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Alkyl and Alkoxycarbonyl Derivatives of Ginkgolide B: Synthesis and Biological Evaluation of PAF Inhibitory Activity

Lihong Hu,[a] Zhongliang Chen,[a,*] Yuyuan Xie,[a] Yuanyin Jiang[b] and Huawu Zhen[c]

[a]*Shanghai Institute of Materia Medica, Academia Sinica, Shanghai 200031, People's Republic of China*
[b]*Second Military Medical University, Shanghai 200433, People's Republic of China*
[c]*Navy 411 Hospital, Shanghai 200081, People's Republic of China*

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Abstract—Alkyl and alkoxycarbonyl derivatives **6**–**24** of ginkgolide B, prepared in one step from ginkgolide B through alkylation and acylation and evaluated for their in vitro ability to inhibit the PAF-induced aggregation of rabbit platelets, show equivalent or superior activities to ginkgolide B.

Introduction

Platelet activating factor (PAF) is the bioactive phospholipid 1-*O*-hexadecyl/octadecyl-2-acetyl-*sn*-glyceryl-3-phosphorylcholine,[1,2] which is released directly from cell membranes and mediates a range of effects on target cells, resulting in a variety of physiological responses.[3,4] PAF appears to be involved in many inflammatory disorders including asthma and endotoxin shock[3,4] and PAF receptor antagonists may be of clinical benefit in such diseases. Among the known types of PAF antagonists, ginkgolides (including ginkgolides A, B, C, J, and M) are especially interesting because of their long history of human use (in the form of extracts of the ginkgo tree, *Ginkgo biloba*), their notable lack of toxicity, and their total resistance to metabolism.[5] The results of clinical trials in phase II and III of ginkgolide B suggested its therapeutic usefulness as a PAF antagonist in inflammatory or autoimmune pathologies, especially renal transplantation and multiple sclerosis.[6] Ginkgolides are unique 20-carbon cage molecules incorporating a *tert*-butyl group and six five-membered rings A–F consisting of a spiro[4.4]nonane system, three lactonic rings, and a tetrahydrofuran ring. The structures of ginkgolides A (**1**), B (**2**), C (**3**), J (**4**), and M (**5**) (Fig. 1) differ only in the number and the position of hydroxyl groups on C_1, C_3, or C_7 of the spirononane framework, which induce strong variations in their anti-PAF potency. Ginkgolide B, with two hydroxyl groups on C_1 and C_3, is the most powerful antagonist. Conversely, ginkgolides C and J, which have a hydroxyl group on C_7, adjacent to the lipophilic *t*-butyl moiety, are less active. In ginkgolide J, the absence of the hydroxyl group on C_1 further decreases its activity in comparison with ginkgolide C. A more drastic loss of antagonistic activity is observed with ginkgolide M, with hydroxyl groups in 1,7 positions. It is, therefore, of interest to synthesize and study the biological activities of ginkgolides by modifying their hydroxyl groups. In our previous study,[7] we found that ring-C-nor-ginkgolide analogues are less active in the anti-PAF potency. As part of our continuing efforts to investigate the relationship between structure and anti-PAF activity, we describe in this paper the preparation and structure–activity relationships of alkyl and alkoxycarbonyl analogues of ginkgolide B, which showed potent inhibitory activity on rabbit platelet aggregation induced by PAF.

Results and Discussion

Corey and co-workers have established the facile alkylation of hydroxyl groups at either C_1 or C_{10} of ginkgolide B.[8] According to their protocol, we have prepared a series of mostly new 1-alkyl, 10-alkyl, and 10-alkoxycarbonyl congeners of ginkgolide B by treating it with appropriate halogenated reagents in the presence of the mild base K_2CO_3. Determination of the position of substitution in these products was based on detailed NMR studies on their HMBC cross peaks, the

*Corresponding author. Tel.: +86-21-6431-1833, ext. 332; fax: +86-21-6437-0269; e-mail: zlchen@server.shcnc.ac.cn

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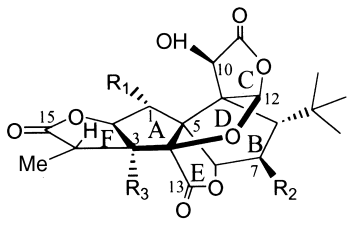


1. ginkgolide A R_1=R_2=H, R_3=OH
2. ginkgolide B R_1=R_3=OH, R_2=H
3. ginkgolide C R_1=R_2=R_3=OH
4. ginkgolide J R_1=H, R_2=R_3=OH
5. ginkgolide M R_1=R_2=OH, R_3=H

Figure 1. Structures of ginkgolides A, B, C, J, and M.

chemical shifts for H-12, and the chemical shifts for their hydroxyl groups (C_1, C_{10}), as well as the NMR spectral analysis of the oxidation products of alkyl analogues, such as compounds **25** and **26**. The chemical shifts of the 1-OH, 3-OH, and 10-OH groups in ginkgolide B occur at 4.89, 6.45, and 7.44 ppm, respectively. By comparison of the ^{1}H NMR data of compounds **7** and **20**, **8** and **21** with those of ginkgolide B, we could determine compounds **7** and **8** were 10-substituted derivatives and compounds **20** and **21** were 1-substituted analogues and these assignments were confirmed by their HMBC cross peaks. Of the two hydroxyl groups, 1-OH and 10-OH, the latter is nearer to H-12. Hence the chemical shift for H-12 is affected when the 10-OH is alkylated or acylated. From the ^{1}H NMR data of compounds **7** and **20**, **8** and **21**, **9** and **22**, **11** and **23**, we observed a simple correlation that values of chemical shifts for H-12 of 10-substituted analogues were found above 6.10 ppm and those of 1-substituted derivatives occurred below 6.10 ppm. Using this correlation, we could determine the substituted positions of all the compounds prepared.

Compounds **6**–**26** were evaluated as PAF antagonists in vitro using an assay involving rabbit platelets (Table 1). Methyl or alkoxymethyl derivatives **6**–**8**, **10** and **21** were only slightly less active than ginkgolide B. Considering unsaturated derivatives **9**–**19** and **22**–**23**, we found that derivatives containing the aromatic ring, carbonyl, and alkoxycarbonyl were more active than the allyl analogue **10**. Examination of the derivatives with substituted aromatic rings suggested that a weak electron-attracting group (-Cl) is more favourable to anti-PAF activity than the strong electron-attracting groups (-F, -NO_2). 1-Substituted analogues are comparable to 10-substituted in their anti-PAF potency, as shown by compounds **7** and **20**, **8** and **21**, **9** and **22**. The oxidized product (**25**) of ginkgolide B is 8 times less active than the parent compound.

It can be seen from this study that modifications at the 1- or 10-hydroxyl group of ginkgolide B can give products with better antagonistic activity than the parent compound. The most active derivative prepared which showed ginkgolide-like activity is the 10-*O*-*p*-chlorobenzyl analogue **17**, which possesses about 4-fold increased potency compared to ginkgolide B in the anti-PAF assay. Further evaluation of these derivatives is in progress in our laboratory.

