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Structure of Bisosthenon, a Novel Dimeric Coumarin from *Citrus* Plants[1)]

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Bisosthenon (1), a new dimeric coumarin, was isolated from the roots of some *Citrus* plants (Rutaceae), and the structure was elucidated to be 1, corresponding to a head-to-head dimer of osthenon (4), which was previously obtained from *Citrus* plants. The photodimerization of 4 gave 1 as well as two other dimeric products, 2 and 3.

Keywords *Citrus*; Rutaceae; coumarin; bisosthenon; osthenon; photodimerization; cyclobutane; dimer; X-ray

Phytochemical studies of *Citrus* plants (Rutaceae) in progress in our laboratories are aimed at characterizing many kinds of new coumarins and acridone alkaloids as well as known components.[2)] We report here the structure elucidation of a novel dimeric coumarin, bisosthenon (1), isolated from roots of some *Citrus* plants: *C. funadoko* HORT. *ex* Y. TANAKA (funadoko), and several hybrid seedlings resulting from crosses of *C. flaviculpus* HORT. *ex* TANAKA (ogonkan) × *C. Tamurana* HORT. *ex* TAKAHASHI (hyuganatsu) and [*C. unshiu* MARC. (miyagawa-wase) × *C. sinensis* OSBEC. (trobita orange)] (kiyomi) × *C. iyo* HORT. *ex* TANAKA (iyo).

Results and Discussion

As reported previously,[2c)] the acetone extract of the dried roots of the *Citrus* plants was subjected successively to silica gel column, preparative centrifugally accelerated thin-layer, and preparative thin-layer chromatographies (TLC) to yield bisosthenon (1) in addition to many other coumarins and/or acridone alkaloids.

Bisosthenon (1) was isolated as colorless prisms, mp 234—237 °C. The molecular formula was determined as $C_{28}H_{24}O_8$ by high-resolution mass spectrometry (HR-MS). In the proton and carbon-13 nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectra, the number of signals observed (Table I) was half of that expected, suggesting that bisosthenon (1) had a completely symmetrical structure. Ultraviolet (UV) bands were observed at λ_{max} 253, 260, and 317 nm. In the ^{1}H-NMR spectrum, a methoxy signal appeared at δ_H 3.60 (6H, singlet). In addition, two pairs of AB-type doublet signals appeared at δ_H 6.09 and 7.47 (each 2H, J = 9.4 Hz), and δ_H 7.11 and 6.52 (each 2H, J = 8.7 Hz). Based on the analysis of the two dimensional H–C correlation spectroscopy (COSY) spectrum, signals of

