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A HIGHLY EFFICIENT PREPARATION OF LUNULARIC ACID AND SOME BIOLOGICAL ACTIVITIES OF STILBENE AND DIHYDROSTILBENE DERIVATIVES

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Key Word Index—Lunularic acid; dihydrostilbenes; stilbenes; hydrangenol; dihydroisocoumarin; sodium borohydride–palladium chloride reduction; dormancy; plant growth inhibitory activity; piscicidal activity; hyaluronidase inhibitory activity.

Abstract—Lunularic acid, an acid possessing dormancy inducing, antifungal, thromboxane synthetase and hyaluronidase inhibitory and plant growth inhibitory activities, was obtained quantitatively from hydrangenol by reduction using sodium borohydride–palladium chloride. Some stilbene and dihydrostilbene derivatives prepared from hydrangenol and its glucoside also showed plant growth inhibitory, hyaluronidase inhibitory and piscicidal activities.

INTRODUCTION

Lunularic acid (**1**), a dihydrostilbenic acid isolated from the liverwort, *Lunularia cruciata* (L.) Dum., possesses dormancy inducing [1], antifungal [2] and plant growth inhibitory activities [3]. Recently, Sankawa *et al.* [4] reported that **1** is present in the higher plant, *Allium chinense* G. Don (= *A. bakeri* Regel.) and shows potent thromboxane synthetase inhibitory activity. Although compound **1** is widely distributed in the Hepaticae [5, 6], and in *Allium* species it is only present in very small amounts.

Stilbene derivatives possessing phenolic hydroxyl groups display estrone-like [7], antimicrobial [8, 9], piscicidal [9, 10], plant growth inhibitory [9], antihypertensive and coronary vasodilatory activities [11]. In the course of our investigations of the physiological activities of natural stilbene and dihydrostilbene derivatives, we showed that some of them also possessed potent hyaluronidase inhibitory activity.

In order to obtain large quantities of these compounds for detailed studies on their biological activities, we looked for a facile synthesis of **1** and its derivatives in high yield and reached the conclusion that the reduction of hydrangenol (**3**) and its glucoside (**2**) with sodium borohydride–palladium chloride [12] was the best method. In this paper, we wish to report the highly efficient preparation of lunularic acid (**1**) and its glucoside (**4**) and the plant growth inhibitory, piscicidal and hyaluronidase inhibitory activities of a number of stilbene and dihydrostilbene derivatives.

RESULTS AND DISCUSSION

Hydrangenol 8-β-D-glucoside (**2**) was easily obtained from the leaves of *Hydrangea macrophylla* Seringe var. *otaksa* Makino (Saxifragaceae) in 100 g amounts [13]. Hydrolysis of **2** with dilute acid gave hydrangenol (**3**) [14] in good yield. Treatment of **3** with sodium borohydride–palladium chloride in methanol at room temperature [12] yielded the stoichiometric amount of lunularic acid (**1**), the spectral (see Tables 1 and 2) and physical data of which were identical to those of authentic lunularic acid (**1**) (see Experimental).

Compound **1** has been obtained: from hydrangenol (**3**) by reduction using sodium–ethanol [1]; by total synthesis from 8-methoxy-3-*p*-methoxyphenylisocoumarin (**16**) prepared from Diels–Alder reaction of 1-methoxycyclohexa-1,3-diene and dimethylallen-1,3-dicarboxylate in 21% yield in five steps [3, 15]; by synthesis from **16** derived from phenyl β-chloropropionate in ten steps [16]. The yield of **1** by these reactions is very poor. The present preparation of **1** is a one step procedure and the work-up of the reaction mixture is very simple.

Treatment of **2** by the same condition as described above afforded lunularic acid 3-β-D-glucopyranoside (**4**) in 87% yield. By previously known methods, several stilbene derivatives (**5**–**15**) were prepared from **2**, **3** or **4** and their structures confirmed by spectral methods (see Tables 1 and 2 and Experimental).

