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## Two Sesquiterpene Polyesters from the Ripe Fruits of *Euonymus japonicus* Thunb

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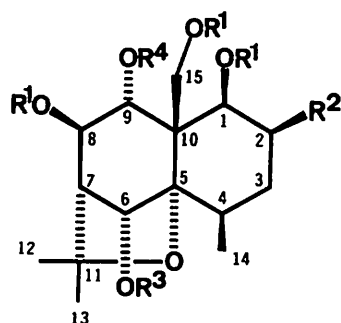
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### Abstract

Two sesquiterpene polyesters have been isolated from the ripe fruits of *Euonymus japonicus* Thunb. (Celastraceae) and shown to be two known compounds,  $1\beta$ ,  $2\beta$ ,  $6\alpha$ ,  $8\beta$ , 15-pentaacetoxy- $9\alpha$ -benzoyloxy- $\beta$ -dihydroagarofuran (Ejap-4) and its 2-deacetoxy derivative (Ejap-3). Some physical data which have not reported in the previous paper are described and the anomalous upfield shift of the  $^1\text{H}$  NMR signal associated with an acetoxy group at C-1 in each of the compounds is discussed.

Various  $\beta$ -dihydroagarofuran sesquiterpenes have been isolated from the plants of Celastraceae.<sup>1-6)</sup> In the continuation of our chemical studies on native plants of Okinawa, we investigated the constituents of the ripe fruits of *Euonymus japonicus* Thunb. (Celastraceae) and isolated two known compounds which have been identified to be Ejap-3 (1) and Ejap-4 (2).<sup>5)</sup> In this paper, we describe some physical data which have been not reported in the previous paper<sup>5)</sup> and the cause of the anomalous upfield shift of the signal associated with an acetoxy group at C-1 in the  $^1\text{H}$  NMR spectrum of each of the compounds. Compounds 1 and 2 were analyzed for  $\text{C}_{30}\text{H}_{38}\text{O}_{11}$  and  $\text{C}_{32}\text{H}_{40}\text{O}_{13}$  by elemental analysis and mass spectroscopy, respectively. The IR spectra of 1 and 2 were very similar, and each contained bands assignable to ester carbonyl groups ( $1740$  and  $1710\text{cm}^{-1}$ ) and a monosubstituted benzene ring ( $1600$ ,  $1500$  and  $710\text{cm}^{-1}$ ). Both showed nearly identical UV spectra [ $1: \lambda_{\text{max}}^{\text{MeOH}}$  229 nm ( $\epsilon$  13400),  $2: \lambda_{\text{max}}^{\text{MeOH}}$  233 nm ( $\epsilon$  13000)], which are consistent with benzoate functions. The  $^1\text{H}$  NMR spectrum of 2 showed characteristic for five acetate groups [ $\delta$  1.45 (3H, s), 2.06 (3H, s), 2.09 (3H, s), 2.19 (3H, s) and 2.25 (3H, s)], two tertiary methyl groups [ $\delta$  1.42 (3H, s) and 1.55 (3H, s)], one secondary methyl group [ $\delta$  1.16 (3H, d,  $J=7.7$  Hz)], and one benzoate group [ $\delta$  7.40-7.45 (2H, m), 7.55-7.59 (1H, m) and 7.97-8.00 (2H, m)]. Furthermore, the  $^1\text{H}$  NMR spectrum of 2 contained five



	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>
1	CH <sub>3</sub> CO	H	CH <sub>3</sub> CO	PhCO
2	CH <sub>3</sub> CO	CH <sub>3</sub> COO	CH <sub>3</sub> CO	PhCO
3	H	H	CH <sub>3</sub> CO	PhCO
4	H	H	CH <sub>3</sub> CO	H

methine signals assignable to protons on carbon atoms carrying five secondary ester groups and an AB quartet assigned to two protons at the C-15. The  $^1\text{H}$  NMR spectrum of 1 was very similar to that of 2 except for the absence in 1 of two signals due to an acetyl methyl and a proton on a carbon atom carrying a secondary acetate group. Analysis of the above data, coupled with inspection of  $^{13}\text{C}$  NMR spectra of 1 and 2, revealed 1 and 2 to be polyesters of  $\beta$ -dihydroagarofuran sesquiterpenes.

