Synthesis and Biological Evaluation of a Natural Ester Sintenin and Its Synthetic Analogues

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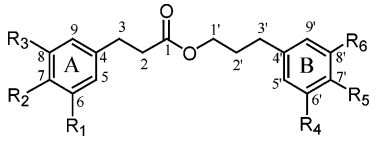
Synthesis of 3-(3,4-dimethoxyphenyl)propyl-3-(3,4-dimethoxyphenyl) propanoate (**18**), a cytotoxic natural ester, was carried out by a convenient synthetic path with a total yield of 49%. Sixteen of its analogues (**19**−**34**) were also prepared. Seventeen unsaturated derivatives of **18**, compounds **1**−**17**, were also synthesized to examine the structure−activity relationship of this type of ester. All of the synthetic compounds were passed through the cytotoxicity screenings on human tumor cell lines, such as PC-3, Hela, A549, BEL7404, CNE, and KB. Some of the esters exhibited moderate inhibitory effects on these tumor cell lines. The phenolic derivatives exhibited the highest cytotoxicity among these derivatives, while the unsaturated esters were more cytotoxic than the saturated analogues. Some of the compounds also exhibited inhibition on α-glucosidase.

Cytotoxic compounds are crucial in the course of finding new leads for antitumor drugs. Chen and co-workers recently reported the isolation of a cytotoxic natural ester, 3-(3,4-dimethoxyphenyl)propyl-3-(3,4-dimethoxyphenyl) propanoate (**18**), from the leaves and stems of *Piper sintenense* scattered in Taiwan. This ester, named sintenin by Chen et al., possessed selective cytotoxicity with an ED_{50} value of 5.4×10^{-7} M against P-388 cells.[1] However, the cytotoxicities on other common human tumor cell lines, e.g., KB, Hela, PC-3, CNE, A549, and BEL7404, were not reported therein. To our knowledge, these kinds of esters have wide biological activity. Lee et al. reported the cytotoxicity of caffeic acid phenethyl ester analogues on oral cancer cells, while Nagaoka et al. also indicated that the caffeic acid phenethyl ester analogues have selective antiproliferative activity on the colon 26-L5 carcinoma cell line.[2,3] To further investigate the cytotoxic nature of compound **18** and to preliminarily explore the structure−activity relationship (SAR) of these types of esters, we have designed a convenient synthetic route to prepare this natural ester (**18**) and its derivatives (**19**−**34**) (Table 1) along with their performance on KB, Hela, PC-3, CNE, A549, and BEL7404 cell lines. Furthermore, the structure of **18** is partially similar to nelumols B−D, the sinapyl alcohol derivatives isolated from *Ligularia nelumbifolia*, which were reported to be cytotoxic to A549, HL-60, and KB cell lines.[4,5] This further stimulated our interest to synthesize the sinapyl sinapate analogues (**1**−**17**) (Table 2) and compare their influence to the cytotoxicity on the six above-mentioned human tumor cell lines.

Moreover, to detect the structure−activity relationship of sintenin (**18**) derivatives, we selected different numbers and patterns of substituents on the aromatic A and/or B rings in the molecule, e.g., to replace the OCH_3 group by OCH_2OCH_3 to prolong the substituents, and to remove the OCH_2OCH_3 group to expose the phenolic OH group. Further modifications were carried out by changing the methoxy and hydrogen by an amine and nitro group to make the aromatic ring more electron-rich or electron-poor. All of the synthetic derivatives (**1**−**34**) were subjected to a cytotoxic screening on PC-3, Hela, A549, BEL7404, CNE, and KB cell lines, which correspond to the tumor diseases found in China. Furthermore, the inhibitory effects of selected compounds on α-glucosidase were also performed to check the relationship between cytotoxicity and α-glucosidase inhibition. The syntheses as well as the biological evaluations of these compounds are reported herein.

Table 1. Synthetic Saturated Esters **18**−**34**



	substituted group[a]					
compound	R_1	R_2	R_3	R_4	R_5	R_6
18	OCH_3	OCH_3	H	OCH_3	OCH_3	H
19	H	OCH_3	H	OCH_3	OCH_3	H
20	H	H	H	H	H	H
21	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	H
22	H	OCH_3	H	H	OCH_3	H
23	OCH_3	OCH_3	OCH_3	H	OCH_3	H
24	H	NH_2	H	OCH_3	OCH_3	H
25	H	OMOM	H	H	H	H
26	H	OH	H	H	H	H
27	H	CH_3	H	H	CH_3	H
28	H	OMOM	H	H	OMOM	H
29	OMOM	OMOM	H	H	OMOM	H
30	OMOM	OMOM	H	H	H	H
31	OH	OH	H	H	H	H
32	H	OMOM	H	H	OCH_3	H
33	H	OH	H	H	OCH_3	H
34	H	OMOM	H	OMOM	OMOM	H

[a] OMOM (OCH_2OCH_3).

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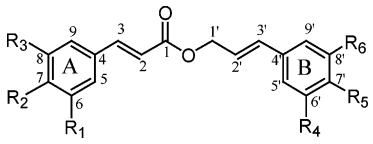
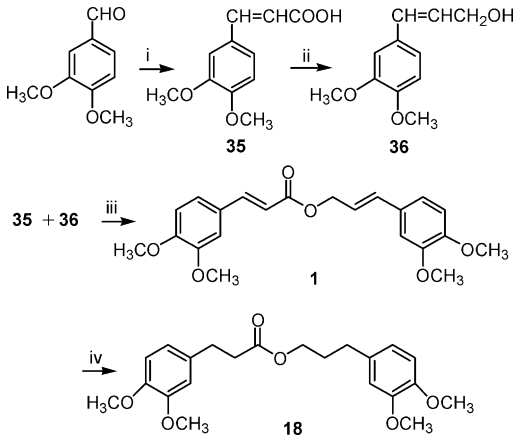
Table 2. Synthetic Unsaturated Esters **1**−**17**



compound	substituted group[a]					
	R_1	R_2	R_3	R_4	R_5	R_6
1	OCH_3	OCH_3	H	OCH_3	OCH_3	H
2	H	OCH_3	H	OCH_3	OCH_3	H
3	H	H	H	H	H	H
4	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	H
5	H	OCH_3	H	H	OCH_3	H
6	OCH_3	OCH_3	OCH_3	H	OCH_3	H
7	H	NO_2	H	OCH_3	OCH_3	H
8	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3
9	OMOM	OMOM	H	H	H	H
10	H	OMOM	H	H	OMOM	H
11	OMOM	OMOM	H	H	OMOM	H
12	H	OMOM	H	H	H	H
13	H	OH	H	H	H	H
14	H	OMOM	H	OMOM	OMOM	H
15	OH	OH	H	H	H	H
16	H	OMOM	H	H	OCH_3	H
17	H	OH	H	H	OCH_3	H

[a] OMOM (OCH_2OCH_3).