Experimental

General experimental procedures

IR spectra were measured with a Perkin–Elmer 559B apparatus. ^{1}H NMR spectra were obtained on a Bruker AMX-400 spectrometer, using acetone-d_6 and DMSO-d_6 as solvents and TMS as internal standard. Mass spectra were measured on an MAT-711 mass spectrometer. C-18-PAF acether was purchased from Sigma Co. Ltd.

Table 1. In vitro biological evaluation of alkyl and alkoxycarbonyl analogues of ginkgolide B

Compound	R_1	R_2	PAF-induced platelet aggregation IC_{50}[a] (μM)
Ginkgolide B			0.128 (0.102–0.145)
6			0.232 (0.197–0.283)
7	H	CH_3	0.571 (0.486–0.653)
8	H	CH_3OCH_2	1.68 (1.57–1.75)
9	H	$PhCH_2OCH_2$	0.0588 (0.0541–0.705)
10	H	CH_2=$CHCH_2$	1.09 (0.857–1.27)
11	H	$CH_3CH_2OOCCH_2$	0.0429 (0.0363–0.0497)
12	H	$PhCOCH_2$	0.121 (0.109–0.142)
13	H	*p*-$MeOC_6H_4COCH_2$	0.106 (0.0872–1.341)
14	H	$PhCH_2$	0.0404 (0.0336–0.512)
15	H	$PhCH(CH_3)$	1.63 (1.45–1.77)
16	H	*p*-$O_2NC_6H_4CH_2$	0.108 (0.0882–0.136)
17	H	*p*-$ClC_6H_4CH_2$	0.0289 (0.0267–0.0304)
18	H	*p*-$FC_6H_4CH_2$	0.0440 (0.336–0.514)
19	H	CH_3CH_2OCO	0.426 (0.407–0.472)
20	CH_3	H	0.344 (0.305–0.374)
21	CH_3OCH_2	H	0.203 (0.128–0.257)
22	$PhCH_2OCH_2$	H	0.0404 (0.0369–0.438)
23	$CH_3CH_2OOCCH_2$	H	0.213 (0.194–0.264)
24	CH_3OCH_2	CH_3OCH_2	2.06 (1.83–2.58)
25			1.00 (0.856–1.24)
26			22.8 (20.3–24.9)

[a]Concentration required to inhibit PAF-induced maximum aggregation by 50%. Parentheses contain 95% confidence limits.

Materials

Ginkgolide B, isolated from Chinese medicinal herb *Ginkgo biloba* L., was used as the starting material.

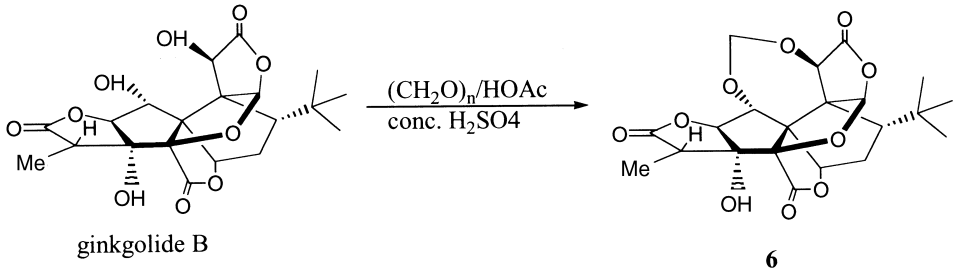
1,10-*O*,*O*-Methyleneginkgolide B (6). To a solution of 200 mg of ginkgolide B in 10 mL of THF were added 2 mL of acetic acid, 140 mg of paraformaldehyde and 0.25 mL of concentrated sulfuric acid (Scheme 1). The reaction mixture was refluxed for 8 h and cooled. The insoluble paraformaldehyde was filtered off and the filtrate was evaporated to give a solid. The solid was taken up in 5 mL of water and the aqueous layer was extracted three times with 5 mL of ethyl acetate. The organic layers were evaporated to give a solid, which was subjected to column chromatography on silica gel. Elution with cyclohexane:acetone (3:1) and evaporation gave **6** (127 mg) as a solid in 61.8% yield. IR (KBr) ν_{max} 3408, 1780, 1774, 1740 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 1.03 (9H, s, *t*-Bu), 1.10 (3H, d, $J=7.0$ Hz, H-16), 1.82 (1H, dd, $J=13.7$, 4.6 Hz, H-8), 2.08 (1H, m, H-7α), 2.21 (1H, dd, $J=13.7$, 4.7 Hz, H-7β), 2.86 (1H, q, $J=7.1$ Hz, H-14), 3.98 (1H, d, $J=8.8$ Hz, H-1β), 5.00 (1H, d, $J=8.9$ Hz, H-2), 5.08 (1H, d, $J=7.6$ Hz, *O*-C**H$_2$**-*O*), 5.14 (1H, d, $J=7.7$ z, *O*-C**H$_2$**-*O*), 5.37 (1H, d, $J=3.6$ Hz, H-6), 5.59 (1 H, s, H-10), 6.16 (1H, s, H-12), 6.75 (1H, s, 3-OH). HREIMS *m*/*z* 436.13604, $C_{21}H_{24}O_{10}$ requires 436.13695; EIMS *m*/*z* 436 $[M]^+$, 421, 392, 374, 349, 334, 303, 277, 249, 215, 111, 83, 57.

General procedure of *O*-alkylation and *O*-acylation of ginkgolide B

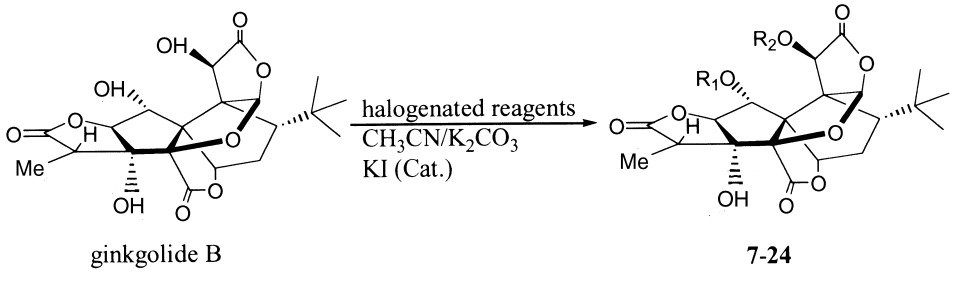
7–24 were prepared according to the previously reported method (Scheme 2).[8] The appropriate halogenated reagent was added to a solution of 333 mg of ginkgolide B in 5 mL of CH_3CN containing 400 mg of K_2CO_3 and a catalytic amount of KI. The mixture was refluxed for 0.5 h. The insoluble K_2CO_3 was filtered off, the filtrate was then removed under reduced pressure and the residue was purified by flash chromatography.