$^1\text{H}$ - $^1\text{H}$  correlation spectroscopy (COSY) (Fig. 1) and spin decoupling experiments allowed the substitution patterns of the nuclei of 2 and 1 to be elucidated as  $1\beta$ ,  $2\beta$ ,  $6\alpha$ ,  $8\beta$ ,  $9\alpha$ , 15-hexaacyloxy- $\beta$ -dihydroagarofuran and its 2-deacetoxy derivative, respectively. Hydrolysis of 1 with dilute methanolic NaOH yielded compounds 3 and 4. Consequently, 1 could be identified as  $1\beta$ ,  $6\alpha$ ,  $8\beta$ , 15-tetraacetoxy-9 $\alpha$ -benzoyloxy- $\beta$ -dihydroagarofuran, Ejap-3 $^{51}$ , and 2 as its  $2\beta$ -acetoxy derivative, Ejap-4. $^{51}$  Furthermore,  $^1\text{H}$ - $^{13}\text{C}$  COSY spectra of 1 and 2 enabled the assignments of the  $^{13}\text{C}$  NMR chemical shifts of the nuclei (Table 1).

It is noteworthy that an acetyl methyl at C-1 in 1 resonances at  $\delta$  1.48 ( $\delta$  1.45 in 2). This anomalous upfield shift can be attributed to an anisotropic shielding effect by a benzoate at C-9 as proposed in case of  $\beta$ -dihydroagarofuran compounds which have an acetate at C-9 and a benzoate at C-1. $^{61}$  Examination of a molecular model of 1 shows the acetyl methyl comes to the shielding zone of the benzene ring in its preferred conformation (Fig. 3).

Table 1.  $^{13}\text{C}$  NMR data for the skeletal carbons of 1 and 2 (100 MHz,  $\text{CDCl}_3$ , TMS as internal standard)

Carbon	1	2
1	73.6 d	71.5 d
2	22.2 t	69.1 d
3	26.2 t	31.0 t
4	33.0 d	32.7 d
5	90.0 s	89.7 s
6	75.0 d	74.8 d
7	53.0 d	53.0 d
8	76.9 d	76.9 d
9	74.3 d	73.9 d
10	52.5 s	52.6 s
11	81.3 s	81.5 s
12	25.7 q	25.7 q
13	30.3 q	30.2 q
14	15.6 q	16.9 q
15	65.3 t	65.5 t

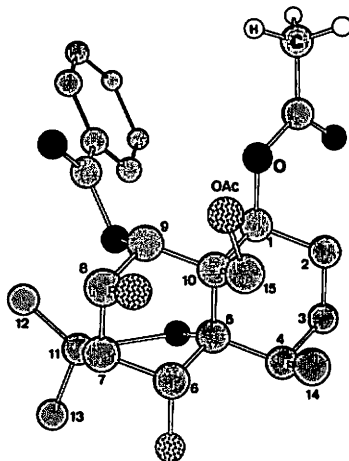


Fig. 3. Postulated conformation of compound 1 in  $\text{CDCl}_3$ .

