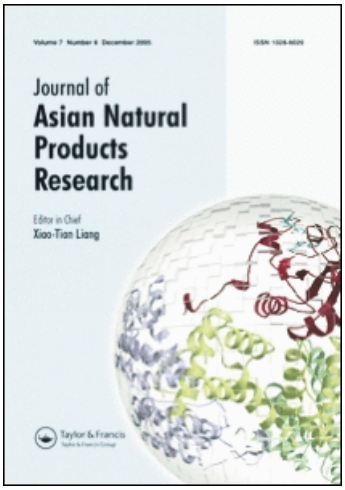

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An attempt to enlarge the B ring of maoecrystal B, an *ent*-kaurane-type diterpene

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An attempt to enlarge the B ring of maoecrystal B, an *ent*-kaurane-type diterpene

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An attempt to enlarge the B ring of maoecrystal B (**6**), an *ent*-kaurane-type diterpene from *Isodon eriocalyx* (Labiatae), to obtain the desired compound **23** via six steps, led to the novel rearranged diterpene compound **22**.

Keywords: *Isodon eriocalyx*; *ent*-Kauranoid; Diterpene; Maoecrystal B; Rearrangement

1. Introduction

Of the more than 300 *ent*-kaurane-type diterpenes from *Isodon* species (Labiatae) [1], no naturally occurring diterpene containing the seven-membered B ring has yet been reported. In 1977, Fujita and co-workers [2,3] reported one novel artificial diterpene (**2**) with a seven-membered B ring, obtained by thallium trinitrate oxidative rearrangement of *ent*-17-norkauran-16-one (**1**). Six years later, another diterpene possessing the seven-membered B ring (**5**) was obtained by refluxing **4** from **3** with Zn [4].

With the aim of enlarging the B ring of the *ent*-kaurane-type diterpenes starting from maoecrystal B (**6**) from *Isodon eriocalyx* [5], treatment of compound **21** derived from maoecrystal B (**6**) by a six-step reaction, mainly including hydrogenation (Pd–C/H_2), glycol protection, LAH reduction, and sulfonation, with NaOH led to the rearranged product **22** instead of the desired compound **23**. During this research, new diterpene derivatives, such as **12**–**22**, and, in particular, a novel 1,10-*seco* kauranoid compound (**22**), were obtained. We report here the preparation and structural elucidation of these compounds.

2. Results and discussion

The attempted cleavage of the 7,20-epoxy in maoecrystal B (**6**) via $LiAlH_4$ reduction [6] failed. The rupture of this bond starting from trickokaurine (**7**) (compounds **6** and **7** were

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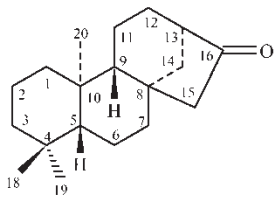
isolated and identified from *Isodon eriocalyx* by the present authors) using TsOH–HOAc gave the expected product **9** in almost quantitative yield (scheme 1). The ^{1}H- and ^{13}C-NMR spectra of **9** showed four acetyl groups (δ_H 1.99, 2.02, 2.09, 2.17, each 3H, s; δ_C see Experimental section) and one keto group (δ_C 205.4 s). In analogy, when the same reaction conditions were applied to eriocalyxin D (**8**), 94% of **10** was obtained (scheme 1). $NaBH_4$ reduction of **9** followed by acetylation with Ac_2O–TsOH gave **11** in 60% yield. The ^{13}C-NMR spectrum of **11** showed the absence of the keto group, and the α-configuration of the 7-OAc group can be deduced from the larger coupling constant ($J_{6\alpha,7\beta} = 10.0$ Hz) between H-6α (δ_H 5.99, dd, $J = 10.0$, 11.6 Hz) and H-7β (δ_H 4.76, d, $J = 10.0$ Hz), indicating that the β-side of **11** is more crowded than that in the keto group at C-6 of **9**.

After the above model experiments, our attention turned to enlargement of the B ring of maoecrystal B (**6**). Hydrogenation of maoecrystal B (**6**) using 10% Pd–C as catalyst



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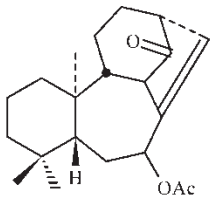

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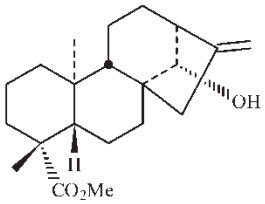

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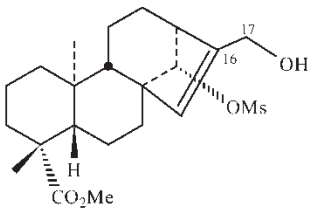

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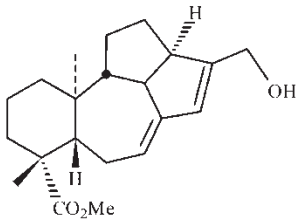

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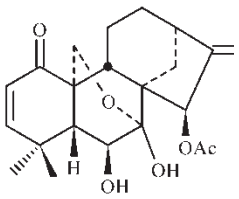
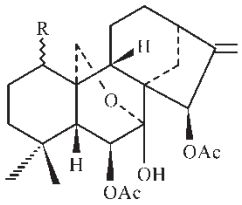
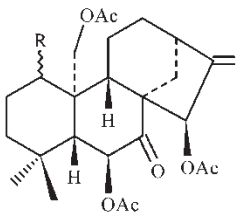


