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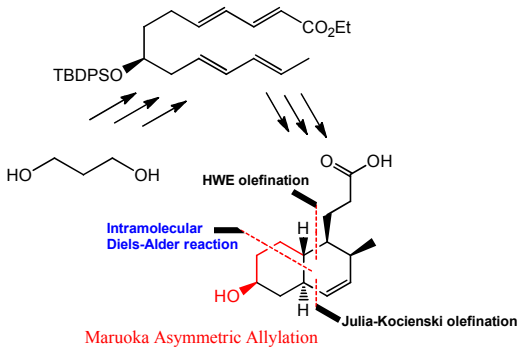

The first total synthesis of the polyketide eujavanoic acid **B** has been accomplished from an easily available and inexpensive starting material 1,3-propane diol. Maruoka asymmetric allylation, Julia olefination, HWE olefination and organocatalyzed intramolecular Diels-Alder reactions are the key steps involved in the present synthesis.

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ARTICLE TYPE

Enantioselective first total synthesis of eujavanoic acid B through organocatalyzed IMDA reaction †

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Abstract: The first total synthesis of the polyketide eujavanoic acid B has been accomplished from an easily available and inexpensive starting material 1,3-propane diol. Maruoka asymmetric allylation, Julia olefination, HWE olefination and organocatalyzed intramolecular Diels-Alder reactions are the key steps involved in the present synthesis.

Introduction

The functionalized and substituted decalins are found in a range of biologically important natural and synthetic compounds.[1] Typical decalin derivatives eujavanoic acids **A** (**1**) and **B** (**2**) **(Fig. 1)** were isolated from *Eupenicillium javanicum* along with several compactin derivatives.[2] The eujavanoic acid **B** (**2**) possesses an interesting *trans*-fused decalin substructure. The structure of the molecule was determined by spectroscopic data and modified Mosher's method. No synthetic efforts towards eujavanoic acid **B** (**2**) have been reported so far.

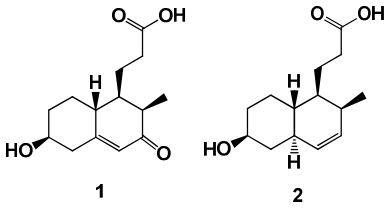

Fig. 1

In continuation of our work[3] on the construction of naturally occurring secondary metabolites for their advanced biological screening, we undertook investigations aimed at developing a concise and enantioselective total synthesis of eujavanoic acid **B**. Herein, we report our successful endeavour which culminated in the first total synthesis of this molecule.

Results and Discussion

The substitution pattern of cyclohexene ring in the eujavanoic acid **B** suggests a synthetic strategy with an intramolecular Diels-Alder reaction[4] as the key step.

