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Chemical and Chemotaxonomical Studies on Filices. LVIII.[1] Chemical Studies on the Constituents of *Monachosorum arakii* TAGAWA (Pteridaceae)

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A novel pterosin-type dinorsesquiterpene, mukagolactone (I), was isolated from the fronds of *Monachosorum arakii* TAGAWA (Pteridaceae), along with three new dinorsesquiterpene dimers, monachosorins A (II), B (III) and C (IV). Their structures were elucidated on the basis of spectroscopic and chemical data. Compound II may have been formed by an aldol-type condensation of 6-(2-hydroxyethyl)-5,7-dimethylindan-1-one and the corresponding 5-formyl compound. The reduction of II afforded III, and the acid isomerization of II gave IV.

Keywords——*Monachosorum arakii*; Pteridaceae; chemotaxonomy; pterosin-type dinorsesquiterpene; dimeric pterosin-type dinorsesquiterpene; aldol-type condensation product

As a continuation of our chemical and chemotaxonomical studies on ferns, the constituents of *Monachosorum arakii* TAGAWA (Japanese name: Himemukagoshida, Pteridaceae) were investigated. From the methanol extracts of the fronds, a new monomeric and three new dimeric pterosin-type dinorsesquiterpenes were isolated and named mukagolactone (I), and monachosorins A (II), B (III) and C (IV), respectively. This paper deals with the structural elucidation of these compounds.

Mukagolactone (I), $C_{13}H_{12}O_3$, was obtained as colorless needles, mp 179—180 °C. It dissolved in alkali and its infrared (IR) spectrum showed no hydroxyl absorption. The ultraviolet (UV) spectrum [λ_{max}^{MeOH} nm ($\log\varepsilon$): 260 (4.26), 269 sh (4.18), 325 (3.54)] is superimposable on that of pterolactone A (V),[2] a pterosin-type sesquiterpene lactone obtained from *Dennstaedtia wilfordii* (MOORE) CHRIST (Pteridaceae). Therefore the presence of the same chromophores as those found in V was expected, and the IR spectral absorptions at 1710 and 1730 cm^{-1} were assignable to a five-membered ring ketone and δ-lactone ketone respectively, which were both conjugated with an aromatic ring. In the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of I, the signals due to the corresponding carbonyl carbons appeared at δ 207.3 and 165.0, while in that of deoxypterolactone A (VI),[2,3] they were seen at δ 211.8 and 164.9. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum ($CDCl_3$) of I was partially similar to that of deoxypterolactone A (VI) and showed signals due to aromatic protons at δ 8.04 (1H, s), oxygenated ethylene protons at δ 4.53 (2H, t, J=7 Hz) and 3.04 (2H, t, J=7 Hz) and aromatic methyl protons at δ 2.64 (3H, s). In contrast to VI, the signals corresponding to the dimethyl groups at C-2 in VI were absent and instead of these, a signal (2H, m) ascribable to methylene protons adjacent to the C-1 ketone appeared at δ3.00—3.21 along with the signal (2H, m) due to the benzylic methylene protons at δ2.68—2.82. These spectral data indicated that mukagolactone is a pterosin-type sesquiterpene

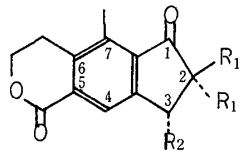
lactone, which is devoid of methyl groups at C-2. Hence, the structure 2-dinordeoxypterolactone A (I) was assigned to mukagolactone, and was confirmed by comparing the ^{13}C-NMR chemical shifts of I with those of deoxypterolactone A (VI) (see the table). The signals of I appeared at almost the same positions as those of VI, except for C-1, C-2 and C-3. The differences of the chemical shifts between I and VI arose from the absence of dimethyl groups at C-2 in I.[4)]