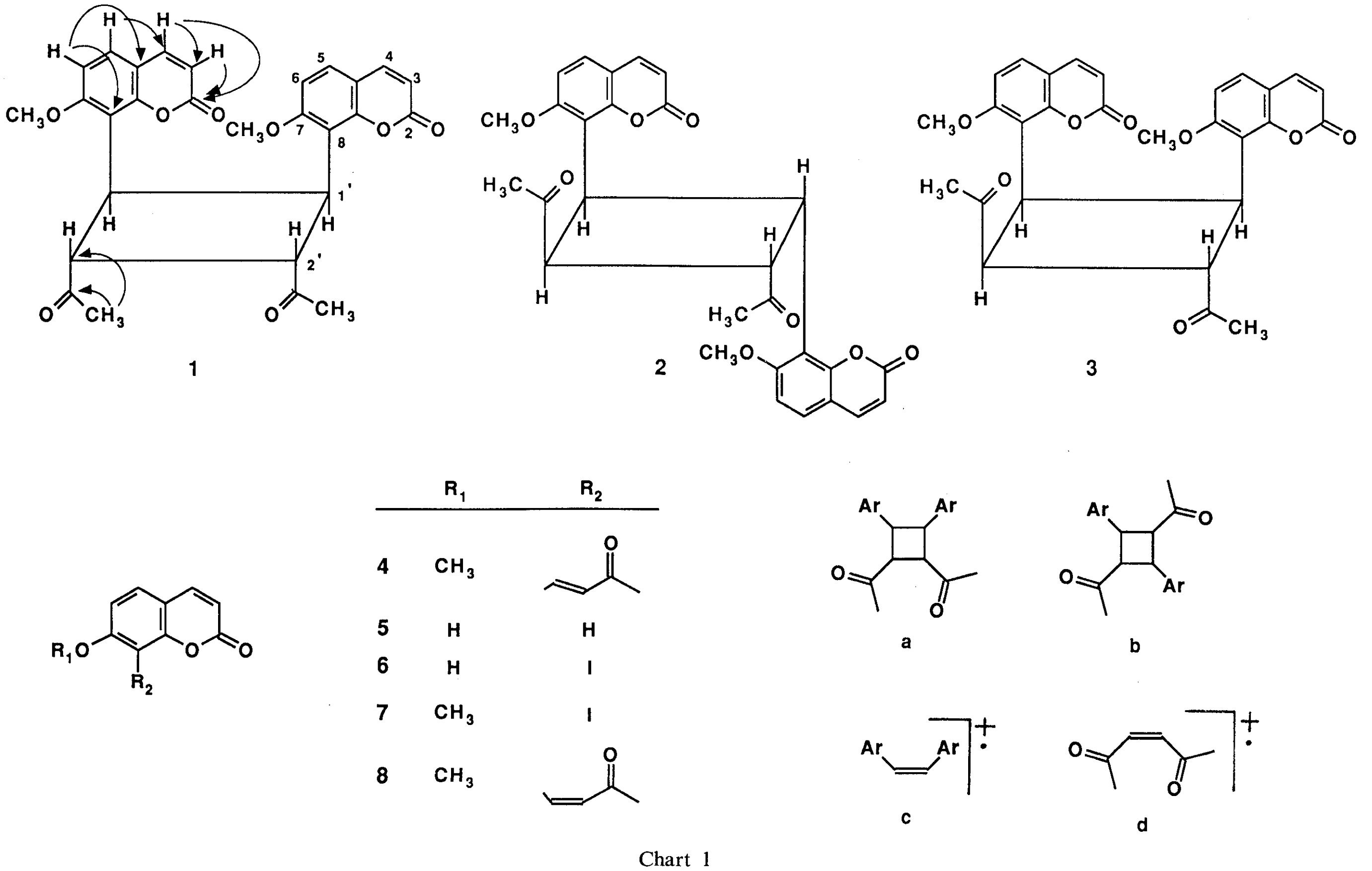

Chart 1

carbons bearing these protons were determined to resonate at δ_C 112.54, 143.68, 126.98, and 106.69, respectively. These spectral data, coupled with the results of examination of the long-range H–C COSY spectrum shown by arrows in formula (**1**), indicated the presence of the 7-methoxy-8-substituted coumarin nucleus in the bisosthenon molecule. The presence of the acetyl moiety in the molecule was deduced from the appearance of the infrared (IR) absorption at ν_{max} 1725 cm^{-1}, a sharp singlet in the NMR spectrum at δ_H 2.27, and a carbonyl carbon singlet at δ_C 208.27. The remaining protons at δ_H 4.93 (2H, doublet-like multiplet, $J=6.7$ Hz) and 4.82 (2H, broad singlet) coupled to each other and signals due to the carbons bearing these protons appeared at δ_C 35.15 and 51.04, respectively. These data were suggestive of a 1,2,3,4-symmetrically-substituted cyclobutane ring system.[3,4] The ^{1}H-NMR signal pattern of bisosthenon was similar to that of osthenon (**4**)[5] isolated previously from some *Citrus* plants,[2d] except for the H-1′ and H-2′ signals. In the differential nuclear Overhauser effect (NOE) experiments on bisosthenon (**1**), a strong negative NOE enhancement was observed at the signal of δ_H 4.82 (H-2′) on irradiation of the signal at δ_H 4.93 (H-1′). Conversely, irradiation of the signal at δ_H 4.82 (H-2′) also caused a strong negative NOE enhancement of the signal at δ_H 4.93 (H-1′). The electron impact mass spectrum (EI-MS) of bisosthenon exhibited a characteristic fragment peak at m/z 244 which corresponded to the half of the molecule, $C_{14}H_{12}O_4$, and also showed peaks at m/z 229, 213 (base peak), and 201, associated, respectively, with loss of a methyl, a methoxy, and an acetyl radical from half of the molecular ion (m/z 244). From the foregoing spectroscopic data, it was concluded that bisosthenon was either the head-to-head (a) or head-to-tail (b) dimer of osthenon (**4**) as shown in Chart 1. According to previous papers,[3,4] the presence of the fragment due to the ion c and/or d in the MS is characteristic of the head-to-head

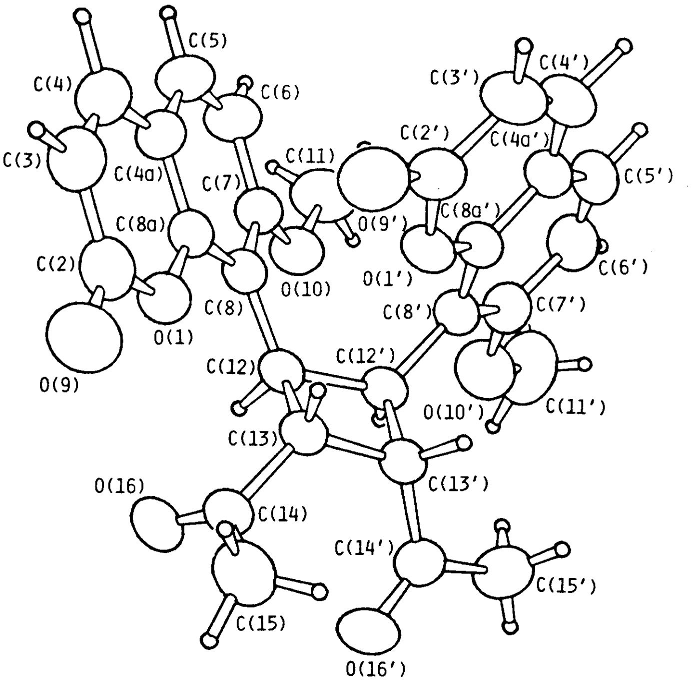

Fig. 1. Structure and Solid-State Conformation of One Enantiomer; Small Circles Represent Hydrogen Atoms

Table I. The ^{1}H- and ^{13}C-NMR Spectra of Bisosthenon (**1**) and Other Photodimerization Products of Osthenon (**4**)

No.	Bisosthenon (**1**) δ_H	δ_C	Product C (**2**) δ_H	δ_C	Product B (**3**) δ_H	δ_C
2		160.43		161.80		160.57 160.43
3	6.09 (2H, d, 9.4)	112.54	6.15 (2H, d, 9.5)	113.14	6.18 (1H, d, 9.4), 6.11 (1H, d, 9.4)	112.67 112.36
4	7.47 (2H, d, 9.4)	143.68	7.56 (2H, d, 9.5)	143.66	7.49 (1H, d, 9.4), 7.45 (1H, d, 9.4)	143.79 143.69
4a		112.54		112.95		112.54 112.42
5	7.11 (2H, d, 8.7)	126.98	7.33 (2H, d, 8.5)	127.65	7.05 (1H, d, 8.7), 7.12 (1H, d, 8.7)	126.68 127.47
6	6.52 (2H, d, 8.7)	106.69	6.89 (2H, d, 8.5)	108.19	6.47 (1H, d, 8.7), 6.42 (1H, d, 8.7)	106.26 106.60
7		153.25		152.95		153.45 153.31
8		115.93		116.63		114.96 114.96
8a		160.27		160.51		160.28 160.21
OCH_3	3.60 (6H, s)	55.35	3.96 (6H, s)	56.03	3.55 (6H, br s)	54.66 55.22
1′	4.93 (2H, m[a])	35.15	4.95 (2H, m[a])	33.71	5.42 (1H, t, 10.7), 4.49 (1H, t, 10.7)	35.21 35.42
2′	4.82 (2H, br)	51.04	4.07 (2H, m[a])	49.34	3.74 (1H, t, 10.4), 5.69 (1H, t, 10.4)	49.74 50.57
3′		208.27		207.66		205.67 209.76
CH_3	2.27 (6H, s)	28.65	2.13 (6H, s)	27.48	1.50 (3H, s), 2.45 (3H, s)	26.87 28.69

Values are in ppm (δ_H and δ_C). ^{1}H- and ^{13}C-NMR spectra were recorded at 400 MHz and 100 MHz, respectively, in $CDCl_3$. Figures in parentheses are coupling constants (J) in hertz (Hz). *a*) Doublet-like multiplet signals (J *ca.* 6.7 Hz).

