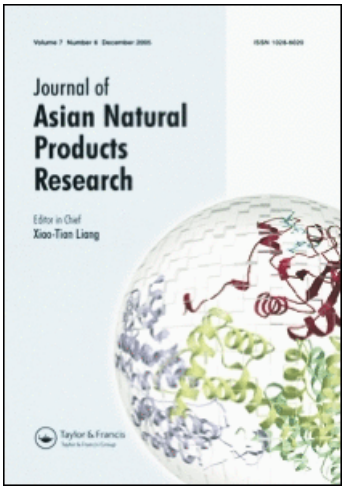

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Total synthesis of natural product (*R*)-4-phenyl-2-*O*-[β-d-xylopyranosyl(1→6)-β-d-glucopyranosyl]butane and its epimer

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Total synthesis of natural product (*R*)-4-phenyl-2-*O*-[β-D-xylopyranosyl(1 → 6)-β-D-glucopyranosyl]butane and its epimer

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The new compound (*R*)-4-phenyl-2-*O*-[β-D-xylopyranosyl(1 → 6)-β-D-glucopyranosyl]butane (**1**) and its epimer (**2**), together with (*R*)-4-phenyl-2-*O*-β-D-glucopyranosyl butane (**24**) and (*S*)-4-phenyl-2-*O*-β-D-glucopyranosyl butane (**25**) were firstly synthesized from 4-phenylbutan-2-one and glucose. The absolute configuration of C-2 for **1** was confirmed as R. Their anti-tumour activities were evaluated.

Keywords: 4-Phenylbutan-2-one; Glucose; Rhododendron athopogonosides; Synthesis

1. Introduction

(*R*)-4-Phenyl-2-*O*-[β-D-xylopyranosyl(1 → 6)-β-D-glucopyranosyl]butane (**1**) (figure 1) was isolated from *Rhododendron athopogonosides* Maxim as a new natural product by our group [1]. The stems and leaves of *Rhododendron athopogonosides* Maxim have traditionally been used as a folk medicine to treat cough, bronchitis, asthma and so on [2–4]. The absolute configuration of C-2 of compound **1** was determined to R by comparison the $[\alpha]_D$ value of aglycone with (*R*)- and (*S*)-4-phenylbutan-2-ol. However, it was disturbing to observe that the $[\alpha]_D$ value of aglycone ($[\alpha]_D^{25} - 3$ ($c = 0.6$ benzene)) was noticeably different from the reported data ($[\alpha]_D^{25} - 21.1$($c = 1.0$ benzene)) [5], in order to secure the absolute configuration of compound **1** and study its biological activities, **1** and its epimer **(2)** (figure 1) were synthesized from 4-phenylbutan-2-one **(3)** and glucose by 11-step reactions.

2. Results and discussion

1 and **2** were synthesized via 4-phenylbutan-2-one **3** and glucose as the starting materials in 11 steps (Scheme 1).

The alcohol **4** was obtained by reduction of **3** with $NaBH_4$ quantitatively. The glycosyl donor thichloroacetimidate **5** (prepared according to the literature [6] from glucose) reacted

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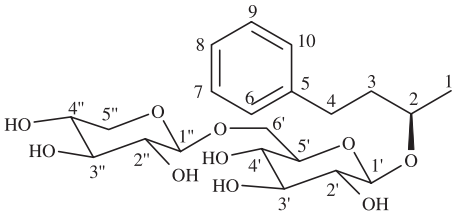

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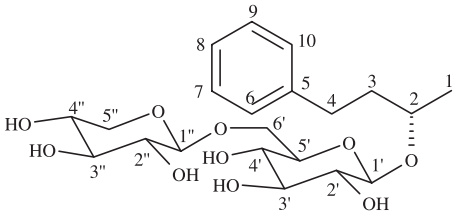


2

Figure 1. Structures of compounds **1** and **2**.

