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Short and efficient synthesis of (+)-subersic acids

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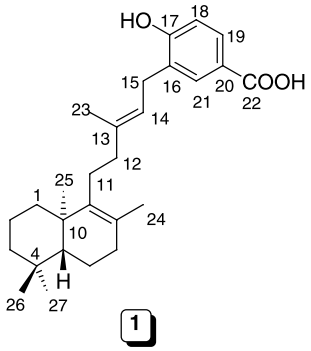
Abstract—An efficient synthesis of (+)-subersic acid, the unnatural enantiomer, has been achieved from sclareol and *p*-hydroxybenzoic acid.

1. Introduction

(−)-Subersic acid was isolated from the sponge *Suberea* sp. by Crews and co-worker.[1] The natural product was an inhibitor of human 15-lipoxygenase, assay that has been employed to discover new marine-sponge derived bioactive compounds. The availability of inhibitors could provide biomolecules that are useful as pharmacological agents.

Recently Mori and co-workers[2] reported the synthesis and absolute configuration of (−)-subersic acid. The acid **1** was synthesized from (*S*)-3-hydroxy-2,2-dimethylcyclohexanone and *p*-hydroxybenzoic acid. The stereochemistry was established as (5*R*,10*R*).



1

(-) Subersic acid

2. Results and discussion

In this work we report the synthesis of (+)-subersic acid from naturally occurring (−)-sclareol. The key step of the synthesis (Scheme 1) was the coupling of the diterpene part with the lithiated arene unit.

The synthesis of the aromatic fragment **6** is summarized in Scheme 2. The starting methyl 4-hydroxybenzoate **2** by treatment with Br_2[3] gives the bromo derivated **3**. Protection of the **3** as methoxymethyl ether[4] and subsequent DIBAL reduction[5] of **4**, gives alcohol **5** in excellent yield. The alcohol **5** was transformed[6] in the THP derivative **6**.

The diterpene fragment **11** necessary for the final coupling was obtained from sclareol according to Scheme 3. Sclareol was acetylated in quantitative yield with acetyl chloride and *N*,*N*-dimethylaniline, affording the diacetyl derivative **7** whose isomerization with bis-(acetonitrile)palladium (II) chloride[7,8] led to diacetate **8** (92%).

Treatment of **8** with HI in benzene[9] gives the monoacetate **9**. The hydrolysis of the acetoxy group of **9** and subsequent halogenation with CBr_4/PPh_3[10,11] gave the allylic bromide **11**.

Scheme 4 shows the final stage of the synthesis to give (+)-subersic acid. The lithiated arene unit was generated from the bromo derivative **6** by treatment with *t*-BuLi. It was then alkylated with the bromide **11** to give the coupling product that was transformed to **12** by removing the THP protective group.

Oxidation of **12** with MnO_2 gives the aldehyde **13** in excellent yield. Treatment of **13** with sodium chlorite[12] and removing of protective group furnished (+)-subersic acid, $[\alpha]_D^{20}=+49$ ($c=0.78$, $CHCl_3$), (−)-subersic acid,[1] $[\alpha]_D^{20}=-46$ ($c=0.5$, $CHCl_3$)

The efficiency of this synthesis allows the availability of the target molecule for activity test as human 15-lipoxygenase inhibitor, that is currently in progress.

