Novel Synthesis of Stagonolide-F, Putaminoxin and Aspinolide-A

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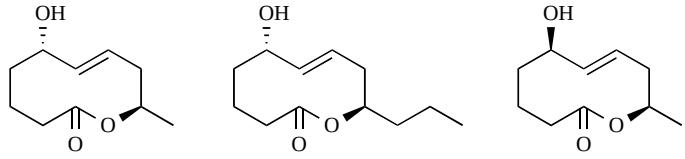
Abstract: Novel synthesis of putaminoxin, stagonolide-F and aspinolide-A have been achieved by utilizing (S) and (R)-malic acid. The key feature of the synthetic strategy includes Horner-Wittig olefination, double bond reduction and Steglich esterification. Olefinic acid for putaminoxin and stagonolide-F was prepared from (S)-malic acid whereas olefinic acid for aspinolide-A was prepared from (R)-malic acid and olefinic alcohols for putaminoxin, stagonolide-F and aspinolide-A were prepared by using Brown's asymmetric allylboration.

Keywords: Decanolides, (S) and (R) malic acid, Horner-Wittig olefination, Steglich esterification, Brown's asymmetric allylboration, Ring closing metathesis (R.C.M.).

INTRODUCTION

Ten-membered lactones commonly known as decanolides have attracted synthetic as well as bioorganic chemists, due to their unique structural properties and interesting biological activities. Some examples, like herbarumin-I, II, III [1, 2], microcarpalide [3] belong to this class of molecules. Stagonolide-F (**1**) [4] was isolated from pycnidial fungus *Stagonospora cirsii*. While Putaminoxin (**2**) [5], a phytotoxic lactone was isolated from the culture of *Phoma putaminum* fungus and aspinolide-A (**3**) [6], was isolated from the cultures of *Aspergillus ochraceus*. The structures of stagonolide-F, putaminoxin and aspinolide-A (as shown in Fig. **1**) were determined by spectroscopic, chemical and synthetic methods [7-9].



1 Stagonolide-F **2** Putaminoxin **3** Aspinolide-A

Fig. (1). Chemical structures of putaminoxin, stagonolide-F and aspinolide-A.

RESULTS AND DISCUSSION

To the best of our knowledge, synthetic routes have been developed in the literature for the preparation of these ten-membered lactones utilizing Sharpless asymmetric epoxidation, Keck allylation and Jacobsen's hydrolytic kinetic resolution methods for introducing stereogenic centers and ring-closing metathesis (RCM) for construction of olefin geometry in their skeleton [7-9]. As part of our studies directed towards the synthesis of biologically active lactone compounds [10-14], herein we report an efficient and convergent formal synthesis of stagonolide-F, putaminoxin and aspinolide-A by employing (S), (R)-malic acid and Brown's asymmetric allylboration. Our initial retrosynthetic plan is outlined in Scheme **1**. All the three lactones inturn could be obtained by the Steglich coupling of olefinic acid fragments and olefinic alcohol. Olefinic acid fragments for stagonolide-F and putaminoxin can be prepared from (S)-malic acid and olefinic acid fragment for aspinolide-A can be prepared from (R)-malic acid.

Olefinic chiral homoallyl alcohols (2*R*)-4-penten-2-ol **14** and (4*R*)-1-hepten-4-ol **15** were synthesized in one step by utilizing Brown's asymmetric allylboration of acetaldehyde and butyraldehyde with (–)-B-allyldiisopinocampheylborane in Et_2O-pentane (1:1) at –100 °C according to the previously reported literature [15, 16] Scheme **2**.

Olefinic acid fragment for stagonolide-F and putaminoxin was prepared from (S) malic acid. Accordingly, (S) malic acid **4** was subjected to reduction by using BH_3.DMS and $B(OMe)_3$ to give (2*S*) butane-1,2,4-triol **7** [17]. Selective 1,3-protection of the triol **5** with p-methoxybenzaldehyde dimethyl acetal, CSA, in CH_2Cl_2 afforded a six membered acetal [18], as *p*-methoxybenzylidene acetal **6** in 80% yield, and 1,2-protection of the triol afforded a five-membered acetal as *p*-methoxybenzylidene acetal in 10% yield. These two acetals

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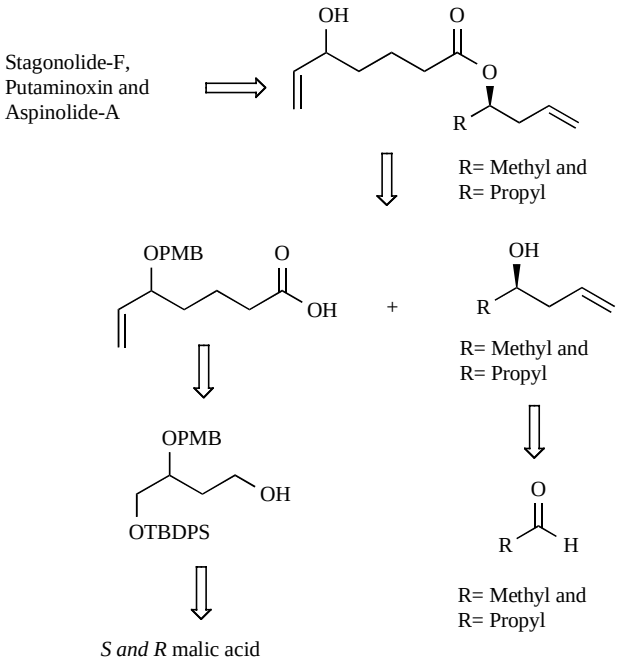
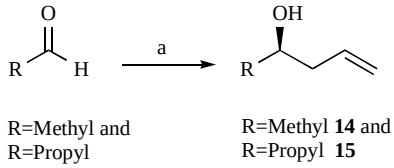


