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ORIGINAL ARTICLE

Synthesis of the amino acid conjugates of *epi*-jasmonic acid

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Abstract The TES ether of the C6-hydroxy derivative of naturally occurring *epi*-jasmonic acid (*epi*-JA) was designed as epimerization-free equivalent of *epi*-JA. The TES ether was synthesized from (1*R*,4*S*)-4-hydroxycyclopent-2-enyl acetate in 13 steps. The acid part of the ether was activated with $ClCO_2Bu^i$ and subjected to condensation with L-amino acid at room temperature for 48 h. The TES group in the condensation product was removed in HCO_2H (0°C, 30 min) and the resulting hydroxyl group was oxidized with Jones reagent (acetone, 0°C, 30 min) to furnish the amino acid conjugate of *epi*-JA. The amino acids examined are L-isoleucine, L-leucine, L-alanine, L-valine, and D-allo-isoleucine, which afforded the conjugates in 48–68% yields with 89–96% diastereomeric purity over the trans isomers. Similarly, the possible three stereoisomers of *epi*-JA were condensed with L-isoleucine successfully, producing the corresponding stereoisomers in good yields.

Keywords *epi*-Jasmonic acid · Amino acid conjugate · Isoleucine · Asymmetric synthesis · Stereoselective

Introduction

The amino acid conjugates of *epi*-JA (Fig. 1) found in plants (Kramell et al. 1997a; Miersch et al. 1992, 1999; Schmidt et al. 1990; Staswick and Tiryaki 2004) are the major components of the jasmonate signaling mediators that regulate stress responses and development in plants (Creelman and Mullet 1997; Tamogami et al. 2008; Walter et al. 2007; Xie et al. 1998). In 2007, the mechanism of the signaling was disclosed at the molecular level, in which the amino acid conjugates promote the SCF^{COI1} complex binding to JAZ repressor proteins, resulting in degradation of JAZ proteins (Chini et al. 2007; Thines et al. 2007). Furthermore, L-isoleucine was found to be the most active component among the amino acids examined (Thines et al. 2007). The conjugates used for the study were synthesized from racemic jasmonic acid (JA) that consists of natural *epi*-JA (**1**), its enantiomer, and the two trans isomers (**3** and **4**) in roughly the thermodynamic ratio of <5:<5:>45:>45 (Kramell et al. 1988, 1997b). Thus, the potency of the isoleucine conjugate **2a** possessing the *epi*-JA component remained unclear. Later, the conjugates **2a** and the trans isomers (**7** and **8**) were separated from the diastereomeric mixture derived from racemic JA and L-isoleucine by HPLC, and the conjugates **2a** and **8** (unnatural isomer) were found to be the active isomers for the promotion, while the trans isomer **7** was less active (Fonseca et al. 2009).

Before the natural isomer **2a** was elucidated to be the most active isomer, we established a stereoselective synthesis of *epi*-JA (**1**) (Ogawa and Kobayashi 2008). We then examined condensation of **1** and L-isoleucine according to the procedure developed for racemic JA and L-isoleucine (Kramell et al. 1988). However, substantial epimerization at C7 took place, producing a mixture of the desired product **2a** and the trans isomer **7** in a 3:7 ratio (Scheme 1, method 1) (Soloshonok 2002). Since the trans isomer is thermodynamically more stable (Seto et al. 1996, 1999), the epimerization at C7 of the cyclopentane ring of less

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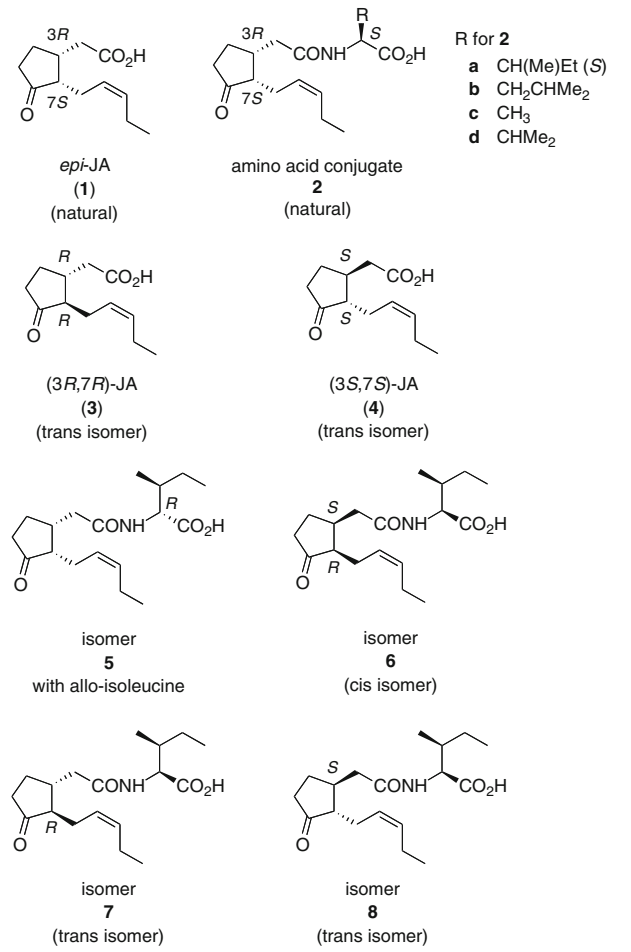
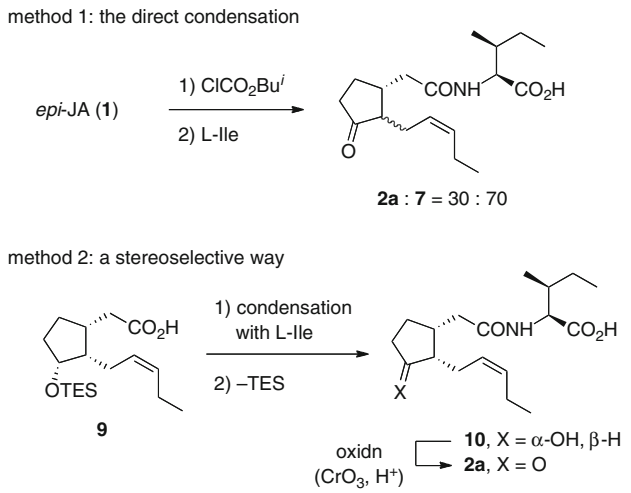


Fig. 1 *epi*-JA amino acid conjugates of *epi*-JA, and related isomers. *JA* jasmonic acid



Scheme 1 Synthesis of **2a** by two methods 1 and 2

stable **2a** is not surprising. To detour the problem of the epimerization, we envisioned a method delineated in Scheme 1, method 2, in which the carbonyl group was restored at the last step. In practice, the method afforded **2a** stereoselectively as communicated recently (Ogawa and Kobayashi 2008). With **2a** synthesized, we studied **2a**-promoted interaction between COI1 and JAZ proteins that are produced by alternative splicing (Chung et al. 2010) and succeeded in obtaining crystal structures of the complex involving **2a**, COI1, and JAZ and their pharmacological data (Sheard et al. 2010). In contrast to the isoleucine conjugate, biological profiles of the natural conjugates with other amino acids are not yet disclosed, though the studies using the trans isomers of the conjugates derived from racemic JA and the L-amino acids have been reported previously. Due to the significance of the stereodefined amino acid conjugates of *epi*-JA and JA as such and as standards for biological investigation, we describe herein synthesis **2a–d** and **5–8**, demonstrating generality of the method.