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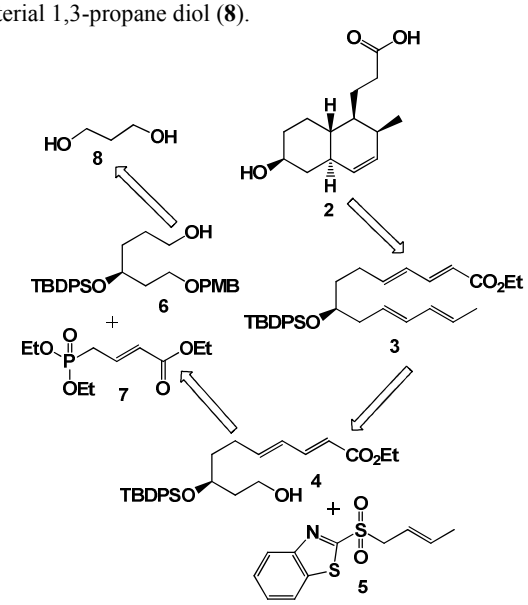
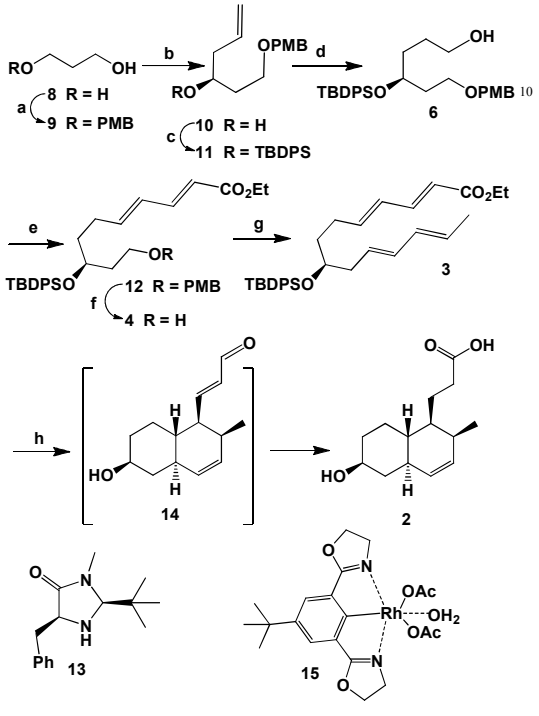
A concurrent study on organocatalyst IMDA reaction by Macmillan and co-worker showed improved enatio- and stereo-selctivities and therefore we adopted these conditions.[5] The retrosynthetic analysis (Scheme 1) reveals that the compound **2** can be prepared from commercially available and cheap starting material 1,3-propane diol (**8**).



Scheme 1. Retrosynthetic analysis for eujavanoic acid B

One of the hydroxyl groups of 1,3-propane diol (**8**) was protected as its PMB ether (**9**) with PMBCl in presence of catalytic amount of TBAI (Scheme 2). The free hydroxyl functionality of **9** was oxidized under Swern condition and the corresponding aldehyde was subjected to Maruoka asymmetric allylation to produce the homoallylic alcohol **10** (97% *ee*, the *ee* value of the compound has been determined by chiral HPLC analysis).[6,3a] The hydroxyl group was then protected as its TBDPS ether in presence of TBDPSCl and imidazole to obtain the compound **11**.[7] As a protecting group, TBDPS was chosen as this was expected to be cleaved in situ during organocatalyzed IMDA reaction because of the utilization of strong Bronsted acid $HClO_4$ as co-catalyst. Hydroboration of **11** with $BH_3.SMe_2$ provided the primary alcohol **6**,[8] which was further oxidized with IBX and the respective aldehyde underwent the Horner-Wadsworth-Emmons

(HWE) olefination with the phosphonate **7**[3f] to afford the ester **12**.[9] The compound **12** was then treated with DDQ to furnish the alcohol **4**, which was oxidized with IBX and the corresponding aldehyde was subjected to Julia olefination[10] with the benzothiazolyl sulfone **5**[3f] to produce the tetraene ester **3**.



Scheme 2. Reagents and condition: (a) PMBCl, TBAI (cat.), THF, 89%; (b) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C; (ii) $TiCl_4$, $Ti(O\text{-}iPr)_4$, *S,S*-BINOL, Allyltributyltin, CH_2Cl_2, 96% ee, 80% (over two steps); (c) TBDPSCl, Imidazole, CH_2Cl_2, 0 °C-rt, 94%; (d) $BH_3.SMe_2$, NaOH, H_2O_2 (30%), 0 °C-rt, 91%; (e) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C; (ii) **7**, LiHMDS, THF, −78 °C, *E*:*Z* = 95:5, 90% (over two steps); (f) DDQ, CH_2Cl_2:H_2O (9:1), 0 °C-rt, 92%; (g) (i) IBX, DMSO, CH_2Cl_2; (ii) **5**, LiHMDS, THF, −78 °C, *E*:*Z* = 75:25, 63% (over two steps); (h) (i) DIBAL-H (1.2 equiv), toluene, −78 °C, 35 min.; (ii) **13**.$HClO_4$ (20 mol%), H_2O/CH_3CN (2% v/v), 4 °C, 24 h, (*endo:exo* = 9:1); (iii) **15** (1 mol%), $(OEt)_2MeSiH$ (1.5 equiv), toluene, 60 °C, 1 h; (iv) TEMPO/BIAB, CH_2Cl_2:H_2O (2:1), 44% (over four steps).