6 maoecrystal B



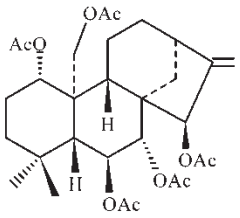
7 R=*β*-OH

8 R=*α*-OH



9 R=*β*-OAc

10 R=*α*-OAc



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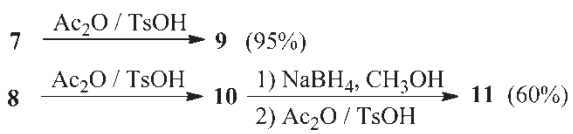
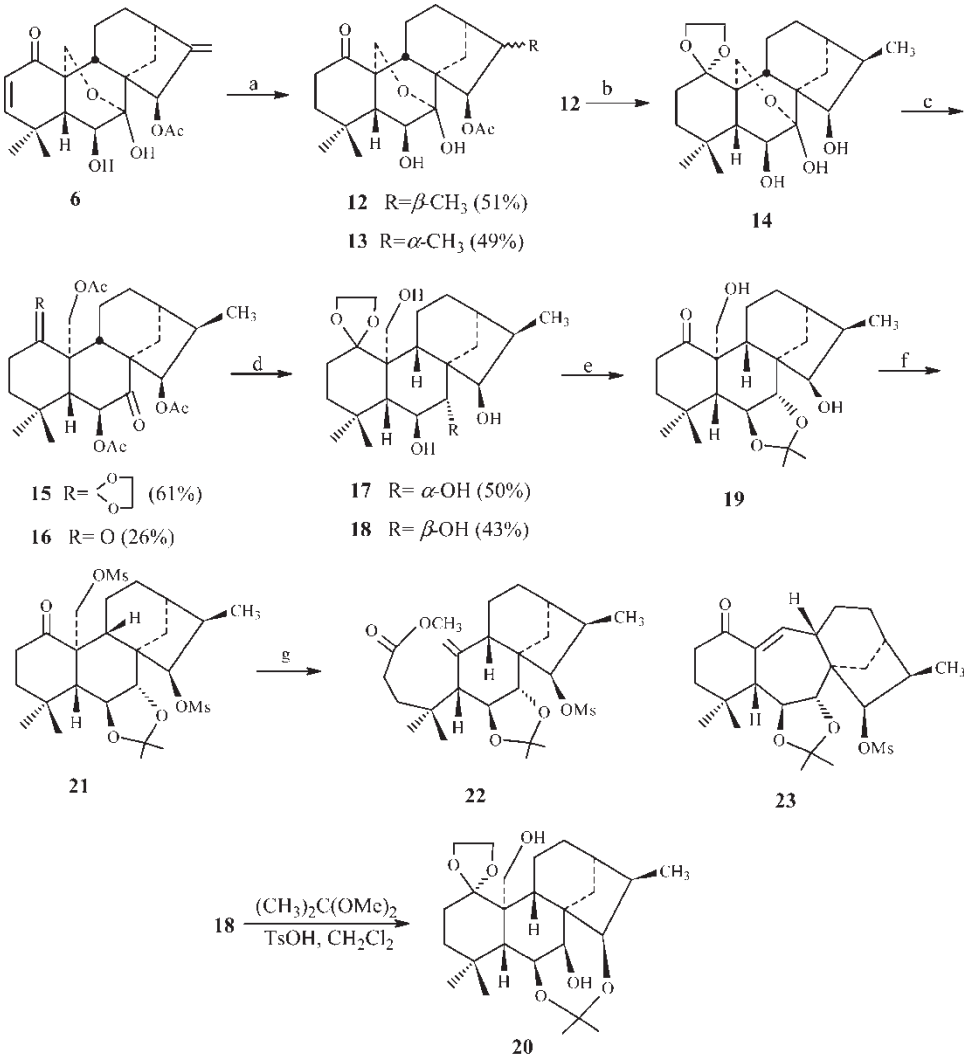


Scheme 1.

produced a pair of epimers at C-16 **12** (51%) and **13** (49%), which can be differentiated by the coupling constant of H-15; for example, the larger coupling constant ($J_{15\alpha,16\beta} = 10.2$ Hz) for **13** with the 16α-methyl group. In contrast, the 16-methyl group of **12** ($J_{15\alpha,16\alpha} = 5.2$ Hz) would be assigned to be in the β-orientation. Compound **12**, upon protection with glycol-TsOH followed by acetylation using Ac_2O–TsOH, gave compound **15** via **14** in 48% overall yield, along with by-product **16** (26%). Their structures were confirmed by comparison of the ^{1}H- and ^{13}C-NMR spectra with those of the analogues **9** and **10**. Protection of the 7-keto group of **15** using glycol-TMSCl was found to be very difficult, probably due to spatial hindrance. Reduction of **15** with $LiAlH_4$



a). 10%Pd-C/H_2, EtOH; b). glycol/TsOH, PhH, 80%; c). Ac_2O/TsOH; d). LAH, THF; e). $(CH_3)_2C(OMe)_2$, TsOH, CH_2Cl_2, 100%; f). MsCl, pyridine, 80%; g). NaOH, CH_3OH, 51%

Scheme 2.