Plant growth inhibitory activity of the dihydrostilbene and stilbene derivatives against rice seeds is shown in Table 3. It can be seen that compounds **1**, **6**, **10** and **12** show inhibition of germination and of elongation of the second coleoptile. The most active compound is methyl hydrangeate (**10**) which completely inhibits germination at a concentration of 150 ppm. Compounds **2**–**5**, **7**–**9**, **11** and **13**–**15** are inactive. Thus, it is obvious that the plant growth inhibitory activity of the stilbene derivatives examined results from the presence of the phenolic hydroxyl groups at C-3 and C-4′.

The piscicidal activity was examined against killi-fish (= *Oryzia latipes*). The fish were killed within one hour by an 8 ppm solution of **12** and **13** and within two hours by

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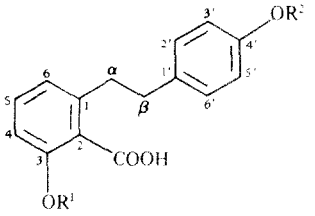
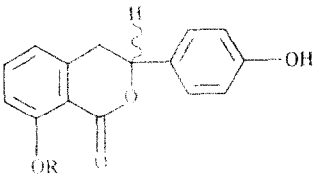
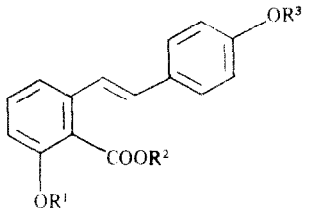


1 $R^1 = R^2 = H$
4 $R^1 = \beta$-D-Glc, $R^2 = H$
5 $R^1 = \beta$-D-GlcAc$_4$, $R^2 = Ac$



2 R = β-D-Glc
3 R = H



6 $R^1 = R^2 = R^3 = H$
7 $R^1 = \beta$-D-Glc, $R^2 = R^3 = H$
8 $R^1 = R^2 = R^3 = Me$
9 $R^1 = R^3 = Me$, $R^2 = H$
10 $R^1 = R^3 = H$, $R^2 = Me$
11 $R^1 = R^3 = Ac$, $R^2 = Me$
12 $R^1 = R^3 = H$, $R^2 = Et$
13 $R^1 = H$, $R^2 = R^3 = Et$
14 $R^1 = R^3 = Ac$, $R^2 = Et$
15 $R^1 = Ac$, $R^2 = R^3 = Et$

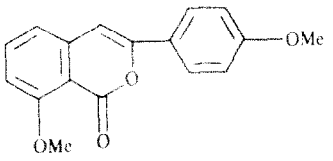


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Table 1. ^{1}H NMR data for

H	1	4	5	6	7	8
4	6.68 *d* (8.3)†	7.70 *d* (7.6)	6.97 *d* (7.3)	6.86 *d* (7.6)	7.11 *d* (7.3)	6.88 *d* (8.1)
5	7.25 *dd* (8.3, 8.3)	7.15 *dd* (7.6, 7.6)	7.26 *dd* (7.3, 7.3)	7.41 *dd* (7.6, 7.6)	7.24 *dd* (7.3, 7.3)	7.33 *dd* (8.1, 8.1)
6	6.78 *d* (8.3)	6.86 *d* (7.6)	6.88 *d* (7.3)	7.18 *d* (7.6)	7.41 *d* (7.3)	7.26 *d* (8.1)
α	3.14 *t* (8.5)	2.96 *t* (8.6)	2.97 *t* (8.5)	7.76 *d* (15.4)	7.18 *d* (16.4)	7.04 *d* (16.1)
β	2.76 *t* (8.5)	2.85 *t* (8.6)	2.92 *t* (8.5)	6.91 *d* (15.4)	7.07 *d* (16.4)	6.91 *d* (16.1)
2′,6′	7.00 *d* (8.6)	7.01 *d* (8.5)	7.16 *d* (8.1)	7.42 *d* (8.6)	7.37 *d* (8.6)	7.40 *d* (8.3)
3′,5′	6.70 *d* (8.6)	6.68 *d* (8.5)	6.96 *d* (8.1)	6.85 *d* (8.6)	6.77 *d* (8.6)	6.90 *d* (8.3)
		4.86 *d* (7.7)	5.08 *d* (7.6)		4.89 *d* (7.6)	
Ac			2.02, 2.05, 2.08, 2.10, 2.28 *s*			
OMe						3.81, 3.84 *s*
CO_2Me						3.95 *s*
CO_2H						
3-OH						
4′-OH						
OCH_2Me						
OCH_2Me						
CO_2CH_2Me						
CO_2CH_2Me						