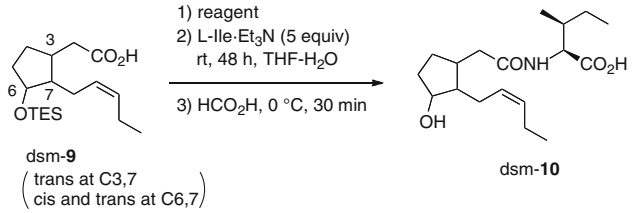
Results and discussion

On the basis of our previous synthesis of 12-oxo-PDA and OPC-8:0 (Ainai et al. 2003), we envisaged that condensation of an epimerization-free acid **9** with L-isoleucine followed by desilylation would afford alcohol **10**, which upon Jones oxidation would furnish **2a** stereoselectively.

The condensation was first examined with a diastereomeric mixture (dsm) of the acid dsm-**9**, which was synthesized from racemic methyl jasmonate through hydrolysis (aqueous NaOH), reduction ($NaBH_4$), and silylation [TESCl (Et_3SiCl), imidazole] in 82% yield. Acid dsm-**9** was activated by a reagent at room temperature for 3 h in THF and mixed with an aqueous solution of L-isoleucine (5 equiv.) and Et_3N (5 equiv.). After 48 h at room temperature, the TES group was removed in HCO_2H (0°C, 30 min) to produce dsm-**10**, which was purified by chromatography on silica gel ($CHCl_3$/EtOAc to $CHCl_3$/EtOAc/HCO_2H). Among the reagents examined (Table 1), $ClCO_2Bu^i$ gave a good yield (entry 8). In relation to the condensation, isoleucine-allyl was condensed to racemic JA (**3** + **4**) in 31% yield, and the allyl group in the product was removed with Bu_3SnH and $Pd(PPh_3)_4$ cat to afford a mixture of the isoleucine conjugate of racemic JA and Ph_3P-oxide. However, the mixture was inseparable by chromatography on silica gel.

With the above results in hand, we undertook synthesis of the optically active conjugate **2a** as shown in Scheme 2 starting from acetate **11** (>99% ee by HPLC), which was converted to bis–TES ether **12** by the eight-step procedure (Nonaka et al. 2010). Swern oxidation of **12** gave aldehyde **13**, which upon Wittig reaction afforded **14** in 83% yield over the two steps. The olefin part of **14** was then changed to the hydroxyl group of **15** in 77% yield. The yield of **15** from **12** was higher than that reported (Nonaka et al. 2010).

Table 1 Condensation of a model acid dsm-**9**[a] with L-isoleucine



Entry	Reagent[b] (equiv.)	Yield[b] (%)
1	WSC (1.3), HOSu (1.3)	43
2	DMT-MM (1.3)	51
3	BOPCl (1.3), Et_3N (1.3)	47
4	HATU (1.3), Et_3N (1.3)	47
5	HBTU (1.3), Et_3N (1.3)	51
6	TCBC (1.5), Et_3N (1.5)	17
7	DCBC (1.5), Et_3N (1.5)	0
8	$ClCO_2Bu^i$ (1.3), Et_3N (1.3)	60
9	$ClCO_2CH(Me)Cl$ (1.3), Et_3N (1.3)	42

[a] A diastereomeric mixture (dsm) prepared from racemic methyl jasmonate

[b] *WSC* 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride; *DMT-MM* 4-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride; *BOPCl* Bis(2-oxo-3-oxazolidinyl)phosphinic chloride; *HATU* 1-[Bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo(4,5-b) pyridinium 3-oxide hexafluorophosphate; *HBTU* 1-[Bis(dimethylamino)methylene]-1*H*-benzotriazolium 3-oxide hexafluorophosphate; *TCBC* 2,4,6-Trichlorobenzoyl chloride

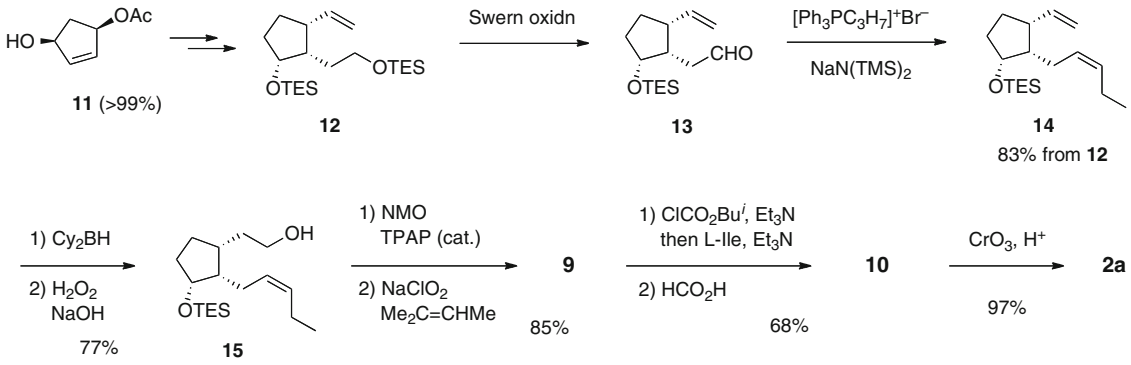
[c] Isolated yields by chromatography on silica gel

Oxidation of alcohol **15** to acid **9** was accomplished using TPAP/NMO and $NaClO_2$ in 85% yield (TPAP, tetrapropylammonium perruthenate; NMO, *N*-methylmorpholine-*N*-oxide). Condensation of **9** with L-isoleucine followed by desilylation under the conditions established above-produced alcohol **10** in 68% yield. Finally, Jones oxidation (CrO_3, H_2SO_4) at 0°C for 30 min gave the isoleucine conjugate **2a** in quantitatively. The isomeric purity of **2a** over the trans isomer **7** (synthesis, see Scheme 5) was 96% by 500 MHz ^{1}H NMR spectroscopy [**2a**, δ 2.84–2.94 (m, 1 H); isomer **7**, δ 2.67 (dd, J = 14.5 Hz, 4.5 Hz, 1 H)]. Furthermore, NH and α-H of the amino acid part in the ^{1}H NMR spectra of **2a** and **5** (synthesis, see below) clearly indicated no epimerization at the α position of leucine: **2a**, δ 4.63 (dd, J = 8.5 Hz, 4.5 Hz, 1 H), 6.30 (d, J = 8.5 Hz, 1 H); isomer **5**, δ 4.78 (dd, J = 9 Hz, 4 Hz, 1 H), 6.42 (d, J = 9 Hz, 1 H). The conjugate **2a** with this purity will be accepted for biological study. With the ^{1}H NMR spectra of **2a** and its C7 epimer **7** in hand, we examined chemical stability of **2a** in CD_3OD by ^{1}H NMR spectroscopy. In contrast to the partial epimerization (4%) induced by the acid during Jones oxidation, the conjugate **2a** was found to be quite stable at room temperature for 3 weeks, whereas addition of K_2CO_3 promoted rapid epimerization to afford a 6:94 mixture of **2a** and **7** after 24 h. The rate of the epimerization appears faster than that of tuberonic acid and much faster than 12-oxo-PDA, though we do not have any reason to explain the difference.