The treatment of ester **3** with DIBAL-H afforded the corresponding aldehyde[11] which was utilized for the organocatalytic intramolecular Diels-Alder[5] reaction in presence of the organo catalyst **13**[5] and $HClO_4$. The IMDA reaction yielded the desired product **14** along with its minor *exo* isomer with excellent diastereoselectivity (9:1). The reversible formation of iminium ions by the biocatalyst with α-β unsaturated carbonyl lowers the activation energy of LUMO of the IMDA substrate and as a result it enhances the reaction rate as well as the selectivity of the reaction.[5] The α,β-unsaturated double bond of **14** was selectively reduced with $(OEt)_2MeSiH$ in presence of catalyst **15**,[12] and subsequently the TEMPO mediated oxidation[13] of aldehyde functionality provided an acid consisting of a mixture of two diastereomers. The major product was purified as the target compound **2** (94% *ee*). The physical properties (specific rotation) and spectral (NMR, IR, MS) data of the compound are well agreed with those reported for natural product.[2]

Conclusions

In conclusion, we have accomplished the first total synthesis of eujavanoic acid **B** with excellent diastereo and enantioselectivities, from a commercially available inexpensive starting material 1,3-propane diol. The synthesis involved well established reactions like Maruoka asymmetric allylation, Julia olefination, HWE olefination and organocatalyzed intramolecular Diels-Alder reactions as the key steps. The method can be well utilized for the synthesis of a wide variety of interesting secondary metabolites possessing similar *trans* –fused decalin substructure.

Experimental Section

General experimental procedure: All commercially available reagents were used directly without further purification unless otherwise stated. The solvents used were all of AR grade and were distilled under a positive pressure of dry nitrogen atmosphere wherever necessary. The progress of the reactions was monitored by analytical thin-layer chromatography (TLC) performed on Merck Silica Gel 60 F_{254} plates. Column chromatography was carried out using silica gel 60 – 120 mesh (Qingdao Marine Chemical, China). IR spectra were recorded on a Perkin-Elmer RX1 FT-IR spectrophotometer and mass spectra on VG-Autospec micromass. NMR spectra were recorded on Gemini 200 MHz spectrometer with tetramethylsilane as internal standard using $CDCl_3$. The chemical shifts are expressed as δ values in parts per million (ppm) and the coupling constants (*J*) are given in hertz (Hz). Yields were of purified compounds and were not optimized. Optical rotations were measured with JASCO DIP 360 digital polarimeter at 25 °C.

Experimental procedures and spectral data of all compounds are given below.

3-((4-Methoxybenzyl)oxy)propan-1-ol (9): Propane-1,3-diol **8** (1 g, 13.1 mmol) was taken in 50 mL of anhydrous THF and NaH (60% dispersion in mineral oil, 576 mg, 14.41 mmol) was added to it portion wise at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. Tetrabutylammonium iodide (TBAI) was added to it followed by the addition of 4-methoxybenzylchloride (PMBCl) (1.8 mL, 13.1 mmol) in THF (5 mL). The reaction mixture was stirred for a further 8 h at room temperature. Water was added carefully to the reaction mixture to quench any excess of NaH. The reaction mixture was then extracted with EtOAc (2 x 50 mL). The organic solution was washed with water (2 x 50 mL), brine (2 x 50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane-EtOAc, 3:2) to afford the compound **9** (2.2 g, 89%) as a reddish liquid. R_f = 0.2 (30% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$): δ 7.28 (2H, d, *J* = 8.5 Hz), 6.88 (2H, d, *J* = 8.5 Hz), 4.45 (2H, s), 3.81 (3H, s), 3.77 (2H, t, *J* = 7.0 Hz), 3.64 (2H, t, *J* = 7.0 Hz), 2.40 (1H, brs), 1.89-

1.81 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): 159.2, 130.0, 129.2, 113.7, 72.8, 69.1, 61.6, 55.2, 31.9; EIMS: *m/z* 197 $[M+H]^+$, Anal. Cald. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.44; H, 8.18.