*Compounds **5**, **8**–**15** were measured in $CDCl_3$ solution, TMS as internal standard. Compounds **1**, **4**, **6** and **7** were
†J = Hz in parenthesis.

the same concentration of **8** and **10**. The activity of these compounds is more significant than the other natural stilbenes tested [9, 10]. Compound **14** showed some activity. However, compounds **1**–**7**, **9**, **11** and **15** showed no activity. It is quite clear from these data that the piscicidal activity of the stilbenes tested is related to the presence of methyl or ethyl ester groups in the molecules.

The anti-hyaluronidase activity of the synthetic stilbene derivatives was tested in the presence of 2.5 mM calcium chloride as activator of the enzyme [17]. Compounds **1**, **6**, **9** and **10** showed concentration-dependent inhibitory activity. Compound **6** showed the strongest inhibitory activity (IC_{50} 0.05 mM) of the compounds tested. This activity is 10 times stronger than that of tranilast (*N*-3′,4′-dimethoxycinnamoylanthranilic acid) which is anti-allergenic agent developed in Japan for oral administration. Compounds **1** and **9** are less active (IC_{50} 0.13 mM in **1** and 0.14 mM in **9**) than **6**, but more active than tranilast. Compound **10** showed the same inhibitory activity (ID_{50} 0.5 mM) as that of tranilast. Details of hyaluronidase inhibitory activity of the other stilbene and isocoumarin derivatives and their application as new antiallergenic agents will be reported elsewhere.

EXPERIMENTAL

Mps: uncorr. The solvents used for spectral determinations were: TMS–$CDCl_3$ [^{1}H (400 MHz) and ^{13}C NMR (100 MHz)]; EtOH (UV) and MeOH ($[\alpha]_D$) unless otherwise stated. IR: KBr.

Bioassay. Plant growth inhibitory activity was measured using a modified method of ref. [18] in which $(Me)_2CO$ instead of MeOH was used to dissolve the test sample. Piscicidal activity was tested using a modified method of ref. [19] in which $(Me)_2CO$ was used in place of MeOH. The inhibitory effect of stilbene derivatives on hyaluronidase was tested by the method of ref. [17].

Extraction and isolation of hydrangenol 8-β-D-glucoside (**2**). Fresh leaves (137 kg) of *Hydrangea macrophylla* var. *otaksa* (= *H. macrophylla* var. *macrophylla*) were heated for 10 min at 90° and extracted (× 3) with hot H_2O (250 l) for 1 hr with stirring. The combined H_2O extract was concd *in vacuo* to 73 l and extracted (× 3) with EtOAc (43 l). The vol. of solvent was reduced *in vacuo* to 5 l and the resultant solution allowed to stand overnight at 0° to ppt. crystals of the isocoumarin glucoside **2** (584 g) [13, 21], whose spectral and physical data were identical to those of authentic [20] and reported hydrangenol 8-β-D-glucoside (**2**) [13].

Acid hydrolysis of **2**. Compound **2** (20.0 g) and 0.5 M H_2SO_4 (600 ml) were refluxed for 1 hr at 80–90° with stirring. The reaction mixture was extracted with EtOAc and the extract was washed (× 2) with H_2O and dried over $MgSO_4$. Evaporation of the solvent gave a residue (11.4 g) which was chromatographed on silica gel (150 g) eluted by $CHCl_3$ containing increasing amounts of EtOAc to give hydrangenol (**3**) (10.4 g) (73.5%), the spectral and physical data of which were identical to those of authentic [20] and reported hydrangenol [14].