10-*O*-Methylginkgolide B (7) and 1-*O*-methylginkgolide B (20). Compounds **7** and **20** were prepared from 333 mg of ginkgolide B and methyl iodide (400 mg) as described by the preceding general procedure to obtain white solids **7** (200 mg, 60.1%) and **20** (92 mg, 26.7%) after flash chromatography (cyclohexane:acetone 2:1). **7**: IR (KBr) ν_{max} 3560, 1778 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 1.03 (9H, s, *t*-Bu), 1.10 (3H, d, $J=7.0$ Hz, H-16), 1.70 (1H, dd, $J=14.2$, 4.4 Hz, H-8), 1.86 (1H, ddd, $J=14.2$, 13.4, 4.4 Hz, H-7α), 2.12 (1H, dd, $J=13.4$, 4.4 Hz, H-7β), 2.84 (1H, q, $J=7.0$ Hz, H-14), 3.63 (3 H, s, OMe), 4.07 (1H, d, $J=6.8$ Hz, H-1β), 4.60 (1H, d, $J=6.9$ Hz, H-2), 4.91 (1H, s, H-10), 5.12 (1 H, d, $J=4.1$ Hz, 1-OH), 5.30 (1H, d, $J=3.9$ Hz, H-6), 6.10 (1H, s, H-12), 6.46 (1 H, s, 3-OH). HREI-MS *m*/*z* 438.15299, $C_{21}H_{26}O_{10}$ requires 438.15260; EIMS *m*/*z* 438 $[M]^+$, 423, 394, 362, 306, 254, 210, 178, 149, 113, 57. **20**: IR (KBr) ν_{max} 3439, 1792 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 1.02 (9H, s, *t*-Bu), 1.12 (3H, d, $J=7.4$ Hz, H-16), 1.70 (1H, dd, $J=14.2$, 4.4 Hz, H-8), 1.91 (1H, ddd, $J=14.2$, 13.4, 4.4 Hz, H-7α), 2.07 (1H, dd, $J=13.5$, 4.6 Hz, H-7β), 2.88 (1H, q, $J=7.1$ Hz, H-14), 3.33 (3 H, s, OMe), 3.79 (1H, d, $J=5.1$ Hz, H-1β), 4.74 (1H, d, $J=4.9$ Hz, H-2), 4.98 (1H, d, $J=5.0$ Hz, H-10), 5.30 (1H, d, $J=3.8$ Hz, H-6), 6.02 (1H, s, H-12), 6.49 (1H, s, 3-OH), 6.77 (1H, d, $J=5.1$ Hz, 10-OH). HREI-MS *m*/*z* 438.15209, $C_{21}H_{26}O_{10}$ requires 438.15260; EI-MS *m*/*z* 438 $[M]^+$, 420, 365, 321, 307, 259, 57.

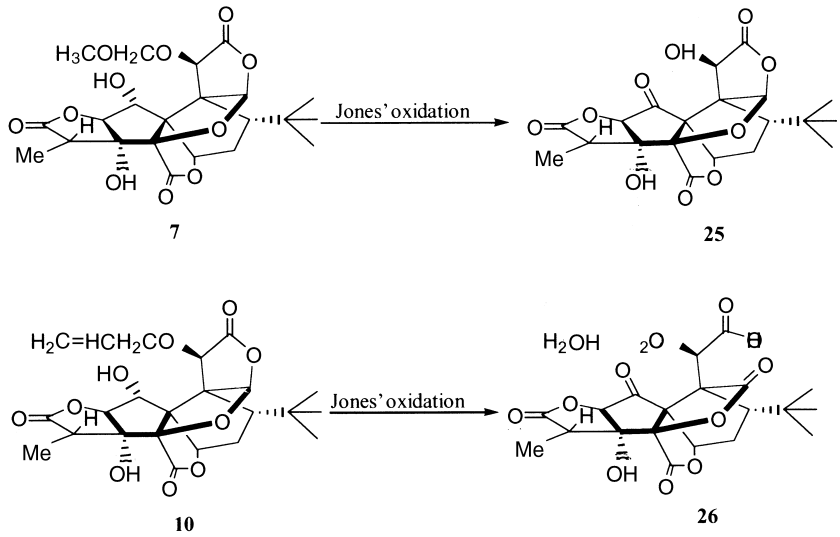
10-*O*-Methoxymethylginkgolide B (8), 1-*O*-methoxymethylginkgolide B (21) and 1,10-*O*-dimethoxymethylginkgolide B (24). Compounds **8**, **21** and **20** were prepared from 333 mg of ginkgolide B and chloromethyl methyl ether (250 mg) as described by the preceding



Scheme 1. Synthesis of 1,10-*O*-*O*-methyleneginkgolide B (**6**).



Scheme 2. Synthesis of 1- or 10-*O*-alkylginkgolide B (**7**–**24**).



Scheme 3. Oxidation of compounds **7** and **10**.

general procedure to obtain white solids **8** (71 mg, 19.2%), **21** (101 mg, 27.4%) and **24** (102 mg, 25.4%) after flash chromatography (cyclohexane:acetone 2:1). **8**: IR (KBr) ν_{max} 3566, 3540, 1786 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 1.20 (9H, s, *t*-Bu), 1.26 (3H, d, J = 7.1 Hz, H-16), 1.92 (1H, dd, J = 14.3, 4.1 Hz, H-8), 2.08 (1H, ddd, J = 14.4, 13.6, 4.3 Hz, H-7α), 2.29 (1H, dd, J = 13.6, 4.2 Hz, H-7β), 3.03 (1H, q, J = 7.1 Hz, H-14), 3.47 (3 H, s, **Me**OCH_2-), 4.27 (1H, d, J = 7.7 Hz, H-1β), 4.66 (1H, d, J = 7.7 Hz, H-2), 5.13 (1H, d, J = 6.4 Hz, MeOC**H_2**-), 5.31 (1H, d, J = 6.4 Hz, MeOC**H_2**-), 5.40 (1H, s, H-10), 5.44 (1H, d, J = 4.1 Hz, H-6), 6.20 (1H, s, H-12),. HREIMS m/z 468.16310, $C_{22}H_{28}O_{11}$ requires 468.16317; EIMS m/z 468 $[M]^+$, 452, 422, 362, 321, 270, 240, 171, 141, 59. **21**: IR (KBr) ν_{max} 3439, 3430, 1774 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 1.16 (9H, s, *t*-Bu), 1.26 (3H, d, J = 7.1 Hz, H-16), 1.93 (1H, dd, J = 14.2, 4.4 Hz, H-8), 2.11 (1H, ddd, J = 14.2, 13.2, 4.4 Hz, H-7α), 2.21 (1H, dd, J = 13.3, 4.1 Hz, H-7β), 3.08 (1H, q, J = 7.1 Hz, H-14), 3.39 (3H, s), (**Me**OCH_2-), 4.28 (1H, d, J = 5.4 Hz, H-1β), 4.45 (1H, d, J = 6.3 Hz, MeOC**H_2**-), 4.80 (1H, d, J = 5.4 Hz, H-2), 4.86 (1H, d, J = 6.3 Hz, MeOC**H_2**), 5.22 (1H, s, H-10), 5.49 (1H, d, J = 3.9 Hz, H-6), 6.08 (1H, s, H-12). HREI-MS m/z 468.16353, $C_{22}H_{28}O_{11}$ requires 468.16317; EI-MS m/z 468 $[M]^+$, 450, 406, 362, 305, 277, 221, 163, 113, 59. **24**: IR (KBr) ν_{max} 3547, 1786 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 1.19 (9H, s, *t*-Bu), 1.26 (3H, d, J = 7.6 Hz, H-16), 1.91 (1H, dd, J = 14.2, 4.4 Hz, H-8), 2.08 (1H, ddd, J = 14.2, 13.2, 4.4 Hz, H-7), 2.24 (1H, dd, J = 13.2, 4.1 Hz, H-7β), 3.04 (1H, q, J = 7.5 Hz, H-14), 3.42 (3H, s, **Me**OCH_2-), 3.43 (3H, s, **Me**OCH_2-), 4.26 (1H, d, J = 4.8 Hz, H-1β), 4.75 (1H, d, J = 6.4 Hz, MeOC**H_2**-), 4.79 (1H, d, J = 6.3 Hz, MeOC**H_2**-), 4.80 (1H, d, J = 4.7 Hz, H-2), 5.02 (1H, d, J = 6.3 Hz, MeOC**H_2**-), 5.20 (1H, d, J = 6.3 Hz, MeOC**H_2**-), 5.32 (1H, s, H-10), 5.54 (1H, d, J = 3.9 Hz, H-6), 6.14 (1H, s, H-12). HREI–MS: m/z 512.18961, $C_{24}H_{32}O_{12}$ requires 512.18938; EI–MS m/z 512 $[M]^+$, 481, 437, 361, 305, 259, 191, 163, 70, 59.