Monachosorin A (II), $C_{26}H_{28}O_4$, was obtained as yellow needles, mp 215—216 °C. The bands at 1705 and 1695 cm^{-1} in the IR spectrum and two sp^2 carbon signals at δ 193.3 (s) and 207.2 (s) in the ^{13}C-NMR (C_5D_5N) spectrum indicated the presence of two five-membered ring ketones which were conjugated with aromatic rings. The ^{13}C-NMR [δ 148.3 (s) and 136.0 (d)] and the ^{1}H-NMR [$\delta_{C_5D_5N}$ 7.45 (s)] spectra revealed the presence of a trisubstituted double bond. The catalytic hydrogenation of II over PtO_2 afforded the dihydro derivative, $C_{26}H_{30}O_4$, mp 206—207 °C, whose IR and ^{1}H-NMR spectra coincided with those of monachosorin B (III). The UV spectrum [λ_{max}^{MeOH} nm (log ε): 219 (4.90), 264 (4.57), 305 (3.92) of the dihydro derivative was closely similar to those of pterosin-type sesquiterpenes[5)] except for the molecular extinction coefficients. The hyperchromic shifts of the UV spectrum as well as the molecular formula $C_{26}H_{30}O_4$ of the dihydro derivative strongly suggested that II was a dimeric pterosin-type dinorsesquiterpene. The ^{13}C-NMR spectrum of II exhibited, in addition to the above mentioned sp^2 carbons signals, the signals of twelve aromatic carbons [two of them at δ 125.5 (d) and 125.9 (d) were due to carbons bearing one hydrogen], three methyl carbons [δ 13.5, 13.6 and 21.3 (each q)] and seven secondary sp^3 carbons. Four triplets at δ 32.6, 32.9, 61.1 and 61.5 were ascribed to the carbons of the hydroxyethylene groups and the remaining three at δ 24.7, 34.0 and 37.3, to methylene carbons of cyclopentenone rings [two of them at δ 24.7 and 37.3 were ascribable to ethylene carbons of a cyclopentenone ring]. In the ^{1}H-NMR spectrum (100 MHz, C_5D_5N) the signals due to ethylene protons of a cyclopentenone ring appeared at δ 2.42—2.62 and 2.64—2.96 (each 2H, m) and a broad singlet (2H) was seen at relatively low field (δ 3.68), which may be due to a deshielding effect of the double bond, and was assignable to the benzylic protons adjacent to the double bond. Two hydroxyethylene groups gave rise to the signals at δ 3.13, 3.27, 3.97 and 4.02 (each 2H, t, J= 7 Hz). Three aromatic methyl groups appeared at δ 2.44, 2.78 and 2.84 (each 3H, s). The latter two were deshielded by ketone groups and were possibly situated at peri-positions to ketones, *i.e.*, the 7- and 7′-position. The former one was not affected by any ketone group and was assigned to a methyl group at C-5. The corresponding methyl group at C-5′ of another moiety was absent. All these observations could be best interpreted on the basis of a structure such as II which resulted from the aldol-type condensation of the pterosin-type dinorsesquiterpene moieties, dinorpterosin Z (=6-(2-hydroxyethyl)-5,7-dimethylindan-1-one, A) and the corresponding formyl derivative (=5-formyl-6-(2-hydroxyethyl)-7-methylindan-1-one, B). This assumption was supported by the fragment ions at m/z 201 ($C_{13}H_{13}O_2$) and 202 ($C_{13}H_{14}O_2$) in the mass spectrum (MS) of II and was confirmed by the following chemical evidence. The ozonolysis of II provided mukagolactone (I) and a dibasic acid (VII). The Jones oxidation of VII gave a tribasic acid, which was converted by methylation with CH_2N_2 to a corresponding triester (VIII). The ^{1}H-NMR spectrum of VIII was compatible with the structure methyl 2,4,-dimethyl-3,6-bis(methoxycarbonylmethyl)benzoate, which would be expected from the proposed structure II. On the other hand, 6-methoxycarbonylmethyl-5,7-dimethylindan-1-one (IX) was synthesized by Nambudiry and Rao's method,[6)] and its condensation product with benzaldehyde was subjected to ozonolysis, followed by methylation with CH_2N_2 to furnish methyl 2,4-dimethyl-3,6-bis(methoxycarbonylmethyl)benzoate. Its spectral data coincided with those of VIII. Thus, a C(2)=C(12′) linking pattern between the two moieties was unequivocally established. In the ^{1}H-NMR spectrum (400 MHz, C_5D_5N) of II, long-range coupling between the methylene protons signal [C(3)-H_2] at δ 3.67 and the signal at δ 7.48

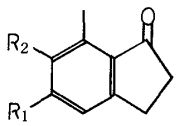
TABLE. ^{13}C Chemical Shifts of I, II, III, IV and VI (in C_5D_5N, δ)

Carbon	I	VI	II	III	IV	Carbon	II	III	IV
1	207.3 (s)	211.8 (s)	193.3 (s)	207.7 (s)[f]	206.7 (s)	1′	207.2 (s)	207.0 (s)[f]	207.2 (s)
2	37.3 (t)	46.0 (s)	148.3 (s)	49.0 (d)	53.0 (d)	2′	37.3 (t)	37.3 (t)	37.3 (t)
3	25.0 (t)[a]	41.7 (t)	34.0 (t)	35.7 (t)	27.1 (t)[l]	3′	24.7 (t)	24.8 (t)	25.0 (t)
4	126.2 (d)	126.2 (d)	125.5 (d)[b]	125.3 (d)[g]	126.0 (d)	4′	125.9 (d)[b]	126.0 (d)[g]	120.4 (d)
5	135.9 (s)	135.9 (s)	144.8 (s)	144.7 (s)	144.7 (s)	5′	143.0 (s)	146.5 (s)	143.7 (s)
6	129.9 (s)	130.3 (s)	136.7 (s)	136.6 (s)[h]	136.3 (s)	6′	138.0 (s)	136.3 (s)[h]	136.3 (s)
7	137.6 (s)	136.6 (s)	137.9 (s)	137.7 (s)[i]	137.4 (s)[m]	7′	137.1 (s)	137.9 (s)[i]	137.0 (s)[m]
8	138.1 (s)	138.4 (s)	135.5 (s)	133.3 (s)	133.5 (s)[n]	8′	134.3 (s)	132.4 (s)	133.0 (s)[n]
9	153.8 (s)	150.8 (s)	150.1 (s)	152.4 (s)	153.4 (s)[o]	9′	153.1 (s)	154.1 (s)	153.7 (s)[o]
12	165.0 (s)	164.9 (s)	21.3 (q)	21.3 (q)	21.1 (q)	12′	136.0 (d)	31.9 (t)	77.4 (d)
13	24.4 (t)[a]	24.5 (t)	32.6 (t)[c]	32.9 (t)[j]	32.9 (t)	13′	32.9 (t)[c]	32.5 (t)[j]	26.2 (t)[l]
14	67.1 (t)	67.0 (t)	61.5 (t)[d]	61.6 (t)[k]	61.1 (t)	14′	61.1 (t)[d]	61.2 (t)[k]	64.3 (t)
15	12.9 (q)	13.0 (q)	13.5 (q)[e]	13.9 (q)	13.8 (q)	15′	13.6 (q)[e]	13.9 (q)	12.8 (q)