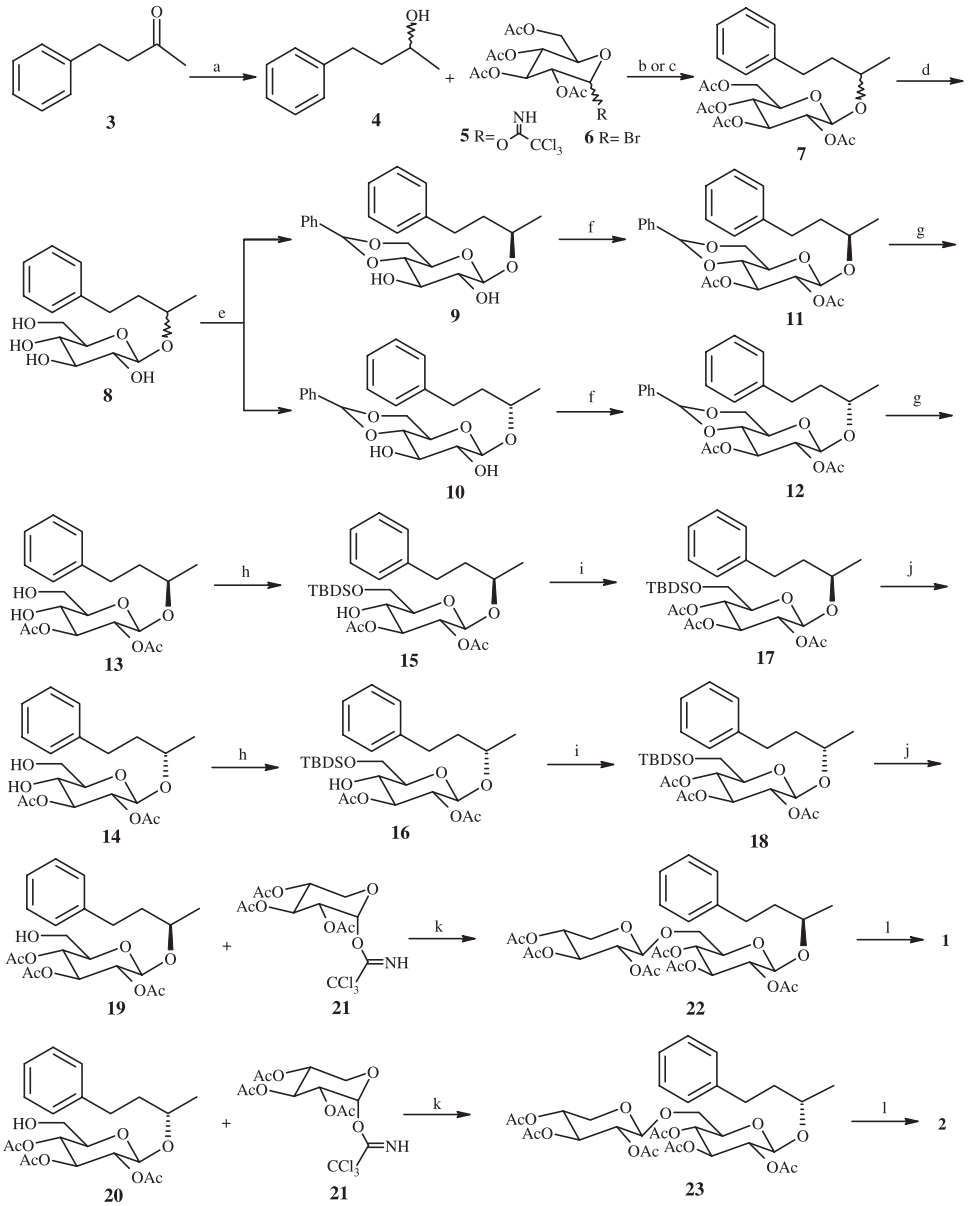
with the acceptor **4** to give the compound **7** under the usual condition using BF_3-Et_2O as the promoter in 30% yield. The reason for the low yield was perhaps the relative low reactivity of secondary alcohol and glycosyl donor. In order to improve the yield, the glycosyl donor was changed to glycosyl bromide [7] and **7** was obtained in 60% yield under the condition using $HgBr_2$ and yellow HgO as the promoter. **7** was δ the mixture of the two diastereoisomers with the ratio of 1:1. The attempt to separate the two isomers by silica gel column chromatography failed. Deacetylation of **7** using NaOMe in anhydrous MeOH gave the completely deprotected compound **8** quantitatively. Selective protection of the 4′,6′-OH by using benzaldehyde dimethyl acetal and p-TsOH provided the diastereomers **9** (2*R*) and **10** (2*S*) which were successively separated by silica gel column chromatography. The absolute configurations of **9** and **10** were determined to be R and S by comparison of the $[\alpha]_D$ value of aglycon (hydrolyzed from **9** and **10** with 0.2 mol/L HCl) with the known values of (*R*)- and (S)-4-phenylbutan-2-ol [5,8], respectively. The $[\alpha]_D$ values of aglycon hydrolyzed from **9** and **10** were similar to the reported data [5,8]. Acetylation of **9** and **10** using Ac_2O and Py afforded **11** and **12**, respectively. Benzylidene acetals of **11** and **12** were removed by 80% AcOH to give **13** and **14** respectively. Selective protection of 6′-OH of **13** and **14** with TBDMSiCl gave **15** and **16**, which were acetylated to give **17** and **18**, respectively. The resulting 6′-OH compounds **19** and **20** were obtained by removing the protective group TBDMSi with 80% AcOH., 19 and **20** reacted with xylosyl trichloroacetimidate **21** [9] in BF_3-Et_2O to give **22** and **23**, which were deprotected by NaOMe to yield the target compounds **1** and **2**, respectively. Removing the benzylidene acetals of **9** and **10** by 80% AcOH gave **24** and **25**, respectively (Scheme 2).

Compounds **1**, **2**, **24** and **25** were evaluated for their anti-tumour activities (table I) and showed no obvious anti-tumour activities.

3. Experimental

3.1 General experimental procedures

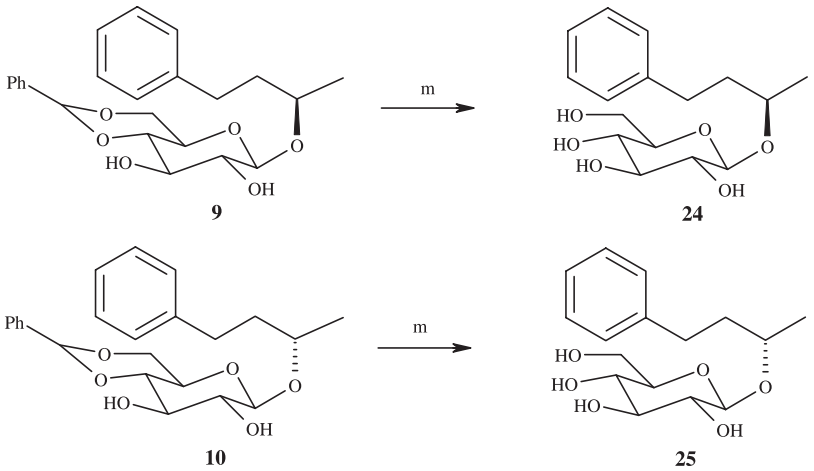
Melting points were determined on a $XT_{4-}100_X$ micro-melting apparatus and are uncorrected. IR spectra were run on a Nicolet Impact-400 spectrometer. Optical rotations were measured on PE-241 digital polarimeter. NMR spectra were recorded on Varian Mercury-400 spectrometer (400 MHz for ^1H and 100 MHz for ^{13}C). Chemical shifts of ^1H and ^{13}C spectra are referenced to the NMR solvents. Mass spectra were obtained on a ZAB-2F spectrometer. TLC was carried out on silica gel (GF_{254}). Column chromatography was run on silica gel (200–300 mesh) from Qingdao Ocean Chemical Factory. Dichloromethane was distilled over P_2O_5.