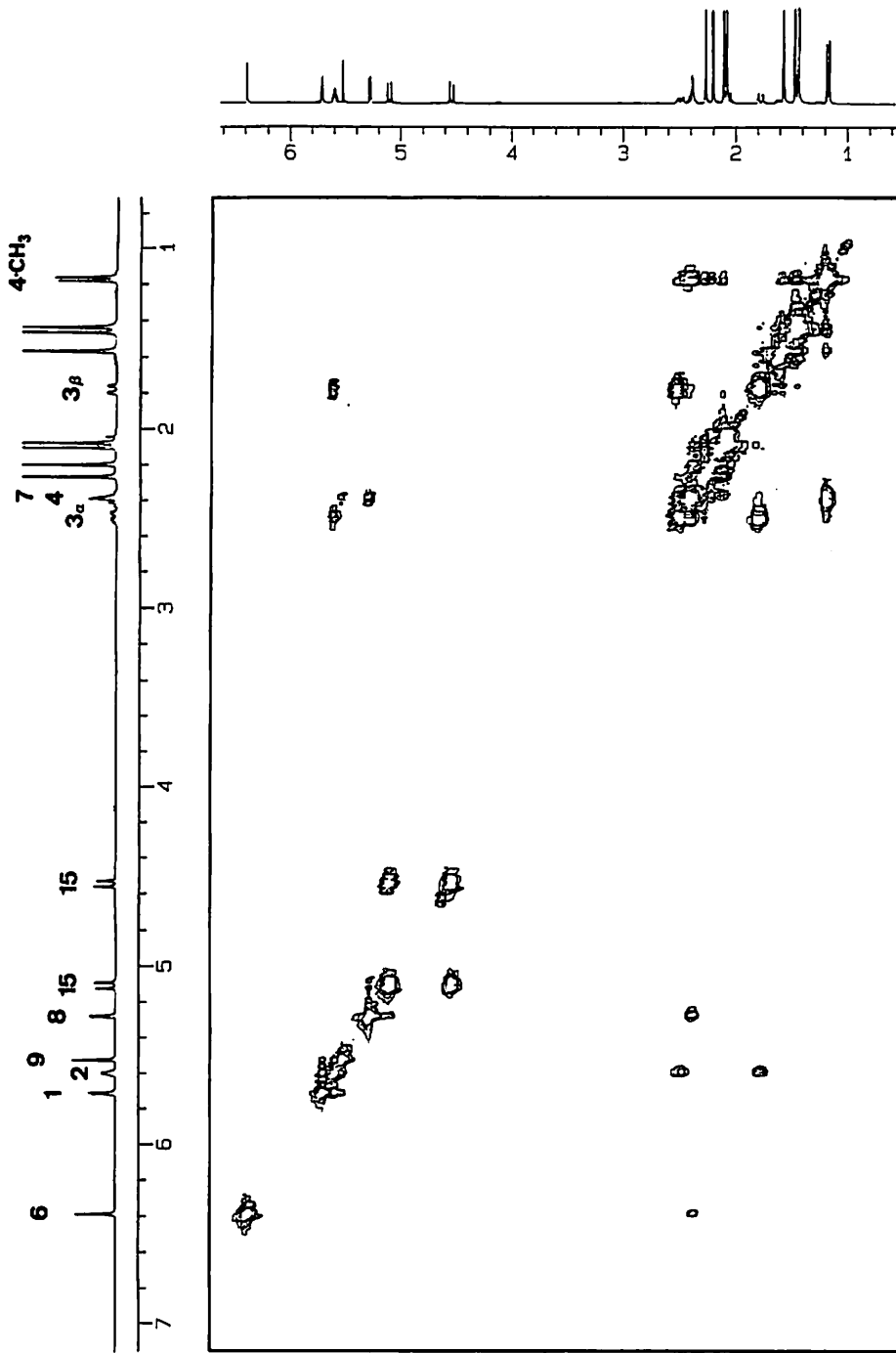


Fig. 1.  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of compound 2 in  $\text{CDCl}_3$ . Signals due to the benzoate group are not showed.