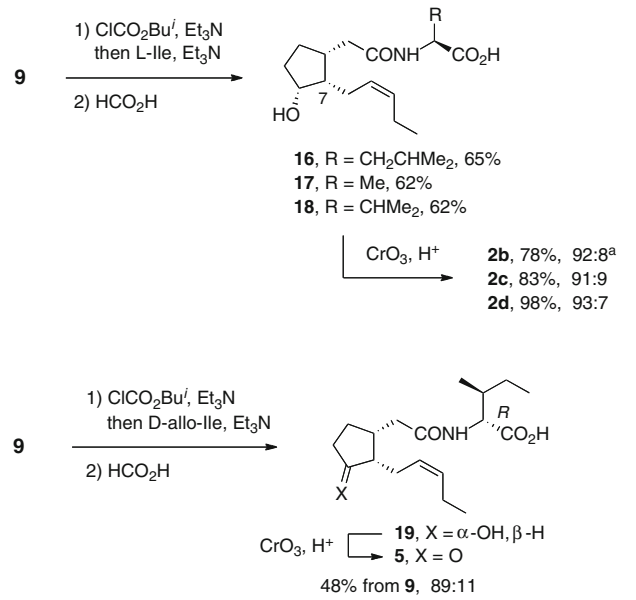
The above three-step sequence was applied to L-leucine, L-alanine, and L-valine as delineated in Scheme 3. In all cases, the condensation with the amino acids (room temperature, 48 h) and the removal of the TES group (HCO_2H, 0°C, 30 min) proceeded uneventfully to afford alcohols **16–18**, which were oxidized to the conjugates **2b–d** in good yields. To determine epimeric purity over the trans isomer (the C7 epimer), the epimer of **2c** (see the supplemental material) was synthesized as well to find the specific signals in the ^{1}H NMR spectrum. With the diagnostic signals for the epimer of **2c** and **7** (epimer of **2a**), those of **2b** and **2d** were assigned by analogy and the epimeric purities for **2b–d** were calculated to be 91–93%.

Similarly, the allo-isoleucine conjugate **5** was synthesized from acid **9** by condensation with D-allo-isoleucine followed by Jones oxidation (Scheme 3). In addition, product **5** was used to determine the epimeric purity of **2a** by ^{1}H NMR spectroscopy (see above).

Next, we investigated synthesis of the isoleucine conjugates of the *epi*-JA isomers delineated in Fig. 1 (i.e., isomers **6–8**).



Scheme 2 Synthesis of the conjugate **2a** through acid **9**



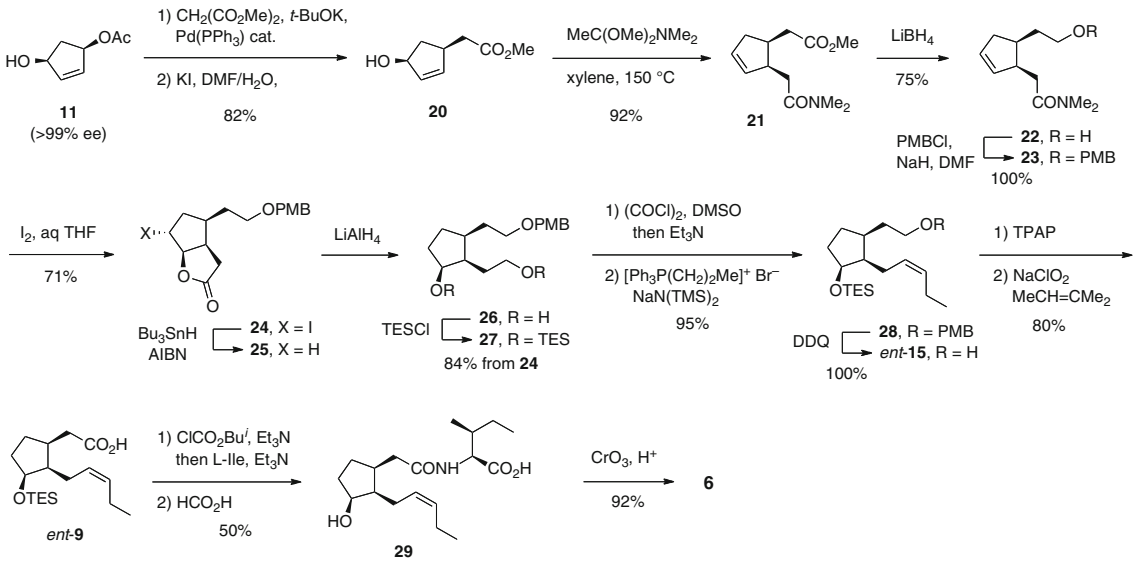
Scheme 3 Synthesis of the amino acid conjugates. [a]Ratio of **2**: C7-epimer

Synthesis of **6**, the isoleucine conjugate with the enantiomer of *epi*-JA, started with the same monoacetate **11** used above (>99% ee by chiral HPLC), to which the CH_2CO_2Me group was attached to give **20** with retention of the configuration of the acetoxy-carbon in 82% yield through palladium-catalyzed allylic substitution with methyl malonate followed by decarboxylation (Acharya and Kobayashi 2006). Transformation of **20** to *ent*-**9** was accomplished using the strategy developed for the synthesis of *epi*-JA (**1**) (Nonaka et al. 2010). Condensation of *ent*-**9** with L-isoleucine followed by desilylation afforded alcohol **29** in 50% yield. Finally, Jones oxidation furnished **6** in 92% yield with a 96:4 diastereomeric ratio of **6** and the C7 isomer **8** by ^{1}H NMR spectroscopy (synthesis of **8**, see below).

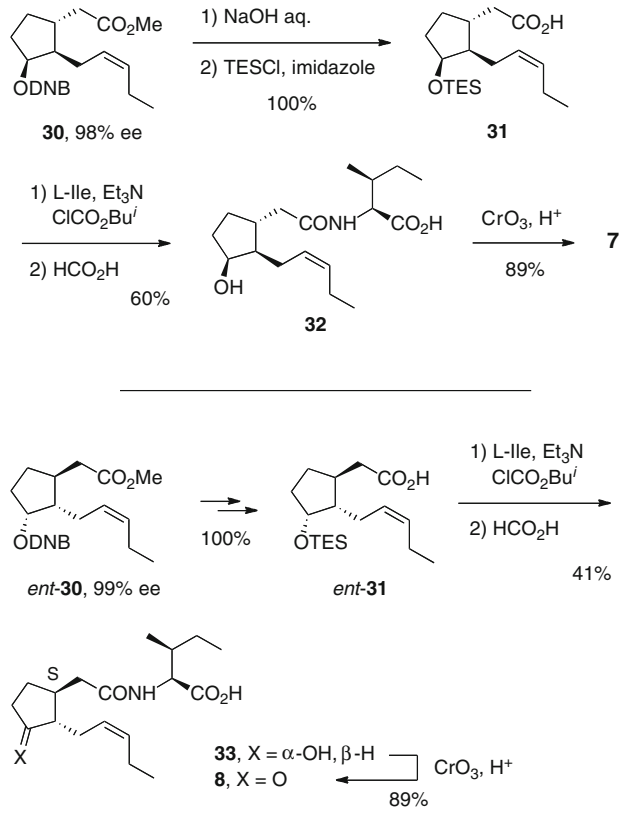
Synthesis of the stereoisomers **7** and **8** possessing the JA moiety required the 3,7-trans acids **31** and *ent*-**31**, respectively. Although monoacetate **11** would be transformed to these acids by a method similar to that presented as above for the synthesis of **9** and *ent*-**9** (Schemes 2, 4), we rather decided to utilize esters **30** and *ent*-**30** since these intermediates are available through the kinetic resolution of the racemic alcohol derived from methyl jasmonate by PPL-assisted acetylation in 5 and 6 steps (to **31** and *ent*-**31**) (Kiyota et al. 2001; Asamitsu et al. 2006), which are shorter than that starting from monoacetate **11** (11 steps). In practice, ester **30** with 98% ee was prepared from racemic methyl jasmonate in 26% yield and transformed to acid **31** through hydrolysis followed by silylation. The acid was subjected to the three-step transformation developed above to furnish the trans stereoisomer **7** in 53% yield from **31**. Diastereomeric purity of **7** over **2a** was >99% by 500 MHz ^{1}H NMR spectroscopy, indicating slower (if any) deprotonation of the hydrogen at C7 of **7** than that of **2a** (96% purity over **7**) during the oxidation. The C3 acetamide chain on the cyclopentanone ring probably prevents the access of the base to the hydrogen at C7. In a similar manner, *ent*-**31** obtained in 19% yield from racemic methyl jasmonate was transformed to the stereoisomer **8** without detectable epimerization by ^{1}H NMR spectroscopy (Scheme 5).