Scheme 1. Retrosynthetic analysis of putaminoxin, stagonolide-F and aspinolide-A.



Scheme 2. Reagents and conditions: (a) (-)-Ipc_2BCl, allyl MgBr, E_2O-pentane (1:1), –100 ^oC, NaOH and H_2O_2, 70%.

were separated by column chromatography. Hydroxy group of **6** was protected as TBDPS ether using TBDPSCl and imidazole in DMF to afford TBDPS protected compound **7** in good yield. Regioselective ring opening of the PMP protected acetal **7** by DIBAL–H proceeded at the sterically less-hindered side to give the unmasked primary alcohol **8** in 81% yield according to the literature procedure [19-24]. Alcohol **8** was oxidized under Swern's oxidative conditions to give the corresponding aldehyde, which without purification (as crude) on Horner-Wittig olefination by two-carbon homologation using ethoxycarbonylmethylene triphenylphosphorane in benzene gave the α,β-unsaturated ester **9** in 78% yield over 2 steps Scheme **3**.

Olefin reduction of compound **9** with PtO_2-H_2 ($NaHCO_3$) (catalytic) in ethylacetate gave compound **10** in 92% yield , which on treatment with TBAF in THF afforded primary alcohol **11** in 88% yield. Olefinic acid fragment **13** was prepared from compound **11** in two steps. Accordingly, Compound **11** was subjected to Swern's oxidative conditions to give the corresponding aldehyde, which on Wittig olefination with $MePh_3Br$ and t-BuOK in THF gave the olefinic ester **12** in 55% yield [25]. Finally, olefinic ester was hydrolyzed with LiOH in THF-methanol-water (2:1:1) to afford the desired olefinic acid fragment **13** in 86% yield for stagonolide-F as well as putaminoxin.

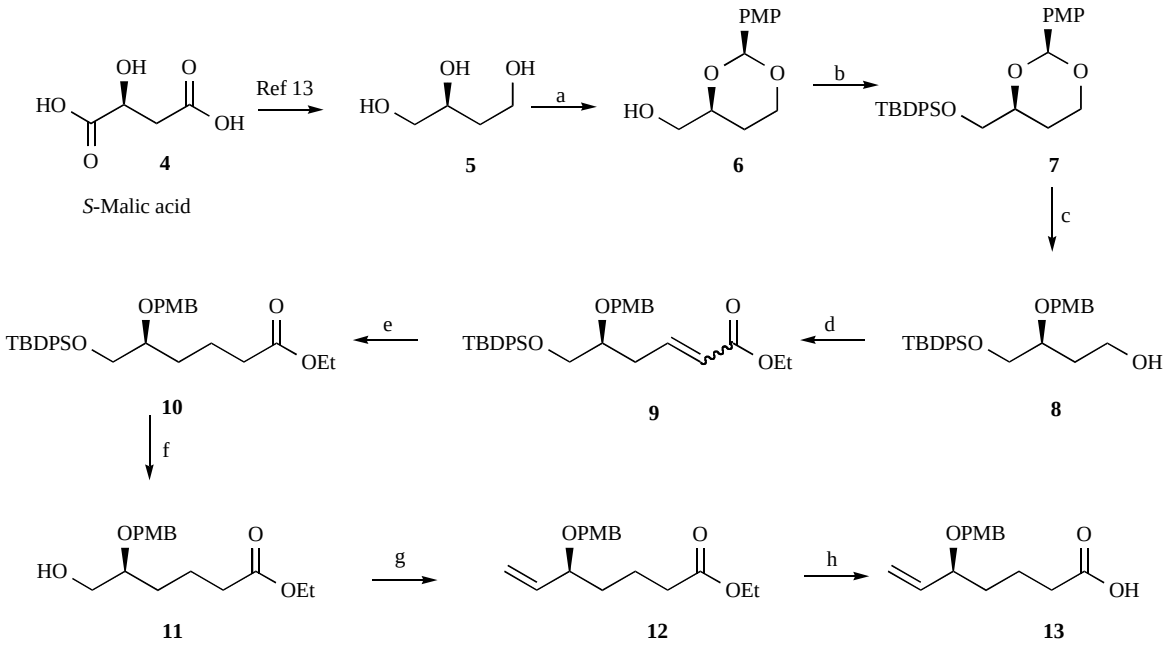
For the synthesis of stagonolide-F and putaminoxin, coupling of the olefinic acid fragment 13, which was obtained from (S) malic acid with (2*R*)-4-penten-2-ol 14 and (4*R*)-1-hepten-4-ol 15 by employing Steglich esterification conditions [26] to give the diene compounds 16 and 17 respectively. PMB group of these dienes were deprotected by using DDQ to give the diene alcohols 18 and 19. These dienes (18 and 19) have allowed the stage to be set for the macrolactonization to obtain stagonolide-F and putaminoxin *via* ring-closing metathesis (R.C.M.) [27-34]. Treatment of the bis-olefin compounds 18 and 19 with the use of the Grubbs' first generation catalyst (20 mol%) under high dilution in dichloromethane at reflux conditions gave a 10:1 (*E*:*Z)* mixture of macrocyclic lactones; from which (*E*)-isomers of 1 and 2 were isolated in 55% yield by silica gel column chromatography. The spectral and analytical data of stagonolide-F 1 and putaminoxin 2 were comparable to the previously reported data in the literature [4, 7, 8] Scheme **4**.