was carried out smoothly to give a mixture which was subjected to chromatography to give compounds **17** (50%) and **18** (43%). In the ^{1}H-NMR spectrum of **17**, the one-proton doublet signal at δ 3.20 ($J = 9.2$ Hz) can be assigned to the H-7 geminal hydroxyl group based on comparison with the parent compound **15**. For **17**, the stereochemistry of H-7 was suggested to be β-oriented with an α-hydroxyl group at C-7. This, and considering the coupling constant ($J_{6,7} = 9.2$ Hz), led to the assignment of the β-configuration for the H-7 group of **17**. Protection of **17** with acetone afforded compound **19** quantitatively. The ^{1}H- and ^{13}C-NMR spectra of **19** showed distinct signals at δ_H 1.33, 1.33 and δ_C 107.1 s, 25.6 q for the acetonylidene moiety. In this case, de-protection of the 1-keto group of **17** is probably due to the presence of HIO_4. Interestingly, another epimer, **18**, under similar conditions gave the 1,4-diol-protected product **20** (100%) (scheme 2), probably due to the very close proximity of the 6,15-dihydroxyl groups. This was the result of a change in conformation of the B ring from the chair form to the boat form of the 7β-hydroxyl group of **20**. Compound **19** was exposed to MsCl–pyridine at room temperature and afforded the dimesylate **21** quantitatively. The ^{1}H- and ^{13}C-NMR spectra of **21** displayed two additional OMs signals at δ_H 3.02, 3.06 (each 3H, s) and δ_C 38.1 q, 38.0 q. Compared with **19**, the chemical shifts of H-15 (δ 4.48, d, $J = 4.2$ Hz) and H_2-20 (δ_H 4.71, 5.06, each 1H, ABq, $J = 10.2$ Hz) were shifted downfield by 0.48, and 0.34, 1.65 ppm, respectively, leading to the assignment of the OMs groups at C-15 and C-20. Unfortunately, an attempt to enlarge the B ring of **21** using 5% NaOH–MeOH (rt, 1.5 h) to obtain **23** via a Wagner–Meerwei rearrangement resulted in **22** (51%), a novel 1,10-seco *ent*-kauranoid diterpene. The ^{1}H- and ^{13}C-NMR spectra of **22**, $C_{25}H_{40}O_7S$ (HRMS), showed an exocyclic double bond (δ_H 5.14, 5.18, each 1H, br.s; δ_C 146.0 s, 113.8 t), one *COOCH*$_3$ group (δ_H 3.66, 3H, s; δ_C 174.8 s, 51.5 q), and one OMs group (δ_H 3.06, 3H, s; δ_C 37.4 q). Finally, the structure was confirmed by 2D NMR (HMQC, ^{1}H–^{1}H COSY, HMBC) (table 1, figure 1). The formation of **22** can be explained by the mechanism depicted in scheme 3. Compound A, with a 1-keto group, first undergoes the addition of $^-OCH_3$ derived from MeOH (A → B), followed by the elimination of a molecule of MeOH, together with the rupture of the C(1)–C(10) bond of B, leading to C (scheme 3).

Table 1. NMR data for compound **22** (^{1}H, 600 MHz; ^{13}C, 125 MHz, $CDCl_3$).

No	δ_H *mult (J=Hz)*	δ_C	*No*	δ_H *mult (J=Hz)*	δ_C
1		174.8 s	13	~1.83 m	41.7 d
2	1.54 m 1.69 m	30.0 t	14	1.25 m	29.6 t
3	1.70 m 1.98 m	35.4 t	15	4.57 d (3.6)	90.4 d
4		34.9 s	16	2.05 m	42.2 d
5	1.97 d (9.0)	54.4 d	17	1.19 d (7.2)	20.3 q
6	3.32 dd (11.4, 9.0)	78.0 d	18	1.10 s	27.0 q
7	3.46 d (11.4)	80.4 d	19	1.11 s	25.2 q
8		49.7 s	20	5.19 s 5.41 s	113.8 t
9	2.33 m	42.5 d	21		109.2 s
10		146.0 s	22	1.31 s	26.8 q
11	~1.8 m	21.5 t	23	1.37 s	26.8 q
12	1.25 m 1.32 m	26.5 t	OCH_3	3.66 s	51.5 q

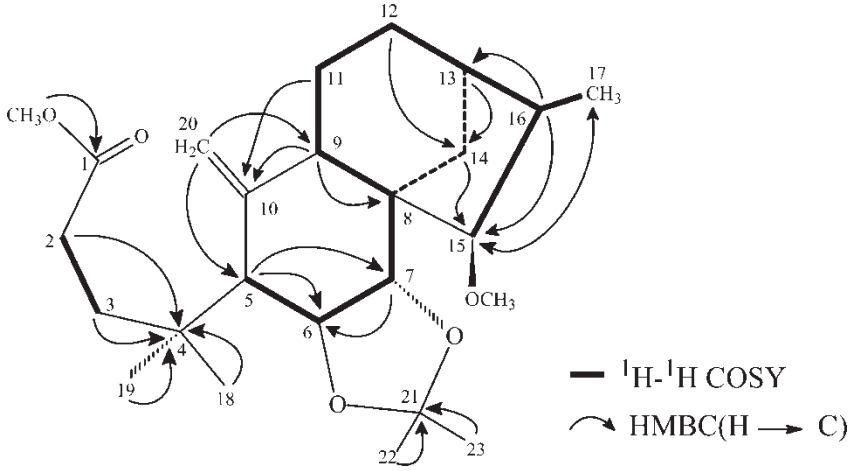


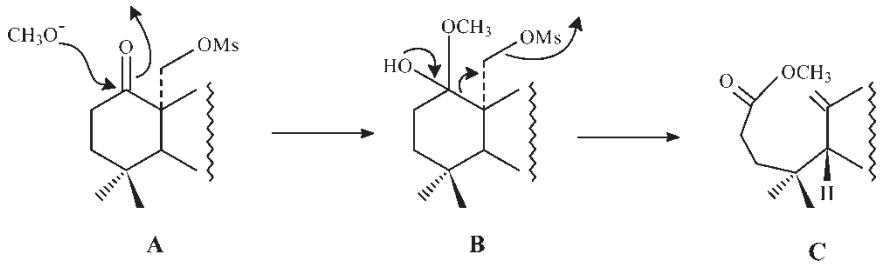
Figure 1. Selected 2D NMR correlations for **22**.

3. Experimental

3.1 General experimental procedures

Melting points were determined on a Kofler block (uncorrected). Optical rotations were measured in a 1.0 dm cell with a PE-314 polarimeter at 20 ± 1°C. IR spectra were recorded on a Nicolet 200 SXV spectrometer. MS spectra were obtained with a Auto-Spec-3000 instrument. ^{1}H- and ^{13}C-NMR spectra were acquired on a Bruker Ac-E 200 or a Varian INOVA-400/54 or a Bruker Avance 600 spectrometer, with TMS as internal standard. Silica gel GF_{254} and H (10–40 μm, Qingdao Sea Chemical Factory, China) were used for TLC and CC. Only key signals in the ^{1}H-NMR spectra, except for **22**, are reported.