Keywords: (+) subersic acid; meroterpenes; sclareol.
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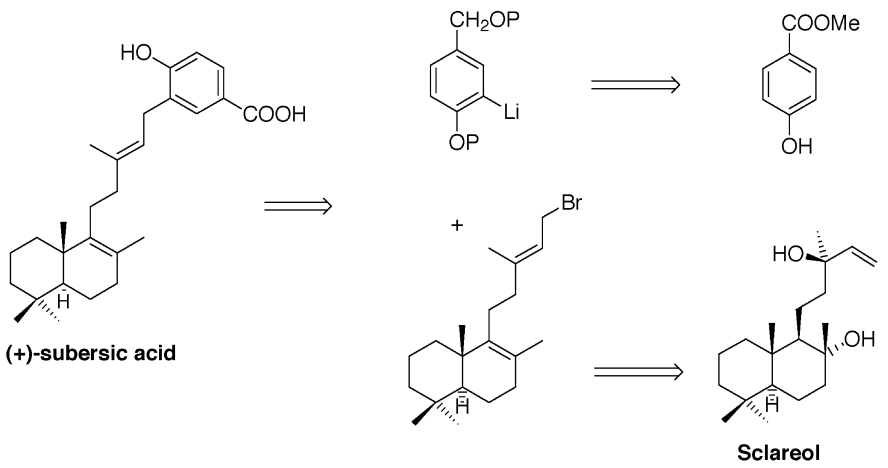
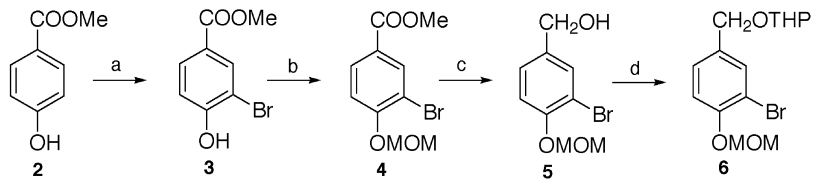
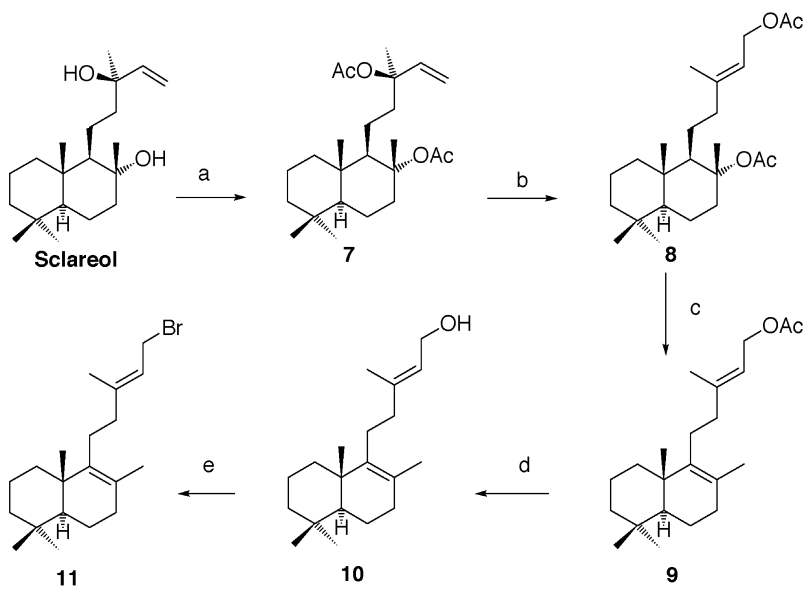


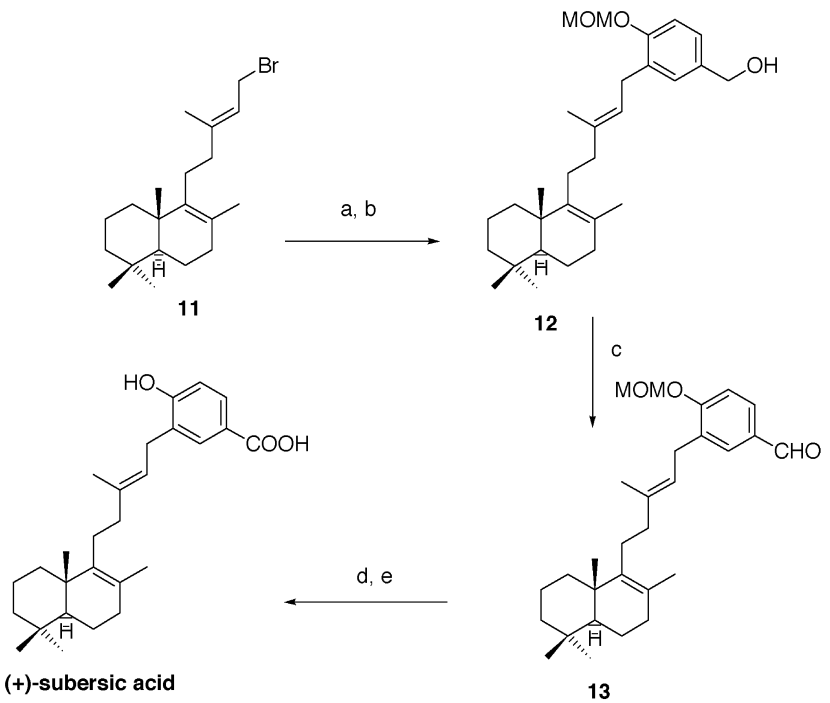
Scheme 1.