Scheme 1. Synthesis of **1** and **2**, Reagents and conditions: a: $NaBH_4$, CH_3OH, 1 h; b: CH_2Cl_2, $BF_3.Et_2O$, − 50°C–r.t., 12 h; c: CH_2Cl_2, $HgBr_2$, yellow HgO, r.t., 12 h; d: MeOH, NaOMe, r.t., 4 h; e: $PhCH(OMe)_2$, DMF, P-TSOH; 50°C; f: Ac_2O, Py, r.t., 12 h, reduce pressure; g: 80% HOAc, 70–80°C, 2 h; h: TBDMSiCl, DMF, DMAP, imidazole, r.t., 4 h; i: Ac_2O, Py, r.t., 5 h; j: 80%HOAc, 70–80°C, 4 h; k: CH_2Cl_2, $BF_3.Et_2O$, − 50°C–r.t., 5 h; l: MeOH, NaOMe, r.t., 3 h.

3.2 General procedures for the synthetic compounds

3.2.1 General procedure for the preparation of glycosyl donors 5, 6 and 21. Glucopyranosyl donors **5** and **6** were prepared from glucose according to refs. [6] and [7], respectively. Xylopyranosyl trichloroacetimidate **21** was prepared from xylose according to the literature [9].



Scheme 2. Synthesis of compounds **24** and **25**. Reagents and conditions: m: 80% HOAc, 70–80°C, 4 h.

3.2.2 Compound 7. BF_3–Et_2O (0.1 ml) was added at −50°C to the solution of **4** (0.75 g, 5 mmol) (prepared from reduction of **3** by $NaBH_4$ in quantitative yield) and **5** (4.93 g, 10 mmol) in 50 ml CH_2Cl_2 which had previously been stirred over freshly activated 4 Å molecule sieve under N_2 at room temperature for 1 h. After that, the temperature was allowed to rise to room temperature and the mixture was stirred for 12 h. Et_3N (1 ml) was added and the mixture was diluted with CH_2Cl_2 (50 ml) and filtered through Celite. The solid was washed with CH_2Cl_2 and the combined filtrate was then washed with H_2O (3 × 50 ml), dried over $MgSO_4$, filtered and concentrated. The crude product was purified by column chromatography on silica gel (PE/EtOAc = 5:1). **7** (0.72 g) was obtained as colourless oil in 30% yield.

The modified method with the glycosyl bromide as the donor: $HgBr_2$ (50 mg, 0.14 mmol) and yellow HgO (2.24 g, 10.3 mmol) were added to the mixture of **4** (0.9 5 g, 6.3 mmol), **6** (2.9 g, 7.1 mmol) in 50 ml anhydrous CH_2Cl_2 and 2 g 4 Å molecule sieve. The mixture was stirred at room temperature for 12 h under N_2 and then filtered through celite; the solid was washed with CH_2Cl_2. the combined filtrate was concentrated. **7** (1.8 g) was obtained by column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.29–7.14 (m, 10H), 5.21 (t, 1H, $J = 9.6$ Hz, H-3′), 5.23 (t, 1H, $J = 9.6$ Hz, H-3′, for isomer), 5.09 (t, 1H, $J = 9.6$ Hz, H-4′), 5.05 (t, 1H, $J = 9.6$ Hz, H-4′, for isomer), 5.01 (dd, 1H, $J = 9.6$ Hz, 8.0 Hz, H-2′, for isomer), 4.97 (dd, 1H, $J = 9.6$ Hz, 8.0 Hz, H-2′), 4.56 (d, 1H, $J = 8.0$ Hz, H-1′, for isomer), 4.53 (d, 1H, $J = 8.0$ Hz, H-1′), 4.26–4.20 (m, 2H, H-6′, two isomers), 4.14–4.08 (m, 2H, H-6′, two isomers), 3.78–3.73 (m, 2H, H-2, two isomers), 3.70–3.64 (m, 2H, H-5′, two isomers), 2.70–2.50 (m, 4H, H-4, two isomers), 2.16–1.91

Table I. Anti-tumour activities of compounds **1**, **2**, **24** and **25**.

	IC_{50} (μg/ml)				
	A549	BEL7402	BGC823	HCT-8	A2780
1	>10	>10	>10	>10	>10
2	>10	>10	>10	>10	>10
24	>10	>10	>10	>10	>10
25	>10	>10	>10	>10	>10

(m, 24H, 8 × CH_3CO, two isomers), 1.89–1.82 (m, 2H, H-3, two isomers), 1.76–1.67 (m, 2H, H-3, two isomers), 1.26 (d, 3H, $J = 6.0$ Hz, H-1 for isomer), 1.12 (d, 3H, $J = 6.0$ Hz, H-1). ESI-MS *m/z* (%): 503 ($[M + Na]^+$, 100).