(*S*)-1-((4-Methoxybenzyl)oxy)hex-5-en-3-ol (10): To a stirred solution of $TiCl_4$ (11 µL, 0.1 mmol) in CH_2Cl_2 (10 mL) was added dried $Ti(O^iPr)_4$ (87 µL, 0.29 mmol) at 0 °C under nitrogen atmosphere and the mixture was allowed to warm to room temperature. After 1.5 h, silver (I) oxide (43.8 mg, 0.19 mmol) was added and the reaction was continued for 6 h under exclusion of direct light. The mixture was diluted with DCM (40 mL) and treated with (*S*)-BINOL (107.5 mg, 0.38 mmol) at room temperature for 2.5 h to furnish the chiral bis-Ti(IV) oxide (*S*, *S*). This complex was cooled to −15 °C and treated sequentially with aldehyde corresponding to the alcohol **9** (To a stirred cold (−78 °C) solution of oxalyl chloride (0.25 mL, 2.9 mmol) in CH_2Cl_2 was added DMSO (0.25 mL, 3.6 mmol). After stirring for 10 min at −78 °C a solution of alcohol **9** (374 mg, 1.9 mmol) was added dropwise to the reaction mixture. The solution was stirred for 15 min at the same temperature and then Et_3N (1.7 mL, 11.8 mmol) was added dropwise. The reaction mixture was stirred at that same temperature for 45 min and then poured into the aqueous saturated NH_4Cl solution. The organic phase was separated and washed with aqueous saturated $NaHCO_3$ solution. The organic phase was dried over Na_2SO_4 and concentrated in vacuum to get the crude aldehyde) and allyltributyltin (0.82 mL, 2.47 mmol) at the same temperature. The mixture was allowed to warm to 0 °C and stirred for 15 h. The mixture was quenched with saturated aq. $NaHCO_3$ (50 mL) and extracted with EtOAc (3 × 30 mL). The extract was dried over anhydrous Na_2SO_4. Evaporation of the solvents and purification of the residue by column chromatography (ethyl acetate / hexane, 1: 9) gave pure **10** (360 mg, 80 %, *ee* 97%) as a yellow liquid. R_f = 0.5 (20% EtOAc/hexane). $[\alpha]_D^{25}$ = −7.2 (*c* = 5.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26 (2H, d, *J* = 8.5 Hz), 6.88 (2H, d, *J* = 8.5 Hz), 5.89-5.75 (1H, m), 5.12-5.06 (2H, m), 4.42 (2H, s), 3.92-3.81 (1H, m), 3.81 (3H, s), 3.71-3.54 (2H, m), 2.25-2.21 (2H, dd, *J* = 6.0, 7.0 Hz), 1.78-1.68 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): 159.1, 134.8, 129.9, 129.1, 117.2, 113.7, 72.7, 70.1, 68.3, 55.1, 41.8, 35.7; ESIMS: *m/z* 259 $[M+Na]^+$, Anal. Cald. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.29; H, 8.58.