TABLE II. Crystal Data[a)]

Molecular formula	$C_{28}H_{24}O_8$
Formula weight	488.50
Crystal system	Triclinic
Space group	$p\bar{1}(C_i^1)$-No. 2
a(Å)	11.003 (2)
b(Å)	13.721 (2)
c(Å)	8.707 (2)
α(°)	106.60 (2)
β(°)	106.41 (2)
γ(°)	73.03 (2)
No. of orientation refls.; θ(°) range	25; 52—67
V(Å^3)	1176 (1)
Z	2
$D_{\text{calcd.}}$ (g cm^{-3})	1.379
μ(CuK_α radiation, $\lambda=1.5418$ Å)	8.0
Temp. (°C)	25
Crystal dimensions (mm)	$0.12 \times 0.24 \times 0.50$
$T_{\text{max.}}:T_{\text{min.}}$	1.00:0.91
Scan type	$\omega-2\theta$
Scan width (°)	$1.10+0.14\tan\theta$
$\theta_{\text{max.}}$ (°)	75
Intensity control refls.;	$1\,\bar{2}\,1; 1\,1\,\bar{2}$
Variation; repeat time (h)	$<1\%$; 2
Total no. of refls. ($+h$, $\pm k$, $\pm l$) recorded	5153
No. of non-equivalent refls. recorded	4820
R_{merge} (on I)	0.027
No. of refls. retained [$I>3.0\sigma(I)$]	3733
No. of parameters refined	422
Extinction correction	2.6×10^{-6}
Goodness-of-fit	2.3
R (R_w)[b)]	0.046 (0.066)
Max. shift:esd in final least-squares cycle	<0.02
Final $\Delta\rho(e/\text{Å}^3)$ max.; min.	0.19; -0.22

a) An Enraf-Nonius CAD-4 diffractometer (CuK_α radiation, incident-beam graphite monochromator) was used for all measurements. Crystallographic calculations were performed on PDP11/44 and MicroVAX computers by use of the Enraf-Nonius Structure Determination Package incorporating the direct methods program MULTAN11/82. Data were corrected for the usual Lorentz and polarization effects; an empirical absorption correction was also applied. $b_R=\sum\|F_O|-|F_C\|/\sum|F_O|$; $R_w=[\sum w(|F_O|-|F_C|)^2/\sum w|F_O|^2]^{1/2}$; $w=1/\sigma^2(|F_O|)$; $\sum w\Delta^2(\Delta=|F_O|-|F_C|)$ was minimized.

TABLE III. Non-hydrogen Atom Fractional Coordinates and Equivalent Isotropic Thermal Parameters, with Estimated Standard Deviations in Parentheses

Atom	x	y	z	B (Å^2)
O(1)	−0.0875 (1)	0.1572 (1)	−0.1155 (2)	3.94 (3)
C(2)	−0.1763 (2)	0.1226 (2)	−0.2527 (2)	4.49 (4)
C(3)	−0.1329 (2)	0.0229 (2)	−0.3564 (3)	5.08 (5)
C(4)	−0.0114 (2)	−0.0346 (2)	−0.3178 (3)	4.90 (5)
C(4a)	0.0790 (2)	0.0025 (1)	−0.1746 (2)	4.02 (4)
C(5)	0.2055 (2)	−0.0542 (2)	−0.1276 (3)	4.90 (5)
C(6)	0.2873 (2)	−0.0153 (2)	0.0145 (3)	4.65 (5)
C(7)	0.2430 (2)	0.0825 (1)	0.1104 (2)	3.66 (4)
C(8)	0.1197 (2)	0.1458 (1)	0.0641 (2)	3.32 (3)
C(8a)	0.0386 (2)	0.1008 (1)	−0.0760 (2)	3.43 (3)
O(9)	−0.2845 (2)	0.1790 (1)	−0.2728 (2)	6.05 (5)
O(10)	0.3151 (1)	0.1226 (1)	0.2583 (2)	4.24 (3)
C(11)	0.4486 (2)	0.0719 (2)	0.3032 (3)	6.06 (7)
C(12)	0.0804 (1)	0.2544 (1)	0.1654 (2)	3.22 (3)
C(13)	−0.0266 (1)	0.3389 (1)	0.0868 (2)	3.26 (3)
C(14)	−0.1609 (2)	0.3628 (1)	0.1224 (2)	3.76 (4)
C(15)	−0.2667 (2)	0.4366 (2)	0.0312 (3)	5.75 (6)
O(16)	−0.1827 (1)	0.3191 (1)	0.2109 (2)	4.58 (3)
O(1′)	0.1776 (1)	0.2684 (1)	−0.1128 (1)	3.79 (3)
C(2′)	0.1653 (2)	0.2292 (2)	−0.2794 (2)	4.40 (4)
C(3′)	0.2774 (2)	0.2138 (2)	−0.3455 (3)	5.72 (6)
C(4′)	0.3906 (2)	0.2298 (2)	−0.2466 (3)	5.49 (5)
C(4a′)	0.4054 (2)	0.2623 (1)	−0.0714 (2)	4.39 (4)
C(5′)	0.5207 (2)	0.2782 (2)	0.0405 (3)	5.23 (5)
C(6′)	0.5262 (2)	0.3086 (2)	0.2046 (3)	5.24 (5)
C(7′)	0.4150 (2)	0.3243 (2)	0.2644 (3)	4.28 (4)
C(8′)	0.2957 (2)	0.3098 (1)	0.1580 (2)	3.46 (3)
C(8a′)	0.2949 (2)	0.2801 (1)	−0.0079 (2)	3.54 (3)
O(9′)	0.0601 (2)	0.2112 (1)	−0.3546 (2)	5.76 (4)
O(10′)	0.4145 (1)	0.3545 (1)	0.4276 (2)	5.57 (4)
C(11′)	0.5315 (3)	0.3685 (2)	0.5457 (4)	7.34 (7)
C(12′)	0.1768 (2)	0.3301 (1)	0.2260 (2)	3.30 (3)
C(13′)	0.0607 (2)	0.4187 (1)	0.1659 (2)	3.34 (3)
C(14′)	0.0253 (2)	0.5109 (1)	0.3012 (2)	4.08 (4)
C(15′)	0.1311 (2)	0.5677 (2)	0.3932 (3)	5.60 (6)
O(16′)	−0.0826 (1)	0.5383 (1)	0.3314 (2)	5.96 (4)

isomer. In the case of bisosthenon, these corresponding fragments at *m*/*z* 376 and 112 ascribed to c and d, respectively, could not be observed even in the enlarged MS, suggesting a head-to-tail dimeric structure b. However, the X-ray crystallographic analysis (*vide infra*) of bisosthenon showed the actual structure to be the head-to-head structure a. On the basis of these results, it is clear that care is required in using MS for the purpose of characterizing the substitution pattern on a cyclobutane ring system.