3.2.3 Compound 8. To the solution of **7** (0.5 g, 1.04 mmol) in 10 ml CH_3OH, was added two drops of 1 M NaOMe in CH_3OH at room temperature. The mixture was concentrated after being stirred at room temperature for 4 h. The crude product was purified by column chromatography on silica gel (CH_2Cl_2/CH_3OH = 9:1). **8** (0.32 g) (1:1 ratio of compound **24** and **25**) was obtained as colourless oil in quantitative yield.

3.2.4 Compounds 9 and 10. To a solution of **8** (0.5 g, 1.6 mmol) and $PhCH(OMe)_2$ (0.3 g, 2 mmol) in dry DMF (15 ml), was added p-TsOH monohydrate(20 mg). The resulting mixture was stirred at 50°C under reduced pressure for 3 h, diluted with EtOAc, then washed with saturated $NaHCO_3$ and H_2O, dried over $MgSO_4$, and concentrated. Chromatography of the residue on a silica gel column (4:1 = PE/acetone) afforded **9** and **10**. In order to determine the absolute configuration of **9** and **10**, **9** and **10** were hydrolyzed with 0.2 mol/L HCl. The procedure is as follows: To a solution of **10** (0.1 g, 0.25 mmol) in benzene, was added 10 ml 0.2 mol/L HCl. The resulting mixture was refluxed for 12 h and then diluted with 20 ml Et_2O. The organic phase was washed with saturated $NaHCO_3$ and water, dried over $MgSO_4$, and concentrated. Aglycon 4-phenylbutan-2-ol (30 mg) was obtained by silical gel column chromatography. The $[\alpha]_D$ value of aglycon ($[\alpha]_D^{25} + 19.8(c = 0.16$, benzene)) was close to the reported $[\alpha]_D$ value of (*S*)-4-phenylbutan-2-ol ($[\alpha]_D^{25} + 21.1(c = 1.00$, benzene)) [8]. Compound **9**: $[\alpha]_D^{25} - 57.9$ ($c = 0.07$, CH_3COCH_3), ^{1}H NMR (400 MHz, acetone-d_6) δ (ppm): 7.49–7.13 (m, 10H), 5.60 (s, 1H), 4.52 (d, 1H, $J = 8.0$ Hz), 4.46 (brs, 1H), 4.30 (brs, 1H), 4.24 (dd, 1H, $J = 10.0$ Hz, 4.2 Hz), 3.89–3.83 (m, 1H), 3.79 (t, 1H, $J = 10.0$ Hz), 3.65 (t, 1H, $J = 10.0$ Hz), 3.50 (dd, 1H, $J = 10.0$, 8.0 Hz), 3.46 (dd, 1H, $J = 10.0$ Hz, 5.2 Hz), 3.34–3.30 (m, 1H), 2.77–2.64 (m, 2H), 1.88–1.69 (m, 2H), 1.18 (d, 3H, $J = 6.4$ Hz). ESI-MS: *m/z* (%) 423 ($[M + Na]^+$, 100). Compound **10**: $[\alpha]_D^{25} - 29.9$ ($c = 0.08$, CH_3COCH_3), ^{1}H NMR (400 MHz, acetone-d_6) δ (ppm): 7.52–7.13 (m, 10H), 5.58 (s, 1H), 4.53 (d, 1H, $J = 8.0$ Hz), 4.49 (brs, 1H), 4.45 (brs, 1H), 4.21 (dd, 1H, $J = 10.4$ Hz, 4.8 Hz), 3.83–3.80 (m, 1H), 3.73 (dd, 1H, $J = 10.0$ δ), 3.66 (dd, 1H, $J = 10.0$, 8.0 Hz), 3.48–3.37 (m, 2H), 3.35–3.31 (m, 1H), 2.84–2.69 (m, 2H), 1.90–1.78 (m, 1H), 1.77–1.69 (m, 1H), 1.23 (d, 3H, $J = 6.4$ Hz). ESI-MS: *m/z* (%) 423 ($[M + Na]^+$, 100).

According to the same procedure as above-mentioned, the $[\alpha]_D$ value of aglycon hydrolysed from **9** ($[\alpha]_D^{25} - 17.5(c = 0.15$, benzene)) was the same as the $[\alpha]_D$ value of (*R*)-4-phenylbutan-2-ol ($[\alpha]_D^{25} - 21.1(c = 1.00$, benzene)). The absolute configuration at C-2 of **9** and **10** was R and S, respectively. Compound (+)-**4**: $[\alpha]_D^{25} + 19.8(c = 0.16$, benzene), ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.34–7.22 (m, 5H), 3.88–3.81 (m, 1H), 2.27–2.69 (m, 2H), 1.91 (brs, 1H), 1.84–1.76 (m, 2H), 1.25 (d, 3H, $J = 6.0$ Hz). EI-MS: *m/z* (%) 150 (M^+, 15), 132 (50), 117 (100), 91 (100), 71 (47), 57 (78). Compound (−)-**4**: $[\alpha]_D^{25} - 17.5(c = 0.15$, benzene); the spectral data of (−)-**4** were the same as those of (+)-**4**.