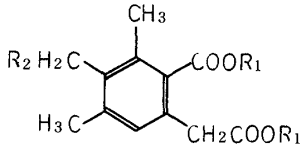
a—*o*) Assignment of chemical shifts may be reversed.



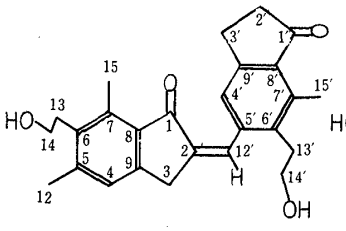
I : $R_1=R_2=H$
V : $R_1=CH_3$, $R_2=OH$
VI : $R_1=CH_3$, $R_2=H$



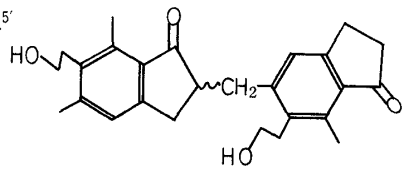
A : $R_1=CH_3$, $R_2=CH_2CH_2OH$
B : $R_1=CHO$, $R_2=CH_2CH_2OH$
IX : $R_1=CH_3$, $R_2=CH_2COOCH_3$



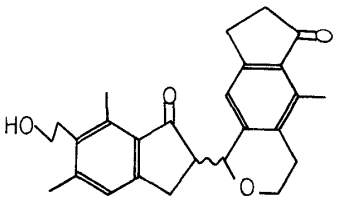
VII : $R_1=H$, $R_2=CH_2OH$
VIII : $R_1=CH_3$, $R_2=COOCH_3$



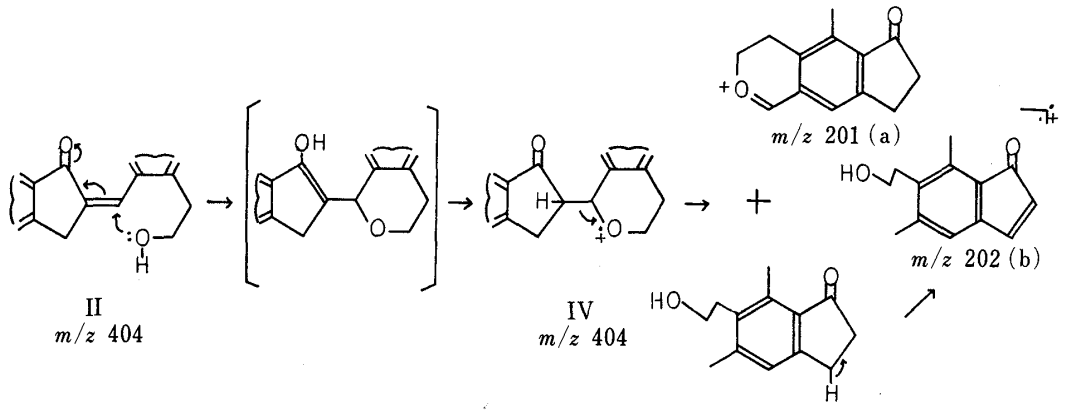
II



III



IV



II
m/z 404

IV
m/z 404

m/z 201 (a)

m/z 202 (b)

Chart. Mass Fragment Ions of II and IV

was observed, so that the latter was assigned to the olefinic proton [C(12′)-H]. In differential nuclear Overhauser enhancement (NOE) experiments, irradiation of the signal at δ 3.67 [C(3)-H_2] enhanced the resonances arising from C(4)-H (δ 7.03) and C(12′)-H (δ 7.48). Therefore, the *cis* relation between C(3)-H_2 and C(12′)-H was confirmed. The spectroscopic data together with the chemical evidence were all consistent with the structure II for monachosorin A.

Monachosorin B, mp 207—208 °C and $[\alpha]_D^{25}$ −6.8° (c=0.77, $CHCl_3$), is a dihydro derivative of monachosorin A (II). The spectroscopic data (^{1}H- and ^{13}C-NMR, UV, IR and MS) were compatible with the structure III.