Single-crystal X-ray analysis established the complete structure and relative stereochemistry of bisosthenon. A view of the structure is provided in Fig. 1. The structural parameters are listed in Tables II—VII.

Next, synthesis of bisosthenon (**1**) from umbelliferone (**5**)[6)] was achieved in the following manner. Umbelliferone (**5**) was converted into 8-iodoumbelliferone (**6**),[7)] followed by methylation with methyl iodide in alkaline solution to afford **7**. Treatment[8)] of **7** with methyl vinyl ketone in the presence of Pd(OAc)$_2$, triethylamine, and tetra-*n*-butylammonium bromide in dimethylformamide gave **4**, which was found to be identical with natural osthenon (**4**) by spectral (IR and ^{1}H-NMR) comparisons. Photodimerization[9)] of **4** in isopropyl alcohol using a high-pressure Hg lamp through a Pyrex glass filter for 26 h at room temperature yielded a single dimeric product in a 15% yield accompanied with a 35% yield of *cis*-osthenon (**8**)[10)] and an 8% recovery of **4**. This dimer was found to be identical with natural bisosthenon (**1**) by spectral comparisons (IR, ^{1}H-NMR and EI-MS). On the other hand, the same reaction in solid-state for 142 h at room temperature gave three dimeric products (A, B, and C in 16, 11, and 2% yields, respectively) accompanied with a 9% yield of the *cis*-isomer (**8**) and a 35% recovery of **4**. The HR-MS of these dimeric products showed them to have the same molecular formula $C_{28}H_{24}O_8$. The similarity of the mass fragmentation patterns also indicated that they were stereoisomers with respect to each other. Spectral comparisons (IR, EI-MS, and ^{1}H-NMR) verified that the most polar product A was identical with natural bisosthenon (**1**). The ^{1}H-NMR spectrum of the second product B at room temperature showed only unresolvable broad signals. However, the spectrum at 50 °C as shown in Table I suggested that B had an unsymmetrical structure unlike the structure of bisosthenon (**1**). The results of spectral studies using H–C COSY indicated the presence of two 7-methoxy-8-substituted coumarin nuclei and two acetyl moieties. Two triplets ($J=10.7$ Hz) at δ_H 4.49 and 5.42 coupled to each other and correlated with carbon signals at δ_C 35.42 and 35.21, respectively, were assignable to benzylic protons on the four-membered ring system. Two other triplets

TABLE IV. Anisotropic Temperature Factor Parameters[a] (× 10^4), with Estimated Standard Deviations in Parentheses

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	403 (5)	528 (6)	528 (6)	−130 (4)	87 (4)	50 (5)
C(2)	512 (8)	705 (10)	510 (9)	−249 (7)	51 (7)	113 (7)
C(3)	698 (10)	736 (11)	528 (9)	−330 (8)	115 (8)	37 (8)
C(4)	767 (10)	582 (9)	558 (9)	−276 (7)	205 (8)	8 (7)
C(4a)	601 (8)	435 (7)	522 (8)	−152 (6)	192 (6)	51 (6)
C(5)	684 (11)	455 (9)	690 (10)	−37 (8)	274 (8)	48 (8)
C(6)	551 (10)	474 (9)	680 (10)	33 (8)	181 (8)	138 (8)
C(7)	472 (7)	438 (7)	494 (7)	−72 (6)	135 (6)	129 (6)
C(8)	406 (6)	419 (7)	473 (7)	−88 (5)	147 (5)	111 (5)
C(8a)	424 (7)	429 (7)	492 (7)	−112 (5)	150 (5)	102 (5)
O(9)	516 (7)	942 (11)	702 (9)	−141 (7)	−6 (7)	134 (8)
O(10)	453 (6)	569 (6)	529 (6)	−27 (5)	75 (5)	155 (5)
C(11)	499 (11)	842 (15)	748 (13)	81 (11)	34 (10)	190 (12)
C(12)	342 (6)	449 (7)	434 (7)	−73 (5)	115 (5)	91 (5)
C(13)	311 (6)	435 (7)	467 (7)	−68 (5)	98 (5)	64 (6)
C(14)	340 (6)	476 (8)	578 (9)	−99 (6)	124 (6)	32 (7)
C(15)	396 (9)	752 (12)	1040 (14)	−15 (8)	130 (9)	346 (10)
O(16)	428 (5)	690 (7)	661 (7)	−155 (7)	189 (4)	109 (5)
O(1′)	440 (5)	560 (6)	434 (5)	−95 (4)	153 (4)	66 (4)
C(2′)	668 (10)	517 (9)	473 (8)	−121 (8)	174 (7)	51 (7)
C(3′)	896 (12)	694 (12)	631 (9)	−62 (10)	404 (7)	108 (8)
C(4′)	718 (10)	637 (11)	844 (10)	−55 (8)	458 (7)	155 (8)
C(4a′)	494 (7)	453 (8)	792 (9)	−34 (6)	319 (6)	145 (7)
C(5′)	379 (7)	576 (9)	1110 (13)	−74 (6)	309 (7)	198 (8)
C(6′)	338 (7)	634 (10)	1012 (14)	−108 (7)	120 (8)	198 (9)
C(7′)	351 (7)	516 (8)	716 (11)	−94 (6)	38 (7)	154 (7)
C(8′)	319 (6)	441 (7)	552 (8)	−70 (5)	104 (5)	114 (6)
C(8a′)	346 (6)	421 (7)	586 (8)	−53 (5)	149 (5)	114 (6)
O(9′)	840 (9)	771 (9)	511 (7)	−217 (7)	123 (7)	31 (7)
O(10′)	479 (7)	921 (10)	619 (8)	−231 (6)	−79 (6)	143 (7)
C(11′)	722 (13)	1055 (16)	910 (16)	−409 (11)	−320 (12)	342 (13)
C(12′)	332 (6)	462 (7)	439 (7)	−76 (5)	89 (5)	78 (6)
C(13′)	345 (6)	429 (7)	488 (7)	−65 (5)	113 (5)	91 (6)
C(14′)	460 (8)	439 (8)	623 (9)	−75 (6)	154 (7)	69 (7)
C(15′)	642 (11)	597 (11)	773 (13)	−207 (9)	143 (10)	−81 (10)
O(16′)	565 (7)	620 (8)	1000 (10)	−95 (6)	374 (6)	−98 (8)

a) In the form: $\exp[-2\pi^2(U_{11}h^2a^{*2}+U_{22}k^2b^{*2}+U_{33}l^2c^{*2}+2U_{12}hka^*b^*+2U_{13}hla^*c^*+2U_{23}klb^*c^*)]$.