3.2.5 Compounds 11 and 12. To the solution of **9** (0.5 g, 1.25 mmol) in 10 ml Py, was added Ac_2O (0.51 g, 5 mmol). The mixture was stirred at room temperature for 12 h, then evaporated. Chromatography of the residue on a silica gel column (10:1 = PE/acetone) afforded **11** (0.58 g). $[\alpha]_D^{25} - 75$ ($c = 0.05$, CH_3COCH_3), ^{1}H NMR (400 MHz, $CDCl_3$) δ

(ppm): 7.46–7.19 (m, 10H), 5.52 (s, 1H), 5.32 (t, 1H, $J = 9.6$ Hz), 5.00 (dd, 1H, $J = 9.6$, 8.0 Hz), 4.62 (d, 1H, $J = 8.0$ Hz), 4.38 (dd, 1H, $J = 10.4$ Hz, 4.8 Hz), 3.86–3.78 (m, 2H), 3.73 (t, 1H, $J = 9.6$ Hz), 3.52–3.49 (m, 1H), 2.73–2.66 (m, 2H), 2.06 (s, 3H), 2.04 (s, 3H), 1.89–1.82 (m, 1H), 1.80–1.75 (m, 1H), 1.15 (d, 3H, $J = 6.4$ Hz). ESI-MS: *m/z* (%) 507 ($[M + Na]^+$, 100). Compound **12** was obtained according to the same procedure. $[\alpha]_D^{25}$ − 38.5 ($c = 0.07$, CH_3COCH_3), ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.44–7.16 (m, 10H), 5.51 (s, 1H), 5.33 (t, 1H, $J = 9.6$ Hz), 5.04 (dd, 1H, $J = 9.6$, 8.0 Hz), 4.66 (d, 1H, $J = 8.0$ Hz), 4.33 (dd, 1H, $J = 10.4$ Hz, 5.2 Hz), 3.83–3.68 (m, 3H), 3.53–3.48 (m, 1H), 2.70–2.66 (m, 1H), 2.61–2.57 (m, 1H), 2.05 (s, 3H), 2.04 (s, 3H), 1.90–1.82 (m, 1H), 1.74–1.70 (m, 1H), 1.27 (d, 3H, $J = 6.0$ Hz). ESI-MS: *m/z* (%) 507 ($[M + Na]^+$, 100).

3.2.6 Compounds 13 and 14. The solution of **11** (0.5 g, 1.03 mmol) in 20 ml 80% HOAc was stirred at 70–80°C for 2 h. The solvent was removed under vacuum to give a residue which was purified by silica gel chromatography. **13** (0.3 g) was obtained as colourless oil. $[\alpha]_D^{25}$ − 47.3 ($c = 0.14$, CH_3COCH_3), ^{1}H NMR (400 MHz, acetone-d_6) δ?(ppm): 7.25–7.13 (m, 5H), 5.07 (t, 1H, $J = 9.6$ Hz), 4.76 (dd, 1H, $J = 9.6$, 8.0 Hz), 4.69 (d, 1H, $J = 8.0$ Hz), 3.90–3.66 (m, 4H), 3.49–3.45 (m, 1H), 2.73–2.64 (m, 2H), 1.96 (s, 3H), 1.95 (s, 3H), 1.80–1.69 (m, 2H), 1.13 (d, 1H, $J = 6.0$ Hz). ESI-MS: *m/z* (%) 419 ($[M + Na]^+$, 100). Compound **14** was obtained by the same procedure above-mentioned. $[\alpha]_D^{25}$ − 3($c = 0.10$, CH_3COCH_3), ^{1}H NMR (400 MHz, acetone-d_6) δ (ppm): 7.29–7.14 (m, 5H), 5.07 (t, 1H, $J = 9.6$ Hz), 4.78 (dd, 1H, $J = 9.6$ δ, 8.0 Hz), 4.72 (d, 1H, $J = 8.0$ Hz), 3.86–3.62 (m, 4H), 3.48–3.42 (m, 1H), 2.74–2.67 (m, 1H), 2.62–2.56 (m, 1H), 2.02 (s, 3H), 2.01 (s, 3H), 1.23 (d, 3H, $J = 6.0$ Hz). ESI-MS: *m/z* (%) 419 ($[M + Na]^+$, 100).

3.2.7 Compounds 15 and 16. To a solution of **13** (0.288 g, 0.73 mmol), TBDMSiCl (164 mg, 1.2 mmol) in 10 ml DMF, were added DMAP (21 mg, 0.17 mmol) and imidazole (197 mg, 2.90 mmol). The resulting mixture was stirred at room temperature for 4 h, diluted with EtOAc (30 ml), then washed with saturated NaCl and H_2O, dried over $MgSO_4$, and concentrated. Chromatography of the residue by silica gel column (6:1 = PE/acetone) afforded **15** (0.28 g). $[\alpha]_D^{25}$ − 40.9 ($c = 0.41$, CH_3COCH_3), ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.27–7.15 (m, 5H), 5.09 (t, 1H, $J = 10.0$ Hz), 4.88 (dd, 1H, $J = 10.0$ Hz, 8.0 Hz), 4.51 (d, 1H, $J = 8.0$ Hz), 3.95 (dd, 1H, $J = 10.5$ Hz, 5.5 Hz), 3.86 (dd, 1H, $J = 10.5$ Hz, 6.5 Hz), 3.80–3.74 (m, 2H), 3.42–3.38 (m 1H), 3.16 (brs, 1H), 2.75–2.69 (m, 1H), 2.66–2.61 (m, 1H), 2.09 (s, 3H), 2.03 (s, 3H), 1.86–1.84 (m, 1H), 1.74–1.70 (m, 1H), 1.12 (d, 3H, $J = 6.0$ Hz), 0.91 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H). ESI-MS: *m/z* (%) 533 ($[M + Na]^+$, 100). According to the same procedure above-mentioned, compound **16** from **14** was obtained as colourless oil in 86% yield. $[\alpha]_D^{25}$ − 8.9 ($c = 0.30$, CH_3COCH_3), ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.30–7.15 (m, 5H), 5.09 (t, 1H, $J = 9.5$ Hz), 4.93 (dd, 1H, $J = 9.5$ Hz, 8.0 Hz), 4.55 (d, 1H, $J = 8.0$ Hz), 3.92 (dd, 1H, $J = 10.0$ Hz, 4.5 Hz), 3.84 (dd, 1H, $J = 10.0$ Hz, 6.0 Hz), 3.74 (t, 1H, $J = 9.5$ Hz), 3.71–3.67 (m, 1H), 3.43–3.39 (m, 1H), 2.71–2.66 (m, 1H), 2.59–2.53 (m, 1H), 2.09 (s, 3H), 2.03 (s, 3H), 1.85–1.79(m, 1H), 1.72–1.67 (m, 1H), 1.25 (d, 3H, $J = 6.5$ Hz), 0.89 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H). ESI-MS: *m/z* (%) 533 ($[M + Na]^+$, 100).