Scheme 2. (a) Br_2, DCM, rt, 24 h, 95%; (b) DMM, P_2O_5, $CHCl_3$, rt, 10 min, 99%; (c) DIBAL-H, DCM, −78°C, 1 h, 99%; (d) DHP, HCl/dioxane 4 M, rt, 10 min, 99%.



Scheme 3. (a) AcCl, *N*,*N*-dimethylaniline, DCM, rt, 24 h, 97%; (b) $PdCl_2(MeCN)_2$, THF, rt, 4 h, 92%; (c) HI, C_6H_6, rt, 11 h, 48%; (d) K_2CO_3/MeOH 3%, rt, 98%; (e) CBr_4, PPh_3, DCM, 0°C, 10 min, 99%.



Scheme 4. (a) **6**, *t*BuLi, THF, −78°C→rt, 3 h; (b) *p*TsOH, MeOH, rt, 1 h, 26% (from **11**); (c) MnO_2, DCM, rt, 3 h, 85%; (d) $NaClO_2$, *t*BuOH, rt, 2 h; (e) HCl 6 M, THF, 45°C, 3 h, 47% (from **13**).

3. Experimental

3.1. General

Unless otherwise stated, all chemicals were purchased as the highest purity commercially available and were used without further purification. Melting points were determined with a Kofler hot stage melting point apparatus and are uncorrected. IR spectra were recorded on a BOMEM 100 FT IR spectrophotometer. ^1H and ^{13}C NMR spectra were performed in deuterochloroform and referenced to the residual peak of $CHCl_3$ at δ 7.26 ppm and δ 77.0 ppm for ^1H and ^{13}C, respectively, using a Bruker WP-200 SY and a BRUKER DRX 400 MHz. Chemical shifts are reported in δ ppm and coupling constants (J) are given in Hz. MS were performed in a VG-TS 250 spectrometer at 70 eV ionizing voltage. Mass Spectra are presented as *m/z* (% rel. int.). HRMS were recorded in a VG Platform spectrometer using Electronic Impact (EI) or Fast Atom Bombardment (FAB) technique. Optical rotations were determined in a Perkin–Elmer 241 polarimeter in 1 dm cells. Diethyl ether, THF and benzene were distilled from sodium, and pyridine and dichloromethane were distilled under argon from CaH_2.

3.1.1. 3-Bromo-4-hydroxybenzoic acid methyl ester (3). To a solution of **2** (1.19 g, 7.8 mmol) in dry DCM (90 mL) was added bromine (0.4 mL, 78.8 mmol) at −5°C dropwise. The mixture was stirred at rt for 24 h. After this time an aq. solution of $Na_2S_2O_3$ 10% was added and the aqueous layer extracted with DCM, dried over Na_2SO_4 and evaporated to give **3** (1.71 g, 95%) as pale yellow solid. Mp: 105°C (hexane–Et_2O); IR (KBr): 3351, 1690, 1508, 1292, 1265, 1044, 970, 764 cm^{-1}; ^1H NMR δ: 8.19 (1H, d, J=2.2 Hz, H-2), 7.92 (1H, dd, J=2.2, 8.4 Hz, H-6), 7.05 (1H, d, J=8.4 Hz, H-5), 3.89 (3H, s, COO*Me*); ^{13}C NMR δ: 166.0 (*C*OOMe), 156.6 (C-4), 134.3 (C-2), 131.2 (C-6), 124.1 (C-1), 116.1 (C-5), 110.3 (C-3), 52.5 (COO*Me*); EIMS *m/z*: 232, 230 $(M)^+$ (34, 34), 201 (80), 199 (81), 171 (6), 152 (42), 121 (100), 93 (22), 69 (26); HREIMS: calcd for $C_8H_7O_3Br$ $(M)^+$: 229.9578, found: 229.9580.

