*S*,5′*R*,6′*R*) chirality was tentatively postulated, although the chirality at C-5 was not established.

3. Concluding remarks

Compounds **1**, **2**, and **3**, having a 5-hydroxy-5,6-*seco*-β-end group, correspond to semi-reduced derivatives of tobiraxanthin A1, B, and C (Fujiwara et al., 2002), respectively. Regarding carotenoids with a 5-hydroxy-5,6-*seco*-β-end group (Britton et al., 2004), only geratoxanthin, 5-hydroxy-5,6-*seco*-β,β-caroten-6-one, was isolated from the young leaves of cycad, *Ceratozamia kuesteriana* and *C. fuscoviridis* (Cardini et al., 1989).

It was also reported that *seco*-carotenoids are formed from a 5,6-epoxy carotenoid precursor by oxidative cleavage of the C-5–C-6 bond (Britton, 1998). Subsequently, reduction of the carbonyl group at C-5 produced the 5-hydroxy-*seco*-carotenoid, as shown in Fig. 3. Therefore, precursors of compounds **1**, **2**, and **3** were assumed to be vioaxanthin di-myristate, (9′*Z*)-violaxanthin 3-myristate, and neoxanthin 3′-myristate, respectively, which were found in the seeds of *P. tobira*. Furthermore, it was assumed that compounds **1**, **2**, and **3** possessed the same chirality as those of the precursors.

In the present investigation, the 5,5′-dihydroxy-derivative of tobiraxanthin A1 i.e., 3,3′-di(tetradecanoyloxy)-5,5′-dihydroxy-5,6,5′,6′-*diseco*-β,β-carotene-,6,6′-dione, was not detected. However, from the aspect of bio-conversion pathway of carotenoid described in Fig. 3, it was assumed that this compound might be present in seeds of *P. tobira* as a very minor component.

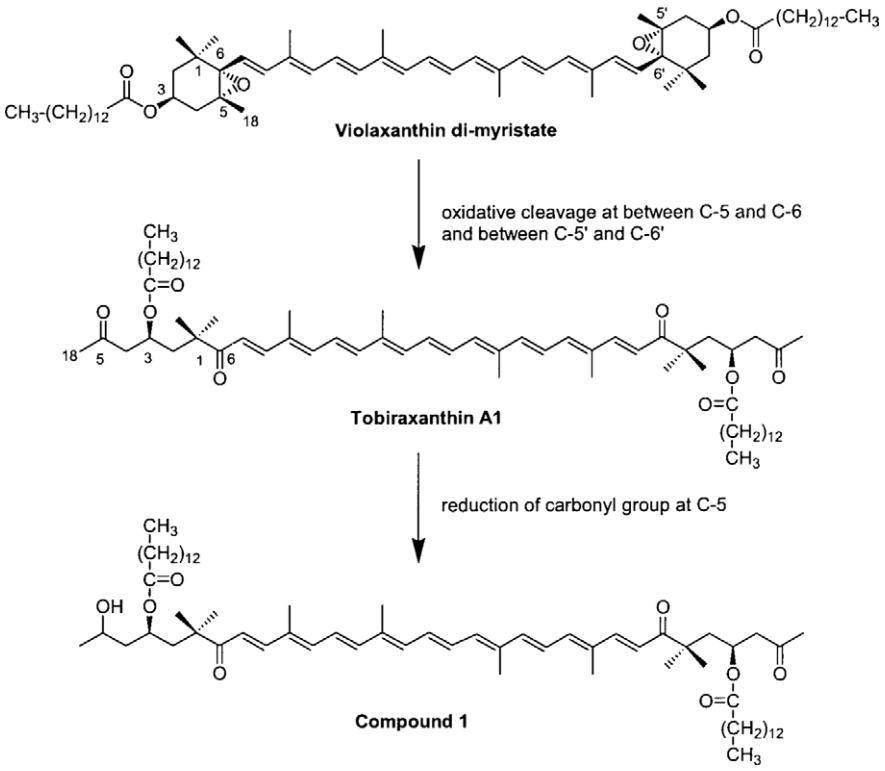

Fig. 3. Proposed biosynthetic pathways of compound **1** from violaxanthin di-myirstate via tobiraxanthin A1.

4. Experimental

4.1. Plant material

The seeds of *P. tobira* were collected in December from plants growing on the bank of the Kamogawa River in Kyoto.

4.2. General experimental procedures

The UV–vis spectra were recorded with a Shimadzu UV-240 spectrophotometer in Et_2O. The positive ion FABMS and EI MS were recorded using a JEOL JMS-SX 102 or JMS-HX 110A mass spectrometer. *m*-nitrobenzyl alcohol was used for matrix of FABMS. The ^1H NMR (300 MHz or 500 MHz) spectra were measured with a Varian XL-300 or INOVA 500 spectrometer in $CDCl_3$ with TMS as an internal standard. The ^{13}C NMR (125 MHz) spectrum was measured with a Varian INOVA 500 spectrometer in $CDCl_3$ with TMS as an internal standard. The CD spectra were recorded in Et_2O at room temperature with a Jasco J-500C spectropolarimeter. HPLC was performed on a Shimadzu LC-6AD with a Shimadzu SPD-6AV spectrophotometer set at 450 nm.