While for the synthesis of aspinolide-A, olefinic acid fragment ent-13 was prepared from (R)-malic acid as the starting material, followed by the same set of reactions as illustrated in Scheme **2**, and is depicted in Scheme **5**. Coupling of the olefinic acid fragment ent-13 with (2*R*)-4-penten-2-ol 14 by employing Steglich esterification conditions gave the diene compound 20. PMB group of this diene was deprotected by using DDQ to give the diene alcohol compound 21 and ring-closing metathesis of the compound 21 can be achieved by using Grubbs' first generation catalyst as reported in the Scheme **4** furnished aspinolide-A (3) in 55% yield after silica gel column chromatography. The spectral and analytical data of aspinolide-A (3) was comparable to the previously reported (natural as well as synthetic compound) data in the literature [6, 9] Scheme **5**.

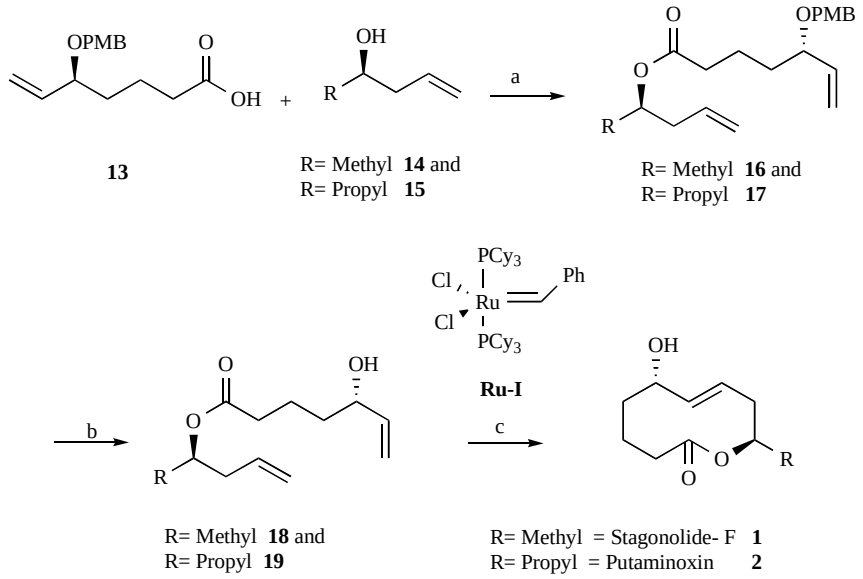
EXPERIMENTAL SECTION

(3*S*)-4-[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy-3-[(4-methoxybenzyl)oxy]butan-1-ol (8)

To a stirred solution of compound **7** (8 g, 17.31 mmol) in dry CH_2Cl_2 (100 mL) at –78 ^oC was added drop wise DIBAL-H (28.86 mL, 34.63 mmol, 1.2 M in toluene). After the reaction mixture had been stirred at the same temperature for 6 h, methanol (10 mL) was added. The reaction mixture was allowed to warm to room temperature then sat. aq. Roche salt (50 mL) was added and the mixture was stirred vigorously for 2 h. The mixture was extracted with dichloromethane (3x100 mL) and organic layers were washed with brine, dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, 60–120 mesh, EtOAc–hexane 2:8) to afford the compound **8** (6.51 g, 81%) as a colorless oil. R_f = 0.5 (30% EtOAc/hexane); $[\alpha]_D^{25}$ = –34 (*c* 1.1, $CHCl_3$). IR (neat): 3429, 2933, 2860, 1612, 1513, 1465, 1247, 1108, 1038, 820, 742, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.68-7.6 (m, 4H), 7.43-7.31 (m, 6H), 7.16 (d, *J* = 8.68 Hz, 2H), 6.8 (d, *J* = 8.68 Hz, 2H), 4.58 (d, *J* = 11.33 Hz, 1H), 4.39 (d, *J* = 11.33 Hz, 1H), 3.78 (s, 3H), 3.75-3.61 (m, 5H), 2.17 (br s, 1H), 1.81-1.69 (m, 2H), 1.06 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2, 135.58, 133.29, 130.5, 129.73, 129.44, 127.71, 113.82, 78.41, 71.79, 65.88,