Conclusion

In summary, we developed a method for synthesis of the isoleucine conjugate **2a** for the first time, and the method



Scheme 4 Synthesis of the isoleucine conjugate **6** with the enantiomer of *epi*-JA part. PMB = 4-$MeOC_6H_4CH_2$



Scheme 5 Synthesis of the isoleucine conjugates of JA and the enantiomer of JA. DNB = 3,5-$(NO_2)_2C_6H_3C(=O)$–

was successfully applied to synthesis of its stereoisomers **5–8** and the conjugates **2b–d** with other amino acids. These compounds are definitely useful not only for the biological study at molecular level but also as standards for estimation of these compounds from natural sources.

Experimental section

General

The IR, specific rotations, and melting points (uncorrected) were measured on a JASCO A-100 spectrophotometer, a JASCO Digital Polarimeter DIP-370, and a Yanako MP-S3, respectively. The 300 MHz ^{1}H and 75 MHz ^{13}C NMR spectra were measured on a Varian Mercury 300, while 500 MHz ^{1}H NMR spectra were done on a Varian VXR-500 s. The chemical shifts of the carbons accompany minus (for C and CH_2) and plus (for CH and CH_3) signs of APT experiments (Attached Proton Test). Chromatographic purification was carried out using spherical silica gel 60 N purchased from Kanto, Japan. TLC plate was purchased from Merck (Silica gel 60 F254).

2-((1*R*,2*S*,3*R*)-2-((*Z*)-Pent-2-en-1-yl)-3-((triethylsilyl)oxy)cyclopentyl)ethanol (**15**)

To a solution of $(COCl)_2$ (0.379 mL, 4.55 mmol) in CH_2Cl_2 (13 mL) was added DMSO (0.646 mL, 9.10 mmol) at −78°C. The mixture was stirred at −78°C for 40 min and a solution of TES ether **12** (350 mg, 0.910 mmol) in CH_2Cl_2 (2 mL) was added dropwise. After 1 h at −78°C, Et_3N (1.27 mL, 9.10 mmol) was added. The resulting mixture was warmed to room temperature with vigorous stirring and diluted with saturated $NaHCO_3$. The product was extracted with CH_2Cl_2 twice. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to afford aldehyde **13**, which was used for the next reaction without further purification.

To an ice-cold suspension of $[Ph_3P(CH_2)_2CH_3]^+Br^-$ (1.05 g, 2.73 mmol) in THF (7 mL) was added NaHMDS (3.0 mL, 1.0 M solution in THF, 3.0 mmol), and the resulting yellow mixture was stirred at 0°C for 1 h and cool to −78°C. DMF (0.76 mL) and a solution of the above aldehyde in THF (2 mL) were added. The resulting mixture was stirred at −78°C for 2 h, warmed to room temperature slowly, stirred overnight, and diluted with saturated NH_4Cl. The product was extracted with EtOAc twice, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give the residue, which was purified by chromatography on silica gel (hexane/EtOAc) to give olefin **14** (222 mg, 83% from **12**).

To an ice-cold solution of olefin **14** (111.4 mg, 0.378 mmol) in THF (5 mL) was added Cy_2BH (Cy = *c*-C_6H_{11}) (2.3 mL, 0.5 M solution in THF, 1.15 mmol) prepared freshly. The solution was stirred at 0°C for 20 min, and 3 N NaOH (5 mL) and 35% H_2O_2 (5 mL) were added to the solution. The resulting mixture was warmed to room temperature slowly and stirred for 2 h. The product was extracted with Et_2O twice. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to afford the residue, which was purified by chromatography on silica gel (hexane/EtOAc) to give alcohol **15** (90.9 mg, 77%): R_f = 0.41 (hexane/EtOAc 5:1). The ^{1}H NMR spectrum of **15** was identical with that reported (Nonaka et al. 2010).

2-((1*R*,2*S*,3*R*)-3-((Triethylsilyl)oxy)-2-((*Z*)-pent-2-en-1-yl)cyclopentyl)acetic acid (**9**)

To a suspension of MS4A (145 mg) in CH_2Cl_2 (1.0 mL), NMO (50.8 mg, 0.434 mmol), TPAP (10.2 mg, 0.0290 mmol), and a solution of alcohol **15** (90.3 mg, 0.289 mmol) in CH_2Cl_2 (2.0 mL) were added. The mixture was stirred at room temperature for 30 min, and passed through a short column of silica gel (hexane to hexane/EtOAc) to give the corresponding aldehyde, which was used for the next reaction

without further purification: $R_f = 0.77$ (hexane/EtOAc 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.58 (q, $J = 7.5$ Hz, 6 H), 0.96 (t, $J = 7.5$ Hz, 9 H), 0.97 (t, $J = 7.5$ Hz, 3 H), 1.37–2.24 (m, 10 H), 2.39–2.65 (m, 2 H), 4.12–4.20 (m, 1 H), 5.28–5.44 (m, 2 H), 9.74 (t, $J = 1.5$ Hz, 1 H).

To a solution of the above aldehyde in *t*-BuOH (1.0 mL), 2-methyl-2-butene (0.33 mL, 2.9 mmol), phosphate buffer (1.0 mL, pH 6.8), and $NaClO_2$ (44 mg, 80%, 0.43 mmol) were added. The mixture was stirred at room temperature for 2 h and diluted with H_2O. The product was extracted with EtOAc several times. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give acid **9** (80 mg, 85% from **15**): $R_f = 0.35$ (hexane/EtOAc 5:1); $[\alpha]_D^{25}$ +5 (*c* 0.60, $CHCl_3$); IR (neat) 3,000, 1,708, 1,413, 1,017 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.58 (q, $J = 7.5$ Hz, 6 H), 0.96 (t, $J = 7.5$ Hz, 9 H), 0.97 (t, $J = 7.5$ Hz, 3 H), 1.50–1.96 (m, 5 H), 1.96–2.25 (m, 4 H), 2.35–2.57 (m, 3 H), 4.12–4.19 (m, 1 H), 5.30–5.43 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0 (−), 7.0 (+), 14.3 (+), 20.8 (−), 23.2 (−), 29.4 (−), 34.1 (−), 36.0 (+), 36.9 (−), 48.7 (+), 75.3 (+), 128.2 (+), 132.2 (+), 180.7 (−); HRMS (FAB) calcd for $C_{18}H_{35}O_3Si$ [$(M + H)^+$] 327.2355, found 327.2359.