10-*O*-Benzyloxymethylginkgolide B (9) and 1-*O*-benzyloxymethylginkgolide B (22). Compounds **9** and **22** were prepared from 333 mg of ginkgolide B and chloromethyl benzyl ether (450 mg) as described by the preceding general procedure to obtain white solids **9** (217 mg, 50.7%) and **22** (63 mg, 14.7%) after flash chromatography (cyclohexane:acetone 2:1). **9**: IR (KBr) ν_{max} 3566, 3540, 1786 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 1.03 (9H, s, *t*-Bu), 1.12 (3H, d, J = 7.0 Hz, H-16), 1.69 (1H, dd, J = 14.3, 4.2 Hz, H-8), 1.89 (1H, ddd, J = 14.3, 13.6, 4.2 Hz, H-7α), 2.14 (1H, dd, J = 13.6, 4.4 Hz, H-7β), 2.86 (1H, q, J = 7.0 Hz, H-14), 4.12 (1H, d, J = 6.8 Hz, H-1β), 4.58 (1H, d, J = 11.7 Hz, $PhCH_2OC$**H_2**-), 4.62 (1H, d, J = 6.8 Hz, H-2), 4.67 (1H, d, J = 12.0 Hz, $PhCH_2OC$**H_2**-), 4.76 (1H, d, 4.76, J = 4.0 Hz, 1-OH), 5.16 (1H, d, J = 6.6 Hz, Ph**CH_2**OCH_2-), 5.26 (1H, d, J = 6.6 Hz, Ph**CH_2**OCH_2-), 5.33 (1H, s, H-10), 5.36 (1H, d, J = 3.7 Hz, H-6), 6.14 (1H, s, H-12), 6.46 (1H, s, 3-OH), 7.31 (5H, m, **Ph**CH_2OCH_2-). HREIMS m/z 544.19483, $C_{28}H_{32}O_{11}$ requires 544.19447; EIMS m/z 544 $[M]^+$, 499, 470, 453, 438, 408, 335, 321, 120, 191, 57. **22:** IR (KBr) ν_{max} 3439, 3430, 1774 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) 1.03 (9H, s, *t*-Bu), 1.13 (3H, d, J = 7.6 Hz, H-16), 1.72 (1H, dd, J = 13.9, 4.1 Hz, H-8), 1.93 (1H, ddd, J = 13.9, 13.7, 3.8 Hz, H-7α), 2.10 (1H, dd, J = 13.7, 4.1 Hz, H-7β), 2.89 (1H, q, J = 7.3 Hz, H-14), β 4.19 (1H, d, J = 4.5 Hz, H-1β), 4.52 (1H, d, J = 11.8 Hz, $PhCH_2OC$**H_2**-), 4.71 (1H, d, J = 11.8 Hz, $PhCH_2OC$**H_2**-), 4.80 (2H, m, Ph**CH_2**OCH_2-), 4.99 (1H, d, J = 3.1 Hz, H-10), 5.39 (1H, d, J = 3.4 Hz, H-6), 6.03 (1H, s, H-12), 6.53 (1H, s, 3-OH), 6.93 (1H, d, J = 3.0 Hz, 10-OH), 7.33 (5H, m, **Ph**CH_2OCH_2-). HREIMS m/z 544.19453, $C_{28}H_{32}O_{11}$ requires 544.19447; EIMS m/z 544 $[M]^+$, 499, 468, 408, 346, 321, 261, 190, 108, 91, 57.

10-*O*-Allylginkgolide B (10). Compound **10** was prepared from 333 mg of ginkgolide B and allyl bromide (339 mg) as described by the preceding general procedure to obtain white solid **10** (320 mg, 87.8%) after flash chromatography (cyclohexane:acetone 2:1). **10**: IR