Monachosorin C (IV), $C_{26}H_{28}O_4$, was obtained as colorless needles, mp 233—234 °C and $[\alpha]_D^{25}$ +11.4° (c=0.5, $CHCl_3$). The MS agreed with that of II, so IV was assumed to be an isomer of II. Furthermore, the treatment of II with acid yielded a mixture of isomers, which was subjected to preparative thin layer chromatography. The separated isomer, mp 232—234 °C, was identical with monachosorin C. Accordingly the planar structure IV was proposed for monachosorin C. The ^{1}H-NMR spectrum ($CDCl_3$) showed two methine proton signals at δ 3.22 (td, J=6 and 2 Hz) and 5.49 (d, J=2 Hz), which were coupled with each other, thus confirming the CH–CH linking between the two moieties. Further evidence was obtained from the MS of IV: the peaks appearing at m/z 201 ($C_{13}H_{13}O_2$) and 202 ($C_{13}H_{14}O_2$) could be attributed to ions a and b (see the chart). The ^{13}C-NMR data were also in agreement with the proposed structure IV (see the table).

Since insufficient materials were available, the stereochemistry of III and IV could not be determined.

Experimental

The instruments used to obtain physical data, the materials and the experimental conditions were the same as those described in part XXXVII[7] of this series unless otherwise specified.

Isolation Procedure——The air-dried *Monachosorum arakii* TAGAWA (1.3 kg), collected in August in Tanba-chōrōgatake, Kyōto Prefecture, was extracted 3 times with methanol (4 l) under reflux for 6 h. The combined extracts (12 l) were passed through an activated charcoal (150 g) column of 7 cm diameter and the column was further eluted with methanol (15 l) and $CHCl_3$–MeOH (3 : 7) (20 l). The fraction eluted with $CHCl_3$–MeOH (3 : 7) was concentrated *in vacuo* to a syrup, which was chromatographed on silica gel (100 g) with $CHCl_3$ (1000 ml, frac. A) and $CHCl_3$–MeOH (9 : 1) (800 ml, frac. B) as eluents. Fraction B was concentrated *in vacuo* to a syrup (4.9 g), which was chromatographed on silica gel (100 g) with *n*-hexane–ethyl acetate (1 : 1) as the eluent. Three main fractions were obtained. Fraction 1 (540 mg) containing mukagolactone (I) was rechromatographed on silica gel with *n*-hexane–ethyl acetate (3 : 2) as the eluent, followed by chromatography on silica gel with $CHCl_3$, and further purified by preparative layer chromatography (PLC, solvent system, *n*-hexane–ethyl acetate (2 : 1)) to yield I (12 mg). Fraction 2 (146 mg) containing monachosorin C (IV) was further purified on a silica gel column with $CHCl_3$–MeOH (70 : 1) as the eluent to yield IV (20 mg). Fraction 3 (130 mg) containing monachosorins A and B, was separated on a silica gel column with *n*-hexane–ethyl acetate (3 : 2), followed by fractional crystallization from a mixture of $CHCl_3$ and ethyl acetate to give monachosorins A (II, 65 mg) and B (III, 20 mg).

Mukagolactone (I)——Colorless needles from a mixture of $CHCl_3$ and *n*-hexane, mp 179—180 °C. UV λ_{max}^{MeOH} nm (log ε): 260 (4.26), 269 sh (4.18), 325 (3.54). IR ν_{max}^{KBr} cm^{-1}: 1730, 1710, 1610, 1590, 1450, 1410, 1290, 1195, 1120, 960, 785. ^{1}H-NMR (in $CDCl_3$) δ: 2.64 (3H, s), 2.68—2.82 (2H, m), 3.04 (t, J=7 Hz), 3.00—3.21 (4H, m, overlapping with δ 3.04), 4.53 (2H, t, J=7 Hz), 8.04 (1H, s). ^{13}C-NMR: Table. MS m/z: 216, 186, 158, 128, 115. Calcd for $C_{13}H_{12}O_3$: 216.0786 (M). Found: 216.0790 (M^+).

Monachosorin A (II)——Yellow needles, mp 215—216 °C. UV λ_{max}^{MeOH} nm (log ε): 218 (4.76), 300 (4.49). IR ν_{max}^{KBr} cm^{-1}: 3380, 2960, 2880, 1705, 1695, 1670, 1635, 1600, 1430, 1360, 1230, 1035, 925. ^{1}H-NMR (in C_5D_5N) δ: 2.44 (3H, s), 2.42—2.62 (2H, m), 2.78 (3H, s), 2.84 (3H, s), 2.64—2.96 (2H, m, overlapping with δ 2.78 and 2.84), 3.13 (2H, t, J=7 Hz), 3.27 (2H, t, J=7 Hz), 3.68 (2H, br s), 3.97 (2H, t, J=7 Hz), 4.02 (2H, t, J=7 Hz), 6.98 (1H, s), 7.45 (2H, s). ^{1}H-NMR (in C_5D_5N, 400 MHz) δ: 2.44 (3H, s), 2.51—2.56 (2H, m), 2.80 (3H, s), 2.82—2.86 (2H, m), 2.86 (3H, s), 3.14 (2H, t, J=7 Hz), 3.28 (2H, t, J=7 Hz), 3.67 (2H, br s), 4.00 (2H, t, J=7 Hz), 4.05 (2H, t, J=7 Hz), 7.03 (1H, s), 7.48 (1H, s), 7.51 (1H, s). ^{13}C-NMR: Table. MS m/z: 404, 386, 359, 202, 201, 200, 159, 131, 115. Calcd for $C_{26}H_{28}O_4$: 404.1985 (M). Found: 404.1980 (M^+).