(2*S*,3*S*)-2-(2-((1*R*,2*S*,3*R*)-3-Hydroxy-2-((*Z*)-pent-2-en-1-yl)cyclopentyl)acetamido)-3-methylpentanoic acid (**10**)

To a solution of acid **9** (25.0 mg, 0.0766 mmol) in THF (1 mL), Et_3N (0.014 mL, 0.099 mmol) and $ClCO_2Bu^i$ (0.013 mL, 0.10 mmol) were added. The mixture was stirred at room temperature for 3 h and filtered through a piece of paper. The remaining precipitates were washed with THF (3 mL). A solution of L-isoleucine (50 mg, 0.38 mmol) and Et_3N (0.053 mL, 0.38 mmol) in H_2O (4 mL) was added to the combined filtrates. The mixture was stirred at room temperature for 48 h, and diluted with saturated NH_4Cl. The resulting mixture was extracted with $CHCl_3$ several times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was diluted with HCO_2H (2 mL) at 0°C. After 30 min at 0°C, the solution was concentrated to give a residue, which was purified by chromatography on silica gel ($CHCl_3$/EtOAc/HCO_2H) to give alcohol **10** (17.0 mg, 68%): $R_f = 0.24$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{25}$ +46 (*c* 0.34, $CHCl_3$); IR (neat) 3,355, 3,300, 1,718, 1,457, 1,064 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, $J = 7.5$ Hz, 3 H), 0.95 (d, $J = 7.5$ Hz, 3 H), 0.97 (t, $J = 7.5$ Hz, 3 H), 1.11–1.71 (m, 5 H), 1.82–2.31 (m, 9 H), 2.55 (dd, $J = 14$, 4 Hz, 1 H), 4.23 (t, $J = 4$ Hz, 1 H), 4.61 (dd, $J = 8.5$, 5 Hz, 1 H), 4.0–4.9 (br s, 2 H), 5.33–5.50 (m, 2 H), 6.10 (d, $J = 8.5$ Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7 (+), 14.3 (+), 15.4 (+), 20.8 (−), 23.2 (−), 25.3 (−), 29.0 (−), 33.0 (−), 36.8 (+), 37.8 (+), 38.4 (−), 48.2 (+), 56.5 (+), 75.6 (+), 127.6 (+), 132.9 (+), 173.9 (−), 174.5 (−); HRMS (FAB) calcd for $C_{18}H_{32}NO_4$ [$(M + H)^+$] 326.2331, found 326.2334.

epi-Jasmonoyl-L-isoleucine (**2a**)

To an ice-cold solution of alcohol **10** (12.2 mg, 0.0375 mmol) in acetone (1 mL), Jones reagent (2 drops, 4 M solution) was added dropwise. The mixture was stirred at 0°C for 30 min and *i*-PrOH was added to quench the excess reagent. The mixture was subjected directly to chromatography on silica gel ($CHCl_3$/EtOAc/HCO_2H) to give the isoleucine conjugate **2a** (11.7 mg, 97%): $R_f = 0.32$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{27}$ +59 (*c* 0.35, $CHCl_3$); IR (neat) 3,346, 1,727, 1,641, 1,546 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (t, $J = 7.5$ Hz, 3 H), 0.95 (d, $J = 7.5$ Hz, 3 H), 0.96 (t, $J = 7.5$ Hz, 3 H), 1.16–1.38 (m, 2 H), 1.44–1.54 (m, 1 H), 1.82–2.10 (m, 7 H), 2.19–2.30 (m, 2 H), 2.34–2.44 (m, 2 H), 2.84–2.94 (m, 1 H), 4.63 (dd, $J = 8.5$, 4.5 Hz, 1 H), 5.34 (dt, $J = 10.5$, 7.5 Hz, 1 H), 5.45 (dt, $J = 10.5$, 7.5 Hz, 1 H), 6.30 (d, $J = 8.5$ Hz, 1 H), 6.1–6.8 (br s, 1 H); ^{1}H NMR (500 MHz, CD_3OD) δ 0.93 (t, $J = 7.5$ Hz, 3 H), 0.95 (d, $J = 7.5$ Hz, 3 H), 0.96 (t, $J = 7.5$ Hz, 3 H), 1.20–1.36 (m, 2 H), 1.47–1.56 (m, 1 H), 1.84–2.16 (m, 6 H), 2.17–2.43 (m, 5 H), 2.76–2.90 (m, 1 H), 4.37 (d, $J = 6.0$ Hz, 1 H), 5.32–5.48 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7 (+), 14.2 (+), 15.5 (+), 20.7 (−), 23.0 (−), 25.2 (−), 25.4 (−), 35.3 (−), 35.8 (−), 36.1 (+), 37.6 (+), 53.1 (+), 56.6 (+), 125.5 (+), 133.6 (+), 172.2 (−), 175.3 (−), 219.9 (−); HRMS (FAB) calcd for $C_{18}H_{30}NO_4$ [$(M + H)^+$] 324.2175, found 324.2183.

epi-Jasmonoyl-L-leucine (**2b**)

According to the synthesis of the conjugate **2a**, acid **9** (24.2 mg, 0.0741 mmol) was condensed with L-leucine (48.6 mg, 0.371 mmol) and the TES group was removed with HCO_2H (1 mL) to afford alcohol **16** (15.7 mg, 65%): $R_f = 0.27$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{23}$ +6 (*c* 0.42, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.92–1.00 (m, 9 H), 1.23–1.32 (m, 1 H), 1.53–1.95 (m, 7 H), 1.96–2.47 (m, 6 H), 2.47–2.58 (m, 1 H), 4.19–4.28 (m, 1 H), 4.54–4.66 (m, 1 H), 5.32–5.49 (m, 2 H), 5.6 (br s, 2 H), 6.61 (d, $J = 7.5$ Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (+), 20.8 (−), 21.9 (+), 22.9 (+), 23.2 (−), 24.9 (+), 28.8 (−), 33.1 (−), 36.6 (+), 38.3 (−), 41.2 (−), 48.1 (+), 51.0 (+), 75.3 (+), 127.6 (+), 132.7 (+), 174.5 (−), 176.1 (−).

Alcohol **16** (13.5 mg, 0.0415 mmol) was oxidized with Jones reagent (4 drops, 4 M solution) to give the leucine conjugate **2b** (10.5 mg, 78%): $R_f = 0.32$ ($CHCl_3$/EtOAc/

HCO_2H 14:6:1); $[\alpha]_D^{24}$ +19 (*c* 0.23, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.90–1.04 (m, 9 H), 1.20–1.34 (m, 1 H), 1.50–1.76 (m, 4 H), 1.82–2.13 (m, 5 H), 2.14–2.49 (m, 4 H), 2.84–2.94 (m, 1 H), 4.50–4.72 (m, 1 H), 5.22–5.58 (m, 2 H), 6.17–6.30 (m, 1 H), 6.6 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (+), 20.7 (−), 21.8 (+), 22.9 (+), 25.0 (+), 25.3 (−), 29.8 (−), 35.3 (−), 35.6 (−), 36.0 (+), 41.1 (−), 46.9 (+), 53.1 (+), 125.5 (+), 133.6 (+), 172.5 (−), 173.8 (−), 220.0 (−); HRMS (FAB) calcd for $C_{18}H_{29}NO_4Na$ $[(M + Na)^+]$ 346.1994, found 346.2005.

epi-Jasmonoyl-L-alanine (**2c**)

According to the synthesis of the conjugate **2a**, acid **9** (21.6 mg, 0.0661 mmol) was condensed with L-alanine (29.4 mg, 0.330 mmol) and the TES group was removed with HCO_2H (1 mL) to afford alcohol **17** (11.6 mg, 62%): $R_f = 0.30$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{23}$ +8 (*c* 0.48, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (d, $J = 7$ Hz, 3 H), 0.96 (t, $J = 7.5$ Hz, 3 H), 1.34–1.40 (m, 1 H), 1.54–1.67 (m, 1 H), 1.70–1.95 (m, 4 H), 1.96–2.58 (m, 6 H), 4.21–4.28 (m, 1 H), 4.48–4.62 (m, 1 H), 5.30–5.49 (m, 2 H), 6.0 (br s, 1 H), 6.98 (d, $J = 7.5$ Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (+), 18.2 (+), 19.0 (+), 20.8 (−), 23.2 (−), 28.9 (−), 33.0 (−), 36.6 (+), 38.2 (−), 48.4 (+), 75.4 (+), 127.6 (+), 132.8 (+), 174.3 (−), 175.8 (−).