Scheme 1: Synthetic Route of Compounds **1** and **18**[a]



[a] (i) 1: malonic acid, Py, piperidine, reflux, 1.5 h; 2: HCl, rt, 1 h; (ii) LAH, THF, rt, 4 h; (iii) CDI, DBU, THF, 45 °C, 1 day; (iv) H_2, Pd/C, EtOAc, rt, 12 h.

Results and Discussion

Synthesis. The synthetic paths are outlined in Scheme 1 and Scheme 2. Scheme 1 describes the procedure of preparing compounds **1** and **18**. The synthesis started from 3,4-dimethoxybenzaldehyde, which was treated with malonic acid in pyridine catalyzed by piperidine (Knoevenagel condensation) to furnish an allylic acid, **35**.[6,7] The allylic alcohol **36** was achieved by reduction of **35** with $LiAlH_4$ in anhydrous THF at room temperature.[8−10] The allylic acid **35** was treated with carbonyldiimidazole (CDI) to form a CDI-adduct that contained an activated carbonyl group, and thus facilitated the condensation of the adduct with the allylic alcohol **36** in the presence of 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) to afford **1** with a yield of 76%. This unsaturated ester **1** was further hydrogenated to give compound **18** in an 84% yield.[11]

Similar preparations were carried out as modeled in Scheme 1, and different aromatic substituents were introduced by changing the benzaldehyde starting materials. A series of unsaturated esters **2**−**8** were thus obtained. Further hydrogenation of the unsaturated esters was performed by palladium-charcoal catalysis and afforded a series of saturated ester derivatives **19**−**24**. The structures of all the synthetic compounds were elucidated mainly on the basis of their ^1H and ^{13}C NMR spectra as well as MS spectral data.

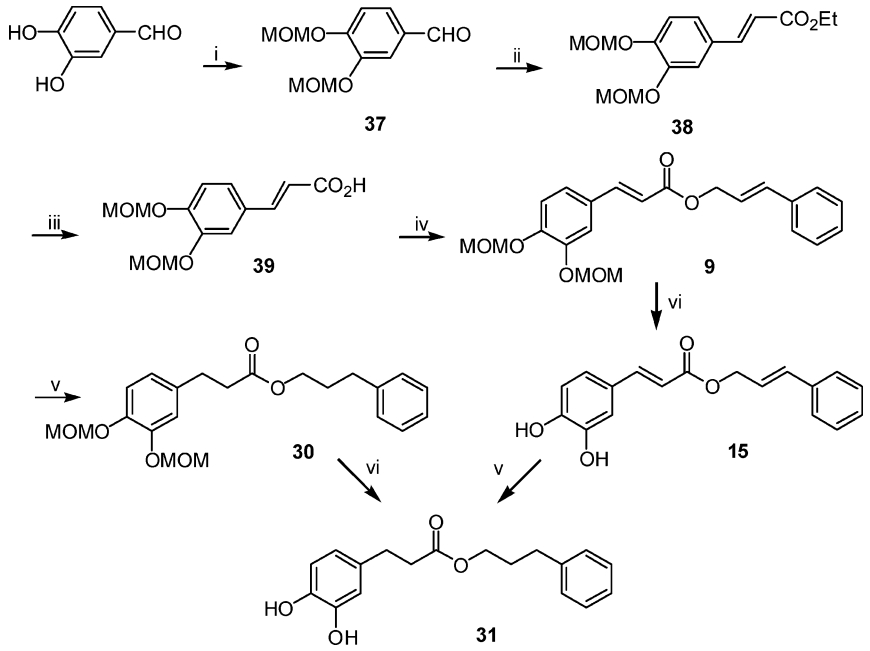
Scheme 2 outlines the synthetic path of the compounds **9**−**17** as well as compounds **25**−**34**. These compounds are mainly substituted by OCH_2OCH_3 and free phenolic OH groups, and therefore utilized a different synthetic schedule. The unsaturated esters **9** and **15** as well as the saturated esters **30** and **31** were selected to be examples in the scheme. The protocol was initiated with 3,4-dihydroxybenzaldehyde, which was reacted with chloromethyl methyl ether in the presence of potassium carbonate under reflux to afford the disubstituted aldehyde **37** in 70% yield.[12] This aldehyde was subjected to a Wittig reaction with ethyl(triphenylphosphoranylidene)acetate in benzene to afford a substituted sinapic acid ethyl ester **38**.[13] The ester was hydrolyzed by potassium hydroxide to afford the substituted sinapic acid **39**, which was then condensed with cinnamic alcohol under the catalysis of dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) to afford the unsaturated ester **9**,[14] which could be hydrogenated under palladium-charcoal (10% Pd−C) catalysis to afford the saturated ester **30**. Furthermore, treatment of **9** and **30** with 10% hydrochloric acid gave the corresponding products **15** and **31**, respectively, which contained free phenolic hydroxyls in the aromatic ring.[11,15]

Cytotoxic Evaluation. All of the synthetic compounds **1**−**34** were subjected to in vitro cytotoxicity screenings on six human tumor cell lines with the marketed agent cisplatin (DDP) employed as a positive control. The tested IC_{50} values for these active compounds are listed in Table 3. Meanwhile, those with IC_{50} values greater than 100 μg/mL on all six tumor cell lines were considered inactive compounds and thus are not included in Table 3. It could be observed that compound **18** showed no significant cytotoxicity to the six selected tumor cell lines. This result is consistent with a former study, in which the natural ester was found to be cytotoxic only to P-388 cells among the three cell lines they tested.[1] Furthermore, its analogues possessing saturated carbon chains between two aromatic rings, **19**−**24**, also exhibited poor cytotoxicity except for compound **21**, which showed moderate cytotoxicity with IC_{50} values of 1.0×10^{-4} and 1.3×10^{-4} M against PC-3 and KB cell lines, respectively. However, three analogues with free phenolic hydroxyls in the aromatic ring, viz., compounds **26**, **31**, and **33**, exhibited stronger and wider cytotoxicity to the six tumor cell lines (Table 3).

Meanwhile, it could be found that the unsaturated esters **1**−**7** exhibited more visible cytotoxicity than those of their saturated analogues **19**−**24**. For example, unsaturated ester **4** showed cytotoxicity to PC-3, Hela, A549, and BEL7404 cell lines, while its corresponding saturated precursor **21** exhibited weaker cytotoxicity limited to PC-3 and KB cells (Table 3). This suggested that the double bonds conjugated to the two aromatic rings might be desirable to promote the cytotoxicity of this type of esters.