3.1.1 Compound 9. To a solution of compound **7** (15 mg, 0.035 mmol) in Ac_2O (2 ml) was added *p*-TsOH (15 mg) and the mixture was stirred at room temperature overnight. After pouring into ice water, the solution was basified with conc. NH_4OH to pH 8. Extraction ($CHCl_3$, 5 ml × 3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–Me_2CO, 100:1) afforded the pure product as a white amorphous powder, 18 mg, (100%). Mp 161–162°C; R_f (98% $CHCl_3$–Me_2CO) 0.41; $[\alpha]_D^{20}$ −97.3 (*c* 0.42, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 2956, 2861, 1750 (COO), 1714 (COO), 1452, 1381, 1236, 1035; δ_H (200 MHz, $CDCl_3$) 0.95 (3H, s, CH_3-19), 1.05 (3H, s, CH_3-18), 1.99, 2.02, 2.09, 2.17



Scheme 3. A plausible mechanism for the reaction pathway from **21** to **22**.

(each 3H, s, OAc × 4), 4.14, 4.49 (each 1H, ABq, $J = 12.4$ Hz, H_2-20), 4.88 (1H, t, $J = 1.6$ Hz, Ha-17), 5.06 (1H, hidden, Hb-17), 5.07 (1H, dd, hidden, H-1α), 5.53 (1H, d, $J = 11.6$ Hz, H-6α), 5.66 (1H, t, $J = 2.4$ Hz, H-15α); δ_C (50 MHz, $CDCl_3$) 205.4 (C-7), 170.0 (*CO*CH_3), 170.0 (*CO*CH_3), 169.6 (*CO*CH_3), 169.4 (*CO*CH_3), 154.2 (C-16), 109.1 (C-17), 80.4 (C-6), 72.1 (C-15), 69.9 (C-1), 64.0 (C-20), 55.8 (C-8), 47.4 (C-5), 42.9 (C-10), 37.0 (C-9), 36.8 (C-13), 35.4 (C-3), 34.5 (C-18), 33.1 (C-4), 32.6 (C-2), 30.4 (C-12), 23.2 (C-14), 22.3 (C-19), 21.2 (CO*CH*$_3$), 21.1 (CO*CH*$_3$), 20.8 (CO*CH*$_3$), 20.7 (CO*CH*$_3$), 16.3 (C-11); *m/z* (ESI) 541 (100, $M^+ + Na$); HR FAB-MS *m/z* 519.2578 $[M + H]^+$ (calcd for $C_{28}H_{39}O_9$, 519.2594).

3.1.2 Compound 10. To a solution of ecriocalyxin D (**8**) (90 mg, 0.21 mmol) in Ac_2O (5 ml) was added *p*-TsOH (100 mg) and the mixture was stirred at room temperature overnight. General work-up and column chromatography (silica gel H, $CHCl_3$–Me_2CO, 60:1) afforded the pure product as a white amorphous powder, 100 mg (94%). Mp 172–173°C; R_f (95% $CHCl_3$–Me_2CO) 0.51; $[\alpha]_D^{20}$ −145.4 (*c* 0.50, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 2940, 1748 (COO), 1710 (COO), 1434, 1229, 1058; δ_H (200 MHz, $CDCl_3$) 0.85 (3H, s, CH_3-19), 1.03 (3H, s, CH_3-18), 1.96, 1.96, 2.03, 2.19 (each 3H, s, OAc × 4), 4.47, 4.49 (each 1H, ABq, $J = 12.8$ Hz, H_2-20), 4.80 (1H, dd, $J = 5.6$, 11.2 Hz, H-1β), 4.82, 5.06 (each 1H, br.s, H_2-17), 5.48 (1H, br.s, H-15α), 5.57 (1H, d, $J = 10.6$ Hz, H-6α); *m/z* (EI) 518 (4, M^+), 416 (80); HR FAB-MS *m/z* 519.2572 $[M + H]^+$ (calcd for $C_{28}H_{39}O_9$, 519.2594).

3.1.3 Compound 11. To a solution of compound **10** (70 mg, 0.14 mmol) in MeOH (5 ml) was added $NaBH_4$ (70 mg, 1.89 mmol) and the mixture was stirred at room temperature for 30 min. The reaction was quenched with saturated NH_4Cl (15 ml). The resulting mixture was extracted with $CHCl_3$ (5 ml × 4). Drying (Na_2SO_4) and evaporation afforded the residue (71 mg); to a solution of this residue in Ac_2O (3 ml) was added *p*-TsOH (70 mg) and the solution was stirred at room temperature for 30 h. Diluting (ice water), basifying (NH_4OH, pH 8), extraction ($CHCl_3$, 10 ml × 3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–Me_2CO, 50:1) afforded the pure product as a white amorphous powder, 45 mg (59%). Mp 91–92°C; R_f (97% $CHCl_3$–Me_2CO) 0.50; $[\alpha]_D^{20}$ −58.4 (*c* 0.41, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 2940, 1745 (COO), 1710, 1472, 1234, 1107, 1044; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, s, CH_3-19), 1.06 (3H, s, CH_3-18), 2.00, 2.04, 2.05, 2.20, 2.25 (each 3H, s, OAc × 5), 4.39, 4.68 (each 1H, ABq, $J = 13.6$ Hz, H_2-20), 4.76 (1H, d, $J = 10.0$ Hz, H-7β), 4.78 (1H, dd, $J = 6.0$, 13.6 Hz, H-1β), 4.92 (1H, d, $J = 1.6$ Hz, Ha-17), 4.95 (1H, d, $J = 2.8$ Hz, Hb-17), 5.22 (1H, t, $J = 2.8$ Hz, H-15α), 5.99 (1H, dd, $J = 10.0$, 11.6 Hz, H-6α); δ_C (50 MHz, $CDCl_3$) 170.6 (*CO*CH_3), 170.3 (*CO*CH_3), 169.9 (*CO*CH_3), 169.8 (*CO*CH_3), 169.8 (*CO*CH_3), 151.3 (C-16), 107.2 (C-17), 82.4 (C-6), 75.7 (C-7), 74.7 (C-15), 70.2 (C-1), 63.9 (C-20), 52.7 (C-5), 49.2 (C-8), 46.9 (C-9), 45.9 (C-10), 38.9 (C-13), 38.1 (C-3), 34.3 (C-18), 33.0 (C-4), 32.2 (C-2), 28.8 (C-12), 26.3 (C-14), 23.1 (C-19), 21.5 (CO*CH*$_3$), 21.4 (CO*CH*$_3$), 21.2 (CO*CH*$_3$), 21.0 (CO*CH*$_3$), 20.6 (CO*CH*$_3$), 18.3 (C-11); *m/z* (ESI) 585 (100, $M^+ + Na$); HR FAB-MS *m/z* 563.2841 $[M + H]^+$ (calcd for $C_{30}H_{43}O_{10}$, 563.2856).