Alcohol **17** (16.2 mg, 0.0572 mmol) was oxidized with Jones reagent (4 drops, 4 M solution) to give the alanine conjugate **2c** (13.5 mg, 83%): $R_f = 0.33$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{23}$ +18 (*c* 0.17, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.84–1.06 (m, 6 H), 1.24–1.36 (m, 1 H), 1.44–2.74 (m, 10 H), 2.82–2.95 (m, 1 H), 4.58–4.68 (m, 1 H), 5.24–5.58 (m, 2 H), 6.20–6.42 (m, 1 H), 6.4–7.2 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (+), 18.0 (+), 19.0 (+), 20.7 (−), 22.9 (−), 25.3 (−), 35.2 (−), 35.6 (−), 35.9 (+), 53.2 (+), 125.5 (+), 133.6 (+), 172.2 (−), 173.0 (−), 220.1 (−); HRMS (FAB) calcd for $C_{15}H_{24}NO_4$ $[(M + H)^+]$ 282.1705, found 282.1708.

epi-Jasmonoyl-L-valine (**2d**)

According to the synthesis of the conjugate **2a**, acid **9** (21.3 mg, 0.0652 mmol) was condensed with L-valine (38.2 mg, 0.326 mmol) and the TES group was removed with HCO_2H (1 mL) to afford alcohol **18** (12.4 mg, 62%): $R_f = 0.36$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{22}$ +24 (*c* 0.54, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.96–1.00 (m, 9 H), 1.23–1.35 (m, 2 H), 1.57–1.67 (m, 1 H), 1.71–1.95 (m, 3 H), 1.96–2.32 (m, 5 H), 2.36–2.48 (m, 1 H), 2.50–2.58 (m, 1 H), 4.22–4.32 (m, 1 H), 4.52–4.62 (m, 1 H), 5.24–5.61 (m, 2 H), 5.4 (br s, 2 H), 6.62–6.78 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (+), 17.8 (+), 19.0 (+), 20.8 (−), 23.2 (−), 28.8 (−), 31.1 (+), 33.0 (−), 36.7 (+), 38.3 (−), 48.2 (+), 57.2 (+), 75.4 (+), 127.6 (+), 132.8 (+), 174.5 (−), 174.7 (−).

Alcohol **18** (13.8 mg, 0.0443 mmol) was oxidized with Jones reagent (3 drops, 4 M solution) to give the valine conjugate **2d** (13.5 mg, 98%): $R_f = 0.39$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{23}$ +29 (*c* 0.18, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.90–1.02 (m, 9 H), 1.22–1.38 (m, 3 H), 1.56–1.67 (m, 1 H), 1.81–1.92 (m, 1 H), 1.95–2.13 (m, 3 H), 2.16–2.30 (m, 2 H), 2.31–2.44 (m, 2 H), 2.82–2.94 (m, 1 H), 4.54 (br s, 1 H), 5.22–5.58 (m, 2 H), 5.7 (br s, 1 H), 6.23–6.47 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (+), 17.8 (+), 19.1 (+), 20.7 (−), 23.0 (−), 25.4 (−), 30.9 (+), 35.3 (−), 35.8 (−), 36.1 (+), 53.1 (+), 57.1 (+), 125.5 (+), 133.6 (+), 172.4 (−), 175.4 (−), 219.9 (−); HRMS (FAB) calcd for $C_{17}H_{27}NO_4Na$ $[(M + Na)^+]$ 332.1838, found 332.1833.

epi-Jasmonoyl-D-allo-isoleucine (**5**)

According to the synthesis of the conjugate **2a**, acid **9** (26.5 mg, 0.0812 mmol) was condensed with D-allo-isoleucine (53.3 mg, 0.406 mmol) and the TES group was removed with HCO_2H (2 mL) to afford alcohol **19** (12.6 mg, 48%): $R_f = 0.25$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{26}$ +21 (*c* 0.162, $CHCl_3$); IR (neat) 3346 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.80–1.01 (m, 9 H), 1.06–1.20 (m, 1 H), 1.22–1.36 (m, 1 H), 1.38–1.54 (m, 1 H), 1.60–1.71 (m, 1 H), 1.72–1.84 (m, 1 H), 1.85–2.40 (m, 8 H), 2.42–2.58 (m, 2 H), 3.9 (br s, 2 H), 4.30 (s, 1 H), 4.64–4.77 (m, 1 H), 5.32–5.50 (m, 2 H), 6.91 (d, $J = 8.5$ Hz, 1 H).

Alcohol **19** (7.9 mg, 0.024 mmol) was oxidized with Jones reagent (2 drops, 4 M solution) to afford the D-allo-isoleucine conjugate **5** (7.9 mg, 100%): $R_f = 0.32$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); ^1H NMR (500 MHz, $CDCl_3$) δ 0.90 (d, $J = 7$ Hz, 3 H), 0.96 (t, $J = 7$ Hz, 3 H), 0.97 (t, $J = 7$ Hz, 3 H), 1.15–1.36 (m, 3 H), 1.38–1.49 (m, 1 H), 1.81–1.90 (m, 1 H), 1.96–2.10 (m, 5 H), 2.26–2.33 (m, 2 H), 2.34–2.45 (m, 3 H), 2.85–2.95 (m, 1 H), 4.78 (dd, $J = 9, 4$ Hz, 1 H), 5.31–5.38 (m, 1 H), 5.40–5.48 (m, 1 H), 6.42 (d, $J = 9$ Hz, 1 H).

Methyl 2-((1*S*,2*R*)-2-(2-(dimethylamino)-2-oxoethyl)cyclopent-3-en-1-yl)acetate (**21**)

To a solution of alcohol **20** (901 mg, 5.77 mmol) in xylene (12 mL), $MeC(OMe)_2NMe_2$ (4.69 mL, 90% purity, 28.9 mmol) was added. The solution was stirred at 150°C (oil bath temperature) for 24 h, cooled to room temperature, and concentrated. The residue was passed through a column of silica gel (hexane/EtOAc) to give amide **21** (1.19 g, 92%): $R_f = 0.23$ (hexane/EtOAc 1:1); $[\alpha]_D^{26}$ +89 (*c* 1.09, $CHCl_3$); IR (neat) 1,735, 1,636, 1,146 cm^{-1}; ^1H

NMR (300 MHz, $CDCl_3$) δ 2.05 (ddq, $J = 16$, 8, 2 Hz, 1 H), 2.16 (dd, $J = 15$, 9 Hz, 1 H), 2.30 (dd, $J = 15$, 9 Hz, 1 H), 2.35 (dd, $J = 15$, 6 Hz, 1 H), 2.47 (dd, $J = 15$, 7 Hz, 1 H), 2.44–2.56 (m, 1 H), 2.70–2.88 (m, 1 H), 2.95 (s, 3 H), 2.99 (m, 3 H), 3.15–3.27 (m, 1 H), 3.68 (s, 3 H), 5.70–5.80 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.2 (−), 35.2 (−), 35.4 (+), 37.28 (+), 37.31 (−), 43.1 (+), 51.5 (+), 129.8 (+), 134.8 (+), 171.9 (−), 173.6 (−); HRMS (FAB) calcd for $C_{12}H_{19}NO_3Na$ [$(M + Na)^+$] 248.1263, found 248.1263.