Moreover, almost all of the compounds containing OCH_2OCH_3 groups in the molecules did not exhibit cytotoxicity except for compound **9**, which exhibited an IC_{50} on KB of 2.0×10^{-4} M, and for compound **16**, which showed cytotoxicity to PC-3 and Hela cell lines with IC_{50} values of 2.3×10^{-4} and 4.6×10^{-5} M, respectively. However, after the OCH_2OCH_3 groups were removed and the phenolic hydroxyls were revealed, the cytotoxicity was elevated

Scheme 2: Synthesis of Esters **9**, **15**, **30**, and **31**[a]



[a] (i) MOMCl, K_2CO_3, acetone, reflux, 4 h, 70%; (ii) $Ph_3P{=}CHCO_2Et$, benzene, reflux, 6 h, 89%; (iii) KOH/H_2O, EtOH, rt, 4 h, 80%; (iv) cinnamic alcohol, DCC, DMAP, CH_2Cl_2, rt, 24 h, 63%; (v) H_2, Pd/C, AcOEt, rt, 12 h, 82%; (vi) 10% HCl, MeOH, reflux, 0.5 h, 34%.

Table 3. Cytotoxicities of Selected Compounds on Six Human Tumor Cell Lines (IC_{50} at 10^{-5} M)[a]

compound	PC-3	Hela	A549	CNE	BEL7404	KB
1	9.2	8.67	18.1	/[b]	13.6	13.3
2	18.1	16.7	/[b]	/[b]	/[b]	/[b]
4	8.0	6.4	17.2	/[b]	21.2	/[b]
7	21.2	/[b]	/[b]	/[b]	/[b]	16.5
8	18.9	4.3	18.0	5.0	/[b]	20.6
9	/[b]	/[b]	/[b]	/[b]	/[b]	20.2
13	14.3	16.0	12.0	16.2	/[b]	/[b]
15	12.3	17.1	7.1	21.4	9.1	5.4
16	22.6	4.6	/[b]	/[b]	/[b]	/[b]
17	8.8	9.5	7.2	4.0	19.3	14.3
21	10.4	/[b]	/[b]	/[b]	/[b]	12.4
26	32.2	31.7	31.7	26.8	21.7	12.9
31	18.9	17.1	13.8	23.5	/[b]	12.5
33	28.3	/[b]	18.6	28.7	10.8	82.0
cisplatin	0.3	0.1	0.3	0.2	0.7	0.04

[a] Key to cell lines: BEL7404, human hepatocellular carcinoma line; CNE, nasopharyngeal carcinoma cell line; KB, human oral epithelial cell line; A549, human lung adenocarcinoma cell line; Hela, human cervical carcinoma cell line; PC-3, human prostate cancer cell line. [b] IC_{50} values greater than 100 μg/mL were considered inactive.

remarkably. This could be reflected from couples of compounds, e.g., **13** vs **12**, **15** vs **9**, **17** vs **16**, **31** vs **30**, etc. (Table 3).

By scrutiny of the initial results, it could also be observed that the unsaturated esters with notable cytotoxicity are those with two methoxy groups existing on the B ring (i.e., compounds **1**, **2**, **4**, and **7**). Nevertheless, compound **8**, which possessed a trimethoxy-substituted B ring and a trimethoxy moiety in the A ring, exhibited a wide and significant cytotoxicity to nearly all of the six tumor cell lines.

Among these synthetic samples, ester **17**, with free phenols in the A ring and a methoxy group in the B ring, showed the strongest cytotoxicity, especially on the cell lines of CNE and PC-3 with IC_{50} values of 4.0×10^{-5} and 8.8×10^{-5} M, respectively. It should also be noticed that the unsaturated ester **15**, which contained two free phenolic hydroxyls in the A ring, exhibited cytotoxicity to KB, BEL 7404, and A549 cell lines with IC_{50} values of 5.4×10^{-5}, 9.1×10^{-5}, and 7.1×10^{-5} M, respectively.

According to the cytotoxic evaluation results, it was suggested that the analogues having one or more free phenol groups are more toxic to human tumor cells than the esters with alkyloxyl or alkyl substituents, and the esters with nitro or amine groups in the aromatic rings. It is clear that the number of methoxy substituents in the B ring is related to the measure of cytotoxicity among the batch of esters. However, the prolongation of the OCH_3 group by OCH_2OCH_3 groups did not intensify the cytotoxicity. In general, unsaturated esters showed more convincing cytotoxicity than their saturated analogues, which might be due to the presence of a large $\pi-\pi$ conjugative system in the unsaturated molecules. These results could serve as fundamental information for further SAR investigation on this type of natural-based esters.

α-Glucosidase Inhibition. α-Glucosidase is a nutritionally and biochemically important enzyme for dietary carbohydrate digestion and post-translational processing of glycoprotein.[16] Inhibition of α-glucosidases causes abnormal functionality of glycoproteins because of incomplete modification of glycans. Suppression of this processing is to be expected for antiviral activity and decreasing of growth rate of tumors.[16] Some glucosidase inhibitors show antitumor metastasis[17] and anti-HIV activities[18] and are also clinically useful for treatment of diabetes.[19]

To the best of our knowledge, some of the cytotoxic compounds also possess inhibition effects on α-glucosidase.[20] Therefore selected synthetic compounds were subjected to an α-glucosidase inhibition assay. It was found that compounds **8**, **13**, **15**, and **31** exhibited IC_{50} values to α-glucosidase at 1.1×10^{-4}, 6.5×10^{-5}, 9.7×10^{-5}, and 7.3×10^{-5} M, respectively. Meanwhile the positive control, acarbose, demonstrated a IC_{50} value to α-glucosidase of 6.8×10^{-4} M. This indicated some relationship between cytotoxicity and α-glucosidase inhibition among this kind of esters.