3.1.4 Compounds 12 and 13. A solution of maoecrystal B (**6**) (2.0 g, 5.15 mmol) in EtOH (100 ml) was treated with 10% Pd–C (200 mg) under an atmospheric pressure of hydrogen

and stirred at room temperature for 2 h. Filtration, evaporation and column chromatography (silica gel H, petroleum ether–acetic ether, 2.5:1) afforded the pure products **12** (white needles, 1.03 g, 51%) and **13** (white needles, 990 mg, 49%).

3.1.4.1 Compound 12. Mp 212–213°C; R_f (50% cyclohexane–acetone) 0.44; $[\alpha]_D^{20}$ + 93.1 (*c* 0.49, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 3433 (OH), 2960, 1721 (COO), 1705, 1493, 1378, 1278, 1045; δ_H (200 MHz, $CDCl_3$) 0.93 (3H, s, CH_3-18), 1.05 (3H, s, CH_3-19), 1.13 (3H, d, $J = 7.0$ Hz, CH_3-17), 2.07 (3H, s, OAc), 3.75 (1H, dd, $J = 2.2$, 8.4 Hz, H-6α), 3.88, 4.29 (each 1H, ABq, $J = 10.2$ Hz, H_2-20), 4.81 (1H, d, $J = 5.2$ Hz, H-15α); δ_C (100 Hz, $CDCl_3$) 213.5 (C-1), 171.2 (*CO*CH_3), 96.7 (C-7), 79.2 (C-15), 72.9 (C-6), 64.6 (C-20), 55.3 (C-5), 52.9 (C-8), 50.4 (C-9), 48.7 (C-10), 42.8 (C-16), 38.5 (C-3), 36.8 (C-13), 35.5 (C-2), 32.4 (C-4), 31.0 (C-12), 30.5 (C-18), 25.9 (C-14), 23.5 (C-19), 21.9 (CO*CH$_3$*), 20.1 (C-17), 17.5 (C-11); *m/z* (EI) 392 (14, M^+), 374 (10, M–H_2O), 331 (63); HR EI-MS *m/z* 392.2244 $[M]^+$ (calcd for $C_{22}H_{32}O_6$, 392.2198).

3.1.4.2 Compound 13. Mp 171–172°C; R_f (50% cyclohexane–acetone) 0.47; $[\alpha]_D^{20}$ + 48.9 (*c* 0.52, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 3458 (OH), 2957, 1720 (COO), 1705, 1495, 1374, 1246, 1050; δ_H (200 MHz, $CDCl_3$) 0.76 (3H, d, $J = 7.6$ Hz, CH_3-17), 0.94 (3H, s, CH_3-19), 1.04 (3H, s, CH_3-18), 2.09 (3H, s, OAc), 3.73 (1H, dd, $J = 2.4$, 7.8 Hz, H-6α), 3.78 (1H, br.s, OH), 3.87, 4.25 (each 1H, ABq, $J = 10.6$ Hz, H_2-20), 5.21 (1H, d, $J = 10.2$ Hz, H-15α); δ_C (100 MHz, $CDCl_3$) 213.5 (C-1), 171.0 (*CO*CH_3), 96.6 (C-7), 73.5 (C-15), 73.0 (C-6), 64.7 (C-20), 56.1 (C-5), 52.9 (C-8), 48.7 (C-10), 42.6 (C-9), 39.3 (C-16), 38.7 (C-3), 35.7 (C-2), 33.6 (C-13), 32.5 (C-4), 30.5 (C-18), 28.0 (C-12), 23.5 (C-19), 21.5 (CO*CH$_3$*), 19.8 (C-14), 16.9 (C-11), 11.4 (C-17); *m/z* (EI) 392 (21, M^+), 374 (12, M–H_2O), 331 (78); HR EI-MS *m/z* 392.2244 $[M]^+$ (calcd for $C_{22}H_{32}O_6$, 392.2198).