3.2.8 Compounds 17 and 18. To a solution of **15** (0.264 g, 0.53 mmol) in 5 ml Py, Ac_2O (81 mg, 0.8 mmol) was added. The resulting mixture was stirred at room temperature for 5 h,

then evaporated. Chromatography of the residue on a silica gel column (10:1 = PE/acetone) afforded **17** (0.25 g). $[\alpha]_D^{25}$ − 24.9 (c = 0.09, CH_3COCH_3), ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.28–7.16 (m, 5H), 5.20 (t, 1H, J = 9.6 Hz), 5.06 (t, 1H, J = 9.6 Hz), 4.95 (dd, 1H, J = 9.6 Hz, 8.0 Hz), 4.53 (d, 1H, J = 8.0 Hz), 3.83–3.75 (m, 1H), 3.73–3.68 (m, 2H), 3.53–3.49 (m, 1H), 2.75–2.71 (m, 1H), 2.67–2.63 (m, 1H), 2.04 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.90–1.84 (m, 1H), 1.75–1.72 (m, 1H), 1.14 (d, 3H, J = 6.0 Hz), 0.88 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H). ESI-MS: m/z (%) 461 ($[M + Na]^+$, 100). Compound **18** was obtained according to the same procedure. $[\alpha]_D^{25}$ + 10.9 (c = 0.09, CH_3COCH_3), ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.30–7.15 (m, 5H), 5.20 (t, 1H, J = 9.6 Hz), 5.00 (t, 1H, J = 9.6 Hz), 4.98 (dd, 1H, J = 9.6 Hz, 8.0 Hz), 4.54 (d, 1H, J = 8.0 Hz), 3.73–3.67 (m, 3H), 3.53–3.48 (m, 1H), 2.72–2.65 (m, 1H), 2.60–2.52 (m, 1H), 2.02 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.87–1.73 (m, 1H), 1.72–1.66 (m, 1H), 1.27 (d, 3H, J = 6.4 Hz), 0.87 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H). ESI-MS: m/z (%) 461 ($[M + Na]^+$, 100).

3.2.9 Compounds 19 and 20. The solution of **17** (0.2 g, 0.36 mmol) in 10 ml 80% HOAc was stirred at 70–80°C for 4 h. The solvent was removed under vacuum to give a residue which was purified by silica chromatography. **19** (0.13 g) was obtained as colourless oil. $[\alpha]_D^{25}$ − 50 (c = 0.11, CH_3COCH_3), ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.28–7.16 (m, 5H), 5.24 (dd, 1H, J = 10, 9.0 Hz), 5.01 (t, 1H, J = 10 Hz), 4.96 (dd, 1H, J = 9.5, 8.5 Hz), 4.54 (d, 1H, J = 8.5 Hz), 3.80–3.74 (m, 1H), 3.68 (dd, 1H, J = 12.5 Hz, 1.5 Hz), 3.55 (dd, 1H, J = 12.5 Hz, 5.5 Hz), 3.49–3.45 (m, 1H), 2.74–2.65 (m,2H), 2.04 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H), 1.91–1.84 (m 1H), 1.79–1.72 (m, 1H), 1.13 (d, 3H, J = 6.5 Hz). ESI-MS: m/z (%) 575 ($[M + Na]^+$, 100). Compound **20** was obtained as the same procedure above-mentioned. $[\alpha]_D^{25}$ − 8.9 (c = 0.08, CH_3COCH_3), ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.30–7.15 (m, 5H), 5.26 (dd, 1H, J = 10, 9.0 Hz), 5.02 (dd, 1H, J = 10.0, 9.0 Hz), 5.01 (dd, 1H, J = 9.0, 8.0 Hz), 4.60 (d, 1H, J = 8.0 Hz), 3.76–3.70 (m, 2H), 3.60 (dd, 1H, J = 12.5 Hz, 5.5 Hz), 3.53–3.49 (m, 1H), 2.72–2.66 (m, 1H), 2.60–2.54 (m, 1H), 2.05 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H), 1.88–1.81 (m, 1H), 1.74–1.68 (m, 1H), 1.28 (d, 3H, J = 6.0 Hz). ESI-MS: m/z (%) 575 ($[M + Na]^+$, 100).