3.1.2. 3-Bromo-4-methoxymethoxybenzoic acid methyl ester (4). To an ice cooled solution of **3** (1.71 g, 7.4 mmol) in dry $CHCl_3$ (50 mL) and dimethoxymethane (50 mL) was added P_2O_5 (10 g, 70.4 mmol). The reaction was stirred for 10 min at rt and then, the mixture was poured into ice and the aqueous layer extracted with Et_2O. The organic layer were collected and washed with aq. solution of $NaHCO_3$ 10% and water, dried over Na_2SO_4 and concentrated to afford **4** (2.03 g, 99%) as a pale yelow solid. Mp: 56°C (hexane–Et_2O); IR (film): 1723, 1599, 1495, 1435, 1289, 1258, 1161, 1115, 1044, 980, 766 cm^{-1}; ^1H NMR δ: 8.24 (1H, d, J=2.2 Hz, H-2), 7.94 (1H, dd, J=2.2, 8.4 Hz, H-6), 7.16 (1H, d, J=8.4 Hz, H-5), 5.31 (2H, s, OCH_2O), 3.89 (1H, s, COO*Me*), 3.52 (3H, s, OCH_3); ^{13}C NMR δ: 165.9 (*C*OOMe), 157.6 (C-4), 135.1 (C-2), 130.6 (C-6), 125.0 (C-1), 114.9 (C-5), 112.6 (C-3), 95.0 (OCH_2O), 56.8 (OCH_3), 52.4 (COO*Me*); EIMS *m/z* 276, 274 $(M)^+$ (44, 56), 245 (22), 196 (58), 125 (848), 107 (30), 77 (75), 63 (100); HREIMS: calcd for $C_{10}H_{11}O_4Br$ $(M)^+$: 273.9841, found: 273.9817.

3.1.3. (3-Bromo-4-methoxymethoxyphenyl)methanol (5). To a solution of **4** (210 mg, 0.8 mmol) in dry DCM (14 mL) under argon, was added a solution of DIBAL-H in toluene (1.5 M, 1.3 mL, 1.9 mmol) at −78°C. The solution was stirred for 1 h and was quenched by addition of MeOH and water. A saturated solution of tartrate Na^+ and K^+ was added, the mixture was stirred for an additional hour and the

aqueous layer was extrated with AcOEt. The collected organic layer were washed with an aq. solution of $NaHCO_3$ 10% and water, dried over Na_2SO_4, concentrated under reduced pressure to give **5** (188 mg, 99%) as a pale brown oil. IR (film): 3380, 1605, 1495, 1404, 1244, 1202, 1159, 1086, 1044, 924, 816 cm^{-1}; ^1H NMR δ: 7.56 (1H, d, J=1.8 Hz, H-2), 7.23 (1H, dd, J=1.8, 8.4 Hz, H-6), 7.11 (1H, d, J=8.4 Hz, H-5), 5.23 (2H, s, OCH_2O), 4.60 (2H, s, H-7), 3.51 (3H, s, OCH_3); ^{13}C NMR δ: 153.4 (C-4), 136.2 (C-1), 132.3 (C-2), 127.4 (C-6), 116.4 (C-5), 113.1 (C-3), 95.4 (OCH_2O), 64.4 (C-7), 56.6 (OCH_3); EIMS m/z: 248, 246 $(M)^+$ (96, 100), 218 (36), 186 (18), 167 (14), 137 (15), 108 (19), 94 (27), 65 (55); HREIMS: calcd for $C_9H_{11}O_3Br$ $(M)^+$: 245.9892, found: 245.9878.