3.1.5 Compound 14. To a solution of compound **12** (500 mg, 1.28 mmol) and *p*-TsOH (100 mg) in PhH (25 ml) was added ethanediol (1.5 ml) and the mixture was stirred under reflux with the azeotropic removal of water for 2.5 h. After cooling to room temperature, filtration afforded the product as white needles. The filtrate was washed with saturated $NaHCO_3$ solution (5 ml) and the water layer was extracted with PhH (5 ml × 2). The combined PhH layer was concentrated to 5 ml and allowed to crystallize at room temperature to give the product as needles (398 mg, 80%). Mp 239–240°C; R_f (95% $CHCl_3$–Me_2CO) 0.55; $[\alpha]_D^{20}$ − 50.2 (*c* 0.50, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 3377 (OH), 3178 (OH), 2953, 2896, 1500, 1453, 1295, 1177, 1101, 1039; δ_H (400 MHz, DMSO-d) 0.92 (3H, s, CH_3-19), 0.98 (3H, d, $J = 7.2$ Hz, CH_3-17), 1.02 (3H, s, CH_3-18), 3.32 (1H, s, 7-OH), 3.45–4.00 (7H, m, hidden, OCH_2CH_2O, H_2-20 and H-6α), 5.18 (1H, s, OH), 5.56 (1H, s, OH), 5.82 (1H, d, $J = 4.8$ Hz, H-15α); δ_C (100 Hz, DMSO-d) 110.4 (C-1), 96.0 (C-7), 79.5 (C-15), 72.9 (C-6), 63.5 (C-20), 62.6 (O*CH$_2$*CH_2O), 61.7 (OCH_2*CH$_2$*O), 57.3 (C-5), 52.6 (C-8), 50.4 (C-9), 42.3 (C-10), 37.3 (C-3), 37.1 (C-16), 36.9 (C-13), 33.5 (C-4), 32.5 (C-18), 31.7 (C-2), 26.5 (C-12, C-14), 22.3 (C-19), 21.2 (C-17), 16.9 (C-11); *m/z* (FAB) 395 (45, H), 377 (100, M–H_2O); HR EI-MS *m/z* 394.2394 $[M]^+$ (calcd for $C_{22}H_{34}O_6$, 394.2355).

3.1.6 Compounds 15 and 16. To a solution of compound **14** (180 mg, 0.45 mmol) in Ac_2O (10 ml) was added *p*-TsOH (110 mg) and the mixture was heated at 50°C for 2.5 h. Work-up

using general methods and column chromatography (silica gel H, $CHCl_3$–Me_2CO, 50:1) afforded the pure product as a white amorphous powder (**15**, 145 mg, 61%; **16**, 56 mg, 26%).

3.1.6.1 Compound 15. Mp 65–66°C; R_f (98% $CHCl_3$–Me_2CO) 0.50; $[\alpha]_D^{20}$ + 9.5 (*c* 0.61, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 2962, 1773 (COO), 1736 (COO), 1458, 1374, 1256, 1077; δ_H (200 MHz, $CDCl_3$) 0.84 (3H, s, CH_3-19), 1.03 (3H, s, CH_3-18), 1.14 (3H, d, J = 7.0 Hz, CH_3-17), 1.95, 1.95, 2.13 (each 3H, s, OAc × 3), 3.89–4.08 (4H, m, OCH_2CH_2O), 4.47 (2H, s, H_2-20), 4.68 (1H, d, J = 5.4 Hz, H-15α), 5.54 (1H, d, J = 10.8 Hz, H-6α); δ_C (50 Hz, $CDCl_3$) 206.2 (C-7), 170.2 (*CO*CH_3), 169.7 (*CO*CH_3), 169.7 (*CO*CH_3), 111.6 (C-1), 86.6 (C-6), 71.8 (C-15), 64.6 (O*C*$H_2$$CH_2$O), 64.4 ($OCH_2$*C*$H_2$O), 63.3 (C-20), 57.7 (C-8), 55.4 (C-4), 49.6 (C-5), 49.5 (C-9), 47.0 (C-10), 38.1 (C-3, C-16), 37.2 (C-13), 33.4 (C-18), 32.2 (C-2), 29.1 (C-14), 28.9 (C-12), 21.9 (CO*C*H_3), 21.2 (C-19), 21.4 (CO*C*H_3), 20.7 (CO*C*H_3), 20.0 (C-17), 19.4 (C-11); *m*/*z* (ESI) 521 (100, M^+ + H); HR FAB-MS *m*/*z* 521.2682 $[M]^+$ (calcd for $C_{28}H_{41}O_9$, 521.2750).

3.1.6.2 Compound 16. Mp 162–163°C; R_f (98% $CHCl_3$–Me_2CO) 0.46; $[\alpha]_D^{20}$ −80.2 (*c* 0.90, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 2935, 1747 (COO), 1721 (COO), 1460, 1378, 1233, 1041; δ_H (200 MHz, $CDCl_3$) 1.13 (3H, s, CH_3-19), 1.19 (3H, d, J = 7.6 Hz, CH_3-17), 1.20 (3H, s, CH_3-18), 2.05, 2.06, 2.13 (each 3H, s, OAc × 3), 4.75, 4.84 (each 1H, ABq, J = 12.4 Hz, H_2-20), 5.13 (1H, d, J = 5.2 Hz, H-15α), 5.49 (1H, d, J = 13.2 Hz, H-6α); δ_C (50 MHz, $CDCl_3$) 209.6 (C-7), 203.6 (C-1), 170.0 (*CO*CH_3), 169.7 (*CO*CH_3), 169.5 (*CO*CH_3), 82.6 (C-6), 73.0 (C-15), 63.2 (C-20), 58.7 (C-8), 54.2 (C-10), 52.6 (C-5), 44.4 (C-9), 40.1 (C-3), 39.6 (C-16), 38.3 (C-13), 36.0 (C-2), 33.4 (C-4, C-18), 32.9 (C-14), 30.2 (C-12), 23.8 (C-19), 21.8 (CO*C*H_3), 20.8 (CO*C*H_3), 20.7 (C-17), 20.3 (CO*C*H_3), 19.2 (C-11); *m*/*z* (EI) 476 (15, M^+), 374 (14), 416 (20), 374 (100); HR FAB-MS *m*/*z* 477.2480 $[M + H]^+$ (calcd for $C_{26}H_{37}O_8$, 477.2488).