Scheme 3. Reagents and conditions: (a) $PMB(OMe)_2$, CSA, dry CH_2Cl_2, 0 °C, 2 h, 80%; (b) TBDPSCl, imidazole, dry DMF, 6 h, 85%; (c) DIBAL-H, dry CH_2Cl_2, –78 °C, 6 h, 81%; (d) (i) $(COCl)_2$, DMSO, Et_3N, –78 °C, 1 h; (ii) Ph_3PCHCO_2Et, benzene, 6 h, reflux, 78% over two steps; (e) PtO_2-H_2, $NaHCO_3$(cat), EtOAc, 12 h, 92%; (f) TBAF (1M), THF, 0.5 h, 88%; (g) (i) $(COCl)_2$, DMSO, Et_3N, –78 °C, 1 h; (ii) $MePh_3Br$, t-BuOK, THF, 0 °C, 1 h, 55 % over two steps; (h) LiOH, MeOH:THF:H_2O (1:2:1), 0 °C to rt, 4 h, 86%.

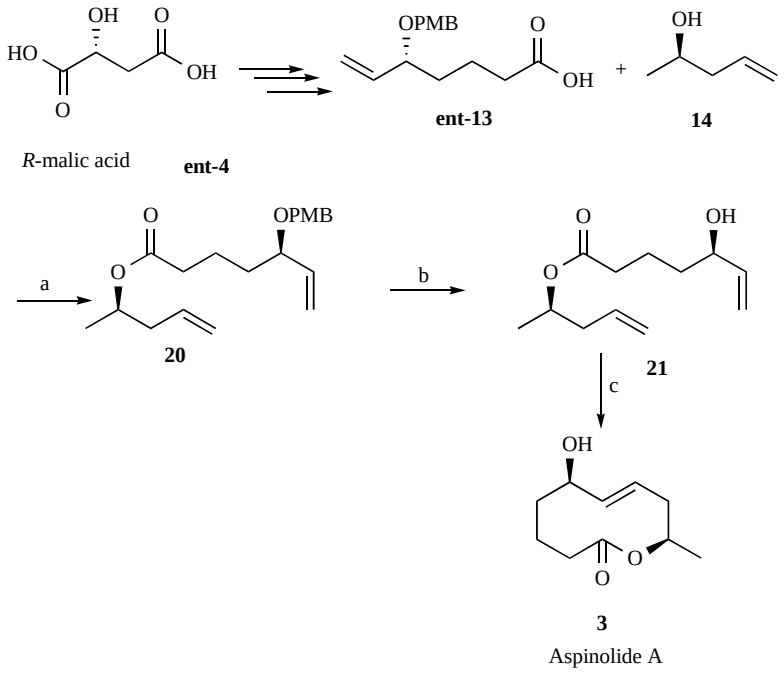


Scheme 4. Reagents and conditions: (a) DCC, DMAP, CH_2Cl_2, 0 °C to rt, 3 h, 81%; (b) DDQ, H_2O:CH_2Cl_2 (1:9), 0 °C to rt, 1 h, 78%; (c) 20 mol% Ru-1, CH_2Cl_2, reflux, 48 h, 55%.

60.62, 55.23, 34.07, 26.81, 19.16; MS-ESIMS: *m/z* $[M+NH_4]^+$: 482; HRMS calcd for ($C_{28}H_{36}O_4NaSi$) 487.228 ; found. 487.229.

Ethyl (*E*,5*S*)-6-[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy-5-[(4-methoxybenzyl)oxy]-2-hexenoate (9)

To a stirred solution of oxalyl chloride (1.64 mL, 19.39 mmol) in dry CH_2Cl_2 (150 mL), DMSO (2.75 mL, 38.79 mmol) was added at –78 °C and stirred at the same temperature for 30 min. Compound **8** (6 g, 12.93 mmol) in dry CH_2Cl_2 (15 mL), was added at –78 °C to the reaction mixture and stirred for 1 h at the same temperature. After 1 h triethylamine (5.39 mL, 38.79 mmol) was added at –78 °C and slowly allowed the reaction mixture to room temperature for 30 min. The reaction mixture was diluted with water (50 mL) and extracted with $CHCl_3$ (3 x 100 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous Na_2SO_4 concentrated under reduced pressure to afford crude aldehyde as yellow syrup. Aldehyde in dry



Scheme 5. Reagents and conditions: (a) DCC, DMAP, CH_2Cl_2, 0 °C to rt, 3 h, 81%; (b) DDQ, H_2O:CH_2Cl_2 (1:9), 0 °C to rt, 1 h, 78%; (c) 20 mol% Ru-1, CH_2Cl_2, reflux, 48 h, 55%.