3.1.4. Tetrahydropyranyloxy derivative of (3-bromo-4-methoxymethoxyphenyl)methanol (6). To a solution of DHP (527 mg, 6.3 mmol) in dry DCM (1 mL) was added a solution of HCl in dioxane (4 M, 30 μL, 0.12 mmol) and 1 min later **5** (664 mg, 2.69 mmol) was added diluted in DCM (20 mL). The reaction was stirred vigorously for 10 min and then an aq. solution of $NaHCO_3$ 10% was added and the aqueous layer was extracted with AcOEt. The organic layer was washed with an aq. solution of $NaHCO_3$ 10% and water, dried over Na_2SO_4 and evaporated to afford an oily residue. The purification by Florisil® chromatography with hexane–AcOEt (95:5) as eluent gave **6** (887 mg, 99%) as a colourless oil. IR (film): 1497, 1244, 1202, 1159, 1121, 1082, 1044, 991, 907, 870, 816 cm^{-1}; ^1H NMR δ: 7.56 (1H, d, J=2.2 Hz, H-2), 7.23 (1H, dd, J=2.2, 8.4 Hz, H-6), 7.11 (1H, d, J=8.4 Hz, H-5), 5.24 (2H, s, OCH_2O), 4.69 (1H, d, J=12.2 Hz, H_a-7), 4.68 (1H, t, J=3.2 Hz, H-2′), 4.40 (1H, d, J=12.2 Hz, H_b-7), 3.90–3.40 (2H, m), 3.51 (3H, s, OCH_3), 1.90–1.45 (6H, m); ^{13}C NMR δ: 153.4 (C-4), 133.6 (C-1), 133.2 (C-2), 128.3 (C-6), 116.2 (C-5), 113.0 (C-3), 97.9 (C-2′), 95.4 (OCH_2O), 67.9 (C-7), 62.4 (C-6′), 56.6 (OCH_3), 30.7 (C-3′), 25.6 (C-5′), 19.5 (C-4′); EIMS m/z: 332, 330 $(M)^+$ (13, 14), 231 (34), 229 (35), 199 (14), 151 (10), 115 (8), 85 (100); HREIMS: calcd for $C_{14}H_{19}O_4Br$ $(M)^+$: 330.0467, found: 330.0448.

3.1.5. 15-Acetoxy-13*E*,8(9)-labdadiene (9). To a stirred solution of **8** (4.55 g, 11.6 mmol) in dry benzene (265 mL) was added HI (19 mL). After 1 h the mixture was diluted with Et_2O and the organic layer was washed successively with aqueous solution of $NaHCO_3$ 10%, $NaHSO_3$ 40% and water, dried over Na_2SO_4 and evaporated to give an oily residue. The purification by silica gel chromatography with hexane–AcOEt (95:5) as eluent gave **9** (1.86 g, 48%) as colourless oil. $[\alpha]_D^{20}$=+53 (c=0.78, $CHCl_3$); IR (film): 1748, 1458, 1387, 1235, 1022 cm^{-1}; ^1H NMR δ: 5.36 (1H, t, J=7.0 Hz, H-14), 4.60 (2H, d, J=7.0 Hz, H-15), 2.20–1.06 (15H, m), 2.07 (3H, s, CH_3COO), 1.74 (3H, s, Me-16), 1.58 (3H, s, Me-17), 0.94 (3H, s, Me-20), 0.89 (3H, s, Me-18), 0.84 (3H, s, Me-19); ^{13}C NMR δ: 171.3 (CH_3COO), 143.3 (C-13), 140.2 (C-9), 126.3 (C-8), 117.8 (C-14), 61.6 (C-15), 52.1 (C-5), 42.0 (C-3), 40.4 (C-12), 39.2 (C-10), 37.2 (C-1), 33.8 (C-7), 33.5 (C-4 and C-18), 26.8 (C-11), 21.9 (C-19), 21.3 (CH_3COO), 20.3 (C-20), 19.7 (C 17), 19.3 (C-6 and C-2), 16.8 (C-16); EIMS m/z: 272 $(M-60)^+$ (64), 257 (100), 229 (10), 204 (78), 119 (45), 77 (55); HREIMS: calcd for $C_{22}H_{36}O_2$ $(M)^+$: 332.2715, found: 332.2738.