Reduction of **3**. To a stirred soln of **3** (3.0 g) in MeOH (500 ml) was added $PdCl_2$ (2.16 g). $NaBH_4$ (1.33 g) was then added to the reaction mixture over a period of 10 min at room temp. and stirring was continued for 1 hr. The resulting mixture was filtered and the filtrate concd *in vacuo* to give the crude dihydrostilbene, which was partitioned between EtOAc and H_2O. The EtOAc extract, after removal of the solvent, gave the required dihydrostilbenic acid **1** (3.10 g) (99.6%). Mp 200–201°; UV λ_{max} nm (log ε): 218 (4.27), 281 (3.53), 287 (3.55) and 310.5 (3.61); IR ν_{max} cm^{-1}: 3475, 3250–2400, 1652, 1605, 1515, 1468, 1445, 1245, 1205 and 825; ^{1}H and ^{13}C NMR: see Tables 1 and 2; HRMS: $[M]^+$ (found; 285.0898; calc. for $C_{15}H_{14}O_4$ 258.0892); EIMS *m/z* (rel. int.): 258 $[M]^+$ (9), 108 (7) and 107 (100); (found: C, 69.93; H, 5.45. $C_{15}H_{14}O_4$ requires C, 69.75; H, 5.46). All these data were in good agreement with those of lunularic acid (**1**) [1, 3, 16].

Reduction of hydrangenol 8-β-D-glucopyranoside (**2**). Compound **2** (3.0 g) was treated in the same manner as described above. The reaction mixture (3.05 g) was chromatographed on silica gel using a $CHCl_3$–MeOH gradient to give lunularic acid 3-*O*-β-D-glucopyranoside (**4**) (2.63 g) (87%); $[\alpha]_D + 11.3°$ (*c* 1.1);

compounds **1**, **14**–**15***

9	10	11	12	13	14	15
6.86 *d* (8.1)	6.88 *d* (8.3)	6.91 *d* (8.1)	6.92 *d* (8.2)	6.89 *d* (7.3)	7.05 *d* (8.1)	7.02 *d* (7.8)
7.38 *d* (8.1, 8.1)	7.34 *dd* (8.3, 8.3)	7.30 *dd* (8.1, 8.1)	7.37 *dd* (8.2, 8.2)	7.34 *dd* (7.3, 7.3)	7.43 *dd* (8.1, 8.1)	7.41 *dd* (7.8, 7.8)
7.31 *d* (8.1)	7.01 *d* (8.3)	7.41 *d* (8.1)	7.06 *d* (8.2)	7.04 *d* (7.3)	7.56 *d* (8.1)	7.55 *d* (7.8)
7.27 *d* (16.1)	7.50 *d* (16.1)	7.06 *d* (16.4)	7.60 *d* (16.1)	7.58 *d* (15.9)	7.21 *d* (16.1)	7.12 *d* (16.1)
7.04 *d* (16.1)	6.71 *d* (16.1)	6.88 *d* (16.4)	6.75 *d* (16.1)	6.74 *d* (15.9)	7.02 *d* (16.1)	7.00 *d* (16.1)
7.44 *d* (8.8)	7.32 *d* (8.8)	7.34 *d* (8.5)	7.37 *d* (8.6)	7.39 *d* (8.8)	7.47 *d* (8.5)	7.40 *d* (8.5)
6.86 *d* (8.8)	6.78 *d* (8.8)	6.95 *d* (8.5)	6.84 *d* (8.6)	6.87 *d* (8.8)	7.04 *d* (8.5)	6.88 *d* (8.5)
		2.14, 2.16 *s*			2.29, 2.30 *s*	2.28 *s*
3.80, 3.90 *s*						
	3.97 *s*	3.79 *s*				
8.50 *br s*						
	11.10 *br s*		11.30 *br s*	11.25 *br s*		
	5.18 *br s*		5.40 *br s*			
			4.43 *q* (7.1)	4.05 *q* (7.0)	4.40 *q* (7.1)	4.04 *q* (7.8)
			1.40 *t* (7.1)	1.41 *t* (7.0)	1.37 *t* (7.1)	1.42 *q* (7.8)
				4.43 *q* (7.0)		4.41 *q* (7.8)
				1.41 *t* (7.0)		1.38 *t* (7.8)

measured in CD_3OD.