Acetylation of II——II (10 mg) was acetylated with Ac_2O–pyridine (1 : 1) at room temperature for 18 h. After

work-up in the usual way, 9 mg of diacetate were obtained. Pale yellow needles, mp 172—173 °C. ^{1}H-NMR (in $CDCl_3$) δ: 1.98 (3H, s), 2.05 (3H, s), 2.47 (3H, s), 2.65 (3H, s), 2.72 (3H, s), 2.60—2.80 (2H, m, overlapping with δ 2.65 and 2.72), 2.92—3.18 (6H, m), 3.82 (2H, s), 4.08 (2H, t, J=7 Hz), 4.13 (2H, t, J=7 Hz), 7.14 (2H, s), 7.32 (1H, s). MS m/z: 488, 428, 413, 402, 401, 385, 368, 341. Calcd for $C_{30}H_{32}O_6$: 488.2197 (M). Found: 488.2221 (M^+).

Catalytic Hydrogenation of II——II (10 mg) in ethyl alcohol (10 ml) was hydrogenated for 2 h by using PtO_2 (20 mg) as catalyst. The reaction mixture was worked up in the usual manner, followed by PLC (solvent system, ethyl acetate–*n*-hexane (5 : 1) to furnish 5.6 mg of colorless needles, mp 206—207 °C (from a mixture of $CHCl_3$ and ethyl acetate). This product was identical (IR and ^{1}H-NMR) with manachosorin B (III).

Treatment of II with Acid——A solution of II (10 mg) in methanol (3 ml) containing 1% HCl was heated on a water bath (50 °C) for 15 min. The reaction mixture was diluted with water (10 ml), and extracted with ether (10 ml × 3). After removal of the solvent, the residue was subjected to PLC (solvent system, ethyl acetate–*n*-hexane (1 : 1)) to yield 7 mg of colorless needles, mp 232—234 °C (from a mixture of $CHCl_3$ and *n*-hexane). This product was identical (IR and ^{1}H-NMR) with monachosorin C (IV).

Ozonolysis of II——A gentle stream of O_3 was passed into a solution of II (30 mg) in acetic acid (15 ml) at room temperature for 1.5 h. The reaction solution was diluted with water (50 ml) and heated on a boiling water bath for 1.5 h, then cooled. The reaction product was extracted with ether (40 ml × 3). The ether layer was washed with water, dried and evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g, $CHCl_3$, $CHCl_3$–MeOH (5 : 1), MeOH) to furnish I (9 mg) and 6-carboxymethyl-2,4-dimethyl-3-(2-hydroxyethyl)benzoic acid (VII, 5 mg), which were used for the next oxidation without further purification.

Jones Oxidation of VII——Jones reagent (8 drops) was added dropwise to an ice-cooled stirred solution of VII (5 mg) in acetone (5 ml), and stirring was continued at 0 °C for 10 min. The resulting solution was diluted with water (20 ml), and extracted with ether (30 ml × 3). The ether layer was washed with water, dried, and evaporated *in vacuo*, and the residue was methylated with an excess of diazomethane in ether in the usual manner to yield 3 mg of VIII. Colorless oil. Calcd for $C_{16}H_{20}O_6$: 308.1259 (M). Found: 308.1258 (M^+). This product was identical (^{1}H-NMR and MS) with synthetic methyl 2,4-dimethyl-3,6-bis(methoxycarbonylmethyl)benzoate.

Monachosorin B (III)——Colorless needles, mp 207—208 °C. $[\alpha]_D^{25}$ −6.8° (c=0.77, $CHCl_3$). UV λ_{max}^{MeOH} nm (log ε): 219 (4.90), 264 (4.57), 305 (3.92). IR ν_{max}^{KBr} cm^{-1}: 3430, 2960, 2930, 1695, 1670, 1600, 1580, 1440, 1380, 1330, 1040. ^{1}H-NMR (in C_5D_5N) δ: 2.41 (3H, s), 2.45—2.65 (2H, m), 2.85 (3H, s), 2.88 (3H, s), 2.70—2.95 (3H, m, overlapping with δ 2.85 and 2.88), 3.15 (t, J=7 Hz), 3.29 (t, J=7 Hz), 2.95—3.40 (7H, m, overlapping with δ 3.15 and 3.29), 3.81 (1H, dd, J=13, 3 Hz), 3.99 (2H, t, J=7 Hz), 4.02 (2H, t, J=7 Hz), 6.98 (1H, s), 7.22 (1H, s). MS m/z: 406, 376, 346, 203, 174, 173, 143. Calcd for $C_{26}H_{30}O_4$: 406.2142 (M). Found: 406.2127 (M^+).