3.1.7 Compounds 17 and 18. To a solution of compound **15** (200 mg, 0.42 mmol) in THF (15 ml) was added $LiAlH_4$ (100 mg, 2.63 mmol) and the solution was stirred at room temperature for 1.5 h. To the reaction solution was added EtOAc (1 ml) and saturated NH_4Cl solution (2 ml). Filtration, washing (EtOAc), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH, 98:2 to 96:4) afforded the pure product as a white amorphous powder (**17**, 90 mg, 50%; **18**, 65 mg, 43%).

3.1.7.1 Compound 17. Mp 112–113°C; R_f (95% $CHCl_3$–CH_3OH) 0.45; $[\alpha]_D^{20}$ −88.2 (*c* 0.50, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 3420 (OH), 2930, 1642, 1458, 1360, 1256, 1050; δ_H (200 MHz, $CDCl_3$) 1.08 (3H, s, CH_3-19), 1.10 (3H, d, J = 7.0 Hz, CH_3-17), 1.17 (3H, s, CH_3-18), 3.20 (1H, d, J = 2.8 Hz, H-7β), 4.02, 4.36 (each 1H, ABq, J = 12.4 Hz, H_2-20); δ_C (50 MHz, $CDCl_3$) 115.0 (C-1), 83.9 (C-6), 77.2 (C-7), 71.7 (C-15), 63.5 (C-20), 62.7 (O*C*$H_2$$CH_2$O), 62.6 ($OCH_2$*C*$H_2$O), 54.4 (C-5), 51.2 (C-8, C-10), 43.7 (C-9), 40.7 (C-13), 38.2 (C-3), 36.9 (C-16), 36.4 (C-18), 33.1 (C-4), 30.9 (C-2), 28.3 (C-12), 27.9 (C-14), 23.1 (C-17, C-19), 20.7 (C-11); *m*/*z* (EI) 396 (3, M^+), 378 (4), 347 (14), 295 (22); HR EI-MS *m*/*z* 396.2552 $[M]^+$ (calcd for $C_{22}H_{36}O_6$, 396.2511).

3.1.7.2 Compound 18. Mp 98–99°C; R_f (90% $CHCl_3$–CH_3OH) 0.46; $[\alpha]_D^{20}$ −19.8 (*c* 0.54, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 3427 (OH), 2926, 1639, 1459, 1369, 1062; δ_H (200 MHz, $CDCl_3$) 1.08 (6H, s, CH_3-18 and CH_3-19), 1.10 (3H, d, J = 8.6 Hz, CH_3-17), 3.53 (1H, d, J = 5.6 Hz, H-15α), 3.58 (1H, d, J = 4.0 Hz, H-7α), 3.87 (1H, dd, J = 4.0, 9.0 Hz, H-6α),

4.05, 4.36 (4H, m, OCH_2CH_2O); δ_C (50 MHz, $CDCl_3$) 114.3 (C-1), 83.5 (C-6), 74.8 (C-7), 69.9 (C-15), 63.7 (C-20), 63.2 (OCH_2CH_2O), 63.0 (OCH_2CH_2O), 52.4 (C-5), 52.2 (C-12), 50.2 (C-8), 49.2 (C-10), 46.5 (C-9), 39.7 (C-13), 39.3 (C-3), 35.5 (C-16), 34.6 (C-18), 33.3 (C-4), 32.2 (C-2), 29.1 (C-14), 22.3 (C-19), 21.0 (C-17), 20.0 (C-11); *m/z* (EI) 396 (1, M^+), 378 (4), 360 (5), 347 (15); HR EI-MS *m/z* 396.2552 $[M]^+$ (calcd for $C_{22}H_{36}O_6$, 396.2511).

3.1.8 Compound 19. To a solution of compound **17** (48 mg, 0.12 mmol) in CH_2Cl_2 (5 ml) was added 2,2-dimethoxypropane (0.08 ml, 0.65 mmol) and *p*-TsOH (10 mg) and the solution was stirred at room temperature for 10 min. Saturated $NaHCO_3$ solution (5 ml) was added and the mixture was stirred vigorously. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (5 ml × 3). Drying (Na_2SO_4) and removal of solvent afforded the product as a white amorphous powder, 48 mg (100%). Mp 236–237°C; R_f (98% $CHCl_3$–CH_3OH) 0.45; $[\alpha]_D^{20}$ −28.2 (*c* 0.40, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 3493 (OH), 3378 (OH), 2956, 1707, 1468, 1380, 1229, 1055; δ_H (400 MHz, $CDCl_3 + CD_3COCD_3$) 1.07 (3H, d, $J = 6.8$ Hz, CH_3-17), 1.13 (3H, s, CH_3-19), 1.33 (3H, s, CH_3-18), 1.33 (6H, s, $C(CH_3)_2$), 2.25 (1H, d, $J = 9.2$ Hz, H-7β), 3.61 (1H, dd, $J = 8.8$, 11.6 Hz, H-6α), 4.00 (1H, d, $J = 5.2$ Hz, H-15α), 4.36, 4.41 (each 1H, ABq, $J = 11.2$ Hz, H_2-20); δ_C (50 MHz, $CDCl_3 + CD_3COCD_3$) 210.1 (C-1), 107.1 (C-21), 80.7 (C-6, C-7), 74.2 (C-15), 59.6 (C-20), 58.6 (C-8), 52.1 (C-5), 48.3 (C-10), 42.4 (C-9), 39.0 (C-16), 35.6 (C-3), 35.3 (C-13), 35.0 (C-2), 31.9 (C-18), 31.2 (C-4), 30.4 (C-14), 26.6 (C-12), 25.6 (C-22), 25.2 (C-23), 24.3 (C-19), 19.7 (C-17), 19.4 (C-11); *m/z* (EI) 377 (1, $M-CH_3$), 347 (4), 237 (40), 155 (100); HR FAB-MS *m/z* 393.2598 $[M + H]^+$ (calcd for $C_{23}H_{37}O_5$, 393.2640).