Table 4. ^{1}H NMR Spectral Data [400 MHz, δ_H (*J*, Hz)] for Compounds **1**−**34** in $CDCl_3$[a]

compound	H-2	H-3	H-1′	H-2′	H-3′	Ar-H
1	6.36 d (16)	7.68 d (16)	4.86 d (6.4)	6.23 dt (16, 6.4)	6.66 d (16)	6.84−7.13 m
2	6.36 d (16)	7.69 d (16)	4.85 d (6.8)	6.24 dt (16, 6.8)	6.65 d (16)	6.80−7.49 m
3	6.50 d (16)	7.75 d (16)	4.89 d (6.4)	6.38 dt (16, 6.4)	6.72 d (16)	7.27−7.56 m
4	6.40 d (16)	7.65 d (16)	4.86 d (6.4)	6.25 dt (16, 6.4)	6.66 d (16)	6.76−6.97 m
5	6.35 d (16)	7.69 d (16)	4.84 d (6.4)	6.26 dt (16, 6.4)	6.66 d (16)	6.83−7.50 m
6	6.36 d (16)	7.64 d (16)	4.85 d (6.8)	6.24 dt (16, 6.8)	6.66 d (16)	6.76−7.37 m
7	6.58 d (16)	7.75 d (16)	4.88 d (6.4)	6.24 dt (16, 6.4)	6.82 d (16)	6.95−7.18 m
8	6.40 d (16)	7.66 d (16)	4.87 d (6.4)	6.30 dt (16, 6.4)	6.64 d (16)	6.77 s, 6.64 s
9	6.37 d (16)	7.66 d (16)	4.87 d (6.4)	6.36 dt (16, 6.4)	6.72 d (16)	6.85−7.62 m
10	6.37 d (16)	7.68 d (16)	4.84 d (6.4)	6.25 dt (16, 6.4)	6.66 d (16)	7.00−7.48 m
11	6.37 d (16)	7.65 d (16)	4.84 d (6.4)	6.25 dt (16, 6.4)	6.66 d (16)	6.99−7.38 m
12	6.37 d (16)	7.70 d (16)	4.87 d (6.4)	6.36 dt (16, 6.4)	6.72 d (16)	7.04−7.51 m
13	6.36 d (16)	7.69 d (16)	4.88 d (6.4)	6.35 dt (16, 6.4)	6.67 d (16)	6.83−7.45 m
14	6.37 d (16)	7.69 d (16)	4.84 d (6.8)	6.25 dt (16, 6.8)	6.63 d (16)	7.00−7.50 m
15	6.42 d (16)	7.52 d (16)	4.80 d (6.4)	6.30 dt (16, 6.4)	6.72 d (16)	6.77−7.48 m
16	6.36 d (16)	7.68 d (16)	4.84 d (6.4)	6.24 dt (16, 6.4)	6.66 d (16)	6.83−7.49 m
17	6.37 d (16)	7.67 d (16)	4.87 d (6.4)	6.36 dt (16, 6.4)	6.71 d (16)	6.94−7.43 m
18	2.63 t (8.4)	2.91 t (8.4)	4.10 t (6.4)	1.92 m	2.61 t (8.4)	6.69−6.80 m
19	2.62 t (8.4)	2.90 t (8.4)	4.09 t (6.4)	1.91 m	2.59 t (8.4)	6.68−7.14 m
20	2.67 t (8.4)	2.97 t (8.4)	4.10 t (6.4)	1.95 m	2.65 t (8.4)	7.16−7.32 m
21	2.66 t (8.0)	2.90 t (8.0)	4.10 t (6.4)	1.91 m	2.61 t (8.4)	6.43−6.80 m
22	2.60 t (8.0)	2.90 t (8.0)	4.07 t (6.4)	1.91 m	2.58 t (8.0)	6.82−7.14 m
23	2.63 t (8.0)	2.90 t (8.0)	4.09 t (6.4)	1.91 m	2.60 t (8.0)	6.42−7.73 m
24	2.63 t (8.0)	2.85 t (8.0)	4.10 t (6.4)	1.91 m	2.58 t (8.0)	6.45−7.02 m
25	2.65 t (8.0)	2.91 t (8.0)	4.11 t (6.4)	1.94 m	2.61 t (8.0)	6.96−7.31 m
26	2.65 t (8.0)	2.89 t (8.0)	4.10 t (6.4)	1.92 m	2.61 t (8.0)	6.75−7.31 m
27	2.70 t (8.0)	2.93 t (8.0)	4.09 t (6.4)	1.92 m	2.63 t (8.0)	7.05−7.12 m
28	2.64 t (8.0)	2.91 t (8.0)	4.12 t (6.4)	1.90 m	2.53 t (8.0)	6.95−7.15 m
29	2.63 t (8.0)	2.89 t (8.0)	4.08 t (6.4)	1.91 m	2.61 t (8.4)	6.79−7.27 m
30	2.66 t (8.0)	2.89 t (8.0)	4.12 t (6.4)	1.91 m	2.61 t (8.4)	6.80−7.31 m
31	2.64 t (8.0)	2.83 t (8.0)	4.09 t (6.4)	1.92 m	2.60 t (8.0)	6.61−7.31 m
32	2.61 t (8.0)	2.91 t (8.0)	4.08 t (6.4)	1.90 m	2.59 t (8.0)	6.83−7.15 m
33	2.64 t (8.0)	2.88 t (8.0)	4.07 t (6.4)	1.92 m	2.58 t (8.0)	6.74−7.26 m
34	2.68 t (8.0)	2.92 t (8.0)	4.09 t (6.4)	1.91 m	2.57 t (8.4)	6.73−7.14 m

[a] Only common characteristics of the synthetic compounds are listed. The individual ^{1}H NMR spectral data of the different substituents for compounds **1**−**34** were listed in the Experimental Section.

Experimental Section

General Experimental Procedures. Melting points were recorded on a Kofler hot-stage instrument and were uncorrected. ESIMS data were recorded on a Bruker Esquire 3000+ spectrometer. HRFABMS spectra were recorded on a VG ZAB-HS spectrometer. The NMR spectra were obtained on a Bruker AM-400 FT-NMR spectrometer with TMS as internal standard. Preparative TLC was performed using silica gel GF_{254} and RP-18 plates (Merck). Enzyme-linked immunosorbent assays were recorded on a BIO-TEK ELX8000 ELISA reader. α-Glucosidase was from Baker's yeast (Sigma, 500 U/mL). 4-Nitrophenyl-α-D-glucopyranoside was from E. Merck. Acarbose was purchased from The First Hospital affiliated with Zhejiang University.

3-(3,4-Dimethoxyphenyl)propenyl-3-(3,4-dimethoxyphenyl)allylate (1). To a stirred solution of malonic acid (3 g, 18 mmol) in Py (5 mL) at room temperature was added 3,4-dimethoxybenzaldehyde (2.8 g, 27 mmol) in Py (7 mL). Piperidine (2 mL) was added to the solution. The mixture was heated at 118 °C for 4 h and was cooled to 0 °C. Then 3 N HCl was added to adjust the pH value to 3, and the mixture was stirred at 0 °C for another 1 h. After suction filtration, the filtrate was crystallized in acetone to afford **35** as a white crystalline solid. To a stirred suspension of LAH (56 mg, 1.5 mmol) in dry THF (8 mL) at room temperature was added a solution of **35** (208 mg, 1 mmol) in THF (10 mL) under argon atmosphere. The solution was stirred for 4 h and was quenched by 8 mL of H_2O. Then 15 mL of 1 N HCl was added, and the mixture was extracted by ether. The ether layers were combined and dried ($MgSO_4$). Evaporation of the solvent followed by CC (hexane/AcOEt, 6:1) afforded a yellow solid, **36** (109 mg, 56% yield). To a stirred solution of **35** (0.20 g, 0.96 mmol) in dry THF (10 mL) was added CDI (0.23 g, 1.44 mmol) in dry THF under argon. The mixture was stirred at 45 °C for 15 min. The solution of **36** (0.21 g, 1.05 mmol) and DBU (0.16 g, 1.05 mmol) in dry THF (10 mL) was then added quickly. The resulting mixture was stirred at 45 °C for 24 h. The mixture was evaporated to afford a residue, which was subjected to flash chromatography to provide **1** (0.28 g, 76% yield) as a white crystalline solid: mp 78 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (6 H, *s*, O*Me*-6′ and O*Me*-6), 3.91 (6 H, s, O*Me*-7′ and O*Me*-7), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 385 ([M + 1]$^+$); HRFABMS *m/z* 384.1569 (calcd for $C_{22}H_{24}O_6$, 384.1573).