Table 2. ^{13}C NMR data of compounds **1**, **4**–**10**, **12** and **13***

C	**1**	**4**	**5**	**6**	**8**	**9**	**10**	**12**	**13**
1	146.5 *s*	140.3 *s*	140.7 *s*	136.4 *s*	136.3 *s*	137.6 *s*	141.3 *s*	141.6 *s*	141.5 *s*
2	115.4 *s*	134.1 *s*†	124.3 *s*	114.5 *s*	109.4 *s*	109.7 *s*	110.5 *s*	111.0 *s*	110.9 *s*
3	163.2 *s*	154.8 *s*	153.6 *s*	155.7 *s*	156.5 *s*	156.9 *s*	156.5 *s*	162.2 *s*	162.4 *s*
4	116.6 *d*	115.3 *d*	112.9 *d*	114.5 *d*	117.4 *d*	118.2 *d*	116.6 *d*	116.6 *d*	116.5 *d*
5	134.8 *d*	129.5 *d*	130.6 *d*	130.8 †	131.2 *d*†	131.2 *d*†	130.6 *d*	130.3 *d*	130.3 *d*
6	123.8 *d*	124.9 *d*	124.5 *d*	116.1 *d*	122.6 *d*	123.2 *d*	119.5 *d*	119.6 *d*	119.3 *d*
1′	135.0 *s*	132.5 *s*†	138.9 *s*	128.9 *s*	129.6 *s*	129.7 *s*	130.4 *s*	130.4 *s*	130.0 *s*
2′,6′	130.8 *d*	130.3 *d*	129.5 *d*	128.9 *d*	127.9 *d*	128.1 *d*	128.1 *d*	128.0 *d*	127.7 *d*
3′,5′	116.5 *d*	116.0 *d*	121.4 *d*	115.7 *d*	114.0 *d*	114.1 *d*	115.7 *d*	115.7 *d*	114.6 *d*
4′	156.8 *s*	156.3 *s*	148.9 *s*	157.3 *s*	159.5 *s*	159.6 *s*	159.5 *s*	155.5 *s*	158.7 *s*
α	39.2 *t*†	37.6 *t*‡	36.9 *t*†	130.5 *d*†	130.3 *d*‡	131.6 *d*‡	134.4 *d*	134.4 *d*	134.2 *d*
β	40.9 *t*†	37.0 *t*‡	35.5 *t*†	122.8 *d*	127.9 *d*	120.8 *d*	127.3 *d*	127.6 *d*	127.4 *d*
COOR	174.8 *s*	178.2 *s*	166.2 *s*	174.3 *s*	168.5 *s*	172.3 *s*	171.7 *s*	171.4 *s*	171.3 *s*
1″		104.4 *d*	99.6 *d*						
2″		75.0 *d*	70.8 *d*						
3″		78.3 *d*	72.1 *d*						
4″		71.2 *d*	68.3 *d*						
5″		77.4 *d*	72.5 *d*						
6″		62.4 *t*	62.0 *t*						
CO_2Me					52.2 *q*		56.6 *q*		
OMe					55.1 *q*	55.3 *q*			
					55.9 *q*	56.2 *q*			
OCH_2Me								14.3 *q*	14.2 *q*
									14.8 *q*
OCH_2Me								61.9 *t*	61.7 *t*
									63.4 *t*

*Compounds **1**, **4** and **6** were measured in CD_3OD solution, TMS as internal standard. Compounds **5**, **8**–**13** were measured in $CDCl_3$.

†‡These values can be interchanged.