3.1.9 Compound 20. To a solution of compound **18** (50 mg, 0.13 mmol) in CH_2Cl_2 (5 ml) was added 2,2-dimethoxypropane (0.09 ml, 0.73 mmol) and *p*-TsOH (10 mg) and the solution was stirred at room temperature for 15 min. General work-up afforded the product as a white amorphous powder, 55 mg (100%). Mp 200–201°C; R_f (98% $CHCl_3$–CH_3OH) 0.50; $[\alpha]_D^{20}$ −17.9 (*c* 0.49, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 3429 (OH), 2931, 1460, 1371, 1251, 1156, 1026; δ_H (400 MHz, $CDCl_3$) 1.05 (3H, s, CH_3-19), 1.08 (3H, s, CH_3-18), 1.14 (3H, d, $J = 7.2$ Hz, CH_3-17), 1.33, 1.47 (each 3H, s, $C(CH_3)_2$), 3.22 (1H, dd, $J = 2.4$, 9.2 Hz, 20-OH), 3.66 (1H, dd, $J = 2.0$, 6.0 Hz, $+D_2O$, d, $J = 5.6$ Hz, H-7α), 3.74 (1H, dd, $J = 9.2$, 12.4 Hz, $+D_2O$, d, $J = 12.8$ Hz, Ha-20), 3.99 (4H, m, OCH_2CH_2O), 4.01 (1H, hidden, H-15α), 4.19 (1H, dd, $J = 2.0$, 12.4 Hz, $+D_2O$, d, $J = 12.0$ Hz, Hb-20), 4.28 (1H, dd, $J = 5.6$, 10.8 Hz, H-6α); δ_C (50 MHz, $CDCl_3$) 114.4 (C-1), 108.4 (C-21), 85.4 (C-6), 81.5 (C-7), 75.2 (C-15), 63.4 (OCH_2CH_2O), 62.7 (OCH_2CH_2O), 61.8 (C-20), 51.3 (C-5), 50.6 (C-8), 47.6 (C-10), 44.0 (C-9), 40.4 (C-16), 38.8 (C-3), 36.7 (C-13), 35.7 (C-18), 33.9 (C-2), 33.3 (C-4), 31.1 (C-14), 27.9 (C-12), 27.8 (C-22), 26.0 (C-23), 23.0 (C-19), 21.2 (C-17), 19.9 (C-11); *m/z* (EI) 436 (3, M^+), 418 (2), 293 (43); HR FAB-MS *m/z* 437.2861 $[M + H]^+$ (calcd for $C_{25}H_{41}O_6$, 437.2903).

3.1.10 Compound 21. To a solution of compound **19** (42 mg, 0.11 mmol) in pyridine (3 ml) was added MsCl (0.1 ml, 1.29 mmol) and the solution was stirred at room temperature for 1.5 h. After removal of solvent, the solution was diluted with saturated $NaHCO_3$ solution. Extraction ($CHCl_3$, 5 ml × 3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–Me_2CO, 80:1.3) afforded the pure product as a white amorphous

powder, 47 mg (80%). Mp 192–193°C; R_f (95% $CHCl_3$–Me_2CO) 0.50; $[\alpha]_D^{20}$ −29.1 (*c* 0.39, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 2928, 2857, 1707, 1461, 1359, 1174, 1023; δ_H (200 MHz, $CDCl_3$) 1.15, 1.25, 1.25, 1.37 (each 3H, s, $CH_3 \times 4$), 3.02, 3.06 (each 3H, s, OMs × 2), 3.26 (1H, d, $J = 9.0$ Hz, H-7β), 3.45 (1H, dd, $J = 9.0$, 11.4 Hz, H-6α), 4.48 (1H, d, $J = 4.2$ Hz, H-15α), 4.81, 5.07 (each 1H, ABq, $J = 10.2$ Hz, H_2-20); δ_C (50 MHz, $CDCl_3$) 208.7 (C-1), 109.7 (C-21), 88.8 (C-15), 80.4 (C-6), 74.6 (C-7), 66.4 (C-20), 57.1 (C-8), 53.5 (C-5), 49.7 (C-10), 41.3 (C-9), 40.1 (C-16), 38.1 (OMs), 38.0 (OMs), 36.9 (C-13), 36.8 (C-3), 35.6 (C-2), 33.1 (C-18), 32.5 (C-4), 30.5 (C-14), 27.5 (C-12), 26.8 (C-22), 26.6 (C-23), 25.4 (C-19), 20.3 (C-11, C-17); *m/z* (EI) 533 (3, M^+–CH_3), 491 (5), 394 (18), 315 (100); HR FAB-MS *m/z* 549.2239 $[M + H]^+$ (calcd for $C_{25}H_{41}S_2O_9$, 549.2192).

3.1.11 Compound 22. A solution of compound **21** (22 mg, 0.04 mmol) in 5% methanolic NaOH (9 ml) was stirred at room temperature for 50 min. Diluting (H_2O), neutralizing (10% HCl), extraction ($CHCl_3$, 5 ml × 3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–Me_2CO, 100:1) afforded the pure product as a white amorphous powder, 10 mg (51%). Mp 143–144°C; R_f (98% $CHCl_3$–Me_2CO) 0.54; $[\alpha]_D^{20}$ −39.2 (*c* 0.40, $CHCl_3$); ν_{max} (KBr) (cm^{-1}): 2930, 2861, 1721 (COO), 1460, 1377, 1155, 1024; δ_H (600 MHz, $CDCl_3$) and δ_C (125 MHz, $CDCl_3$) see table 1; *m/z* (ESI) 507 (100, $M^+ + Na$); HR FAB-MS *m/z* 485.2549 $[M + H]^+$ (calcd for $C_{25}H_{41}SO_7$, 485.2573).

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