(KBr) ν_{max} 3539, 3502, 1793, 1776 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 1.02 (9H, s, *t*-Bu), 1.11 (3H, d, J = 7.1 Hz, H-16), 1.71 (1H, dd, J = 14.2, 4.1 Hz, H-8), 1.89 (1H, ddd, J = 14.1, 13.6, 4.1 Hz, H-7α), 2.13 (1H, dd, J = 13.5, 4.2 Hz, H-7β), 2.84 (1H, q, J = 7.1 Hz, H-14), 4.12 (1H, d, J = 6.7 Hz, H-1β), 4.12 (1H, dd, J = 11.6, 4.8 Hz, CH_2=CHC**H$_2$**-), 4.63 (1H, d, J = 6.7 Hz, H-2), 4.77 (1H, dd, J = 12.9, 4.9 Hz, CH_2=CHC**H$_2$**-), 5.09 (1H, s, H-10), 5.16 (1H, d, J = 10.5 Hz, C**H$_2$**=CHCH$_2$-), 5.29 (1H, d, J = 17.5 Hz, C**H$_2$**=CHCH$_2$-), 5.33 (1H, d, J = 3.7 Hz, H-6), 5.95 (1H, m, CH_2=C**H**CH$_2$-), 6.13 (1H, s, H-12), 6.50 (1H, s, 3-OH). ^1H NMR (acetone-d_6, 400 MHz) δ 1.17 (9H, s, *t*-Bu), 1.26 (3H, d, J = 7.1 Hz, H-16), 1.94 (1H, dd, J = 14.4, 4.6 Hz, H-8), 2.09 (1H, m, H-7α), 2.28 (1H, dd, J = 13.6, 4.6 Hz, H-7β), 3.03 (1H, q, J = 7.1 Hz, H-14), 4.25 (1H, d, J = 7.8 Hz, H-1β), 4.33 (1H, dd, J = 11.7, 6.3 Hz, CH_2=CHC**H$_2$**-), 4.68 (1H, d, J = 7.8 Hz, H-2), 4.92 (1H, dd, J = 11.7, 6.3 Hz, CH_2=CHC**H$_2$**-), 5.25 (1H, s, H-10), 5.40 (1H, d, J = 4.3 Hz, H-6), 5.42 (1H, dd, J = 10.7, 1.0 Hz, C**H$_2$**=CHCH$_2$-), 6.08 (2H, m, C**H$_2$**=C**H**CH$_2$-), 6.18 (1H, s, H-12). HREIMS m/z 464.16803, $C_{23}H_{28}O_{10}$ requires 464.16825; EIMS m/z 464 $[M]^+$, 449, 421, 405, 387, 364, 335, 307, 221, 135, 113, 95, 69, 57.

10-*O*-Ethyloxycarbonylmethylginkgolide B (11) and 1-*O*-ethyloxycarbonylmethylginkgolide B (23). Compounds **11** and **23** were prepared from 333 mg of ginkgolide B and ethyl α-bromoacetate (467 mg) as described by the preceding general procedure to obtain white solids **11** (313 mg, 78.3%) and **23** (49 mg, 12.1%) after flash chromatography (cyclohexane:acetone 2:1). **11**: IR (KBr) ν_{max} 3481, 1784, 1743 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 1.16 (9H, s, *t*-Bu), 1.26 (3H, d, J = 7.0 Hz, H-16), 1.28 (3H, t, J = 7.1 Hz, C**H$_3$**CH$_2$OOCCH$_2$-), 1.96 (1H, ddd, J = 14.3, 13.6, 4.2 Hz, H-7α), 2.07 (1H, m, H-8), 2.28 (1H, dd, J = 13.6, 4.4 Hz, H-7β), 3.01 (1H, q, J = 7.1 Hz, H-14), 4.27 (2H, q, J = 7.1 Hz, CH$_3$C**H$_2$**OOCCH$_2$-), 4.28 (1H, d, J = 7.6 Hz, H-1β), 4.54 (1H, d, J = 15.6 Hz, CH$_3$CH$_2$OOCC**H$_2$**-), 4.67 (1H, d, J = 7.7 Hz, H-2), 4.98 (1H, d, J = 15.7 Hz, CH$_3$CH$_2$OOCC**H$_2$**-), 5.44 (1H, d, J = 3.9 Hz, H-6), 5.38 (1H, s, H-10), 6.19 (1H, s, H-12). HREIMS m/z 510.17365, $C_{24}H_{30}O_{12}$ requires 510.17373; EIMS m/z 510 $[M]^+$, 492, 437, 362, 323, 259, 95, 57. **23**: IR (KBr) ν_{max} 3440, 1794, 1730 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 1.16 (9H, s, *t*-Bu), 1.25 (3H, d, J = 7.0 Hz, H-16), 1.25 (3H, t, J = 7.1 Hz, C**H$_3$**CH$_2$OOCCH$_2$-), 2.16 (1H, ddd, J = 14.3, 13.6, 4.2 Hz, H-7α), 2.24 (1H, dd, J = 13.6, 4.4 Hz, H-7β), 2.24 (1H, m, H-8), 3.05 (1H, q, J = 7.0 Hz, H-14), 4.19 (1H, d, J = 5.9 Hz, H-1β), 4.20 (2H, q, J = 7.1 Hz, CH$_3$C**H$_2$**OOCCH$_2$-), 4.33 (1H, d, J = 5.1 Hz, H-2), 4.33 (1H, d, J = 15.9 Hz, CH$_3$CH$_2$OOCC**H$_2$**-), 4.95 (1H, d, J = 16.1 Hz, CH$_3$CH$_2$OOCC**H$_2$**-), 5.23 (1H, s, H-10), 5.51 (1H, d, J = 3.9 Hz, H-6), 6.08 (1H, s, H-12). HREIMS m/z 510.17370, $C_{24}H_{30}O_{12}$ requires 510.17373; EIMS m/z 510 $[M]^+$, 495, 437, 363, 333, 259, 231, 163, 83, 57.

10-*O*-Phenacylginkgolide B (12). Compound **12** was prepared from 333 mg of ginkgolide B and 2-chloroacetophenone (433 mg) as described by the preceding general procedure to obtain white solid **12** (380 mg, 89.2%) after flash chromatography (cyclohexane:acetone 2:1). **12**: IR (KBr) ν_{max} 3419, 1786, 1691 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 1.05 (9H, s, *t*-Bu), 1.12 (3H, d, J = 7.0 Hz, H-16), 1.78 (1H, dd, J = 14.2, 4.1 Hz, H-8), 1.92 (1H, ddd, J = 14.1, 13.6, 4.1 Hz, H-7α), 2.18 (1H, dd, J = 13.6, 4.3 Hz, H-7β), 2.83 (1H, q, J = 7.1 Hz, H-14), 4.11 (1H, dd, J = 7.7, 3.0 Hz, H-1β), 4.71 (1H, d, J = 7.7 Hz, H-2), 5.31 (1H, d, J = 17.7 Hz, PhCOC**H$_2$**-), 5.38 (1H, s, H-10), 5.40 (1H, d, J = 3.7 Hz, H-6), 5.65 (1H, d, J = 17.6 Hz, PhCOC**H$_2$**-), 5.78 (1H, d, J = 3.2 Hz, 1-OH), 6.25 (1H, s, H-12), 6.56 (1H, s, 3-OH), 7.59 (2H, d, J = 7.6 Hz, **Ph**COCH$_2$-), 7.73 (1H, t, J = 7.5 Hz, **Ph**COCH$_2$-), 7.92 (2H, d, J = 8.1 Hz, **Ph**COCH$_2$-). ^1H NMR (acetone-d_6, 400 MHz) δ 1.18 (9H, s, *t*-Bu), 1.27 (3H, d, J = 7.0 Hz, H-16), 1.99 (1H, dd, J = 13.6, 4.3 Hz, H-8), 2.11 (1H, ddd, J = 14.1, 13.6, 4.1 Hz, H-7α), 2.28 (1H, dd, J = 13.6, 4.3 Hz, H-7β), 3.04 (1H, q, J = 7.0 Hz, H-14), 4.34 (1H, d, J = 7.7 Hz, H-1), 4.72 (1H, d, J = 7.7 Hz, H-2), 5.48 (1H, d, J = 17.3 Hz, PhCOC**H$_2$**-), 5.49 (1H, s, H-10), 5.51 (1H, d, J = 4.0 Hz, H-6), 5.85 (1H, d, J = 17.3 Hz, PhCOC**H$_2$**-), 6.23 (1H, s, H-12), 7.59 (2H, d, J = 7.8 Hz, **Ph**COCH$_2$-), 7.73 (1H, t, J = 7.8 Hz, **Ph**COCH$_2$-), 8.01 (2H, d, J = 7.8 Hz, **Ph**COCH$_2$-). HREIMS m/z 542.17820, $C_{28}H_{30}O_{11}$ requires 542.17882; EIMS m/z 542 $[M]^+$, 524, 498, 469, 451, 408, 379, 323, 294, 120, 105, 91, 77, 57.