toluene, which is obtained in the above step was added C-2 Horner-Wittig reagent (5.39 g, 15.50 mmol) and stirred for 2 h. After 2 h toluene was evaporated and extracted with EtOAc (3x 100 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under vacuo. The residue was purified by column chromatography (silica gel, 60–120 mesh, EtOAc–hexane 5:95) to afford the compound **9** (5.36 g, 78%) as a light yellow oil. R_f = 0.5 (20% EtOAc/hexane); $[\alpha]_D^{25}$ –20.2 (*c* 1, $CHCl_3$); IR (neat): 2933, 2859, 1718, 1655, 1513, 1465, 1249, 1173, 1109, 1039, 821, 704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.66-7.62 (m, 4H), 7.43-7.34 (m, 6H), 7.17 (d, *J* = 8.78 Hz, 2H), 6.98-6.92 (m, 1H), 6.8 (d, *J* = 8.78 Hz, 2H), 5.85 (d, 1H), 4.49 (d, *J* = 10.73 Hz, 1H), 4.39 (d, *J* = 10.73 Hz, 1H), 4.18 (q, *J* = 6.8 Hz, 2H), 3.79 (s, 3H), 3.72 (dd, *J* = 4.87, 9.75, 15.61 Hz, 1H), 3.61 (dd, *J* = 4.87, 9.75, 15.61 Hz, 1H), 3.57 (p, *J* = 4.87 Hz, 1H), 2.56-2.50 (m, 1H), 2.46-2.40 (m, 1H), 1.28 (t, *J* = 6.8 Hz, 1H), 1.05 (m, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3, 159.11, 145.36, 135.55, 133.30, 133.22, 130.39, 129.68, 129.28, 127.67, 123.37, 113.7, 77.98, 71.62, 65.25, 60.09, 55.20, 34.65, 26.78, 19.16, 14.26; MS-ESIMS: *m/z* $[M+NH_4]^+$: 550; HRMS calcd for ($C_{32}H_{40}O_5NaSi$) 555.2542 ; found. 555.2563.

Ethyl (5*S*)-6-[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy-5-[(4-methoxybenzyl)oxy]hexanoate (10)

Compound **9** (5 g, 9.39 mmol) dissolved in dry ethyl acetate (75 mL) was added catalytic amount of PtO_2 and $NaHCO_3$ under a hydrogen atmosphere and stirred for 12 h. After completion of the reaction, it was filtered through a celite pad. Concentration of the filtrate gives the crude product, which was purified by column chromatography (silica gel, 60–120 mesh, EtOAc/hexane 5:95) to afford the compound **10** (4.62 g, 92%) as a light yellow oil. R_f = 0.5 (20% EtOAc/hexane); $[\alpha]_D^{25}$ –40.2 (*c* 1, $CHCl_3$); IR (neat): 2933, 2859, 1734, 1612, 1513, 1247, 1110, 1037, 821, 742, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.67-7.63 (m, 4H), 7.43-7.35 (m, 6H), δ 7.2 (d, *J* = 7.8 Hz, 2H), 6.82 (d, *J* = 7.8 Hz, 2H), 4.58 (d, *J* = 10.73 Hz, 1H), 4.39 (d, *J* = 10.73 Hz, 1H), 4.09 (q, *J* = 6.8, 14.63 Hz, 2H), 3.78 (s, 3H), 3.72 (dd, *J* = 5.85, 10.73 Hz, 1H), 3.6 (dd, *J* = 5.85, 10.73 Hz, 1H), 3.46 (m, 1H), 2.25-2.20 (m, 2H), 1.74-1.48 (m, 4H), 1.23 (t, *J* = 6.8, 14.63 Hz, 3H), 1.05 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.58, 159.02, 135.56, 133.47, 131.03, 129.6, 129.3, 127.62, 113.65, 78.84, 71.72, 66.06, 60.12, 55.19, 34.26, 31.08, 26.8, 20.91, 19.15, 14.2; MS-ESIMS: *m/z* $[M+NH_4]^+$: 552; HRMS calcd for ($C_{32}H_{42}O_5NaSi$) 557.269 ; found. 557.271.

Ethyl (5*S*)-6-hydroxy-5-[(4-methoxybenzyl)oxy]hexanoate (11)

To a stirred solution of Compound **10** (4.5 g, 8.42 mmol) in dry THF (50 mL) was added tetrabutylammoniumfluoride (TBAF) (8.42 mL, 8.42 mmol, 1 M in toluene) at 0 °C for 30 min. After 30 min, the reaction mixture was quenched with sat. aq. NH_4Cl then THF was evaporated and extracted with EtOAc (3x75 mL) and organic layers were washed with brine, dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, 60–120 mesh, EtOAc–hexane 3:7) to afford the compound **11** (2.2 g, 88%) as a colorless oil. R_f = 0.5 (50% EtOAc/hexane); $[\alpha]_D^{25}$ –7.2 (*c* 1, $CHCl_3$); IR (neat): 3445, 2937, 2872, 1730, 1612, 1513, 1461, 1248, 1175, 1034, 822, 755 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 7.8 Hz, 2H), 6.88 (d, *J* = 7.8 Hz, 2H), 4.54 (d, *J* = 10.73 Hz, 1H), 4.49 (d, *J* = 10.73 Hz, 1H), 4.12 (q, *J* = 6.8 Hz, 2H), 3.8 (s, 3H), 3.69 (m, 1H), 3.54-3.49 (m, 2H), 2.3 (t, 3H), 1.74-1.50 (m, 4H), 1.25 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz,