3-(3,4-Dimethoxyphenyl)propenyl-3-(3-methoxyphenyl)-allylate (2). The method of preparation of **2** was similar to that used for the preparation of **1**: white crystalline solid; mp 66−67 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91 (3 H, s, O*Me*-7), 3.89 (3 H, s, O*Me*-7′), 3.84 (3 H, s, O*Me*-6′), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 355 ([M + 1]$^+$); HRFABMS *m/z* 354.1468 (calcd for $C_{21}H_{22}O_5$, 354.1467).

3-Phenylpropenyl-3-phenylallylate (3). The method of preparation of **3** was similar to that used for the preparation of **1**: white crystalline solid; mp 60−61 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.63; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 265 ([M + 1]$^+$); HRFABMS *m/z* 264.1153 (calcd for $C_{18}H_{16}O_2$, 264.1150).

3-(3,4-Dimethoxyphenyl)propenyl-3-(2,3,4-trimethoxyphenyl)allylate (4). The method of preparation of **4** was similar to that used for the preparation of **1**: white crystalline solid; mp 77−78 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.27; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (6 H, s, O*Me*-6′ and O*Me*-6), 3.86 (6 H, s, O*Me*-7′ and O*Me*-7), 3.85 (3 H, s, O*Me*-8), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 437 ([M + Na]$^+$); HRFABMS *m/z* 414.1674 (calcd for $C_{23}H_{26}O_7$, 414.1679).

3-(3-Methoxyphenyl)propenyl-3-(3-methoxyphenyl)allylate (5). The method of preparation of **5** was similar to that used for the preparation of **1**: white crystalline solid; mp 63−

Table 5. ^{13}C NMR Spectral Data [100 MHz, δ (ppm)] for Selected Compounds in $CDCl_3$

C no.	1	2	3	4	10	11	12	18	19	25	27[a]	28	29
1	167.0	167.0	166.7	166.9	167.0	166.8	167.0	172.9	173.0	173.0	173.0	173.0	172.9
2	120.1	115.5	117.8	110.8	121.4	121.5	115.7	36.1	36.1	36.1	36.0	36.1	36.0
3	144.9	133.8	145.0	134.9	144.2	144.5	144.6	30.5	30.3	30.1	30.3	30.3	30.4
4	134.2	127.0	134.3	121.0	133.7	130.1	123.3	133.0	132.5	133.9	135.5	133.9	134.5
5	109.2	127.0	126.6	127.0	129.6	115.6	126.6	111.5	113.8	129.3	129.0	129.2	116.6
6	151.0	114.2	130.3	147.1	116.2	149.1	116.4	148.7	148.7	116.2	128.2	116.2	147.1
7	149.0	161.3	128.8	148.7	158.9	157.1	158.9	147.4	147.1	155.6	155.3	155.4	145.5
8	115.4	114.2	130.3	153.3	116.2	116.1	116.4	111.1	111.4	116.2	128.2	116.2	116.6
9	122.7	127.0	126.6	117.1	129.6	128.8	126.6	120.0	120.1	129.3	129.0	129.2	129.3
1′	65.2	64.9	65.1	63.9	65.2	65.2	65.0	63.7	63.7	63.8	63.8	63.7	63.7
2′	127.2	121.3	128.0	111.4	127.8	123.4	126.6	30.3	30.3	30.1	30.2	30.3	30.2
3′	129.1	129.2	128.5	129.8	132.5	123.4	128.0	31.4	31.6	32.1	31.4	31.2	31.2
4′	134.2	129.7	134.3	129.7	133.7	133.8	134.1	133.6	133.7	141.1	137.9	134.5	134.9
5′	108.5	108.7	126.6	104.9	129.6	127.8	123.3	111.5	113.8	128.4	129.0	129.2	129.3
6′	151.0	148.9	130.3	139.8	116.2	116.3	129.7	148.7	157.9	128.4	128.2	116.2	116.2
7′	149.0	144.6	128.8	144.7	157.1	147.3	128.0	147.4	147.1	126.0	155.3	155.6	155.4
8′	110.8	111.1	130.3	107.5	116.2	116.3	139.7	111.1	111.0	128.4	128.2	116.2	116.2
9′	121.1	120.1	126.6	111.0	129.6	127.8	123.3	120.1	129.2	128.4	129.0	129.2	129.3
OMe-6	55.7			55.7		56.2		55.7					56.1
OMe-7	55.8	55.3		55.8	56.0	56.0	56.1	55.8	55.2	55.9		55.9	55.9
OMe-8				56.0									
OMe-6′	55.7	55.7		55.7				55.7	55.7				
OMe-7′	55.8	55.8		55.8	56.0	56.3		55.8	55.8			55.9	55.9
OCH_2O-6						95.1							95.3
OCH_2O-7					94.3	94.3	94.0			94.4		94.9	94.4
OCH_2O-6′													
OCH_2O-7′					94.3	95.5						94.9	94.4

[a] Methyl signals: 21.0.

64 °C (hexane); R_f (hexane/AcOEt, 6:1) 0.70; ^1H NMR (400 MHz, $CDCl_3$) δ 3.84 (6 H, s, O*Me*-7′ and O*Me*-7), other data see Table 4; ESIMS *m/z* 324 ([M]$^+$); HRFABMS *m/z* 324.1358 (calcd for $C_{20}H_{20}O_4$, 324.1362).

3-(3-Methoxyphenyl)propenyl-3-(2,3,4-trimethoxyphenyl)allylate (6). The method of preparation of **6** was similar to that used for the preparation of **1**: white crystalline solid; mp 62−63 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.21; ^1H NMR (400 MHz, $CDCl_3$) δ 3.90 (3 H, s, O*Me*-6), 3.88 (6 H, s, O*Me*-7′ and O*Me*-7), 3.78 (3 H, s, O*Me*-8), other data see Table 4; ESIMS *m/z* 385 ([M + 1]$^+$); HRFABMS *m/z* 384.1579 (calcd for $C_{22}H_{24}O_6$, 384.1573).