2-((1*R*,5*S*)-5-(2-Hydroxyethyl)cyclopent-2-en-1-yl)-*N*,*N*-dimethylacetamide (**22**)

To an ice-cold solution of amide **21** (993 mg, 4.41 mmol) in Et_2O (8.8 mL), EtOH (0.38 mL, 6.62 mmol) and $LiBH_4$ (3.3 mL, 2.0 M solution in THF, 6.6 mmol) were added. The mixture was stirred at room temperature overnight and diluted with H_2O and EtOAc. The organic phase was separated, and the aqueous phase was extracted with EtOAc twice. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc to EtOAc) to give alcohol **22** (652 mg, 75%): $R_f = 0.15$ (EtOAc); $[\alpha]_D^{23}$ +116 (*c* 0.772, $CHCl_3$); IR (neat) 3,405, 1,629, 1,400, 1,055 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.48–1.80 (m, 3 H), 2.03 (ddq, $J = 19$, 11, 2.5 Hz, 1 H), 2.16 (dd, $J = 15$, 9 Hz, 1 H), 2.32–2.50 (m, 3 H), 2.96 (s, 3 H), 2.99 (s, 3 H), 3.08–3.24 (m, 1 H), 3.60–3.78 (m, 2 H), 5.71–5.77 (m, 1 H), 5.78–5.83 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.3 (−), 33.5 (−), 35.6 (+), 37.2 (−), 37.5 (+), 37.8 (+), 43.5 (+), 62.2 (−), 130.2 (+), 135.4 (+), 172.9 (−); HRMS (FAB) calcd for $C_{11}H_{20}NO_2$ [$(M + H)^+$] 198.1494, found 198.1491.

2-((1*R*,5*S*)-5-(2-((4-Methoxybenzyl)oxy)ethyl) cyclopent-2-en-1-yl)-*N*,*N*-dimethylacetamide (**23**)

To an ice-cold mixture of NaH (143 mg, 60% dispersion in mineral oil, 3.58 mmol) in DMF (25 mL) was added alcohol **22** (641 mg, 3.25 mmol) in DMF (8 mL). After 10 min at 0°C, PMBCl (*p*-$MeOC_6H_4CH_2Cl$) (0.488 mL, 3.58 mmol) was added. The mixture was stirred at room temperature for 24 h, and diluted with H_2O. The product was extracted with EtOAc several times. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give the PMB ether **23** (1.03 g, 100%): $R_f = 0.68$ (EtOAc); $[\alpha]_D^{23}$ +101 (*c* 1.11, $CHCl_3$); IR (neat) 1,735, 1,647, 1,248, 1,036 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50–1.66 (m, 1 H), 1.72–1.86 (m, 1 H), 1.93–2.07 (m, 1 H), 2.11 (dd, $J = 15$, 10 Hz, 1 H), 2.31–2.45 (m, 3 H), 2.96 (s, 3 H), 2.99 (s, 3 H), 3.05–3.20 (m, 1 H), 3.41–3.54 (m, 2 H), 3.80 (s, 3 H), 4.44 (s, 2 H), 5.69–5.769 (m, 1 H), 5.78–5.85 (m, 1 H), 6.88 (dm, $J = 9$ Hz, 2 H), 7.22–7.30 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.7 (−), 33.4 (−), 37.2 (−), 37.4 (+), 38.3 (+), 43.6 (+), 55.3 (+), 69.7 (−), 72.8 (−), 113.8 (+), 129.4 (+), 130.2 (+), 130.6 (−), 135.6 (+), 159.5 (−), 172.5 (−); HRMS (FAB) calcd for $C_{19}H_{28}NO_3$ [$(M + H)^+$] 318.2069, found 318.2064.

(3a*R*,4*R*,6*R*,6a*R*)-6-Iodo-4-(2-((4-methoxybenzyl)oxy)ethyl)hexahydro-2*H*-cyclopenta[*b*]furan-2-one (**24**)

To an ice-cold solution of amide **23** (331 mg, 1.04 mmol) in THF (10 mL) and H_2O (10 mL), I_2 (528 mg, 2.08 mmol) was added. The mixture was stirred at room temperature for 3 h and diluted with aqueous $Na_2S_2O_3$. The resulting mixture was extracted with EtOAc twice. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give the residue, which was purified by chromatography on silica gel (hexane/EtOAc) to give iodolactone **24** (307 mg, 71%): $R_f = 0.72$ (hexane/EtOAc 3:1); $[\alpha]_D^{27}$ –11 (*c* 0.99, $CHCl_3$); IR (neat) 1,784, 1,611, 1,512, 1,171 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.60–1.84 (m, 3 H), 2.08 (dd, $J = 15$, 6 Hz, 1 H), 2.49 (dd, $J = 19$, 5 Hz, 1 H), 2.57 (dd, $J = 19$, 10 Hz, 1 H), 2.76–2.93 (m, 1 H), 3.04–3.17 (m, 1 H), 3.38–3.53 (m, 2 H), 3.80 (s, 3 H), 4.38–4.48 (m, 3 H), 5.25 (d, $J = 6.5$ Hz, 1 H), 6.89 (dm, $J = 9$ Hz, 2 H), 7.26 (dm, $J = 9$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.0 (+), 29.0 (−), 30.1 (−), 37.8 (+), 39.3 (+), 40.3 (−), 55.3 (+), 68.4 (−), 72.8 (−), 92.8 (+), 113.9 (+), 129.3 (+), 130.3 (−), 159.3 (−), 176.5 (−); HRMS (FAB) calcd for $C_{17}H_{21}O_4NaI$ [$(M + Na)^+$] 439.0382, found 439.0385.

(1*S*,2*R*,3*S*)-2-(2-Hydroxyethyl)-3-(2-((4-methoxybenzyl)oxy)ethyl)cyclopentanol (**26**)

To a solution of iodolactone **24** (752 mg, 1.81 mmol) in benzene (18 mL), Bu_3SnH (0.974 mL, 3.62 mmol) and AIBN (3.0 mg, 0.018 mmol) were added. After being stirred at 110°C (oil bath temperature) overnight, the solution was cooled to room temperature and diluted with 1 N NaOH. The resulting mixture was extracted with EtOAc twice. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to afford lactone **25**, which was used for the next reaction without further purification: $R_f = 0.52$ (hexane/EtOAc 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17–1.41 (m, 1 H), 1.62–1.80 (m, 4 H), 1.97–2.15 (m, 2 H), 2.41 (dd, $J = 19$, 6 Hz, 1 H), 2.49 (dd, $J = 19$, 10 Hz, 1 H), 2.88–3.01 (m, 1 H), 3.39–3.52 (m, 2 H), 3.81 (s, 3 H), 4.42 (s, 2 H), 5.02 (t, $J = 7$ Hz, 1 H), 6.88 (dm, $J = 8.5$ Hz, 2 H), 7.22 (dm, $J = 8.5$ Hz, 2 H).

To an ice-cold solution of the above lactone in Et_2O (18 mL), $LiAlH_4$ (206 mg, 5.43 mmol) was added at 0°C. After 1 h of stirring at room temperature, the reaction was quenched by the addition of 10% NaOH (1.6 mL) and H_2O (2.0 mL). The resulting mixture was filtered through a pad of Celite, and the filtrate was concentrated to afford the residue, which was passed through a short column of silica gel (hexane/EtOAc to EtOAc) to give diol **26** (445 mg, 84% from **24**): $R_f = 0.38$ (EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40–2.14 (m, 10 H), 2.20–2.80 (m, 2 H), 3.35–3.54 (m, 2 H), 3.64 (ddd, $J = 10$, 9, 4 Hz, 1 H), 3.81 (s, 3 H), 3.75–3.89 (m, 1 H), 4.22–4.30 (m, 1 H), 4.40 (d, $J = 11.5$ Hz, 1 H), 4.44 (d, $J = 11.5$ Hz, 1 H), 6.84–6.92 (m, 2 H), 7.22–7.30 (m, 2 H).