10-*O*-*p*-Methoxyphenacylginkgolide B (13). Compound **13** was prepared from 333 mg of ginkgolide B and 2-bromo-*p*-methoxyacetophenone (640 mg) as described by the preceding general procedure to obtain white solid **13** (405 mg, 90.1%) after flash chromatography (cyclohexane:acetone 2:1). **13**: IR (KBr) ν_{max} 3410, 1790, 1680, 1601 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 1.18 (9H, s, *t*-Bu), 1.27 (3H, d, J = 7.0 Hz, H-16), 1.99 (1H, dd, J = 14.2, 4.3 Hz, H-8), 2.08 (1H, ddd, J = 14.1, 13.6, 4.1 Hz, H-7α), 2.28 (1H, dd, J = 13.3, 4.4 Hz, H-7β), 3.03 (1H, q, J = 7.0 Hz, H-14), 3.92 (3H, s, *p*-**Me**OC$_6$H$_4$COCH$_2$-), 4.34 (1H, d, J = 7.8 Hz, H-1β), 4.71 (1H, d, J = 7.8 Hz, H-2), 5.41 (1H, d, J = 16.9 Hz, *p*-MeOC$_6$H$_4$COC**H$_2$**-), 5.47 (1H, s, H-10), 5.51 (1H, d, J = 3.9 Hz, H-6), 5.78 (1H, d, J = 17.1 Hz, *p*-MeOC$_6$H$_4$-COC**H$_2$**-), 6.22 (1H, s, H-12), 7.09 (2H, d, J = 8.8 Hz, *p*-MeOC$_6$**H$_4$**COCH$_2$-), 7.98 (2H, d, J = 8.7 Hz, *p*-MeOC$_6$**H$_4$**COCH$_2$-). HREIMS m/z 572.18986, $C_{29}H_{32}O_{12}$ requires 572.18938; EIMS m/z 572 $[M]^+$, 554, 528, 499, 443, 408, 388, 350, 165, 150, 135, 77, 57.

10-*O*-Benzylginkgolide B (14). Compound **14** was prepared from 333 mg of ginkgolide B and benzyl chloride (355 mg) as described by the preceding general procedure to obtain white solid **14** (264 mg, 65.3%) after flash chromatography (cyclohexane:acetone 2:1). **14**: IR (KBr) ν_{max} 3529, 1780 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 1.01 (9H, s, *t*-Bu), 1.12 (3H, d, J = 7.1 Hz, H-16), 1.73 (1H, dd, J = 14.2, 4.3 Hz, H-8), 1.87 (1H, ddd, J = 14.1, 13.6, 4.1 Hz, H-7), 2.13 (1H, dd, J = 13.3, 4.4 Hz, H-7β), 2.87 (1H, q, J = 7.0 Hz, H-14), 4.15 (1H, dd, J = 6.7, 3.2 Hz, H-1β), 4.62 (1H, d, J = 6.7 Hz, H-2), 4.67 (1H, d, J = 11.3 Hz, C$_6$H$_5$C**H$_2$**-), 4.79 (1H, d, J = 3.2 Hz, 1-OH), 5.25 (1H, s, H-10), 5.31 (1H, d, J = 3.7 Hz, H-6), 5.35 (1H, d, J = 11.4 Hz, C$_6$H$_5$C**H$_2$**-), 6.19 (1H, s, H-12), 6.49 (1H, s, 3-OH), 7.36 (5H, m,

$C_6\mathbf{H_5}CH_2$-). HREIMS *m/z* 514.18308, $C_{27}H_{30}O_{10}$ requires 514.18390; EIMS *m/z* 514 $[M]^+$, 423, 408, 335, 245, 221, 177, 91, 57.

10-*O*-α-Methylbenzylginkgolide B (15). Compound **15** was prepared from 333 mg of ginkgolide B and α-methylbenzyl chloride (394 mg) as described by the preceding general procedure to obtain white solid **15** (194 mg, 46.7%) after flash chromatography (cyclohexane:acetone 2:1). **15**: IR (KBr) ν_{max} 3502, 1790 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 0.66 (9H, s, *t*-Bu), 1.12 (3H, d, *J* = 7.1 Hz, H-16), 1.53 (1H, dd, *J* = 14.6, 4.1 Hz, H-8), 1.60 (3H, d, *J* = 6.4 Hz, $C_6H_5CH(C\mathbf{H_3})$-), 1.73 (1H, ddd, *J* = 14.1, 13.6, 4.1 Hz, H-7α), 2.87 (1H, q, *J* = 7.0 Hz, H-14), 3.00 (1H, dd, *J* = 13.3, 4.2 Hz, H-7β), 4.26 (1H, d, *J* = 6.4 Hz, H-1β), 4.68 (1H, d, *J* = 6.4 Hz, H-2), 5.11 (1H, q, *J* = 6.6 Hz, $C_6H_5C\mathbf{H}(CH_3)$-), 5.13 (1H, s, H-10), 5.38 (1H, d, *J* = 3.7 Hz, H-6), 6.07 (1H, s, H-12), 7.33 (5H, m, $C_6\mathbf{H_5}CH(CH_3)$-). ^1H NMR (acetone-d_6, 400 MHz) δ 0.76 (9H, s, *t*-Bu), 1.27 (3H, d, *J* = 7.1 Hz, H-16), 1.70 (3H, d, *J* = 6.5 Hz, $C_6H_5CH(C\mathbf{H_3})$-), 1.78 (1H, dd, *J* = 14.6, 4.1 Hz, H-8), 1.92 (1H, ddd, *J* = 14.1, 13.6, 4.1 Hz, H-7α), 2.14 (1H, dd, *J* = 13.3, 4.2 Hz, H-7β), 3.06 (1H, q, *J* = 7.1 Hz, H-14), 4.36 (1H, d, *J* = 7.4 Hz, H-1β), 4.71 (1H, d, *J* = 7.6 Hz, H-2), 5.24 (1H, s, H-10), 5.42 (1H, d, *J* = 3.7 Hz, H-6), 5.42 (1H, m, $C_6H_5C\mathbf{H}(CH_3)$-), 6.12 (1H, s, H-12), 7.33–7.49 (5H, m, $C_6\mathbf{H_5}CH(CH_3)$-). HREIMS *m/z* 528.19959, $C_{28}H_{32}O_{10}$ requires 528.19955; EIMS *m/z* 528 $[M]^+$, 513, 484, 380, 361, 335, 321, 105, 57.