3-(3,4-Dimethoxyphenyl)propenyl-3-(3-nitrophenyl)allylate (7). The method of preparation of **7** was similar to that used for the preparation of **1**: yellow crystalline solid; mp 89−90 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.26; ^1H NMR (400 MHz, $CDCl_3$) δ 3.91 (3 H, s, O*Me*-6′), 3.89 (3 H, s, O*Me*-7′), other data see Table 4; ESIMS *m/z* 392 ([M + Na]$^+$); HRFABMS *m/z* 369.1211 (calcd for $C_{20}H_{19}NO_6$, 369.1212).

3-(2,3,4-Trimethoxyphenyl)propenyl-3-(2,3,4-trimethoxyphenyl)allylate (8). The method of preparation of **8** was similar to that used for the preparation of **1**: white crystalline solid; mp 60−62 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.27; ^1H NMR (400 MHz, $CDCl_3$) δ 3.89 (3 H, s, O*Me*-6′), 3.88 (3 H, s, O*Me*-6), 3.86 (6 H, s, O*Me*-7′ and O*Me*-7), 3.83 (6 H, s, O*Me*-8 and O*Me*-8′), other data see Table 4; ESIMS *m/z* 467 ([M + Na]$^+$); HRFABMS *m/z* 444.1769 (calcd for $C_{24}H_{28}O_8$, 444.1784).

3-Phenylpropenyl-3-(3,4-dimethoxymethoxyphenyl)allylate (9). To a stirred solution of **38**[12,13] (98 mg, 0.33 mmol) in 5 mL of ethanol was added a solution of potassium hydroxide (65 mg) in 4 mL of H_2O. The mixture was heated to reflux for 4 h. Evaporation of ethanol was followed by adding 2 mL of water. Then 5 mL of 1 N HCl was added to get a white suspension. The mixture was then extracted by ether, and the ether layers were washed with brine and dried ($MgSO_4$). The solution was evaporated to afford **39** as a white solid (70 mg, 80% yield). To a stirred solution of **39** (0.13 g, 0.50 mmol) in dry CH_2Cl_2 (8 mL) was added DCC (0.11 g, 0.55 mmol) in dry CH_2Cl_2 (5 mL) under argon. The mixture was stirred at room temperature for 5 min until a white suspension occurred. A solution of cinnamic alcohol (0.07 g, 0.55 mmol) and DMAP (0.01 g, 0.10 mmol) in dry CH_2Cl_2 was then added to the mixture. The suspension was stirred at room temperature for 24 h. The mixture was filtered through a Celite layer and evaporated. The residue was purified by column chromatography eluted with 10% AcOEt/hexane to afford white solid **9** (120 mg, 63% yield): mp 32−33 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.53; ^1H NMR (400 MHz, $CDCl_3$) δ 5.27 (2 H, s, *OCH$_2$O*-7), 5.26 (2 H, s, *OCH$_2$O*-6), 3.53 (3 H, s, O*Me*-7), 3.52 (3 H, s, O*Me*-6), other data see Table 4; ESIMS *m/z* [M + Na]$^+$ 407; HRFABMS *m/z* 384.1566 (calcd for $C_{22}H_{24}O_6$, 384.1573).

3-(3-Methoxymethoxyphenyl)propenyl-3-(3-methoxymethoxyphenyl)allylate (10). The method of preparation of **10** was similar to that used for the preparation of **9**: white crystalline solid; mp 30 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.60; ^1H NMR (400 MHz, $CDCl_3$) δ 5.21 (4 H, s, *OCH$_2$O*-7′ and *OCH$_2$O*-7), 3.48 (6 H, s, O*Me*-7′ and O*Me*-7), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 384 ([M]$^+$); HRFABMS *m/z* 384.1563 (calcd for $C_{22}H_{24}O_6$, 384.1573).

3-(3-Methoxymethoxyphenyl)propenyl-3-(3,4-dimethoxymethoxyphenyl)allylate (11). The method of preparation of **11** was similar to that used for the preparation of **9**: white crystalline solid; mp 32−33 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.32; ^1H NMR (400 MHz, $CDCl_3$) δ 5.27 (2 H, s, *OCH$_2$O*-7), 5.26 (2 H, s, *OCH$_2$O*-6), 5.18 (2 H, s, *OCH$_2$O*-7′), 3.53 (3 H, s, O*Me*-7), 3.52 (3 H, s, O*Me*-6), 3.48 (3 H, s, O*Me*-7′), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 467 ([M + Na]$^+$); HRFABMS *m/z* 444.1781 (calcd for $C_{24}H_{28}O_8$, 444.1784).

3-Phenylpropenyl-3-(3-methoxymethoxyphenyl)allylate (12). The method of preparation of **12** was similar to that used for the preparation of **9**: white crystalline solid; mp 52−53 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.54; ^1H NMR (400 MHz, $CDCl_3$) δ 5.22 (2 H, s, *OCH$_2$O*-7), 3.49 (3 H, s, O*Me*-7), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 347([M + Na]$^+$); HRFABMS *m/z* 324.1369 (calcd for $C_{20}H_{20}O_4$, 324.1362).

3-Phenylpropenyl-3-(3-hydroxyphenyl)allylate (13). The method of preparation of **13** was similar to that used for the preparation of **9**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.19; ^1H NMR (400 MHz, $CDCl_3$) δ 5.87 (1 H, s, *OH*-7), other data see Table 4; ESIMS *m/z* 303 ([M + Na]$^+$); HRFABMS *m/z* 280.1087 (calcd for $C_{18}H_{16}O_3$, 280.1099).

3-(3,4-Dimethoxymethoxyphenyl)propenyl-3-(3-methoxymethoxyphenyl) allylate (14). The method of preparation of **14** was similar to that used for the preparation of **9**: white crystalline solid; mp 65−66 °C (hexane); R_f (hexane/

AcOEt, 3:1) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.26 (2 H, s, *OCH$_2$O*-7), 5.24(2 H, s, *OCH$_2$O*-7′), 5.21 (2 H, s, *OCH$_2$O*-6′), 3.53 (3 H, s, O*Me*-7), 3.52 (3 H, s, O*Me*-7′), 3.48 (3 H, s, O*Me*-6′), other data see Table 4; ESIMS *m/z* 445 ([M + 1]$^+$); HRFABMS *m/z* 444.1776 (calcd for $C_{24}H_{28}O_8$, 444.1784).