(*S*)-tert-Butyl((1-((4-methoxybenzyl)oxy)hex-5-en 3yl)oxy) diphenyl silane (11): To a stirred solution of alcohol **10** (342 mg, 1.45 mmol) in anhydrous CH_2Cl_2 (10 mL) was added imidazole (296 mg, 4.35 mmol) and TBDPS-Cl (0.3 mL, 15.35 mmol) at 0 °C. Reaction mixture was stirred at room temperature for 2 h. After completion of the reaction it was diluted with CH_2Cl_2 and washed with water, brine and dried over anhydrous Na_2SO_4. Removal of solvent in vacuum and purification by silica gel column chromatography (5% ethyl acetate in hexane) afforded **11** (650 mg, 94% yield) as a colorless liquid. R_f = 0.8 (10% EtOAc/hexane). $[\alpha]_D^{25}$ = +14.5 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (4H, d, *J* = 8.0 Hz), 7.43-7.32 (6H, m), 7.15 (2H, d, *J* = 8.0 Hz), 6.84 (2H, d, *J* = 8.0 Hz), 5.75-5.65 (1H, m), 4.96-4.85 (2H, m), 4.26 (2H, s), 3.93 (1H, m), 3.80 (3H, s), 3.50-3.40 (2H, m), 2.21 (1H, dd, *J* = 7.0, 13.0 Hz), 2.14 (1H, dd, *J* = 7.0, 13.0 Hz), 1.81-1.75 (2H, m), 1.04 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$): 159.0, 135.9, 134.4, 130.6, 129.5, 129.1, 127.5, 127.4, 117.1, 113.7, 72.4, 70.4, 66.6, 55.2, 41.6, 36.1, 27.0, 19.4; ESIMS: *m/z* 497 $[M+Na]^+$, Anal. Cald. for $C_{30}H_{38}O_3Si$: C, 75.90; H 8.07. Found: C, 76.05; H, 8.03.

(*S*)-4-((tert-Butyldiphenylsilyl)oxy)-6-((4-methoxybenzyl)oxy) hexan-1-ol (6): To a stirred solution of **11** (0.60 g, 1.27 mmol) in dry THF (4 mL) was added $BH_3.Me_2S$ (0.12 mL, 0.6 mmol) while maintaining the temperature at 0 °C. The reaction mixture was stirred at the same temperature for a period of 5 h. This was then treated with the very slow addition of 3N NaOH until the reaction mixture became basic at the same temperature. To this was added H_2O_2 (30%, 0.1 mL, 0.66 mmol) and the reaction mixture stirred over a period of 1.5 h, and then extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with brine (2 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane-EtOAc, 3:2) to afford **6** (540 mg, 91%) as a colorless liquid. R_f = 0.2 (30% EtOAc/hexane). $[\alpha]_D^{32}$ = −8.7 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (4H, d, *J* = 8.0 Hz), 7.44-7.32 (6H, m), 7.15 (2H, d, *J* = 8.0 Hz), 6.84 (2H, d, *J* = 8.0 Hz), 4.26 (2H, s), 3.95-3.93 (1H, m), 3.80 (3H, s), 3.46-3.37 (4H, m), 1.82-1.73 (2H, m), 1.56-1.43 (5H, m), 1.04 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$): 159.0, 135.9, 134.2, 130.5, 129.5, 129.1, 127.5, 113.7, 72.4, 70.6, 66.7, 62.8, 55.2, 36.2, 32.9, 27.8, 27.0, 19.4; ESIMS: *m/z* 493 $[M+Na]^+$, Anal. Cald. for $C_{30}H_{40}O_4Si$: C, 73.13; H 8.18. Found: C, 73.26; H, 8.14.