3.2.10 Compounds 22 and 23. To the solution of **19** (0.3 g, 0.68 mmol) and xylopyranosyl trichloroacetimidate **(21)** (0.42 g, 1.0 mmol) in 20 ml anhydrous CH_2Cl_2 which had previously been stirred over freshly activated 4 Å molecule sieve under N_2 at room temperature for 1 h, was added $BF_3{\cdot}Et_2O$ (0.05 ml) at − 50°C. After that, the temperature was allowed to rise to room temperature and the mixture was stirred at room temperature for 5 h. Et_3N (0.1 ml) was added and the mixture was dilute with CH_2Cl_2 (30 ml) and filtered through a layer of Celite. The residue was washed with CH_2Cl_2 and the combined filtrate was then washed with H_2O (3 × 10 ml), dried over $MgSO_4$, filtered and concentrated. The crude product was purified by column chromatography on silica gel (PE/EtOAc = 5:1). **22** (0.35 g) was obtained as colourless oil. $[\alpha]_D^{25}$ − 41.5 (c = 0.12, CH_3COCH_3), ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.28–7.14 (m, 5H), 5.19 (t, 1H, J = 9.6 Hz), 5.12 (t, 1H, J = 8.0 Hz), 5.01–4.86 (m, 4H), 4.57 (d, 1H, J = 6.4 Hz), 4.52 (d, 1H, J = 8.0 Hz), 4.11 (dd, 1H, J = 7.0 Hz, 12.0 Hz), 3.85–3.81 (m, 2H), 3.65–3.60 (m, 2H), 3.31 (dd, 1H, J = 12.0 Hz, 8.4 Hz), 2.76–2.62 (m, 2H), 2.05–1.99 (m, 18H, 6 × CH_3), 1.86–1.73 (m, 2H), 1.13 (d, 1H, J = 6.4 Hz). ESI-MS: m/z (%) 719 ($[M + Na]^+$, 100). Compound **23** was obtained as colourless oil according to the same procedure. $[\alpha]_D^{25}$ − 16.5 (c = 0.13, CH_3COCH_3),

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.30–7.14 (m, 5H), 5.19 (t, 1H, $J = 9.6$ Hz), 5.11 (t, 1H, $J = 8.4$ Hz), 5.00–4.85 (m, 4H), 4.55 (d, 1H, $J = 6.4$ Hz), 4.54 (d, 1H, $J = 8.4$ Hz), 4.13 (dd, 1H, $J = 12$ Hz, 4.0 Hz), 3.81–3.58 (m, 3H), 3.34 (dd, 1H, $J = 12$ Hz, 8.4 Hz), 2.70–2.53 (m, 2H), 2.08–1.97(m, 18H, 6 × CH_3), 1.86–1.68 (m, 2H), 1.27 (d, 3H, $J = 6.0$ Hz). ESI-MS: *m/z* (%) 719 ([M + Na]$^+$, 100).

3.2.11 Compounds 1 and 2. To the solution of **22** (0.2 g, 0.29 mmol) in 5 ml CH_3OH, was added two drops of 1 M NaOMe in CH_3OH at room temperature. The resulting mixture was stirred at room temperature for 3 h, then evaporated. The crude product was purified by column chromatography on silica gel (CH_2Cl_2/CH_3OH = 9:1). **1** (0.1 g) was obtained as colourless powder in quantitative yield. mp: 180–181°C, $[\alpha]_D^{25}$ − 77.6 ($c = 0.05$, EtOH; $[\alpha]_D^{20}$ − 81.0 for natural product). ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 7.26–7.20 (m, 4H, H-6, H-7, H-9 and H-10), 7.14 (t, 1H, $J = 7.0$ Hz), 4.96–4.87 (m, 6H, 6 × OH), 4.24 (d, 1H, $J = 7.5$ Hz, H-1″), 4.16 (d, 1H, $J = 7.5$ Hz, H-1′), 3.92 (d, 1H, $J = 10.5$ Hz, H-6′), 3.79 (m, 1H, H-2), 3.67 (dd, 1H, $J = 11.5$ Hz, 5.5 Hz, H–H-5″), 3.57 (dd, 1H, $J = 10.5$ Hz, 6.0 Hz, H-6′), 3.29–3.24 (m, 2H, H-3″ and H-4″), 3.16–3.05 (m, 3H, H-3′, H-4′ and H-5′), 3.02–2.92 (m, 3H, H-2′, H-2″ and 5″), 2.70–2.57 (m, 2H, H-4), 1.79–1.72 (m, 1H, H-3), 1.67–1.60 (m, 1H, H-3), 1.11 (d, 3H, $J = 6.0$ Hz). ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 142.3 (C-5), 128.3 (C-7 and C-9), 128.2 (C-6 and C-10), 125.5 (C-8), 104.4 (C-1″), 100.7 (C-1′), 76.8 (C-3′), 76.5 (C-5′), 75.7 (C-3″), 73.3 (C-2′), 73.3 (C-2″), 72.7 (C-2), 69.9 (C-4′), 69.5 (C-4″), 68.4 (C-6′), 65.6 (C-5″), 38.8 (C-3), 31.2 (C-4), 19.7 (C-1). FAB-MS: *m/z* (%) 467 ([M + Na]$^+$, 100), 115 (50), 91 (55). IR (KBr, cm^{-1}): 3386, 2972, 2925, 2848, 1078, 1041. HRFAB-MS: *m/z* 467.1889 [M + Na]$^+$ (calcd for $C_{21}H_{32}O_{10}Na$, 467.1893). The spectral data were the same as the reported natural product [1].