3.1.6. 15-Hydroxy-13*E*,8(9)-labdadiene (10). A solution of K_2CO_3 in methanol (3%, 56 mL) was added to **9** (1.86 g, 5.6 mmol) and the reaction was stirred vigorously at rt for 4 h until no starting material remained. Then water was added and the mixture was concentrated to remove the methanol and the aqueos layer was extracted with Et_2O. The organic layer was washed with water, dried over Na_2SO_4 and evaporated to provide **10** (1.59 g, 98%) as a colourless oil. $[\alpha]_D^{20}$=+62 (c=0.46, $CHCl_3$); IR (film): 3352, 1669, 1458, 1443, 1375, 1003 cm^{-1}; ^1H NMR δ: 5.42 (1H, t, J=6.9 Hz, H-14), 4.15 (2H, d, J=6.9 Hz, H-15), 2.15–1.90 (6H, m, H-12, H-11 and H-7), 1.85–1.78 (1H, m, H_a-1) 1.70 (3H, s, Me-16), 1.70–1.37 (5H, m, H-2, H-6 and H_a-3), 1.57 (3H, s, Me-17), 1.20–1.10 (3H, m, H_b-3, H_a-1 and H-5), 0.94 (3H, s, Me-20), 0.88 (3H, s, Me-18), 0.83 (3H, s, Me-19); ^{13}C NMR δ: 140.6 (C-13), 140.1 (C-9), 126.0 (C-8), 122.6 (C-14), 59.3 (C-15), 51.9 (C-5), 41.8 (C-3), 40.1 (C-12), 39.0 (C-10), 37.0 (C-1), 33.6 (C-7), 33.3 (C-4 and C-18), 26.7 (C-11), 21.7 (C-19), 20.1 (C-20), 19.4 (C 17), 19.0 (C-6 and C-2), 16.3 (C-16); EIMS m/z: 290 $(M)^+$(7), 245 (5), 205 (100), 149 (48), 109 (93), 69 (82); HREIMS: calcd for $C_{20}H_{34}O$ $(M)^+$: 290.2610, found: 290.2599.

3.1.7. 15-Bromo-13*E*,8(9)-labdadiene (11). To a solution of **10** (233 mg, 0.66 mmol) in dry DCM (5.5 mL) was added CBr_4 (230 mg, 0.79 mmol) and PPh_3 (289 mg, 1.10 mmol) at 0°C portionwise. The reaction was stirred for 10 min at rt and diluted with hexane. The mixture was filtered through a short pad of Celite™, the solvent was evaporated and hexane was added to the residue in order to remove the PPh_3, the process was repeated three times to give **11** (229 mg, 99%) as pale yellow oil. IR (film): 1653, 1456, 1387, 1375, 1200, 1119 cm^{-1}; ^1H NMR δ: 5.55 (1H, t, J=8.4 Hz, H-14), 4.03 (2H, d, J=8.4 Hz, H-15), 2.20–1.05 (15H, m), 1.74 (3H, s, Me-16), 1.57 (3H, s, Me-17), 0.94 (3H, s, Me-20), 0.88 (3H, s, Me-18), 0.83 (3H, s, Me-19); ^{13}C NMR δ: 144.5 (C-13), 139.9 (C-9), 126.2 (C-8), 119.8 (C-14), 51.8 (C-5), 41.8 (C-3), 40.2 (C-12), 39.0 (C-10), 37.0 (C-1), 33.6 (C-7), 33.3 (C-4 and C-18), 29.8 (C-15), 26.5 (C-11), 21.7 (C-19), 20.1 (C-20), 19.5 (C 17), 19.0 (C-6 and C-2), 16.0 (C-16); EIMS m/z: 354, 352 $(M)^+$ (8, 10), 277 (22), 205 (100), 149 (48), 109 (68), 69 (50); HREIMS: calcd for $C_{20}H_{33}Br$ $(M)^+$: 352.1766, found: 352.1778.