TABLE V. Hydrogen Atom Fractional Coordinates,[a] Isotropic Temperature Factors, and Bonded Distances; Estimated Standard Deviations Are Shown in Parentheses

Atom	x	y	z	B (Å^2)	d (Å)
H(3)	−0.190 (2)	−0.002 (2)	−0.455 (3)	3.2 (5)	0.95 (2)
H(4)	0.019 (2)	−0.108 (2)	−0.401 (3)	3.8 (6)	1.08 (2)
H(5)	0.235 (2)	−0.119 (2)	−0.194 (3)	3.6 (6)	0.93 (2)
H(6)	0.374 (2)	−0.055 (2)	0.052 (3)	2.7 (5)	0.97 (2)
H(11A)	0.482 (2)	0.122 (2)	0.412 (3)	3.9 (6)	1.04 (2)
H(11B)	0.450 (2)	0.003 (2)	0.308 (3)	3.4 (5)	0.95 (3)
H(11C)	0.496 (3)	0.064 (2)	0.217 (3)	5.8 (8)	0.99 (3)
H(12)	0.054 (2)	0.251 (1)	0.261 (2)	1.0 (3)	0.97 (2)
H(13)	−0.035 (2)	0.324 (2)	−0.032 (2)	2.1 (4)	0.98 (2)
H(15A)	−0.338 (2)	0.469 (2)	0.088 (3)	4.6 (6)	0.97 (2)
H(15B)	−0.239 (2)	0.497 (2)	0.020 (3)	4.4 (6)	1.00 (3)
H(15C)	−0.292 (3)	0.400 (3)	−0.083 (4)	9.1 (11)	0.98 (3)
H(3′)	0.253 (2)	0.195 (2)	−0.477 (3)	5.6 (7)	1.07 (2)
H(4′)	0.474 (2)	0.219 (2)	−0.296 (3)	4.1 (6)	1.08 (3)
H(5′)	0.593 (2)	0.266 (2)	−0.008 (3)	4.6 (7)	0.95 (3)
H(6′)	0.610 (2)	0.319 (2)	0.295 (3)	3.9 (6)	1.05 (2)
H(11′A)	0.491 (2)	0.395 (2)	0.670 (3)	4.1 (6)	1.21 (3)
H(11′B)	0.602 (2)	0.309 (2)	0.532 (3)	4.5 (6)	0.95 (2)
H(11′C)	0.571 (3)	0.408 (2)	0.518 (3)	6.6 (8)	0.90 (4)
H(12′)	0.208 (2)	0.343 (1)	0.351 (2)	1.8 (4)	1.02 (2)
H(13′)	0.075 (2)	0.449 (1)	0.074 (2)	1.3 (4)	1.07 (2)
H(15′A)	0.107 (3)	0.619 (2)	0.464 (4)	7.1 (9)	0.83 (3)
H(15′B)	0.210 (3)	0.522 (3)	0.426 (4)	8.0 (10)	0.93 (3)
H(15′C)	0.160 (3)	0.589 (3)	0.310 (4)	9.5 (11)	1.01 (4)

a) Hydrogen atoms bear the same labels as the atoms to which they are bonded.

TABLE VI. Interatomic Distances (Å) and Angles (°), with Estimated Standard Deviations in Parentheses