10-*O*-*p*-Nitrobenzylginkgolide B (16). Compound **16** was prepared from 333 mg of ginkgolide B and *p*-nitrobenzyl chloride (480 mg) as described by the preceding general procedure to obtain white solid **16** (406 mg, 92.3%) after flash chromatography (cyclohexane:acetone 2:1). **16**: IR (KBr) ν_{max} 3543, 1786, 1524, 1348 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 0.98 (9H, s, *t*-Bu), 1.12 (3H, d, *J* = 7.1 Hz, H-16), 1.73 (1H, dd, *J* = 14.2, 4.3 Hz, H-8), 1.92 (1H, ddd, *J* = 14.1, 13.6, 4.1 Hz, H-7α), 2.15 (1H, dd, *J* = 13.3, 4.4 Hz, H-7β), 2.89 (1H, q, *J* = 7.2 Hz, H-14), 4.20 (1H, d, *J* = 6.6 Hz, H-1β), 4.63 (1H, d, *J* = 6.5 Hz, H-2), 4.81 (1H, d, *J* = 13.7 Hz, *p*-$O_2NC_6H_4C\mathbf{H_2}$-), 5.25 (1H, s, H-10), 5.39 (1H, d, *J* = 3.8 Hz, H-6), 5.49 (1H, d, *J* = 13.7 Hz, *p*-$O_2NC_6H_4C\mathbf{H_2}$-), 6.17 (1H, s, H-12), 7.64 (2H, d, *J* = 8.6 Hz, *p*-$O_2NC_6\mathbf{H_4}CH_2$-), 8.20 (2H, d, *J* = 8.5 Hz, *p*-$O_2NC_6\mathbf{H_4}CH_2$-). ^1H NMR (acetone-d_6, 400 MHz) δ 1.16 (9H, s, *t*-Bu), 1.26 (3H, d, *J* = 7.1 Hz, H-16), 1.97 (1H, dd, *J* = 14.3, 3.9 Hz, H-8), 2.13 (1H, ddd, *J* = 14.0, 13.4, 4.3 Hz, H-7α), 2.28 (1H, dd, *J* = 13.4, 4.3 Hz, H-7β), 3.04 (1H, q, *J* = 7.1 Hz, H-14), 4.33 (1H, d, *J* = 7.2 Hz, H-1β), 4.64 (1H, d, *J* = 7.5 Hz, H-2), 5.01 (1H, d, *J* = 12.3 Hz, *p*-$O_2NC_6H_4C\mathbf{H_2}$-), 5.42 (1H, d, *J* = 2.3 Hz, H-6), 5.42 (1H, s, H-10), 6.21 (1H, s, H-12), 5.64 (1H, d, *J* = 12.2 Hz, *p*-$O_2NC_6H_4C\mathbf{H_2}$-), 7.77 (2H, d, *J* = 8.7 Hz, *p*-$O_2NC_6\mathbf{H_4}CH_2$-), 8.28 (2H, d, *J* = 8.6 Hz, *p*-$O_2NC_6\mathbf{H_4}CH_2$-). HREIMS *m/z* 559.16837, $C_{27}H_{29}O_{12}N$ requires 559.16898; EIMS *m/z* 559 $[M]^+$, 529, 405, 335, 106, 57.

10-*O*-*p*-Chlorobenzylginkgolide B (17). Compound **17** was prepared from 333 mg of ginkgolide B and *p*-chlorobenzyl chloride (451 mg) as described by the preceding general procedure to obtain white solid **17** (423 mg, 98.3%) after flash chromatography (cyclohexane:acetone 2:1). **17**: IR (KBr) ν_{max} 3535, 1790 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 1.18 (9H, s, *t*-Bu), 1.25 (3H, d, *J* = 7.1 Hz, H-16), 1.94 (1H, dd, *J* = 14.3, 4.0 Hz, H-8), 2.01 (1H, ddd, *J* = 14.3, 13.9, 4.3 Hz, H-7α), 2.25 (1H, dd, *J* = 13.3, 4.3 Hz, H-7β), 3.02 (1H, q, *J* = 7.1 Hz, H-14), 4.26 (1H, d, *J* = 7.6 Hz, H-1), 4.62 (1H, d, *J* = 7.7 Hz, H-2), 4.84 (1H, d, *J* = 10.6 Hz, *p*-$ClC_6H_4C\mathbf{H_2}$-), 5.33 (1H, d, *J* = 3.8 Hz, H-6), 5.40 (1H, s, H-10), 5.46 (1H, d, *J* = 10.8 Hz, *p*-$ClC_6H_4C\mathbf{H_2}$-), 6.20 (1H, s, H-12), 7.47 (2H, d, *J* = 8.3 Hz, *p*-$ClC_6\mathbf{H_4}CH_2$-), 7.51 (2H, d, *J* = 8.1 Hz, *p*-$ClC_6\mathbf{H_4}CH_2$-). HREIMS *m/z* 548.14432, $C_{27}H_{29}O_{10}{}^{35}Cl$ requires 548.14493; EIMS *m/z* 548 $[M]^+$, 405, 335, 125, 57.