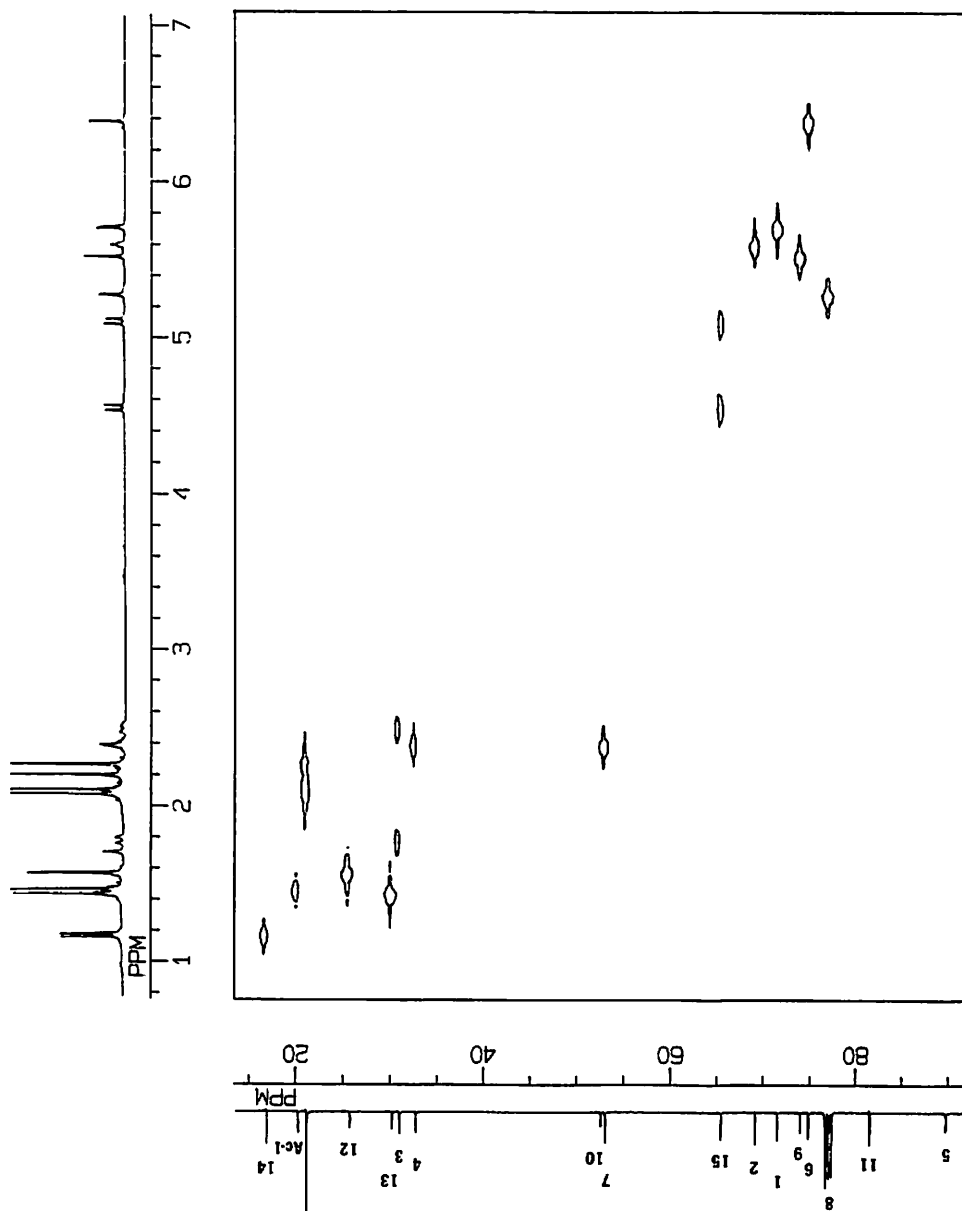


Fig. 2.  $^1\text{H}$ - $^{13}\text{C}$  COSY spectrum of compound 2 in  $\text{CDCl}_3$ . Signals associated with the benzoate group and  $\text{sp}^2$  carbon atoms in five acetate groups are not showed.

### Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded on a PERKIN ELMER 1600 FT IR spectrometer. Ultraviolet (UV) spectra were measured in MeOH on a JASCO UVIDEQ-610 spectrometer. Optical rotations were determined using a 2 dm cell of 3 ml capacity on a ATAGO A-55 digital polarimeter. Nuclear magnetic resonance (NMR) spectra were recorded at 93.94 kG (400 MHz for  $^1\text{H}$ , 100 MHz for  $^{13}\text{C}$ ) in  $\text{CDCl}_3$  on a JEOL JNM-400 FT NMR instrument. Chemical shifts were reported as values in parts per million relative to tetramethylsilane ( $\delta=0.00$ ) as an internal standard and coupling constants in Hz (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet). Analytical thinlayer chromatography (TLC) was conducted on precoated TLC plates, silica gel 60 F-254 (layer thickness 0.25mm) manufactured by E. Marck. Preparative TLC was performed by using 0.5mm precoated silica gel 60 PF-254 plates manufactured by E. Merck. Silica gel (Wakogel C-200) was used for column chromatography.

**Isolation of Compound 1.** Fresh ripe fruits (4.2 kg) of *Euonymus japonicus* Thunb. were crushed with 95% ethanol in a blender. After filtration, the extract was concentrated and the residue was partitioned between ether and water. The residue of the organic layer was chromatographed on a silica gel column to give a mixture of 1 and 2. PTLC separation (benzene-ethyl acetate=9:1) gave 520mg of 1 and 490mg of 2. Pure samples of 1 and 2 were obtained by recrystallization from ethyl acetate-methanol.

**Compound 1.** Colorless flat prisms; mp 133-137° :  $[\alpha]_D^{23} -13^\circ$  (c 1.173,  $\text{CHCl}_3$ ); UV  $\lambda_{\text{max}}^{\text{MeOH}}$  nm ( $\epsilon$ ): 199 (8200), 229 (13400), 272 (740) and 280 (710); IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 2975, 2920, 1740, 1710, 1600, 1500, 1450, 1362, 1278, 1230, 1150, 1100, 1050, 1020, 710;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  0.98 (3H, d,  $J=7.3$  Hz,  $\text{CH}_3$ -4), 1.42 (3H, s,  $\text{CH}_3$ -13), 1.46 (1H, m, H. or  $\beta$ -3), 1.48 (3H, s,  $\text{CH}_3\text{CO}$ ), 1.56 (3H, s,  $\text{CH}_3$ -12), 1.6 (1H, m, H. or  $\beta$ -2), 1.98 (1H, m, H. or  $\beta$ -2), 2.10 (3H, s,  $\text{CH}_3\text{CO}$ ), 2.19 (3H, s,  $\text{CH}_3\text{CO}$ ), 2.26 (3H, s,  $\text{CH}_3\text{CO}$ ), 2.22-2.35 (2H, m, H.-4 and H. or  $\beta$ -3), 2.37 (1H, br d,  $J=3.2$  Hz,  $\text{H}_\beta$ -7), 4.61 and 4.64 (2H, AB q,  $J=12.6$  Hz,  $\text{CH}_2\text{OAc}$ -15), 5.27 (1H, d,  $J=3.2$  Hz, H.-8), 5.51 (1H, s,  $\text{H}_\beta$ -9), 5.58 (1H, dd,  $J=12.0, 4.6$  Hz, H.-1), 6.35 (1H, br s,  $\text{H}_\beta$ -6), 7.43-7.47 (2H, m, ArH), 7.56-7.61 (1H, m, ArH), 8.01-8.04 (2H, m, ArH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ): see Table 1 for the skeletal carbons.  $\delta$  20.8 (q,  $\text{CH}_3\text{CO}$ -1), 21.2 (q,  $\text{CH}_3\text{CO}$ ), 21.3 (q,  $\text{CH}_3\text{CO}$ ), 21.3 (q,  $\text{CH}_3\text{CO}$ ), 128.5 (d, C-3 of the benzoate), 128.7 (s, C-1 of the benzoate), 130.1 (d, C-2 of the benzoate), 133.7 (d, C-4 of the benzoate), 164.6 (s,  $\text{CH}_3\text{CO}$ ), 169.6 (s,  $\text{CH}_3\text{CO}$ ), 169.7 (s,  $\text{CH}_3\text{CO}$ ), 169.8 (s,  $\text{CH}_3\text{CO}$ ), 170.6 (s,  $\text{CH}_3\text{CO}$ ); FABMAS  $m/z$ : 575  $[\text{M}+\text{H}]^+$ , 532  $[\text{M}-\text{CH}_2\text{CO}]^+$ , 515  $[\text{M}+\text{H}-\text{AcO}]^+$ , 105  $[\text{PhCO}]^+$ ; (found: C, 61.9; H, 6.8.  $\text{C}_{30}\text{H}_{38}\text{O}_{11}$   $1/2$   $\text{H}_2\text{O}$  requires: C, 61.7; H, 6.7%). The  $^1\text{H}$  NMR spectrum was identical with that of Ejap-3.<sup>5)</sup>