(a) Bond lengths			
O(1)–C(2)	1.376 (2)	O(1′)–C(2′)	1.378 (2)
O(1)–C(8a)	1.378 (2)	O(1′)–C(8a′)	1.377 (2)
C(2)–C(3)	1.439 (3)	C(2′)–C(3′)	1.441 (4)
C(2)–O(9)	1.212 (3)	C(2′)–O(9′)	1.215 (3)
C(3)–C(4)	1.343 (3)	C(3′)–C(4′)	1.337 (3)
C(4)–C(4a)	1.427 (3)	C(4′)–C(4a′)	1.437 (3)
C(4a)–C(5)	1.392 (3)	C(4a′)–C(5′)	1.396 (3)
C(4a)–C(8a)	1.399 (2)	C(4a′)–C(8a′)	1.405 (3)
C(5)–C(6)	1.378 (3)	C(5′)–C(6′)	1.358 (4)
C(6)–C(7)	1.394 (3)	C(6′)–C(7′)	1.399 (4)
C(7)–C(8)	1.400 (2)	C(7′)–C(8′)	1.407 (3)
C(7)–O(10)	1.365 (2)	C(7′)–O(10′)	1.363 (3)
C(8)–C(8a)	1.393 (2)	C(8′)–C(8a′)	1.382 (2)
C(8)–C(12)	1.508 (2)	C(8′)–C(12′)	1.507 (3)
O(10)–C(11)	1.424 (2)	O(10′)–C(11′)	1.427 (3)
C(12)–C(13)	1.549 (2)	C(12′)–C(13′)	1.569 (2)
C(12)–C(12′)	1.580 (2)	C(13)–C(13′)	1.551 (2)
C(13)–C(14)	1.518 (3)	C(13′)–C(14′)	1.503 (2)
C(14)–C(15)	1.503 (3)	C(14′)–C(15′)	1.500 (3)
C(14)–O(16)	1.210 (3)	C(14′)–O(16′)	1.216 (3)
(b) Bond angles			
C(2)–O(1)–C(8a)	122.7 (1)	C(2′)–O(1′)–C(8a′)	122.7 (1)
O(1)–C(2)–C(3)	117.3 (2)	O(1′)–C(2′)–C(3′)	117.1 (2)
O(1)–C(2)–O(9)	116.3 (2)	O(1′)–C(2′)–O(9′)	115.8 (2)
C(3)–C(2)–O(9)	126.4 (2)	C(3′)–C(2′)–O(9′)	127.1 (2)
C(2)–C(3)–C(4)	120.9 (2)	C(2′)–C(3′)–C(4′)	120.8 (2)
C(3)–C(4)–C(4a)	120.9 (2)	C(3′)–C(4′)–C(4a′)	121.5 (2)
C(4)–C(4a)–C(5)	123.4 (2)	C(4′)–C(4a′)–C(5′)	125.1 (2)
C(4)–C(4a)–C(8a)	118.4 (2)	C(4′)–C(4a′)–C(8a′)	117.4 (2)
C(5)–C(4a)–C(8a)	118.2 (2)	C(5′)–C(4a′)–C(8a′)	117.4 (2)
C(4a)–C(5)–C(6)	120.7 (2)	C(4a′)–C(5′)–C(6′)	121.3 (2)
C(5)–C(6)–C(7)	119.4 (2)	C(5′)–C(6′)–C(7′)	120.0 (2)
C(6)–C(7)–C(8)	122.4 (2)	C(6′)–C(7′)–C(8′)	121.5 (2)
C(6)–C(7)–O(10)	122.6 (2)	C(6′)–C(7′)–O(10′)	122.7 (2)
C(8)–C(7)–O(10)	115.0 (1)	C(8′)–C(7′)–O(10′)	115.8 (2)
C(7)–C(8)–C(8a)	115.7 (1)	C(7′)–C(8′)–C(8a′)	116.2 (2)
C(7)–C(8)–C(12)	120.4 (1)	C(7′)–C(8′)–C(12′)	120.2 (2)
C(8a)–C(8)–C(12)	123.9 (1)	C(8a′)–C(8′)–C(12′)	123.5 (2)
O(1)–C(8a)–C(4a)	119.7 (1)	O(1′)–C(8a′)–C(4a′)	120.0 (1)
O(1)–C(8a)–C(8)	117.0 (1)	O(1′)–C(8a′)–C(8′)	116.5 (2)
C(4a)–C(8a)–C(8)	123.3 (2)	C(4a′)–C(8a′)–C(8′)	123.5 (2)
C(7)–O(10)–C(11)	118.7 (1)	C(7′)–O(10′)–C(11′)	120.1 (2)
C(8)–C(12)–C(13)	120.4 (1)	C(8′)–C(12′)–C(13′)	114.7 (2)
C(8)–C(12)–C(12′)	120.2 (1)	C(12)–C(12′)–C(8′)	123.0 (1)
C(13)–C(12)–C(12′)	89.9 (1)	C(12)–C(12′)–C(13′)	88.6 (1)
C(12)–C(13)–C(13′)	90.4 (1)	C(13)–C(13′)–C(12′)	90.2 (1)
C(14)–C(13)–C(13′)	120.2 (1)	C(13)–C(13′)–C(14′)	120.7 (2)
C(12)–C(13)–C(14)	117.2 (1)	C(12′)–C(13′)–C(14′)	113.9 (1)
C(13)–C(14)–C(15)	116.4 (2)	C(13′)–C(14′)–C(15′)	115.4 (2)
C(13)–C(14)–O(16)	121.4 (1)	C(13′)–C(14′)–O(16′)	122.0 (2)
C(15)–C(14)–O(16)	122.1 (2)	C(15′)–C(14′)–O(16′)	122.6 (1)

($J = 10.7$ Hz) at δ_H 3.74 and 5.69, correlated with signals at δ_C 49.74 and 50.57, respectively, were ascribed to protons on the carbons attached to the acetyl groups. In NOE experiments, irradiation of the benzylic proton at δ_H 4.49 gave a 12% enhancement of another benzylic proton signal at δ_H 5.42. On irradiation of the signal of the proton on the carbon having an acetyl group at δ_H 3.74, an 11% area increase of the signal of the benzylic proton at δ_H 5.42 was observed. Contrariwise, on irradiation of the benzylic proton signal at δ_H 5.42, 13 and 11% enhancements of the other benzylic proton at δ_H 4.49 and the proton on the carbon bearing the acetyl group at δ_H 3.74 were also observed, respectively. On the basis of these results, the structure of product B was proposed to be **3**.[11] The remaining minor product C gave symmetrical ^{1}H- and

TABLE VII. Torsion Angles[a] (°), with Estimated Standard Deviations in Parentheses