$CDCl_3$): δ = 173.38, 159.09, 130.27, 129.28, 113.7, 78.73, 71.06, 63.76, 60.18, 55.08, 34.04, 30.13, 20.61, 14.07; MS-ESIMS: *m/z* $[M+Na]^+$: 319; HRMS calcd for ($C_{16}H_{24}O_5Na$) 319.1521 ; found. 319.1535.

Ethyl (5*S*)-5-[(4-methoxybenzyl)oxy]-6-heptenoate (12)

To a stirred solution of oxalyl chloride (0.9 mL, 10.64 mmol), in dry CH_2Cl_2 (40 mL) DMSO (1.5 mL, 21.28 mmol) was added at –78 °C and stirred at the same temperature for 30 min. Compound **11** (2.1 g, 7.09 mmol) in dry CH_2Cl_2 (10 mL), was added at –78 °C to the reaction mixture and stirred for 1 h at the same temperature. After 1h triethylamine (2.96 mL, 21.28 mmol) was added at –78 °C and allowed the reaction mixture to room temperature for 30 min. The reaction mixture was diluted with water (20 mL) and extracted with $CHCl_3$ (3 x 40 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na_2SO_4 concentrated under reduced pressure to afford crude aldehyde as yellow syrup. To methyltriphenylphosphonium bromide (3.80 g, 10.66 mmol) in dry THF (50 mL) under a nitrogen atmosphere at 0 °C was added t-BuOK (1.03 g, 9.22 mmol) and stirred for 4 h at the same temperature. To this orange yellow ylide solution, the above crude aldehyde in dry THF (8 mL) was added and stirred at same temperature for 1 h. The reaction mixture was quenched with saturated aqueous NH_4Cl solution (10 mL). The mixture was filtered over a celite pad and the residue was washed with ether (20 mL). THF was evaporated then extracted with EtOAc (3 x 40 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under vacuo. The residue was purified by column chromatography (silica gel, 60–120 mesh, EtOAc–hexane 5:95) to afford the compound **12** (1.15 g, 55%) as a colorless liquid. R_f = 0.8 (10% EtOAc/hexane); $[\alpha]_D^{25}$ –50.2 (*c* 1, $CHCl_3$); IR (neat): 2936, 2863, 1733, 1612, 1513, 1459, 1246, 1173, 1035, 820, 757 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.16 (d, *J* = 8.78 Hz, 2H), 6.86 (d, *J* = 8.78 Hz, 2H), 5.72 (m, 1H), 5.2 (m, 2H), 4.53 (d, *J* = 11.7 Hz, 1H), 4.28 (d, *J* = 11.7 Hz, 1H), 4.1 (q, *J* = 6.83, 14.63 Hz, 2H), 3.8 (s, 3H), 3.71 (q, *J* = 5.85, 12.68 Hz, 1H), 2.27 (m, 2H), 1.76-1.48 (m, 4H), 1.24 (t, *J* = 6.83, 14.63 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.59, 158.89, 138.88, 130.55, 129.15, 117.13, 113.56, 79.55, 69.53, 60.02, 55.05, 34.68, 33.93, 20.76, 14.09; MS-ESIMS: *m/z* $[M+H]^+$: 293; HRMS calcd for ($C_{17}H_{24}O_4Na$) 315.157; found. 315.158.

(5*S*)-5-[(4-Methoxybenzyl)oxy]-6-heptenoic acid (13)

To a stirred solution of **12** (1 g, 3.42 mmol) in MeOH (5 mL): THF (10 mL): H_2O (5 mL) (1:2:1) at 0 °C was added Lithium hydroxide monohydrate (0.29 g, 6.84 mmol) was added. The reaction mixture was allowed to stir at room temperature for 4 h. After completion of the reaction; it was poured in to 0.5 N HCl and extracted with EOAc (3x25 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4 and concentrated under vacuo. The residue was purified by column chromatography (silica gel, 60–120 mesh, EtOAc–hexane 5:95) to afford the compound **15** (0.78 g, 86%) as a colorless liquid. R_f = 0.5 (60% EtOAc/hexane); $[\alpha]_D^{25}$ +26.2 (*c* 1, $CHCl_3$); IR (neat): 3410, 1710, 1612, 1513, 1300, 1247, 1175, 1035, 929, 822, 758 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.30 Hz, 2H), 6.86 (d, *J* = 8.30 Hz, 2H), 5.78-5.66 (m, 1H), 5.30-5.19 (m, 2H), 4.52 (d, *J* = 11.33 Hz, 1H), 4.25 (d, *J* = 11.33 Hz, 1H), 3.8 (s, 3H), 3.71 (q, *J* = 6.79, 13.59 Hz, 1H), 2.33 (m, 2H), 1.8-1.49 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.63, 159.22, 138.87, 130.70, 129.29, 117.33, 113.70, 79.58, 69.62, 55.18, 34.62, 33.75, 20.57; MS-ESIMS: *m/z* $[M+Na]^+$: 287; HRMS calcd for ($C_{15}H_{20}O_4Na$) 287.125 ; found. 287.124.