Monachosorin C (IV)——Colorless needles from a mixture of $CHCl_3$ and *n*-hexane, mp 233—234 °C. $[\alpha]_D^{25}$ +11.4° (c=0.5, $CHCl_3$). UV λ_{max}^{MeOH} nm (log ε): 218 (4.99), 265 (4.62), 307 (4.00). IR ν_{max}^{KBr} cm^{-1}: 3610, 1705, 1680, 1605, 1585, 1440, 1125, 1055, 825. ^{1}H-NMR (in $CDCl_3$): 2.41 (3H, s), 2.59 (3H, s), 2.74 (3H, s), 2.66—2.80 (5H, m, overlapping with δ 2.74), 3.01 (t, J=7 Hz), 2.90—3.16 (5H, m, overlapping with δ 3.01), 3.22 (1H, td, J=6, 2 Hz), 3.58 (1H, dd, J=12, 4 Hz), 3.74 (2H, t, J=7 Hz), 4.11 (1H, ddd, J=12, 6, 2 Hz), 5.49 (1H, d, J=2 Hz), 6.97 (1H, s), 7.11 (1H, s). MS m/z: 404, 386, 359, 202, 201, 200, 159, 131, 115. Calcd for $C_{26}H_{28}O_4$: 404.1985 (M). Found: 404.1960 (M^+).

Synthesis of Methyl 2,4-Dimethyl-3,6-bis(methoxycarbonylmethyl)benzoate (VIII)

3,5-Dimethylbenzyl Bromide (X)——A mixture of mesitylene (63.0 g, 0.53 mol), *N*-bromosuccinimide (96 g, 0.54 mol) and benzoyl peroxide (300 mg) in dry carbon tetrachloride (200 ml) was refluxed for 1 h under anhydrous conditions. After filtration, the filtrate was evaporated *in vacuo*, and the residue was distilled *in vacuo* (10 mmHg) to give X (95 g). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3020, 2930, 1610, 1480, 1310, 850. ^{1}H-NMR (in $CDCl_3$, 60 MHz) δ: 2.12 (6H, s), 4.20 (2H, s), 6.78 (1H, s), 6.80 (2H, s).

Diethyl (3,5-Dimethylphenylmethyl)malonate (XI)——A solution of X (17.9 g, 0.09 mol) in dimethylformamide (125 ml) was added dropwise over a period of 20 min to a suspension of diethyl malonate (14.4 g, 0.09 mol) and anhydrous potassium carbonate (9 g) in dimethylformamide (125 ml) under stirring at 150 °C, and stirring was continued at 150 °C for 9 h. The solvent was largely distilled off *in vacuo*, water (200 ml) was added, and the mixture was extracted with ether (200 ml × 3). After evaporation, the residue was purified by column chromatography on silica gel [130 g, *n*-hexane–benzene (1 : 1)] to furnish XI (15.8 g). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2980, 1730 (ester C=O), 1610, 1470, 1370, 910, 850. ^{1}H-NMR (in $CDCl_3$, 60 MHz) δ: 1.18 (6H, t, J=7 Hz, $-CH_2\underline{CH_3}$ × 2), 2.22 (6H, s, Ar-$C\underline{H_3}$ × 2), 3.12 (2H, d, J=8 Hz, Ar-$C\underline{H_2}$–CH<), 3.62 (1H, t, J=8 Hz, $-CH_2-C\underline{H}<$), 4.12 (4H, q, J=7 Hz, $CO_2\underline{CH_2}CH_3$ × 2), 6.78 (3H, s, Ar-H × 3). MS m/z: 278, 233, 204, 187, 159, 119. Calcd for $C_{16}H_{22}O_4$: 278.1516 (M). Found: 278.1513 (M^+).

Diethyl (4-Chloromethyl-3,5-dimethylphenylmethyl)malonate (XII)——Dry hydrogen chloride gas was bubbled through a solution of XI (12.5 g) in tetrachloroethane (160 ml) containing paraformaldehyde (2.2 g) and anhydrous zinc chloride (36 g) at 80 °C for 4.5 h. The mixture was cooled and washed thoroughly with water to remove the zinc salt and free mineral acid. After removal of the solvent, the residue (11.4 g) was subjected to column chromatography on silica gel (170 g, benzene) to give an inseparable mixture (5.1 g) of diethyl (4-chloromethyl-3,5-dimethylphenylmethyl)malonate (XII) and its isomer bearing a chloromethyl group at C-2. ^{1}H-NMR (in $CDCl_3$, 60 MHz) δ: 1.22 (6H, t, J=7 Hz), 2.38 (6H × 2/3 + 3H × 1/3, s, Ar-3,5-$C\underline{H_3}$), 2.48 (3H × 1/3, s, Ar-3-$C\underline{H_3}$), 3.30 (2H,

d, $J=8$ Hz), 3.78 (1H, t, $J=8$ Hz), 4.15 (4H, q, $J=7$ Hz), 4.62 (2H × 2/3, s, Ar-4-C$\underline{H}_2$Cl), 4.72 (2H × 1/3, s, Ar-2-C$\underline{H}_2$Cl), 6.90 (2H, s). Calcd for $C_{17}H_{23}ClO_4$: 326.1282 and 328.1256 (M). Found: 326.1272 and 328.1248 (M^+).