C(8a)–O(1)–C(2)–C(3)	0.3 (3)	C(8a')–O(1')–C(2')–C(3')	−8.4 (3)
C(8a)–O(1)–C(2)–O(9)	179.3 (2)	C(8a')–O(1')–C(2')–O(9')	171.4 (2)
C(2)–O(1)–C(8a)–C(4a)	−2.2 (3)	C(2')–O(1')–C(8a')–C(4a')	6.9 (2)
C(2)–O(1)–C(8a)–C(8)	178.4 (2)	C(2')–O(1')–C(8a')–C(8')	−173.3 (2)
O(1)–C(2)–C(3)–C(4)	1.5 (4)	O(1')–C(2')–C(3')–C(4')	4.8 (4)
O(9)–C(2)–C(3)–C(4)	−177.4 (3)	O(9')–C(2')–C(3')–C(4')	−175.1 (3)
C(2)–C(3)–C(4)–C(4a)	−1.3 (4)	C(2')–C(3')–C(4')–C(4a')	0.3 (4)
C(3)–C(4)–C(4a)–C(5)	179.2 (2)	C(3')–C(4')–C(4a')–C(5')	178.4 (2)
C(3)–C(4)–C(4a)–C(8a)	−0.7 (3)	C(3')–C(4')–C(4a')–C(8a')	−2.1 (3)
C(4)–C(4a)–C(5)–C(6)	−178.3 (2)	C(4')–C(4a')–C(5')–C(6')	−179.7 (2)
C(8a)–C(4a)–C(5)–C(6)	1.6 (3)	C(8a')–C(4a')–C(5')–C(6')	0.7 (3)
C(4)–C(4a)–C(8a)–O(1)	2.4 (3)	C(4')–C(4a')–C(8a')–O(1')	−1.4 (2)
C(4)–C(4a)–C(8a)–C(8)	−178.3 (2)	C(4')–C(4a')–C(8a')–C(8')	178.8 (2)
C(5)–C(4a)–C(8a)–O(1)	−177.5 (2)	C(5')–C(4a')–C(8a')–O(1')	178.2 (2)
C(5)–C(4a)–C(8a)–C(8)	1.8 (3)	C(5')–C(4a')–C(8a')–C(8')	−1.6 (2)
C(4a)–C(5)–C(6)–C(7)	−0.9 (4)	C(4a')–C(5')–C(6')–C(7')	0.2 (4)
C(5)–C(6)–C(7)–C(8)	−3.1 (3)	C(5')–C(6')–C(7')–C(8')	−0.3 (4)
C(5)–C(6)–C(7)–O(10)	175.2 (2)	C(5')–C(6')–C(7')–O(10')	179.8 (2)
C(6)–C(7)–C(8)–C(8a)	6.1 (3)	C(6')–C(7')–C(8')–C(8a')	−0.5 (3)
C(6)–C(7)–C(8)–C(12)	−175.2 (2)	C(6')–C(7')–C(8')–C(12')	−178.4 (2)
O(10)–C(7)–C(8)–C(8a)	−172.3 (2)	O(10')–C(7')–C(8')–C(8a')	179.4 (2)
O(10)–C(7)–C(8)–C(12)	6.4 (3)	O(10')–C(7')–C(8')–C(12')	1.5 (3)
C(6)–C(7)–O(10)–C(11)	11.5 (3)	C(6')–C(7')–O(10')–C(11')	−1.8 (4)
C(8)–C(7)–O(10)–C(11)	−170.1 (2)	C(8')–C(7')–O(10')–C(11')	178.3 (2)
C(7)–C(8)–C(8a)–O(1)	173.9 (2)	C(7')–C(8')–C(8a')–O(1')	−178.4 (2)
C(7)–C(8)–C(8a)–C(4a)	−5.5 (3)	C(7')–C(8')–C(8a')–C(4a')	1.4 (2)
C(12)–C(8)–C(8a)–O(1)	−4.8 (3)	C(12')–C(8')–C(8a')–O(1')	−0.6 (2)
C(12)–C(8)–C(8a)–C(4a)	175.9 (2)	C(12')–C(8')–C(8a')–C(4a')	179.3 (1)
C(7)–C(8)–C(12)–C(13)	156.0 (2)	C(7')–C(8')–C(12')–C(13')	118.5 (2)
C(7)–C(8)–C(12)–C(12')	46.2 (2)	C(7')–C(8')–C(12')–C(12)	−136.0 (2)
C(8a)–C(8)–C(12)–C(13)	−25.4 (3)	C(8a')–C(8')–C(12')–C(13')	−59.3 (2)
C(8a)–C(8)–C(12)–C(12')	−135.3 (2)	C(8a')–C(8')–C(12')–C(12)	46.2 (2)
C(8)–C(12)–C(13)–C(14)	102.5 (2)	C(8')–C(12')–C(13')–C(14')	−117.0 (2)
C(8)–C(12)–C(13)–C(13')	−132.8 (2)	C(8')–C(12')–C(13')–C(13)	118.9 (2)
C(12')–C(12)–C(13)–C(14)	−131.9 (1)	C(12)–C(12')–C(13')–C(14')	117.0 (2)
C(12')–C(12)–C(13)–C(13')	−7.2 (1)	C(12)–C(12')–C(13')–C(13)	−7.1 (1)
C(8)–C(12)–C(12')–C(8')	14.1 (2)	C(13)–C(12)–C(12')–C(13')	7.1 (1)
C(8)–C(12)–C(12')–C(13')	133.0 (2)	C(13)–C(12)–C(12')–C(8')	−111.7 (2)
C(12)–C(13)–C(14)–C(15)	−173.8 (2)	C(12')–C(13')–C(14')–C(15')	60.9 (2)
C(12)–C(13)–C(14)–O(16)	1.4 (2)	C(12')–C(13')–C(14')–O(16')	−120.4 (2)
C(14)–C(13)–C(13')–C(12')	129.5 (2)	C(12)–C(13)–C(13')–C(14')	−111.0 (1)
C(14)–C(13)–C(13')–C(14')	11.2 (2)	C(12)–C(13)–C(13')–C(12')	7.3 (1)
C(13')–C(13)–C(14)–C(15)	78.3 (2)	C(13)–C(13')–C(14')–C(15')	166.5 (2)
C(13')–C(13)–C(14)–O(16)	−106.6 (2)	C(13)–C(13')–C(14')–O(16')	−14.8 (2)

[a] The torsion angle A–B–C–D is defined as positive if, when viewed along the B–C bond, atom A must be rotated clockwise to eclipse atom D.

^{13}C-NMR signal patterns (Table I) which overall were similar to those of **1** after allowing for some chemical shift differences. In the NOE experiments, irradiation of the signal at δ_H 4.95 (H-1'), one of the protons on the four membered ring system, gave 7 and 3% enhancements of the respective signals at δ_H 4.07 (H-2') and 2.13 (acetyl methyl-H), whereas irradiation of the signal at 4.07 (H-2') caused 8 and 4% area increases of the signals at δ_H 4.95 (H-1') and 2.13 (acetyl methyl-H), respectively. Because the structure having a *cis*, *cis*, *cis*-cyclobutane ring system may be excluded due to the severe steric strain among substituents, we propose the alternative structure (**2**) having a *trans*, *cis*, *trans*-cyclobutane ring system for C.

Experimental

All melting points were measured on a micromelting point hot-stage apparatus (Yanagimoto). ^{1}H- and ^{13}C-NMR spectra in $CDCl_3$ were recorded on GX-270 (JEOL) and GX-400 (JEOL) spectrometers, respectively, and differential NOE and H–C COSY spectra were taken with a GX-400 spectrometer on $J=5$ Hz. Chemical shifts are shown in δ-values (ppm) with tetramethylsilane (TMS) as an internal reference. EI-MS were taken with an M-52 (Hitachi) spectrometer having a direct inlet system, and HR-MS with an M-80 (Hitachi) spectrometer. UV spectra were determined in methanol and IR spectra were recorded in $CHCl_3$, unless otherwise stated.