(1*R*)-1-Methyl-3-butenyl (5*S*)-5-[(4-methoxybenzyl)oxy]-6-heptenoate (16)

To a stirred solution of the compound **13** (0.25 g, 0.947 mmol) in dry CH_2Cl_2 (10 mL), DCC (0.39 g, 1.89 mmol) (2*R*)-4-penten-2-ol (0.09 g, 1.04 mmol) and DMAP (catalytic amount) were added at 0 °C and stirred at room temperature for 3 h. After completion of the reaction, the reaction mixture was filtered through Celite pad and extracted with CH_2Cl_2 (3x15 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 60–120 mesh, EtOAc–hexane 4:96) to afford **16** (0.255 g, 81%) as a liquid. R_f = 0.8 (20% EtOAc/hexane); $[\alpha]_D^{25}$ –30.2 (*c* 1, $CHCl_3$); IR (neat): 2976, 2935, 1730, 1612, 1513, 1247, 1174, 1074, 821, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.309 Hz, 2H), 6.87 (d, *J* = 8.309 Hz, 2H), 5.8-5.65 (m, 2H), 5.24-5.17 (m, 2H), 5.11-5.03 (m, 2H), 4.95 (m, 1H), 4.51 (d, *J* = 11.33 Hz, 1H), 4.26 (d, *J* = 11.33 Hz, 1H), 3.79 (s, 3H), 3.71 (q, *J* = 6.79, 13.59, 19.64 Hz, 1H), 2.38-2.20 (m, 4H), 1.75-146 (m, 4H), 1.19 (d, *J* = 6.04 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.13, 159.02, 138.81, 133.69, 130.71, 129.26, 117.59, 117.20, 113.70, 79.70, 69.76, 69.66, 55.21, 40.25, 34.79, 34.35, 20.94, 19.47; MS-ESIMS: *m/z* $[M+Na]^+$: 355; HRMS calcd for ($C_{20}H_{28}O_4Na$) 355.188 ; found. 355.187.

(1*R*)-1-Propyl-3-butenyl (5*S*)-5-[(4-methoxybenzyl)oxy]-6-heptenoate (17)

Compound **17** was prepared from **13** (0.2 g, 0.75 mmol) as a liquid in 81% yield according to the procedure described for compound **16**. IR (neat): 2956, 2868, 1731, 1612, 1513, 1459, 1246, 1173, 1082, 922, 821, 755 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.2 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 2H), 5.71 (m, 2H), 5.2 (m, 2H), 5.04 (m, 2H), 4.9 (p, *J* = 5.8, 12.2, 18.12 Hz, 1H), 4.52 (d, *J* = 11.4 Hz, 1H), 4.27 (d, *J* = 11.4 Hz, 1H), 3.8 (s, 3H), 3.69 (q, *J* = 6.3, 13.0, 20.4 Hz, 1H), 2.35-2.20 (m, 4H), 1.77-1.43 (m, 6H), 1.40-1.22 (m, 2H), 0.9 (t, *J* = 7.36, 14.54 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.19, 158.97, 138.9, 133.77, 130.65, 129.21, 117.42, 117.14, 113.64, 79.63, 72.72, 69.61, 55.14, 38.64, 35.68, 34.78, 34.27, 20.95, 18.49, 13.83; MS-ESIMS: *m/z* $[M+Na]^+$ 383; HRMS calcd for ($C_{22}H_{32}O_4Na$) 383.2198; found. 383.2212.

(1*R*)-1-Methyl-3-butenyl (5*S*)-5-hydroxy-6-heptenoate (18)

To a solution of **16** (0.175 g, 0.52 mmol) in CH_2Cl_2:H_2O [10:1 mL] was added dichlorodicyanoquinone (DDQ) (0.13 g, 0.58 mmol) at 0 °C. The solution was stirred for 1 h. After

the reaction was completed, it was quenched with sodium bicarbonate and the solution was filtered through a pad of Celite. The Celite pad was washed with CH_2Cl_2 (3x10 mL). The combined filtrate was concentrated, and purification by column chromatography (silica gel, 60–120 mesh, EtOAc–hexane 4:96) to afford the compound **18** (0.088 g, 78%) colorless liquid. R_f = 0.3 (30% EtOAc/hexane); $[\alpha]_D^{25}$ + 7.2 (*c* 1, $CHCl_3$); IR (neat): 3442, 2978, 2931, 1729, 1643, 1424, 1378, 1177, 920 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 5.93-5.69 (m, 2H), 5.26-5.03 (m, 4H), 4.97 (m, 1H), 4.09 (q, *J* = 6.04, 12.84 Hz, 1H), 2.4-2.2 (m, 4H), 1.84-1.63 (m, 2H), 1.61-1.51 (m, 2H), 1.2 (d, *J* = 6.04 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.11, 141.05, 133.83, 117.93, 115.10, 72.60, 69.91, 40.22, 36.17, 34.24, 20.70, 19.46; MS-ESIMS: *m/z* $[M+Na]^+$: 235; HRMS calcd for ($C_{12}H_{20}O_3Na$) 235.131; found. 235.131.