Diethyl (4-Cyanomethyl-3,5-dimethylphenylmethyl)malonate (XIII)[8]——A solution of XII (3.70 g, 0.0113 mol) containing its isomer in dimethylsulfoxide (100 ml) was added, during over a period of 20 min, to a stirred suspension of sodium cyanide (560 mg, 0.0114 mol) in dimethylsulfoxide (100 ml) at 20 °C. The mixture was stirred for 3 h at 37 ± 2 °C, then poured into ice-water (250 ml). The ether extracts (200 ml × 3) were washed with water, and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was chromatographed on silica gel (60 g, benzene–ether (40 : 1)) to furnish XIII (1.98 g). Colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2980, 2260 (C≡N), 1730 (ester C=O), 1615, 1590, 1450, 1375, 1210, 1035, 860. ^{1}H-NMR (in $CDCl_3$, 60 MHz) δ: 1.22 (6H, t, $J=7$ Hz), 2.35 (6H, s), 3.12 (2H, d, $J=7$ Hz), 3.58 (2H, s, Ar-C$\underline{H}_2$CN), 3.50—3.88 (3H, m, overlapping with δ 3.58, –CH$_2$–C$\underline{H}$<), 4.15 (4H, q, $J=7$ Hz), 6.92 (2H, s). MS *m/z*: 317, 271, 243, 226, 198. Calcd for $C_{18}H_{23}NO_4$: 317.1625 (M). Found: 317.1604 (M^+).

3-(4-Carboxymethyl-3,5-dimethylphenyl)propionic Acid (XIV)——A solution of nitrile diester (XIII, 1.1 g) in glacial acetic acid (5 ml) and concentrated hydrochloric acid (30 ml) was refluxed for 18 h. A further 30 ml of concentrated hydrochloric acid was added and refluxing was continued for further 18 h. The reaction mixture was diluted with water and evaporated *in vacuo*. The residue was extracted with ether (50 ml × 3) and the extract was washed with water, dried over Na_2SO_4, and evaporated. The residue was chromatographed on Sephadex LH-20 (MeOH), and silica gel (26 g, $CHCl_3$–ethyl acetate (1 : 1)) to furnish XIV (500 mg). Colorless needles, mp 194—196 °C from a mixture of benzene and ethyl acetate. IR ν_{max}^{KBr} cm^{-1}: 3300—2800 (OH), 1710 (COOH), 1620, 1580, 1420, 870. ^{1}H-NMR (in $CDCl_3$ + CD_3OD) δ: 2.30 (6H, s, Ar-C$\underline{H}_3$ × 2), 2.73 (4H, m, Ar-C$\underline{H}_2$–C$\underline{H}_2$–COOH), 3.64 (2H, s, Ar-C$\underline{H}_2$–COOH), 6.85 (2H, s, Ar-H × 2). MS *m/z*: 236, 218, 191, 177, 145, 131. Calcd for $C_{13}H_{16}O_4$: 236.1047 (M). Found: 236.1054 (M^+).

6-Methoxycarbonylmethyl-5,7-dimethylindan-1-one (IX)——A mixture of dicarboxylic acid (XIV, 470 mg) and polyphosphoric acid [prepared from phosphorus pentoxide (25 g) and phosphoric acid (15 ml)] was heated at 100 °C for 1.5 h under stirring. The mixture was poured into ice-water and extracted with ether (150 ml × 3). The ether layer was washed with water, dried over Na_2SO_4, and evaporated *in vacuo*, then the residue was chromatographed on silica gel (20 g, $CHCl_3$–MeOH (20 : 1)), followed by methylation with excess diazomethane in ether in the usual manner to yield IX (280 mg). Colorless needles, mp 90—91 °C from a mixture of $CHCl_3$ and *n*-hexane. UV λ_{max}^{MeOH} nm (log ε): 217 (4.63), 259 (4.29), 303 (3.59). IR ν_{max}^{KBr} cm^{-1}: 2960, 1730 (ester C=O), 1700 (five membered ring ketone), 1600, 1580, 1430, 1260, 1000, 865, 810. ^{1}H-NMR (in $CDCl_3$) δ: 2.38 (3H, s, C_5-C$\underline{H}_3$), 2.64 (3H, s, C_7-C$\underline{H}_3$), 2.63 (2H, t, $J=6$ Hz, overlapping with δ 2.64, CO–C$\underline{H}_2$–CH$_2$–), 3.00 (2H, t, $J=6$ Hz, CO–CH$_2$–C$\underline{H}_2$–Ar), 3.68 (3H, s, OC$\underline{H}_3$), 3.74 (2H, s, Ar-CH$_2$–COOC$\underline{H}_3$), 7.10 (1H, s, Ar-H). ^{13}C-NMR (in C_5D_5N) δ: 206.8 (C-1), 37.2 (C-2), 24.7 (C-3), 126.0 (C-4), 144.4 (C-5), 133.0 (C-6), 137.7 (C-7), 132.3 (C-8), 155.1 (C-9), 21.2 (C-12), 34.2 (C-13), 171.5 (C-14), 13.6 (C-15), 51.8 (O$\underline{C}$H$_3$). MS *m/z*: 232 (M^+), 201 ($M^+ - OCH_3$), 173 ($M^+ - COOCH_3$), 172 ($M^+ - HCOOCH_3$). Calcd for $C_{14}H_{16}O_3$: 232.1098 (M). Found: 232.1093 (M^+).