**Compound 2.** Colorless prisms; mp 245-247° :  $[\alpha]_D^{23} +4.2^\circ$  (c 1.204,  $\text{CHCl}_3$ ); UV  $\lambda_{\text{max}}^{\text{MeOH}}$  nm ( $\epsilon$ ): 202 (9160), 233 (13100), 274 (1050), 284 (737); IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 2970, 2925, 1740, 1710, 1600, 1500, 1450, 1365, 1278, 1230, 1145, 1100, 1040, 1020, 710;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.16 (3H, d,  $J=7.7$  Hz,  $\text{CH}_3$ -4), 1.42 (3H, s,  $\text{CH}_3$ -13), 1.45 (3H, s,  $\text{CH}_3\text{CO}$ ), 1.55 (3H, s,  $\text{CH}_3$ -12), 1.76 (1H, br dd,  $J=15.0, 3.0$  Hz,  $\text{H}_\beta$ -3), 2.06 (3H, s,  $\text{CH}_3\text{CO}$ ), 2.09 (3H, s,  $\text{CH}_3\text{CO}$ ), 2.19 (3H, s,  $\text{CH}_3\text{CO}$ ), 2.25 (3H, s,  $\text{CH}_3\text{CO}$ ), 2.38 (1H, br qd,  $J=7.7, 6.6$  Hz, H.-4), 2.39 (1H, br d,  $J=2.9$  Hz,  $\text{H}_\beta$ -7), 2.49 (1H, ddd,  $J=15.0, 6.6, 4.0$  Hz, H.-3), 4.52 and 5.09 (2H, AB q,  $J=12.8$  Hz,  $\text{CH}_2\text{OAc}$ -15), 5.26 (1H,