(1*R*)-1-Propyl-3-butenyl (5*S*)-5-hydroxy-6-heptenoate (19)

19 was prepared from **17** as a liquid in 79% yield according to the procedure described for compound **18** IR (neat): 3440, 2959, 2872, 1730, 1642, 1379, 1173, 993, 919; ^1H NMR (300 MHz, $CDCl_3$): δ = 5.89-5.64 (m, 2H), 5.24-5.01 (m, 4H), 5.91 (m, 1H), 4.06 (q, *J* = 6.04, 12.08 Hz, 1H), 2.31-2.25 (m, 4H), 1.78-1.61 (m, 2H), 1.59-1.47 (m, 4H), 1.39-1.25 (m, 2H), 0.916 (t, *J* = 7.55, 14.35 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ =173.58, 140.85, 133.92, 117.47, 114.66, 72.91, 72.54, 38.63, 36.18, 35.67, 34.17, 20.72, 18.49, 13.82; HRMS calcd for ($C_{14}H_{24}O_3Na$) 263.1623; found. 263.1616.

(1*R*)-1-Methyl-3-butenyl (5*R*)-5-[(4-methoxybenzyl)oxy]-6-heptenoate) (20)

Compound **20** was prepared from **ent-13** (0.2 g, 0.756 mmol) as a liquid in 81% yield according to the procedure described for compound **16**. R_f = 0.8 (20% EtOAc/hexane); $[\alpha]_D^{25}$ + 28.2 (*c* 1, $CHCl_3$); IR (neat): 2976, 2935, 1730, 1612, 1513, 1246, 1174, 1074, 821, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.18 (d, *J* = 8.49 Hz, 2H), 6.80 (d, *J* = 8.49 Hz, 2H), 5.77-5.62 (m, 2H), 5.20-5.14 (m, 2H), 5.06-5.01 (m, 2H), 4.92 (m, 1H), 4.49 (d, *J* = 11.52 Hz, 1H), 4.23 (d, *J* = 11.52 Hz, 1H), 3.75 (s, 3H), 3.65 (q, *J* = 6.6, 12.6 Hz, 1H), 2.34-2.18 (m, 4H), 1.72-1.41 (m, 4H), 1.17 (d, *J* = 6.23, Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.88, 158.86, 138.67, 133.52, 130.51, 129.07, 117.45, 117.03, 113.51, 79.46, 69.54, 54.97, 40.09, 34.62, 34.14, 20.77, 19.31; MS-ESIMS: *m/z* $[M+Na]^+$: 355; HRMS calcd for ($C_{20}H_{28}O_4Na$) 355.1885 ; found. 355.1873.

(1*R*)-1-methyl-3-butenyl (5*R*)-5-hydroxy-6-heptenoate (21)

Compound **21** was prepared from **20** (0.15 g, 0.45 mmol) as a yellow liquid in 78% yield according to the procedure described for compound **18**. R_f = 0.3 (30% EtOAc/hexane); $[\alpha]_D^{25}$ – 9.8 (*c* 1, $CHCl_3$); IR (neat): 3436, 3079, 2978, 2934, 1729, 1643, 1424, 1378, 1177, 921 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.88-5.65 (m, 2H), 5.29-5.03 (m, 4H), 4.93 (m, 1H), 4.07 (q, 1H), 2.36-2.22 (m, 4H), 1.77-1.61 (m, 2H), 1.55-1.48 (m, 2H), 1.20 (d, *J* = 6.83, 14.63 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.05, 140.83, 133.5, 117.51, 114.45, 72.33, 69.78, 40.08, 36.05, 34.12, 20.61, 19.32; MS-ESIMS: *m/z* $[M+Na]^+$: 235; HRMS calcd for ($C_{12}H_{20}O_3Na$) 235.1310; found. 235.1320.

Spectral and analytical data of all the three lactones 1, 2 and 3 are comparable to the previously reported data in the literature [4-9].

CONCLUSION

In conclusion all the three ten membered lactones namely stagonolide-F, putaminoxin and aspinolide-A have been synthesized combining the "ex-chiral pool" methodology, which involved transformation of enantiopure malic acid and Brown's asymmetric allylboration. All the three ten memberd lactones are prepared in a common synthetic route. The syntheses of related compounds of ten membered lactones are underway in our laboratory.

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