3-Phenylpropenyl-3-(3,4-dihydroxyphenyl)allylate (15). To a solution of **14** (0.04 g, 0.10 mmol) in CH_3OH (5.0 mL) was added 10% HCI (1.0 mL). The resulting mixture was refluxed for 30 min and then poured into cold water and extracted with AcOEt. The organic phase was washed with a saturated solution of $NaHCO_3$ and brine and then dried (Na_2SO_4). After removal of the solvent, the residue was chromatographyed over silica gel. Elution with petroleum ether/AcOEt (8:1) yielded **15** (10 mg, 34% yield) as a colorless oil: R_f (hexane/AcOEt, 3:1) 0.11; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (1 H, s, *OH*-7), 8.99 (1 H, s, *OH*-6), other data see Table 4; ESIMS *m/z* 319 ([M + Na]$^+$); HRFABMS *m/z* 296.1058 (calcd for $C_{18}H_{16}O_4$, 296.1049).

3-(3-Methoxyphenyl)propenyl-3-(3-methoxymethoxyphenyl)allylate (16). The method of preparation of **16** was similar to that used for the preparation of **9**: white crystalline solid; mp 49−50 °C (hexane); R_f (hexane/AcOEt, 3:1) 0.20; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.21 (2 H, s, *OCH$_2$O*-7), 3.82 (3 H, s, O*Me*-7′), 3.48 (3 H, s, O*Me*-7), other data see Table 4; ESIMS *m/z* 354 ([M]$^+$); HRFABMS *m/z* 354.1474 (calcd for $C_{21}H_{22}O_5$, 354.1467).

3-(3-Methoxyphenyl)propenyl-3-(3-hydroxyphenyl)allylate (17). The method of preparation of **17** was similar to that used for the preparation of **9**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.18; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 (1 H, s, *OH*-7), 3.93 (3 H, s, O*Me*-7′), other data see Table 4; ESIMS *m/z* 310 ([M]$^+$); HRFABMS *m/z* 310.1212 (calcd for $C_{19}H_{18}O_4$, 310.1205).

3-(3,4-Dimethoxyphenyl)propyl-3-(3,4-dimethoxyphenyl)propanoate (18). The mixture of **1** (0.10 g, 0.26 mmol) and 10% Pd/C (0.01 g) was suspended in AcOEt (15 mL) and was pressurized by H_2 gas overnight. The resulted mixture was filtered through kieselguhr and evaporated. The residue was purified by column chromatography eluted with 25% AcOEt/hexane to afford **18** (83 mg, 84%) as a colorless oil: R_f (hexane/AcOEt, 3:1) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 (6 H, s, O*Me*-6′ and O*Me*-6), 3.86 (3 H, s, O*Me*-7), 3.85 (3 H, s, O*Me*-7′), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 406 ([M + H_2O]$^+$); HRFABMS *m/z* 388.1880 (calcd for $C_{22}H_{28}O_6$, 388.1886).

3-(3,4-Dimethoxyphenyl)propyl-3-(3-methoxyphenyl)-propanoate (19). The method of preparation of **19** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (3 H, s, O*Me*-6′), 3.86 (3 H, s, O*Me*-7), 3.78 (3 H, s, O*Me*-7′); ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 376 ([M + H_2O]$^+$); HRFABMS *m/z* 358.1783 (calcd for $C_{21}H_{26}O_5$, 358.1780).

3-Phenylpropyl-3-phenylpropanoate (20). The method of preparation of **20** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.66; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 4; ESIMS *m/z* 286 ([M + H_2O]$^+$); HRFABMS *m/z* 268.1460 (calcd for $C_{18}H_{20}O_2$, 268.1463).

3-(3,4-Dimethoxyphenyl)propyl-3-(2,3,4-trimethoxyphenyl)propanoate (21). The method of preparation of **21** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.28; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 (3 H, s, O*Me*-6), 3.86 (3 H, s, O*Me*-6′), 3.84 (6 H, s, O*Me*-7′ and O*Me*-7), 3.81 (3 H, s, O*Me*-8), other data see Table 4; ESIMS *m/z* 402 ([M + H_2O]$^+$); HRFABMS *m/z* 384.1569 (calcd for $C_{23}H_{30}O_7$, 384.1573).

3-(3-Methoxyphenyl)propyl-3-(3-methoxyphenyl)propanoate (22). The method of preparation of **22** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 6:1) 0.71; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (6 H, s, O*Me*-7′ and O*Me*-7), other data see Table 4; ESIMS *m/z* 346 ([M + H_2O]$^+$); HRFABMS *m/z* 328.1676 (calcd for $C_{20}H_{24}O_4$, 328.1675).

3-(3-Methoxyphenyl)propyl-3-(2,3,4-trimethoxyphenyl)-propanoate (23). The method of preparation of **23** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (6 H, s, O*Me*-7 and O*Me*-7′), 3.81 (3 H, s, O*Me*-6), 3.78 (3 H, s, O*Me*-8), other data see Table 4; ESIMS *m/z* 406 ([M + H_2O]$^+$); HRFABMS *m/z* 388.1882 (calcd for $C_{22}H_{28}O_6$, 388.1886).

3-(3,4-Dimethoxyphenyl)propyl-3-(3-aminophenyl)propanoate (24). The method of preparation of **24** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.13; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.30 (2 H, s, *NH$_2$*-7), 3.87 (3 H, s, O*Me*-6′), 3.86 (3 H, s, O*Me*-7′), other data see Table 4; ESIMS *m/z* 344 ([M + 1]$^+$); HRFABMS *m/z* 343.1782 (calcd for $C_{20}H_{25}NO_4$, 343.1784).

3-Phenylpropyl-3-(3-methoxymethoxyphenyl)propanoate (25). The method of preparation of **25** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15 (2 H, s, *OCH$_2$O*-7), 3.47 (3 H, s, O*Me*-7), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 329 ([M + 1]$^+$); HRFABMS *m/z* 328.1671 (calcd for $C_{20}H_{24}O_4$, 328.1675).

3-Phenylpropyl-3-(3-hydroxyphenyl)propanoate (26). The method of preparation of **26** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 (1 H, s, *OH*-7), other data see Table 4; ESIMS *m/z* 285 ([M + 1]$^+$); HRFABMS *m/z* 284.1420 (calcd for $C_{18}H_{20}O_3$, 284.1412).

3-(3-Methylphenyl)propyl-3-(3-methylphenyl)propanoate (27). The method of preparation of **27** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.26; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (3 H, s, *Me*-7′), 2.33 (3 H, s, *Me*-7), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 314 ([M + H_2O]$^+$); HRFABMS *m/z* 296.1768 (calcd for $C_{20}H_{24}O_2$, 296.1776).