d,  $J=2.9$  Hz, H <sub>$\beta$</sub> -8), 5.51(1H, s, H <sub>$\beta$</sub> -9), 5.59(1H, ddd,  $J=4.0, 4.0, 3.0$  Hz, H <sub>$\alpha$</sub> -2), 5.70(1H, d,  $J=4.0$  Hz, H <sub>$\alpha$</sub> -1), 6.37(1H, br s, H <sub>$\beta$</sub> -6), 7.40-7.45(2H, m, ArH), 7.55-7.59(1H, m, ArH), 7.97-8.00(2H, m, ArH); <sup>13</sup>C NMR (CDCl<sub>3</sub>): <sup>13</sup>C NMR (CDCl<sub>3</sub>): see Table 1 for the skeletal carbons.  $\delta$  20.3(q, CH<sub>3</sub>CO-1), 21.1(q, CH<sub>3</sub>CO), 21.2(q, C x 3, CH<sub>3</sub>CO), 128.4(d, C-3 of the benzoate), 128.4(s, C-1 of the benzoate), 130.1(d, C-2 of the benzoate), 133.7(d, C-4 of the benzoate), 164.6(s, CH<sub>3</sub>CO), 169.2(s, CH<sub>3</sub>CO), 169.5(s, CH<sub>3</sub>CO), 169.7(s, CH<sub>3</sub>CO), 169.8(s, CH<sub>3</sub>CO), 170.5(s, CH<sub>3</sub>CO); FDMS  $m/z$  633 [M+H]<sup>+</sup>, 632[M]<sup>+</sup>, 617[M-CH<sub>3</sub>]<sup>+</sup>; (Found: C, 60.4; H, 6.3. C<sub>32</sub>H<sub>40</sub>O<sub>13</sub> requires: C, 60.8; H, 6.3%). The <sup>1</sup>H NMR spectrum was identical with that of Ejap-4.<sup>5)</sup>

*Partial hydrolysis of compound 1.* A Solution of 9mg of 1 in 1.5ml of 1% methanolic NaOH and 1.5ml of methanol was stirred at room temperature for 2 hrs. The reaction mixture was neutralized with dilute HCl. Solvent removal followed by chromatographic separation (PTLC) afforded compounds 3 (1mg) and 4 (1mg).

*Compound 3.* IR  $\nu_{\text{max}}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 2931, 1730, 1709, 1277, 1245, 1107; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.92(3H, d,  $J=8$  Hz, CH<sub>3</sub>-4), 1.40(3H, s, CH<sub>3</sub>-12 or 13), 1.42(3H, s, CH<sub>3</sub>-12 or 13), 2.06(3H, s, COCH<sub>3</sub>-6), 2.36(1H, d,  $J=3$  Hz, H <sub>$\beta$</sub> -7), 3.88 and 4.38(2H, AB q,  $J=12$  Hz, CH<sub>2</sub>OH-15), 4.33(1H, d,  $J=3$  Hz, H <sub>$\alpha$</sub> -8), 4.46(1H, dd,  $J=12, 4$  Hz, H <sub>$\alpha$</sub> -1), 5.66(1H, s, H <sub>$\beta$</sub> -9), 5.81(1H, br s, H <sub>$\beta$</sub> -6), 7.40-7.45(2H, m, ArH), 7.52-7.55(1H, m, ArH), 8.02-8.06(2H, m, ArH); FDMS  $m/z$  450 [M+2H]<sup>+</sup>, 449[M+H]<sup>+</sup>, 433[M-CH<sub>3</sub>]<sup>+</sup>, 105 [PhCO]<sup>+</sup>.

*Compound 4.* IR  $\nu_{\text{max}}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 2931, 1731, 1369, 1255, 1091, 1016; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.96(3H, d,  $J=8$  Hz, CH<sub>3</sub>-4), 1.40(3H, s, CH<sub>3</sub>-12 or 13), 1.56(3H, s, CH<sub>3</sub>-12 or 13), 2.08(3H, s, COCH<sub>3</sub>-6), 2.38(1H, d,  $J=3$  Hz, H <sub>$\beta$</sub> -7), 3.88 and 4.44(2H, AB q,  $J=12$  Hz, CH<sub>2</sub>OH-15), 4.31(1H, br s, H <sub>$\beta$</sub> -9), 4.44(1H, dd,  $J=12, 4$  Hz, H <sub>$\alpha$</sub> -1), 4.51(1H, d,  $J=3$  Hz, H <sub>$\alpha$</sub> -8), 5.75(1H, s, H <sub>$\beta$</sub> -6); FDMS  $m/z$  346 [M+2H]<sup>+</sup>, 345[M+H]<sup>+</sup>, 344 [M]<sup>+</sup>, 329[M-CH<sub>3</sub>]<sup>+</sup>.

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