3.1.8. Coupling reaction of 11 with 6:12. To a solution of **6** (433 mg, 1.3 mmol) in THF (4 mL) was added a solution of *t*BuLi in pentane (1.7 M, 1.6 mL, 2.8 mmol) at −78°C under argon. The reaction was stirred for 1 h and **11** (132 mg, 0.4 mmol) was added diluted in THF (4 mL) via cannula. After 1 h the reaction was quenched by addition of a saturated aq. solution of NH_4Cl (2 mL) and extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4 and evaporated to provide an oily residue. This residue was redissolved in methanol (2 mL) and *p*TsOH (245 mg, 1.3 mmol) was added. The mixture was stirred for 1 h then water was added and concentrated under reduced pressure. The aqueous layer was extracted with Et_2O, the organic layer was washed with aq. solution of $NaHCO_3$ 10% and water, dried over Na_2SO_4 and evaporated to give an oily residue. Flash chromatography with benzene–AcOEt (98:2) as eluent gave **12** (32 mg, 26%) as a colourless oil. $[\alpha]_D^{20}$=+22 (c=0.16, $CHCl_3$); IR (film): 3397, 1507, 1458, 1375, 1248, 1198, 1152, 1078, 1011, 924, 818 cm^{-1}; ^1H

NMR δ: 7.16 (1H, d, J=2.0 Hz, H-21), 7.15 (1H, dd, J=9.2, 2.0 Hz, H-19), 7.04 (1H, d, J=9.2 Hz, H-18), 5.20 (2H, s, OCH_2O), 4.60 (2H, s, H-22), 3.47 (3H, s, MeO), 3.35 (2H, d, J=7.1 Hz, H-15), 2.00–1.80 (5H, m, H-12, H-7 and H_a-1), 1.75 (3H, s, Me-23), 1.60–1.40 (5H, m, H-2, H-6 and H_a-3), 1.57 (3H, s, Me-24), 1.40–1.20 (5H, m, H-11, H_b-3, H_b-1, H-5), 0.93 (3H, s, Me-25), 0.88 (3H, s, Me-26), 0.83 (3H, s, Me-27); ^{13}C NMR δ: 154.5 (C-17), 140.4 (C-9), 137.0 (C-13), 134.0 (C-20), 131.1 (C-16), 129.5 (C-21), 128.8 (C-19), 125.7 (C-8), 121.6 (C-14), 113.9 (C-18), 94.3 (OCH_2O), 65.2 (C-22), 55.9 (CH_3O), 51.9 (C-5), 41.8 (C-3), 40.4 (C-12), 39.0 (C-10), 37.0 (C-1), 33.6 (C-7), 33.3 (C-4 and C-26), 29.6 (C-15), 28.6 (C-11), 21.6 (C-27), 20.1 (C-25), 19.5 (C-24), 19.0 (C-6 and C-2), 16.1 (C-23); EIMS m/z 441 $(M+H)^+$ (1), 423 (6), 391 (11), 205 (22), 149 (64); HREIMS: calcd for $C_{29}H_{45}O_3$ $(M+H)^+$: 441.3369, found: 441.3367.

3.1.9. Oxidation of 12:13. To a solution of **12** (32 mg, 0.07 mmol) in dry DCM (10 mL) was added MnO_2 (212 mg, 2.4 mmol). The reaction was stirred at rt for 3 h and then was filtered through a short pad of silica gel and Celite™, the solvent was removed to afford an oily residue. Column chromatography on silica gel with hexane–AcOEt (95:5) as eluent gave **13** (28 mg, 85%) as colourless oil. $[\alpha]_D^{20}$=+25 (c=0.65, $CHCl_3$); IR (film): 1651, 1435, 1364, 1248, 1152, 1119, 1080, 949 cm^{-1}; ^{1}H NMR δ: 9.87 (1H, s, H-22), 7.70 (1H, d, J=2.0 Hz, H-21), 7.29 (1H, dd, J=8.8, 2.0 Hz, H-19), 7.17 (1H, d, J=8.8 Hz, H-18), 5.30 (2H, s, OCH_2O), 5.30 (1H, t, J=7.0 Hz, H-14), 3.48 (3H, s, MeO), 3.38 (2H, d, J=7.0 Hz, H-15), 2.15–1.10 (15H, m), 1.75 (3H, s, Me-23), 1.57 (3H, s, Me-24), 0.93 (3H, s, Me-25), 0.87 (3H, s, Me-26), 0.82 (3H, s, Me-27); ^{13}C NMR δ: 191.6 (C-22), 160.2 (C-17), 140.6 (C-13), 138.3 (C-9), 131.8 (C-20), 131.1 (C-21), 130.6 (C-16), 130.4 (C-19), 126.1 (C-8), 120.9 (C-14), 113.4 (C-18), 94.1 (OCH_2O), 56.5 (CH_3O), 52.1 (C-5), 42.0 (C-3), 40.7 (C-12), 39.2 (C-10), 37.2 (C-1), 33.8 (C-7), 33.6 (C-4 and C-26), 28.8 (C-15), 27.4 (C-11), 21.9 (C-27), 20.3 (C-25), 19.7 (C-24), 19.3 (C-6 and C-2), 16.5 (C-23).