3-(3-Methoxymethoxyphenyl)propyl-3-(3-methoxymethoxyphenyl)propanoate (28). The method of preparation of **28** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.62; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.16 (2 H, s, *OCH$_2$O*-7), 5.15 (2 H, s, *OCH$_2$O*-7′), 3.48 (3 H, s, O*Me*-7), 3.47 (3 H, s, O*Me*-7′), 2.91 (2 H, t, J = 8.0 Hz, H-3), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 406 ([M + H_2O]$^+$); HRFABMS *m/z* 388.1876 (calcd for $C_{22}H_{28}O_6$, 388.1886).

3-(3-Methoxymethoxyphenyl)propyl-3-(3,4-dimethoxymethoxyphenyl)propanoate (29). The method of preparation of **29** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (2 H, s, *OCH$_2$O*-6), 5.20 (2 H, s, *OCH$_2$O*-7), 5.16 (2 H, s, *OCH$_2$O*-7′), 3.52 (3 H, s, O*Me*-6), 3.51 (3 H, s, O*Me*-7), 3.48 (3 H, s, O*Me*-7′), other data see Table 4; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 5; ESIMS *m/z* 466 ([M + H_2O]$^+$); HRFABMS *m/z* 448.2090 (calcd for $C_{24}H_{32}O_8$, 448.2097).

3-Phenylpropyl-3-(3,4-dimethoxymethoxyphenyl)propanoate (30). The mixture of **14** (0.05 g, 0.13 mmol) and 10% Pd/C (0.01 g) was suspended in AcOEt (15 mL) and was pressurized by H_2 gas overnight. The resulted mixture was filtered through kieselguhr and evaporated. The residue was purified by column chromatography eluted with 25% AcOEt/hexane to afford **30** (47 mg, 93%) as a colorless oil; R_f (hexane/AcOEt, 3:1) 0.54; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (2 H, s, *OCH$_2$O*-6), 5.20 (2 H, s, *OCH$_2$O*-7), 3.52 (3 H, s, O*Me*-6), 3.51 (3 H, s, O*Me*-7), other data see Table 4; ESIMS *m/z* 406 ([M + H_2O]$^+$); HRFABMS *m/z* 388.1869 (calcd for $C_{22}H_{28}O_6$, 388.1886).

3-(3-Hydroxyphenyl)propyl-3-(3-hydroxyphenyl)propanoate (31). The mixture of **15** (0.06 g, 0.22 mmol) and 10% Pd/C (0.01 g) was suspended in AcOEt (15 mL) and was pressurized by H_2 gas overnight. The resulting mixture was filtered through kieselguhr and evaporated. The residue was purified by column chromatography eluted with 25% AcOEt/hexane to afford **31** (54 mg, 82%) as a colorless oil; R_f (hexane/AcOEt, 3:1) 0.13; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (1 H, s, *OH*-6), 5.77 (1 H, s, *OH*-7), other data see Table 4; ESIMS *m/z* 318 ([M + H_2O]$^+$); HRFABMS *m/z* 300.1353 (calcd for $C_{18}H_{20}O_4$, 300.1362).

3-(3-Methoxyphenyl)propyl-3-(3-methoxymethoxyphenyl)propanoate (32). The method of preparation of **32** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15

(2 H, s, *OCH*$_2$*O*-7), 3.79 (3 H, s, O*Me*-7′), 3.29 (3 H, s, O*Me*-7), other data see Table 4; ESIMS *m/z* 376 ([M + H_2O]$^+$); HRFABMS *m/z* 358.1786 (calcd for $C_{21}H_{26}O_5$, 358.1780).

3-(3-Methoxyphenyl)propyl-3-(3-hydroxyphenyl)propanoate (33). The method of preparation of **33** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.20; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (1 H, brs, *OH*-7), 3.79 (3 H, s, O*Me*-7′), other data see Table 4; ESIMS *m/z* 332 ([M + H_2O]$^+$); HRFABMS *m/z* 314.1523 (calcd for $C_{19}H_{22}O_4$, 314.1518).

3-(3,4-Dimethoxymethoxyphenyl)propyl-3-(3-methoxymethoxyphenyl)propanoate (34). The method of preparation of **34** was similar to that used for the preparation of **18**: colorless oil; R_f (hexane/AcOEt, 3:1) 0.39; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 (2 H, s, *OCH*$_2$*O*-6′), 5.23 (2 H, s, *OCH*$_2$*O*-7′), 5.14 (2 H, s, *OCH*$_2$*O*-7), 3.46 (3 H, s, O*Me*-6′), 3.63 (3 H, s, O*Me*-7′), 3.52 (3 H, s, O*Me*-7), other data see Table 4; ESIMS *m/z* 466 ([M + H_2O]$^+$); HRFABMS *m/z* 448.2067 (calcd for $C_{24}H_{32}O_8$, 448.2097).

Cytotoxicity Assay. The cytotoxicity activity of test compounds was performed in 96-well microtiter plates by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. After the cells attached to the substratum, monolayers of cells were incubated with culture medium containing the compounds at different concentrations for 72 h. Control cells were treated with the same volume of deionized water (DI) as the stock of the test agent for examination of the solvent effect. Then 10 μL of MTT (final concentration 5 mg/mL) was added to each well. After 3 h incubation, the supernatant was then removed and the cells were dissolved in DMSO (200 μL/well). The optical density was measured spectrophotometrically at 570 nm on an enzyme-linked immunosorbent assay reader. The 50% cytotoxic concentration (CC_{50}) was calculated as the compound concentration required to reduce the MTT signal by 50% compared with untreated control cultures.

α-Glucosidase Inhibition Assay. The activities of glucosidase were determined in a 96-well plate, and the assay was based on the cleavage of an α-1,6 glucosidic bond in the substrate to release *p*-nitrophenol, which is detected by its absorbance at 405 nm. A reaction mixture consisted of 25 μL of α-glucosidase (0.2 U/mL), 25 μL of 23.2 mM substrate (*p*-nitrophenyl-α-D-glucopyranoside) solution, 25 μL of various concentration of samples, and 175 μL of 67 mM phosphate buffer (pH 6.8). The final volume of the reaction was 250 μL. The reaction mixture was incubated for 15 min at 37 °C, then 50 μL of 1 M Na_2CO_3 was added to the incubation solution to stop the reaction. The negative control was prepared by adding phosphate buffer instead of the sample in the same way as test. Acarbose was utilized as positive control. The blank was prepared by adding phosphate buffer instead of the α-glucosidase in the same way as test. The inhibition rates (%) = $[(OD_{\text{negative control}} - OD_{\text{blank}}) - (OD_{\text{test}} - OD_{\text{test blank}})]/(OD_{\text{negative blank}} - OD_{\text{blank}}) \times 100\%$. IC_{50} value of sample was calculated by the IC_{50} calculative software.

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