2-Benzylidene-6-methoxycarbonylmethyl-5,7-dimethylindan-1-one (XV)——Sodium metal (250 mg) in absolute methanol (8 ml) was added to a solution of IX (120 mg) in absolute methanol (5 ml) containing benzaldehyde (0.25 ml) under stirring. After being stirred for 30 min at room temperature, the reaction mixture was diluted with water (30 ml) and the resulting precipitates were collected by filtration, washed with water, dried and recrystallized from methanol to give XV (150 mg). Colorless needles, mp 161—162 °C. UV λ_{max}^{MeOH} nm (log ε): 204 (4.48), 228 sh (4.15), 322 (4.47). IR ν_{max}^{KBr} cm^{-1}: 1725 (ester C=O), 1675 (five-membered ring C=O), 1625, 820 (trisubstituted double bond), 1595, 1250. ^{1}H-NMR (in $CDCl_3$) δ: 2.36 (3H, s, C_5-C$\underline{H}_3$), 2.71 (3H, s, C_7-C$\underline{H}_3$), 3.67 (3H, s, OC$\underline{H}_3$), 3.70 (2H, s, Ar-C$\underline{H}_2$–COOCH$_3$), 3.79 (2H, d, $J=1.5$ Hz, Ar-C$\underline{H}_2$–C=CH–), 7.10 (1H, s, Ar-4-H), 7.46 (t, $J=1.5$ Hz, –CH$_2$–C=C$\underline{H}$–Ar), 7.28—7.60 (6H, m, overlapping with δ 7.46, Ar-H × 5). ^{13}C-NMR (in C_5D_5N) δ: 194.4 (C-1), 136.0 (C-2), 31.6 (C-3), 125.7 (C-4), 144.7 (C-5), 134.0 (C-6), 138.6 (C-7), 132.3 (C-8), 149.8 (C-9), 132.9 (C-10), 21.4 (C-12), 34.3 (C-13), 171.5 (C-14), 14.0 (C-15), 51.9 (O$\underline{C}$H$_3$), 136.0 (C-1′), 130.9 (C-2′), 129.2 (C-3′), 129.6 (C-4′), 129.2 (C-5′), 130.9 (C-6′). MS *m/z*: 320, 261, 247, 233, 202. Calcd for $C_{21}H_{20}O_3$: 320.1411 (M). Found: 320.1411 (M^+).

Methyl 2,4-Dimethyl-3,6-bis(methoxycarbonylmethyl)benzoate (VIII)——XV (120 mg) in acetic acid (16 ml) was oxidized with ozone for 2 h at room temperature. The resulting solution was diluted with water (16 ml) and heated on a boiling water bath for 1.5 h, then cooled. The mixture was further diluted with water (34 ml) and extracted with $CHCl_3$ (50 ml) and ether (50 ml × 3). The ether layer was washed with water, dried over Na_2SO_4 and evaporated *in vacuo*. The residue was methylated with excess diazomethane in ether in the usual manner and the product was chromatographed on silica gel (10 g, ethyl acetate–*n*-hexane (1 : 4)) to yield VIII (40 mg). Colorless oil. UV λ_{max}^{MeOH} nm (log ε): 280 (2.83). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2950, 1725 (ester C=O), 1600 (benzene ring), 1435, 1270, 1150, 1050. ^{1}H-NMR (in $CDCl_3$) δ: 2.27 (3H, s, C_4-C$\underline{H}_3$), 2.33 (3H, s, C_2-C$\underline{H}_3$), 3.60 (2H, s, C_3-C$\underline{H}_2$–COOCH$_3$), 3.66 (6H, s, OC$\underline{H}_3$ × 2), 3.68 (2H, s, C_6-C$\underline{H}_2$–COOCH$_3$), 3.86 (3H, s, OC$\underline{H}_3$), 6.94 (1H, s, C_5-H). ^{13}C-NMR (in $CDCl_3$) δ: 171.4 (s), 171.1 (s), 169.9 (s), 139.1 (s), 135.0 (s), 132.4 (s), 131.5 (s), 130.4 (d), 130.1 (s), 52.0 (q), 39.2 (t), 35.2 (t), 20.5 (q), 17.5 (q). MS *m/z*: 308, 277, 276, 248, 233, 217, 189. Calcd for $C_{16}H_{20}O_6$: 308.1259 (M). Found: 308.1259 (M^+).

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References and Notes

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