Compound **2** was obtained from **23** as colourless oil according to the same procedure mentioned above. $[\alpha]_D^{25}$ − 40.7 ($c = 0.1$, EtOH). ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 7.27–7.20 (m, 4H, H-6, H-7, H-9 and H-10), 7.14 (t, 1H, $J = 7.0$ Hz, H-8), 5.02–4.83 (m, 6H, 6 × OH), 4.22 (d, 1H, $J = 7.5$ Hz, H-1″), 4.17 (d, 1H, $J = 8.0$ Hz, H-1′), 3.89 (d, 1H, $J = 10$ Hz, H-6′), 3.71 (m, 1H, H-2), 3.64 (m, 1H, H-5″), 3.51 (dd, 1H, $J = 10$ Hz, 6.0 Hz, H-6′), 3.29–3.22 (m, 2H, H-5′ and H-4″), 3.15–3.11 (m, 1H, H-3′), 3.10–2.92 (m, 5H, H-2′, H-4′, H-2″, H-3″ and H-5″), 2.70–2.60 (m, 2H, H-4), 1.78–1.71 (m, 1H, H-3), 1.68–1.62 (m, 1H, H-3), 1.18 (d, 3H, $J = 6.5$ Hz). ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 142.4 (C-5), 128.3 (C-7 and C-9), 128.2 (C-6 and C-10), 125.5 (C-8), 103.9 (C-1″), 102.8 (C-1′), 76.6 (C-3′), 76.5 (C-3″), 75.7 (C-5′), 74.7 (C-2), 73.5 (C-2″), 73.3 (C-2′), 69.9 (C-4′), 69.5 (C-4″), 68.3 (C-6′), 65.6 (C-5″), 38.3 (C-3), 30.6 (C-4), 21.8 (C-1). IR (KBr, cm^{-1}): 3369, 2925, 1653, 1603, 1165, 1039. FAB-MS: *m/z* (%) 467 ([M + Na]$^+$, 55), 91 (100). HRFAB-MS: *m/z* 467.1889 [M + Na]$^+$ (calcd for $C_{21}H_{32}O_{10}Na$, 467.1893).

3.2.12 Compounds 24 and 25. The solution of **9** (0.2 g, 0.5 mmol) in 10 ml 80% HOAc was stirred at 70–80°C for 4 h. The solvent was removed under vacuum to give a residue which was purified by silica gel chromatography. **24** (0.12 g) was obtained as colourless oil. $[\alpha]_D^{25}$ − 43.4 ($c = 0.12$, EtOH), ^{1}H NMR (400 MHz, acetone-d_6) δ (ppm): 7.24–7.19 (m, 4H, Ar–H), 7.12–7.09 (m, 1H, Ar–H), 4.35 (d, 1H, $J = 8.0$ Hz, H-1′), 3.89–3.85 (m, 1H, H-2), 3.82 (dd, 1H, $J = 12$ Hz, 2.4 Hz, H-6′), 3.66 (dd, 1H, $J = 12$ Hz, 5.2 Hz, H-6′), 3.41–3.16 (m, 4H, H-2′, H-3′, H-4′ and H-5′), 2.77–2.58 (m, 2H, H-4), 1.87–1.77 (m, 1H, H-3), 1.73–1.64 (m, 1H, H-3), 1.15 (d, 3H, $J = 7.5$ Hz, H-1). ^{13}C NMR (100 MHz, acetone-d_6) δ (ppm):

143.5 (C-5), 129.3 (C-7 and C-9), 129.0 (C-6 and C-10), 126.3 (C-8), 101.9 (C-1′), 78.0 (C-3′), 77.2 (C-5′), 74.8 (C-2′), 73.8 (C-2), 71.8 (C-4′), 63.1 (C-6′), 39.9 (C-3), 32.2 (C-4), 20.0 (C-1). FAB-MS: *m/z* (%) 335 ($[M + Na]^+$, 85), 115 (60), 91 (100). IR (KBr, cm^{-1}): 3388, 2970, 2927, 1603, 1496, 1454, 1379, 1076, 1028. HRFAB-MS: *m/z* 335.1475 $[M + Na]^+$ (calcd for $C_{16}H_{24}O_6Na$, 335.1471).

Compound **25** was obtained by the same procedure above-mentioned. $[\alpha]_D^{25} - 14.7$ ($c = 0.14$, EtOH), ^1H NMR (400 MHz, acetone-d_6) δ (ppm): 7.26–7.13 (m, 4H, Ar–H), 7.12–7.10 (m, 1H, Ar–H), 4.37 (d, 1H, $J = 7.6$ Hz, H-1′), 3.78 (d, 1H, $J = 11.2$ Hz, H-6′), 3.69–3.60 (m, 2H, H-2 and H-6′), 3.43–3.18 (m, 4H, H-2′, H-3′, H-4′ and H-5′), 2.77–2.62 (m, 2H, H-4), 1.87–1.78 (m, 1H, H-3), 1.73–1.64 (m, 1H, H-3), 1.21 (d, 3H, $J = 6.4$ Hz, H-1). ^{13}C NMR (100 MHz, acetone-d_6) δ (ppm): 143.5 (C-5), 129.2 (C-7 and C-9), 129.0 (C-6 and C-10), 126.3 (C-8), 104.0 (C-1′), 78.0 (C-3′), 77.1 (C-5′), 76.3 (C-2′), 75.1 (C-2), 71.7 (C-4′), 63.0 (C-6′), 39.5 (C-3), 32.0 (C-4), 22.3 (C-1). IR (KBr, cm^{-1}): 3340, 2970, 2931, 1616, 1495, 1371, 1163, 1082, 1026. FAB-MS: *m/z* (%) 335 ($[M + Na]^+$, 100), 115 (25), 91 (60). HRFAB-MS: *m/z* 335.1463 $[M + Na]^+$ (calcd for $C_{16}H_{24}O_6Na$, 335.1471).

3.3 Biological evaluation

3.3.1 Anti-tumour activities. Anti-tumour activities of compounds **1**, **2**, **24** and **25** against human cell lines were evaluated using the MTT assay. The results are given as IC_{50} values and are shown in table I.

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