3.1.10. Oxidation and deprotection of 13: (+)-subersic acid. To a solution of **13** (21 mg, 0.05 mmol) in *t*BuOH (1 mL) and 2-methyl-2-butene (3 mL) was added a solution of NaH_2PO_4 (36 mg) in water (0.24 mL) and $NaClO_2$ (0.15 mL, 0.5 mmol). The reaction was stirred for 2 h and aq. solution of HCl 2 M and water was added. The aqueous layer was extracted with Et_2O, the organic layer was washed with water, dried over Na_2SO_4 and evaporated to give an oily residue. This residue was redissolved in THF (2.5 mL) and a aq. solution of HCl (1 mL) was added. The reaction was stirred for 3 h at 45°C then water was added and the aqueous layer was extracted with AcOEt. The organic layer was washed successively with aq. solution of $NaHCO_3$ 10% and brine, dried over Na_2SO_4 and concentrated to afford a residue. The purification by silica gel chromatography with $CHCl_3$ as eluent gave (+)-subersic acid (9 mg, 47%) as colourles solid. $[\alpha]_D^{20}$=+49 (c=0.78, $CHCl_3$). IR (film): 3308, 1684, 1607, 1456, 1410, 1387, 1277, 1175, 1123, 1099, 739 cm^{-1}; ^{1}H NMR δ: 7.90 (1H, d, J=2.1 Hz, H-21), 7.89 (1H, dd, J=9.0, 2.1 Hz, H-19), 6.86 (1H, d, J=9.0 Hz, H-18), 5.35 (1H, t, J=7.1 Hz, H-14), 3.42 (2H, d, J=7.1 Hz, H-15), 2.15–1.90 (7H, m, H-12, H-11, H-7 and H_a-1), 1.83 (3H, s, Me-23),1.60–1.35 (5H, m, H-2, H_a-3 and H-6), 1.58 (3H, s, Me-24), 1.25–1.10 (3H, m, H_b-1,H_b-3 and H-5), 0.95 (3H, s, Me-25), 0.88 (3H, s, Me-26), 0.87 (3H, s, Me-27); ^{13}C NMR δ: 171.1 (C-22), 159.4 (C-17), 140.6 (C-13), 140.1 (C-9), 132.6 (C-21), 130.4 (C-19), 126.8 (C-16), 126.0 (C-8), 121.6 (C-20), 120.0 (C-14), 115.7 (C-18), 51.9 (C-5), 41.8 (C-3), 40.4 (C-12), 39.0 (C-10), 37.0 (C-1), 33.6 (C-7), 33.3 (C-4 and C-26), 29.6 (C-15), 27.0 (C-11), 21.6 (C-27), 20.1 (C-25), 19.5 (C-24), 19.0 (C-6 and C-2), 16.4 (C-23); FABMS m/z 411 $(M+1)^+$ (1), 341 (4), 313 (4), 219 (5), 154 (32). HRFABMS: calcd for $C_{27}H_{39}O_3$: 411.2899, found: 411.2893. The assignments for the spectra, ^{1}H NMR and ^{13}C NMR for subersic acid were done by 2D correlation experiments HMQC and HMBC.

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