Table 3. Plant growth inhibitory activity of stilbene and dihydrostilbene derivatives against rice seeds [18]

Compound		Sample concentration (ppm)			
		50	150	300	500
1	G*	0%‡	16%	100%	100%
	C†	0	10	25	53
6	G	0	5	53	91
	C	0	0	3	17
10	G	8	93	100	100
	C	0	16	86	87
12	G	38	49	62	69
	C	0	0	11	15
2–5, **7–9**, **11**, **13–15**	G	0	0	0	0
	C	0	0	0	0

*Germination.

†Second coleoptile.

‡Inhibition ratio against control. The root and second coleoptile lengths of grown plant were measured and the average values calculated.

UV λ_{max} nm (log ε): 215 (4.11), 224.5 (4.14) and 279.5 (3.36); IR ν_{max} cm^{-1}: 3350, 3200–2500, 1650, 1600, 1575, 1540, 1450, 1400, 1240 and 1060; ^1H and ^{13}C NMR: see Tables 1 and 2; (found: C, 57.76; H, 5.95. $C_{21}H_{24}O_9 \cdot H_2O$ requires C, 57.53; H, 5.98).

Compound **5**. Mp 153–155° (from Et_2O); $[\alpha]_D$ −34.3 (*c* 0.7, $CHCl_3$); UV λ_{max} nm (log ε): 211.5 (4.39), 217.5 (4.34) and 272 (3.23); IR ν_{max} cm^{-1}: 1760, 1705, 1610, 1240, 1060, 1050 and 1035; ^1H and ^{13}C NMR: see Tables 1 and 2; (found: C, 58.00; H, 5.46. $C_{31}H_{32}O_{14} \cdot H_2O$ requires C, 57.41; H, 5.59).

Compound **6**. Mp 179–181° (lit. [21] 180–181°); UV λ_{max} nm (log ε): 213 (4.38), 300 (4.16) and 337.5 (4.15); IR ν_{max} cm^{-1}: 3250–2400, 1665, 1590, 1515, 1465 and 1230; ^1H and ^{13}C NMR: see Tables 1 and 2; HRMS: $[M]^+$ (found: 256.0735; calc. for $C_{15}H_{12}O_4$: 256.0736); EIMS *m/z* (rel. int.): 256 $[M]^+$ (100), 238 (96), 210 (73), 182 (32), 181 (47) and 134 (22); (found: C, 70.25; H, 4.65. $C_{15}H_{12}O_4$ requires C, 70.30; H, 4.72).

Compound **7**. $[\alpha]_D$ −2.0° (*c* 1.0); UV λ_{max} nm (log ε): 211.5 (3.78), 308.5 (3.75) and 320 (3.79); IR ν_{max} cm^{-1}: 3450–2400, 1650, 1600, 1510, 1460, 1400, 1240 and 1065; ^1H NMR: see Table 1; (found: C, 57.87; H, 5.48. $C_{21}H_{22}O_{11} \cdot H_2O$ requires C, 57.79; H, 5.54).

Compound **8**. Mp 110–111° (from EtOH–Et_2O); UV λ_{max} nm (log ε): 225 (4.28), 307.5 (4.39) and 320 (4.46); IR ν_{max} cm^{-1}: 1725, 1610, 1595, 1275, 1255, 1180, 1115, 1080, 1070 and 1030; ^1H and ^{13}C NMR: see Tables 1 and 2; HRMS: $[M]^+$ (found: 298.1226; calc. for $C_{18}H_{18}O_4$: 298.1205); EIMS *m/z* (rel. int.): 298 $[M]^+$ (100), 267 (31), 252 (11), 239 (13), 165 (12) and 152 (11); (found: C, 72.64; H, 6.05. $C_{18}H_{18}O_4$ requires C, 72.46; H, 6.08).