(*S*,2*E*,4*E*)-Ethyl8-((tert-butyldiphenylsilyl)oxy)-10-((4 methoxy- benzyl)oxy)deca-2,4-dienoate(12): To a stirred solution of phosphonate **7** (594 mg, 2.4 mmol) in anhydrous THF (10 mL) at −78 °C was added LiHMDS (1 M in THF, 1.9 mL, 1.92 mmol), after 20 min of stirring to this solution at the same temperature was added the prepared aldehyde corresponding to the alcohol **6** (455 mg, 0.96 mmol) (The aldehyde was prepared by the oxidation of alcohol **6**, utilizing the Swern oxidation procedure as mentioned earlier for compound **9**) in THF (10 mL), and the resulting solution was stirred at −78 °C for 6 h. After the aldehyde was completely consumed the reaction mixture was quenched with aqueous NH_4Cl solution (5 mL) and the mixture was extracted into EtOAc (3 x 10 mL), dried over Na_2SO_4, concentrated in vacuum and the crude product was purified on silica gel (10% EtOAc/hexane) to yield the desired diene ester **12** (500 mg, 90%). R_f = 0.5 (10% EtOAc/Hexane). $[\alpha]_D^{32}$ = +54.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (4H, d, *J* = 8.0 Hz), 7.45-7.35 (6H, m), 7.16 (2H, d, *J* = 8.0 Hz), 7.14 (1H, dd, *J* = 10.0, 16.50 Hz), 6.86 (2H, d, *J* = 8.0 Hz), 5.98-5.94 (1H, m), 5.85-5.80 (1H, m), 5.73 (1H, d, *J* = 16.50 Hz), 4.30 (2H, d, *J* = 4.0 Hz), 4.23-4.19 (2H, q, *J* = 7.0 Hz), 3.93 (1H, m), 3.80 (3H, s), 3.51-3.44 (2H, m), 2.16-2.05 (2H, m), 1.84-1.73 (2H, m), 1.58-1.49 (2H, m), 1.31 (3H, t, *J* = 7.0 Hz), 1.04 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$): 167.2, 159.0, 145.0, 143.9, 135.9, 134.3, 130.5, 129.5, 129.1, 128.3, 127.5, 119.1, 113.7, 72.4, 70.2, 66.6, 60.1, 55.2, 36.3, 35.7, 28.3, 27.0, 19.4, 14.3; ESIMS: *m/z* 609 $[M+Na]^+$, Anal. Cald. for $C_{36}H_{46}O_5Si$: C, 73.68; 7.90 H. Found: C, 73.82; H, 7.94.

(*S*,2*E*,4*E*)-Ethyl 8-((tert-butyldiphenylsilyl)oxy)-10-hydroxy-deca 2, 4- dienoate (4): To a stirred solution of the compound **12** (465 mg, 0.79 mmol) in CH_2Cl_2 and water (9:1) DDQ (270 mg, 1.2 mmol) was added at 0 °C and stirred for 2 h. After complete conversion of the reaction, the mixture was quenched with $NaHCO_3$ and left it for another more 2 h. Finally, the reaction mixture was worked up and dried over Na_2SO_4, concentrated in vacuum and the crude product was purified on silica gel column chromatography (10% EtOAc/hexane) to yield the desired alcohol **4** (340 mg, 92%). R_f = 0.2 (10% EtOAc/Hexane). $[\alpha]_D^{32}$ = 40.0 (*c* = 1.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69 (4H, d, *J* = 8.0 Hz), 7.46-7.36 (6H, m), 7.12 (1H, dd, *J* = 10.0, 16.50 Hz), 5.95 (1H, m), 5.78 (1H, m), 5.70 (1H, d, *J* = 15.5 Hz), 4.21 (2H, q, *J* = 7.5 Hz), 3.94 (1H, m), 3.75-3.67 (2H, m), 2.16-1.96 (2H, m), 1.84-1.79 (1H, m), 1.72-1.60 (2H, m), 1.56-1.49 (1H, m), 1.30 (3H, t, *J* = 7.0 Hz), 1.06 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$): 167.2, 144.7, 135.8, 133.9, 133.8, 129.8, 129.7, 128.4, 127.6, 119.2, 71.2, 60.1, 59.6, 37.8, 35.2, 28.4, 26.9, 19.2, 14.2; ESIMS: *m/z* 467 $[M+H]^+$, Anal. Cald. for $C_{28}H_{38}O_4Si$: C, 72.06; H, 8.21. Found: C, 72.21; H, 8.24.