4.3. Extraction and isolation of carotenoids

The seeds of *P. tobira* (30 kg) were washed with *n*-hexane to remove the viscous matter on the surface and then extracted with MeOH (2×10 l) at room temperature. The combined MeOH solubles were partitioned into Et_2O-*n*-hexane (1:1) by addition of H_2O. The organic layer was washed with H_2O and then evaporated under reduced pressure. The residual red-colored oil was applied to a silica gel column using an increasing percentage of Et_2O in hexane, then Me_2CO and MeOH. The fraction eluted with Et_2O was subjected to HPLC on ODS with $CHCl_3$–MeCN (1:4) to yield **1** (2 mg). The fraction eluted with Me_2CO was subjected to HPLC on ODS with $CHCl_3$–MeCN (1:4) to yield **2** (1 mg). The fraction eluted with MeOH was subjected to HPLC on ODS with $CHCl_3$–MeCN (1:4) to yield **3** (3 mg). The carotenoid compositions of the seeds of *P. tobira* were as follows; β-carotene (0.8% of total carotenoid), violaxanthin (4.0%), (9*Z*)-violaxanthin (12.0%), luteoxanthin (8.0%), auroxanthin (8.0%), antheraxanthin (0.8%), (9*Z*)-antheraxanthin (2.0%), (9*Z*)-mutatoxanthin (2.0%), neoxanthin (2.0%), (9′*Z*)-neoxanthin (6.0%), (9′*Z*)-neochrome (4.0%), (9′*Z*)-latoxanthin (2.0%), pittosporumxanthins (carotenoid tocopherol complexes) (24.0%), tobiraxanthin A1 (3.2%), tobiraxanthin A2 (2.4%), tobiraxanthin A3 (2.4%), tobiraxanthin B (1.2%), tobiraxanthin C (1.6%), tobiraxanthin D (0.4%), compound **1** (0.8%), compound **2** (0.4%), compound **3** (1.2%), other unidentified carotenoids (10.8%).

4.4. (3*S*,3′*S*,5′?)-3,3′-Di(tetradecanoyloxy)-5′-hydroxy-5,6,5′,6′-diseco-β,β-carotene-5,6,6′-trione(*1*)

Reddish solid; for ^1H NMR (300 MHz $CDCl_3$) spectroscopic assignments, see Table 1; HRFABMS: Calc. for $C_{68}H_{110}O_8$ (M^+): 1054.8201; Found: 1054.8208; FIMS (probe) 70 eV, *m*/*z* (rel. int): *m*/*z* 826 $[M-(C_{14}H_{28}O_2)]^+$(5), 598 $[M-2(C_{14}H_{28}O_2)]^+$(10), 228 (10), 57 (100); CD λ, (Δε) in Et_2O: 220 (+9), 235 (0), 248 (−3), 255(0), 294 (+18.6), 313 (0), 368(−5.8); UV–vis: λ_{max} nm (Et_2O) 440, 468, 500; Key NOESY correlations: H-16/H-3, H-7, and H-17, H-17/H-3, H-7, and H-16, H-18/H-4, H-19/H-7 and H-11, H-20/H-11 and H-15, H-16′/H-3′, H-7′ and H-17′, H-17′/H-3′, H-7′, and H-16′, H-18′/H-4′, H-19′/H-7′ and H-11′, H-20′/H11′ and H-15′.

4.5. (3*S*,5?,3′*S*,5′*R*,6′*S*,9′*Z*)-3- Tetradecanoyloxy-5′,6′-epoxy-5,3′-dihydroxy-5′,6′-dihydro-5,6-seco-β,β-caroten-6-one (*2*)

Reddish solid; for ^1H NMR (300 MHz $CDCl_3$) spectroscopic assignments, see Table 1; HRFABMS: Calcd for $C_{54}H_{82}O_6(M^+)$: 828.6268; Found: 828.6272; EIMS (probe) 70 eV, *m*/*z* (rel. int): *m*/*z* 600 $[M-(C_{14}H_{27}O_2)]^+$(15), 228 (10), 43 (100); CD λ, (Δε) in Et_2O: 230 (−0.5), 260 (0), 285 (−1.5), 310 (0), 325 (+3.5), 350 (0), 375 (−1.6), 400 (0); UV–vis: $\lambda_{max}(Et_2O)$ 455, 479 nm. Key NOESY correlations : H-16/H-3, H-7 and H-17, H-17/ H-3, H-7 and H-16, H-18/H-4, H-19/H-7 and H-11, H-20/ H-11 and H-15, H-16′/H-3′, H-19′/H-7′ and H-10′, H-20′/H11′ and H-15′.

4.6. (3*S*,5?,3′*S*,5′*R*,6′*R*)-3-tetradecanoyloxy-5, 3′,5′-trihydroxy-6′,7′-didehydro-5′,6′-dihydro-5,6-seco-β,β-caroten-6-one (*3*)

Reddish solid; for ^1H NMR (500 MHz $CDCl_3$) and ^{13}C NMR (125 MHz $CDCl_3$) spectroscopic assignments, see Tables 1 and 2; HRFABMS: Calcd for $C_{54}H_{82}O_6$ (M^+): 828.6268; Found 828.6270; EIMS (probe) 70 eV, *m*/*z* (rel. int): *m*/*z* 600 $[M-(C_{14}H_{27}O_2)]^+$(20), 228 (10), 57 (100); CD λ, (Δε) in Et_2O: 230 (−0.5), 260 (0), 285 (−1.0), 305 (0), 335 (+3.2), 350 (0), 370 (−1.6), 395 (0); UV–vis: λ_{max} (Et_2O) 457, 481; Key HMBC correlations: Fig. 2; Key NOESY correlations : H-16/H-3, H-7 and H-17, H-17/ H-3, H-7 and H-16, H-18/H-4, H-19/H-7 and H-11, H-20/ H-11 and H-15, H-16′/H-3′, H-19′/H-11′, H-20′/H11′ and H-15′.

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