10-*O*-*p*-Fluorobenzylginkgolide B (18). Compound **18** was prepared from 333 mg of ginkgolide B and *p*-fluorobenzyl chloride (405 mg) as described by the preceding general procedure to obtain white solid **18** (405 mg, 96.7%) after flash chromatography (cyclohexane:acetone 2:1). **18**: IR (KBr) ν_{max} 3531, 1790, 1514 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 1.00 (9H, s, *t*-Bu), 1.12 (3H, d, *J* = 7.0 Hz, H-16), 1.71 (1H, dd, *J* = 14.2, 4.1 Hz, H-8), 1.80 (1H, ddd, *J* = 14.3, 13.9, 4.3 Hz, H-7α), 2.12 (1H, dd, *J* = 13.0, 4.0 Hz, H-7β), 2.87 (1H, q, *J* = 7.2 Hz, H-14), 4.16 (1H, d, *J* = 6.7 Hz, H-1β), 4.62 (1H, d, *J* = 7.1 Hz, H-2), 4.65 (1H, d, *J* = 11.3 Hz, *p*-$FC_6H_4C\mathbf{H_2}$-), 5.23 (1H, s, H-10), 5.31 (1H, d, *J* = 5.0 Hz, H-6), 5.32 (1H, d, *J* = 10.6 Hz, *p*-$FC_6H_4C\mathbf{H_2}$-), 6.17 (1H, s, H-12), 6.50 (1H, s, 3-OH), 7.19 (2H, dd, *J* = 8.7, 6.5 Hz, *p*-$FC_6\mathbf{H_4}CH_2$-), 7.42 (2H, dd, *J* = 8.5, 5.6 Hz, *p*-$FC_6\mathbf{H_4}CH_2$-). ^1H NMR (acetone-d_6, 400 MHz) δ 1.19 (9H, s, *t*-Bu), 1.25 (3H, d, *J* = 7.1 Hz, H-16), 1.96 (1H, dd, *J* = 14.2, 4.1 Hz, H-8), 2.05 (1H, ddd, *J* = 14.3, 13.9, 4.3 Hz, H-7α), 2.25 (1H, dd, *J* = 13.0, 4.0 Hz, H-7β), 3.02 (1H, q, *J* = 7.1 Hz, H-14), 4.25 (1H, d, *J* = 7.8 Hz, H-1β), 4.61 (1H, d, *J* = 7.5 Hz, H-2), 4.84 (1H, d, *J* = 10.3 Hz, *p*-$FC_6H_4C\mathbf{H_2}$-), 5.31 (1H, d, *J* = 3.9 Hz, H-6), 5.40 (1H, s, H-10), 6.20 (1H, s, H-12), 5.44 (1H, d, *J* = 10.3 Hz, *p*-$FC_6H_4C\mathbf{H_2}$-), 7.21 (2H, dd, *J* = 8.7, 6.5 Hz, *p*-$FC_6\mathbf{H_4}CH_2$-), 7.54 (2H, dd, *J* = 8.5, 5.6 Hz, *p*-$FC_6\mathbf{H_4}CH_2$-). HREIMS *m/z* 532.17432, $C_{27}H_{29}O_{10}F$ requires 532.17450; EIMS *m/z* 532 $[M]^+$, 423, 405, 335, 221, 145, 109, 57.

10-*O*-Ethoxycarbonylginkgolide B (19). Compound **19** was prepared from 333 mg of ginkgolide B and ethyl chloroformate (304 mg) as described by the preceding general procedure to obtain white solid **19** (349 mg, 89.4%) after flash chromatography (cyclohexane:acetone 2:1). **19**: IR (KBr) ν_{max} 3531, 1790, 1720 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 1.00 (9H, s, *t*-Bu), 1.11 (3H, d, *J* = 7.0 Hz, H-16), 1.23 (3H, t, *J* = 6.7 Hz, $C\mathbf{H_3}CH_2OOC$-), 1.78 (1H, m, H-7α), 1.78 (1H, m, H-8), 2.16 (1H, dd, *J* = 13.0, 4.0 Hz, H-7β), 2.86 (1H, q, *J* = 7.2 Hz, H-14), 4.16 (1H, d, *J* = 6.2 Hz, H-1β), 4.23 (2H, m, $CH_3C\mathbf{H_2}OOC$-), 4.61 (1H, d, *J* = 6.2 Hz, H-2), 5.38 (1H, d, *J* = 2.0 Hz, H-6), 5.93 (1H, s, H-10), 6.18 (1H, s, H-12), 6.52 (1H, s, 3-OH). ^1H NMR (acetone-d_6, 400 MHz) δ 1.15 (9H, s, *t*-Bu), 1.27 (3H, d, *J* = 7.0 Hz, H-16), 1.31 (3H, t, *J* = 7.1 Hz, $C\mathbf{H_3}CH_2OOC$-), 2.01 (1H, m, H-7α), 2.01 (1H, m, H-8), 2.29 (1H, m, H-7β),

3.03 (1H, q, $J=7.1$ Hz, H-14), 4.24 (1H, d, $J=7.1$ Hz, H-1β), 4.32 (2H, q, $J=7.1$ Hz, $CH_3C\mathbf{H_2}OOC$-), 4.69 (1H, d, $J=7.1$ Hz, H-2), 5.48 (1H, d, $J=3.0$ Hz, H-6), 6.10 (1H, s, H-10), 6.32 (1H, s, H-12). HREIMS m/z 496.15843, $C_{23}H_{28}O_{12}$ requires 496.15808; EIMS m/z 496 $[M]^+$, 481, 452, 405, 306, 247, 191, 163, 95, 57.

1-Oxoginkgolide B (25). Compound **25** was prepared from compound **8** (50 mg) by Jones' oxidation to obtain white solid **25** (27 mg, 59.9%) after flash chromatography (cyclohexane:acetone 2:1) (Scheme 3). **25**: IR (KBr) ν_{max} 3423, 1782 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 1.05 (9H, s, *t*-Bu), 1.26 (3H, d, $J=7.7$ Hz, H-16), 2.33 (1H, ddd, $J=14.2$, 14.2, 4.5 Hz, H-7α), 2.46 (1H, dd, $J=14.6$, 6.0 Hz, H-8), 2.72 (1H, dd, $J=13.9$, 6.0 Hz, H-7β), 2.92 (1H, q, $J=7.7$ Hz, H-14), 4.70 (1H, s, H-2), 5.19 (1H, d, $J=4.4$ Hz, H-6), 5.29 (1H, s, H-10), 6.20 (1H, s, H-12). HREIMS m/z 422.12109, $C_{20}H_{22}O_{10}$ requires 422.12130; EIMS m/z 422 $[M]^+$, 404, 378, 360, 332, 304, 294, 260, 191, 57.

Compound 26. 26 was prepared from compound **10** (50 mg) by Jones' oxidation to obtain white solid **26** (33 mg, 63.4%) after flash chromatography (cyclohexane:acetone 2:1) (Scheme 3). **26**: IR (KBr) ν_{max} 3427, 1801 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 1.12 (9H, s, *t*-Bu), 1.26 (3H, d, $J=7.2$ Hz, H-16), 2.15 (1H, dd, $J=14.2$, 6.8 Hz, H-7β), 2.69 (1H, ddd, $J=14.1$, 14.1, 4.7 Hz, H-7α), 2.29 (1H, dd, $J=13.8$, 5.0 Hz, H-8), 2.84 (1H, q, $J=7.2$ Hz, H-14), 4.16 (2H, m, $CH_2{=}CHC\mathbf{H_2}$-), 4.68 (1H, s, H-2), 5.07 (1H, s, H-10), 5.24 (1H, dd, $J=11.3$, 1.2 Hz, $C\mathbf{H_2}{=}CHCH_2$-), 5.36 (1H, dd, $J=17.2$, 1.4 Hz, $C\mathbf{H_2}{=}CHCH_2$-), 5.48 (1H, d, $J=4.5$ Hz, H-6), 5.96 (1H, m, $CH_2{=}C\mathbf{H}CH_2$-). HREIMS m/z 478.14783, $C_{23}H_{26}O_{11}$ requires 478.14752; EIMS m/z 478 $[M]^+$, 421, 391, 321, 261, 207, 179, 69, 57.

Biological assay: inhibition of platelet aggregation in vitro

The procedures used were exactly as reported previously.[7]

References and Notes

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