(*S*,2*E*,4*E*,10*E*,12*E*)-Ethyl 8-((tert-butyldiphenylsilyl)oxy) tetra- deca-2,4,10,12-tetraenoate(3): Alcohol **4** (295 mg, 0.632 mmol) was oxidized with IBX to furnish the corresponding aldehyde. To a solution of the sulfone **5** (158 mg, 0.632 mmol) and the aldehyde corresponding to the alcohol **4** in anhydrous THF (50 mL), argon was bubbled to degas the reaction mixture for 30 min, cooled it at −78 °C and KHMDS (1.2 mL, 0.5 M in toluene, 0.632 mmol) was added drop wise. The reaction was warmed to 0 °C and stirred for 2 h and then quenched with a saturated solution of NH_4Cl (15 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated to a residue. Purification of the residue on silica gel column using EtOAc/hexane (2%) as eluent, afforded Julia product **3** (200 mg, 63%) as a yellow liquid. R_f = 0.8 (10% EtOAc/hexane). $[\alpha]_D^{32}$ = +27.8 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68-7.66 (4H, d, *J* = 8.0 Hz), 7.45-7.35 (6H, m), 7.17 (1H, dd, *J* = 16.0, 10.0 Hz), 6.15-5.82 (3H, m), 5.75 (1H, d, *J* = 16.0 Hz), 5.67-5.48 (1H, m), 5.44-5.32 (1H, m), 5.18 (1H, m), 4.20 (2H, q, *J* = 7.5 Hz), 3.76 (1H, m), 2.38-2.04 (4H, m), 1.72 (3H, d, *J* = 7.0 Hz), 1.59-1.45 (2H, m), 1.29 (3H, t, *J* = 7.0 Hz), 1.05 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$): 167.2, 144.9, 135.9, 134.2, 132.8, 131.5, 130.4, 129.8, 129.5, 128.3, 127.5, 127.1, 126.8, 119.5, 72.4, 60.1, 40.0, 35.2, 35.0, 31.6, 28.4, 27.0, 19.3, 14.3; ESIMS: *m/z* 503 $[M+H]^+$, Anal. Cald. for $C_{32}H_{42}O_3Si$: C, 76.45; H, 8.42. Found: C, 76.51; H, 8.39.

3-((1*S*,2*S*,4a*R*,6*S*,8a*S*)-6-Hydroxy-2-methyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)propanoic acid (2): To a stirred solution of ester (**3**) (145 mg, 0.29 mmol) in toluene at -78 °C, 1.2 equivalent (1.25 M, 0.3 mL) DIBAL-H was added and stirred for 35 min at the same temperature. The reaction was quenched with slow addition of saturated aqueous solution of sodium potassium tartrate. The reaction mixture was extracted with EtOAc, dried over Na_2SO_4 and concentrated under high vacuum. The crude aldehyde was directly utilized for organocatalytic intramolecular Diels-Alder step, adding 1mL of 2% v/v H_2O/CH_3CN and then cooled to 4 °C, then adding the MacMillan organo catalyst **13**.$HClO_4$ (20 mol%, 14.0 mg). This sequence of operations yielded the desired *endo* bicyclo[4.4.0]decane aldehyde (**14**) along with its minor *exo* isomer, alpha-beta unsaturated double bond of which was selectively reduced by heating the mixture of aldehyde, rhodium catalyst (**15**) (1.0 mol%, 2.0 mg) and $(OEt)_2MeSiH$ (0.44 mmol, 0.07 mL) in toluene at 60 °C over a period of 1 h. The product was then subjected to TEMPO/BIAB oxidation of aldehyde functionality to acid function leading to an acid mixure (30 mg, 44% over four steps) of two diastereomers. The major product was isolated as natural eujavanoic acid B (**2**) as micro crystal in excellent enantioselectivity (94% *ee*). $[\alpha]_D^{25}$ = + 35.2 (*c* = 0.20, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.60 (1H, ddd, *J* = 2.9, 4.7, 9.7 Hz), 5.33 (1H, d, *J* = 9.7 Hz), 3.56 (1H, tt, *J* = 10.5, 4.2 Hz), 2.40 (1H, ddd, *J* = 6.5, 9.5, 15.7 Hz), 2.29-2.22 (2H, m), 2.04 (1H, brd), 1.91-1.70 (4H, m), 1.49 (1H, m), 1.35 (1H, m), 1.17-1.01 (4H, m), 0.95 (3H, d, *J* = 7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): 175.0, 133.7, 131.5, 70.7, 43.4, 42.9, 41.8, 39.6, 37.1, 32.9, 32.2, 28.3, 25.1, 15.2; ESIMS: *m/z* 261 $[M+Na]^+$. Anal. Cald. for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.64; H, 9.24.

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References

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