Compound **9**. Mp 116–118° (from *n*-hexane–MeOH); UV λ_{max} nm (log ε): 222.5 (4.27), 306 (4.46) and 318 (4.45); IR ν_{max} cm^{-1}: 3400–2300, 1715, 1660, 1600, 1265, 1245, 1220, 1170, 1115, 1065 and 1020; ^1H and ^{13}C NMR: see Tables 1 and 2; (found: C, 71.58; H, 5.63. $C_{17}H_{16}O_4$ requires C, 71.82; H, 5.67).

Compound **10**. Mp 114–115.5° (from $CHCl_3$–*n*-hexane); UV λ_{max} nm (log ε): 208 (4.32), 220 (4.35), 302.5 (4.26) and 320 (4.29); IR ν_{max} cm^{-1}: 3375, 1670, 1600, 1590, 1585, 1515, 1350, 1340, 1280, 1265, 1205, 1170, 1150 and 1000; ^1H and ^{13}C NMR: see Tables 1 and 2; HRMS: $[M]^+$ (found: 270.0900; calc. for $C_{16}H_{14}O_4$; 270.0892); EIMS *m/z* (rel. int.): 270 $[M]^+$ (100), 238 (89), 210 (76), 182 (33), and 181 (42); (found: C, 71.14; H, 5.13. $C_{16}H_{14}O_4$ requires C, 71.10; H, 5.22).

Compound **11**. Mp 133–134° (from Et_2O); UV λ_{max} nm (log ε): 211 (4.22), 225 (4.15), 302 (4.37) and 310 (4.36); IR ν_{max} cm^{-1}: 1762, 1725, 1596, 1272, 1240, 1195, 1185 and 1160; ^1H NMR: see Table 1; (found: C, 67.47; H, 5.10. $C_{20}H_{18}O_6$ requires C, 67.79; H, 5.12).

Compound **12**. Mp 120–121° (from EtOAc–*n*-hexane); UV λ_{max} nm (log ε): 207.5 (4.34), 219 (4.34), 302 (4.21) and 330 (4.22); IR ν_{max} cm^{-1}: 3375, 1655, 1610, 1595, 1585, 1510, 1450, 1255, 1200 and 1160; ^1H and ^{13}C NMR: see Tables 1 and 2; EIMS *m/z* (rel. int.): 284 $[M]^+$ (77), 239 (22), 238 (100), 210 (81), 182 (27), 181 (37), 153 (13) and 152 (15); (found: C, 71.59; H, 5.66. $C_{17}H_{16}O_4$ requires C, 71.82; H, 5.67).

Compound **13**. Mp 100.5–102.0°; UV λ_{max} nm (log ε): 209 (4.27), 221 (4.29), 310 (4.24) and 327.5 (4.25); IR ν_{max} cm^{-1}: 3450, 1655, 1605, 1595, 1510, 1450, 1250, 1230, 1215, 1170, 1160 and 1040; ^1H and ^{13}C NMR: see Tables 1 and 2; EIMS *m/z* (rel. int.): 312 $[M]^+$ (100), 266 (89), 239 (25), 210 (52), 181 (35), 153 (22) and 152 (22); (found: C, 73.13; H, 6.41. $C_{19}H_{20}O_4$ requires C, 73.06; H, 6.45).

Compound **14**. Mp 108–109° (from Et_2O); UV λ_{max} nm (log ε): 208.5 (4.29), 227.5 (4.20) and 302.5 (4.41); IR ν_{max} cm^{-1}: 1762, 1722, 1600, 1505, 1370, 1275, 1245, 1200, 1185 and 1100; ^1H NMR: see Table 1; (found: C, 68.16; H, 5.42. $C_{21}H_{20}O_6$ requires C, 68.47; H, 5.47).

Compound **15**. Mp 91–93° (from Et_2O–*n*-hexane); UV λ_{max} nm (log ε): 213.5 (4.19), 232.5 (4.04) and 323 (4.44); IR ν_{max} cm^{-1}: 1770, 1715, 1605, 1595, 1510, 1280, 1245, 1195 and 1170; ^1H NMR: see Table 1; (found: C, 71.17; H, 6.25. $C_{21}H_{22}O_5$ requires C, 71.17; H, 6.26).

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