Extraction and Isolation The acetone extract of the dried roots (800 g) of several hybrid seedlings resulting from a cross of ogonkan (ki-mikan) (*Citrus flaviculpus* HORT. *ex* TANAKA) × hyuganatsu (*C. Tamurana* HORT. *ex* TAKAHASHI) were treated in the manner reported in a previous paper,[2b)] and the AcOEt eluate from silica gel chromatography was rechromatographed over silica gel. The dichloromethane fraction was subjected to preparative, centrifugally accelerated TLC (Chromatotron) and then the benzene–AcOEt eluate was subjected to preparative TLC [iso-Pr_2O, acetone–hexane (1 : 1), acetone–$CHCl_3$ (1 : 9), and acetone–hexane (1 : 1) successively] to afford bisosthenon (**1**) (8.9 mg, 0.0011% yield). Analogous treatments of the acetone extracts of the roots of funadoko (*C. funadoko* HORT. *ex* TANAKA) and several hybrid seedlings resulting from a cross of kiyomi [*C. unshiu* MARC. (miyagawa-wase) × *C. sinensis* OSBEC. (trobita orange)] × iyo (*C. iyo* HORT. *ex* TANAKA) also afforded bisosthenon (**1**) in 0.0022 and 0.0013% yields, respectively. Isolation and characterization of other components of these *Citrus* plants will be reported elsewhere.

Bisosthenon (1) Colorless prisms, mp 234—237 °C. HR-MS: Calcd for $C_{28}H_{24}O_8$: 488.1469. Found: 488.1451. UV λ_{max} nm: 253 (sh), 260, 317. IR ν_{max} cm^{-1}: 1725, 1720, 1605. EI-MS m/z (%): 488 (M^+, 1), 445 (20), 403 (6), 244 (18, Found: 244.0740. Calcd for $C_{14}H_{12}O_4$: 244.0735), 229 (27), 213 (100), 201 (16), 189 (16).

Synthesis of Osthenon (4)[2b,5)] A mixture of 8-iodoumbelliferone (**6**)[6)]

(600 mg), methyl iodide (443 mg), and anhydrous K_2CO_3 (574 mg) in acetone (20 ml) was refluxed for 5 h in an oil bath. Diluted HCl was added, and the mixture was extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with water, dried over anhydrous $MgSO_4$, and then evaporated to dryness to give **7** in 95% yield as colorless needles, mp 155—157 °C; IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1740, 1610, 1545, 1290. ^{1}H-NMR δ_H: 7.58 (1H, d, J = 9.4 Hz, H-3), 7.44 (1H, d, J = 8.7 Hz, H-5), 6.81 (1H, d, J = 8.7 Hz, H-6), 6.27 (1H, d, J = 9.4 Hz, H-3), 4.00 (3H, s, 7-OMe). EI-MS m/z (%): 302 (M^+, 100%), 274 (35), 259 (43). Methyl vinylketone (100 mg) was added dropwise to a solution of **7** (20 mg) in dimethylformamide (DMF) (3.0 ml) containing $Pd(OAc)_2$ (10 mg), tetra-*n*-butylammonium bromide (20 mg), and NEt_3 (1 drop). The whole was refluxed for 30 min, then methyl vinyl ketone (20 mg) and $Pd(OAc)_2$ (10 mg) were added. After 2 h, the reaction mixture was diluted with water and extracted with AcOEt. The extract was washed with water, dried over anhydrous $MgSO_4$, and concentrated to dryness *in vacuo*. The residue was subjected to preparative TLC (hexane : acetone = 2 : 1) to give **4** as colorless prisms in 60% yield, mp 131—133 °C, IR $\nu_{\max}$ cm^{-1}: 1740, 1690, 1660, 1620, 1600, 1580, 1300, 1285, 1250. ^{1}H-NMR δ_H: 7.98 (1H, d, J = 16.8 Hz, H-1'), 7.65 (1H, d, J = 9.4 Hz, H-4), 7.46 (1H, d, J = 8.7 Hz, H-5), 7.34 (1H, d, J = 16.8 Hz, H-2'), 6.91 (1H, d, J = 8.7 Hz, H-6), 6.31 (1H, d, J = 9.4 Hz, H-3), 4.00 (3H, s, 7-OMe), 2.43 (3H, s, OAc). EI-MS m/z (%): 244 (M^+, 15), 229 (48), 213 (100), 201 (38), 186 (18), 173 (15). This product was identical with authentic osthenon (**4**)[2b,5] as judged from spectral comparisons (IR and ^{1}H-NMR).

Photodimerisation of Osthenon (4) (a) A solution of **4** (40 mg) in iso-PrOH (13 ml) was irradiated with a high pressure Hg-lamp through a Pyrex glass filter for 26 h at room temperature. The solvent was evaporated off *in vacuo* and the residue was subjected to preparative TLC (benzene : AcOEt = 1 : 1) to give **1** (5.8 mg, 15% yield) as colorless prisms, mp 234—237 °C. This product was found to be identical with natural bisosthenon (**1**) by spectral comparisons (IR, ^{1}H-NMR, and EI-MS). *cis*-Osthenon (**8**)[10] was also obtained in 35% yield, with 8% recovery of osthenon (*trans*-isomer) (**4**). (b) Crystalline osthenon (**4**) was irradiated with a high pressure Hg lamp through a Pyrex glass filter for 142 h at room temperature. The solid was dissolved in acetone and subjected to preparative TLC (benzene : acetone = 10 : 1) to give products A, B, and C in 16, 11, and 2% yields, respectively, accompanied with a 9% yield of *cis*-osthenon (**8**) and 35% recovery of **4**. Product A was found to be identical with natural bisosthenon (**1**) on the basis of spectral comparisons (IR, ^{1}H-NMR, and EI-MS). B (**3**): Colorless amorphous powder. HR-MS: Calcd for $C_{28}H_{24}O_8$: 488.1470. Found: 488.1489. UV $\lambda_{\max}$ nm: 256, 260, 298 (sh), 317. IR $\nu_{\max}$ cm^{-1}: 1720, 1710, 1600. EI-MS m/z (%) 488 (M^+, 2), 445 (10), 403 (9), 244 (23), 229 (23), 213 (100), 201 (14), 189 (17). C (**2**): Colorless amorphous powder. HR-MS: Calcd for $C_{28}H_{24}O_8$: 488.1469. Found: 488.1426. UV $\lambda_{\max}$ nm: 253, 261, 306 (sh), 320. IR $\nu_{\max}$ cm^{-1}: 1725, 1720, 1600. EI-MS m/z (%): 488 (M^+, 1), 445 (11), 403 (7), 244 (25), 229 (21), 213 (100), 201 (15), 189 (13).

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11) The structure of B reported in the preliminary communication[2b)] should be revised to formula **3**.