((1*S*,2*R*,3*S*)-3-(2-((4-Methoxybenzyl)oxy)ethyl)-2-(2-((triethylsilyl)oxy)ethyl)-1-((triethylsilyl)oxy))cyclopentane (**27**)

A solution of diol **26** (445 mg, 1.51 mmol), TESCl (0.76 mL, 4.53 mmol), and imidazole (411 mg, 6.44 mmol) in DMF (15 mL) was stirred at room temperature for 18 h, and diluted with saturated $NaHCO_3$. The resulting mixture was extracted with EtOAc twice. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give the residue, which was purified by chromatography on silica gel (hexane/EtOAc) to give TES ether **27** (812 mg, 100%): $R_f = 0.77$ (hexane/EtOAc 3:1); $[\alpha]_D^{27}$ –0.4 (*c* 0.89, $CHCl_3$); IR (neat) 1,513, 1,247, 1,096 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.58 (q, $J = 8$ Hz, 6 H), 0.59 (q, $J = 8$ Hz, 6 H), 0.95 (t, $J = 8$ Hz, 9 H), 0.97 (t, $J = 8$ Hz, 9 H), 1.36–1.86 (m, 9 H), 1.90–2.06 (m, 1 H), 3.34–3.51 (m, 2 H), 3.52–3.64 (m, 1 H), 3.65–3.75 (m, 1 H), 3.80 (s, 3 H), 4.12 (q, $J = 4$ Hz, 1 H), 4.39 (d, $J = 12$ Hz, 1 H), 4.44 (d, $J = 12$ Hz, 1 H), 6.87 (dm, $J = 8.5$ Hz, 2 H), 7.26 (dm, $J = 8.5$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.5 (−), 5.0 (−), 6.9 (+), 7.0 (+), 28.2 (−), 28.6 (−), 31.7 (−), 33.5 (−), 36.3 (+), 44.1 (+), 55.3 (+), 62.6 (−), 69.6 (−), 72.5 (−), 75.4 (−), 76.7 (+), 113.8 (+), 129.2 (+), 131.0 (−), 159.1 (−); HRMS (FAB) calcd for $C_{29}H_{55}O_4Si_2$ [$(M + H)^+$] 523.3639, found 523.3634.

((1*S*,2*R*,3*S*)-3-(2-((4-Methoxybenzyl)oxy)ethyl)-2-((*Z*)-pent-2-en-1-yl)-1-((triethylsilyl)oxy))cyclopentane (**28**)

According to the conversion of silyl ether **12** to the Wittig product **14**, TES ether **27** (300 mg, 0.559 mmol) was converted to the aldehyde with $(COCl)_2$ (0.24 mL, 2.8 mmol), DMSO (0.40 mL, 5.6 mmol), and Et_3N (0.78 mL, 5.59 mmol). The crude aldehyde was subjected to Wittig reaction with anion derived from $[Ph_3P(CH_2)_2CH_3]^+$ Br^- (647 mg, 1.68 mmol) and NaHMDS (1.9 mL, 1.0 M solution in THF, 1.9 mmol) to afford olefin **28** (230 mg, 95% from **27**): $R_f = 0.73$ (hexane/EtOAc 3:1); $[\alpha]_D^{25}$ –27 (*c* 0.43, $CHCl_3$); IR (neat) 1,513, 1,248, 1,006 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.57 (q, $J = 7.5$ Hz, 6 H), 0.95 (t, $J = 7.5$ Hz, 12 H), 1.08–1.44 (m, 3 H), 1.48–1.62 (m, 2 H), 1.64–2.24 (m, 7 H), 3.36–3.52 (m, 2 H), 3.80 (s, 3 H), 4.17 (dt, $J = 3$, 5 Hz, 1 H), 4.40 (d, $J = 11.5$ Hz, 1 H), 4.45 (d, $J = 11.5$ Hz, 1 H), 5.29–5.47 (m, 2 H), 6.87 (dm, $J = 9$ Hz, 2 H), 7.26 (dm, $J = 9$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.1 (−), 7.0 (+), 14.4 (+), 20.7 (−), 25.7 (−), 29.0 (−), 34.1 (−), 35.6 (−), 38.9 (+), 52.3 (+), 55.3 (+), 69.7 (−), 72.6 (−), 74.7 (+), 113.8 (+), 128.8 (+), 129.3 (+), 130.9 (−), 131.8 (+), 159.1 (−); HRMS (FAB) calcd for $C_{26}H_{44}O_3SiNa$ [$(M + Na)^+$] 455.2957, found 455.2963.

2-((1*S*,2*R*,3*S*)-3-((Triethylsilyl)oxy)-2-((*Z*)-pent-2-en-1-yl)cyclopentyl)ethanol (*ent*-**15**)

To an ice-cold solution of the PMB ether **28** (201 mg, 0.465 mmol) in CH_2Cl_2 (4.8 mL), H_2O (0.25 mL) and DDQ (158 mg, 0.696 mmol) were added. The mixture was stirred at 0°C for 3 h and diluted with saturated $NaHCO_3$. The resulting mixture was extracted with EtOAc twice. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc to EtOAc) to give alcohol *ent*-**15** (144 mg, 100%): $R_f = 0.46$ (hexane/EtOAc 3:1); $[\alpha]_D^{24}$ –5 (*c* 0.43, $CHCl_3$); IR (neat) 3,344, 1,056, 1,005 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.58 (q, $J = 8$ Hz, 6 H), 0.95 (t, $J = 8$ Hz, 9 H), 0.96 (t, $J = 7.5$ Hz, 3 H), 1.11–1.46 (m, 4 H), 1.55–2.40 (m, 8 H), 3.56–3.78 (m, 2 H), 4.18 (dt, $J = 5$, 8 Hz, 1 H), 5.31–5.47 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.1, 7.0, 14.4, 20.7, 25.8, 29.0, 34.1, 38.4, 38.9, 52.1, 62.4, 74.7, 128.8, 132.0; HRMS (FAB) calcd for $C_{18}H_{37}O_2Si$ [$(M + H)^+$] 313.2563, found 313.2561.

2-((1*S*,2*R*,3*S*)-3-((Triethylsilyl)oxy)-2-((*Z*)-pent-2-en-1-yl)cyclopentyl)acetic acid (*ent*-**9**)

According to the oxidation of alcohol **15** to acid **9**, alcohol *ent*-**15** (110 mg, 0.353 mmol) was oxidized with NMO (62 mg, 0.53 mmol) and TPAP (12.4 mg, 0.0353 mmol) to give the corresponding aldehyde, which was used for the next reaction without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.58 (q, $J = 8$ Hz, 6 H), 0.95 (t, $J = 8$ Hz, 9 H), 0.96 (t, $J = 7.5$ Hz, 3 H), 1.12–1.42 (m, 2 H), 1.56–1.84 (m, 2 H), 1.96–2.36 (m, 5 H), 2.63 (dq, $J = 2$, 12 Hz, 1 H), 4.19 (dt, $J = 2.5$, 6 Hz, 1 H), 5.32–5.44 (m, 2 H).

The above aldehyde was further oxidized with $NaClO_2$ (60 mg, 80% purity, 0.53 mmol) to afford acid *ent*-**9**

(92.5 mg, 80%): $R_f = 0.37$ (hexane/EtOAc 3:1); $[\alpha]_D^{24}$ +3 (*c* 0.35, $CHCl_3$); IR (neat) 3,100, 1,709, 1,413, 1,057, 1,005, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.57 (q, $J = 8$ Hz, 6 H), 0.95 (t, $J = 8$ Hz, 9 H), 0.96 (t, $J = 7.5$ Hz, 3 H), 1.20–1.42 (m, 2 H), 1.54–1.82 (m, 2 H), 1.96–2.26 (m, 7 H), 2.59 (dd, $J = 13$, 2 Hz, 1 H), 4.19 (dt, $J = 3$, 4.5 Hz, 1 H), 5.34–5.44 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.1 (−), 7.0 (+), 14.3 (+), 20.7 (−), 25.8 (−), 29.1 (−), 34.0 (−), 38.5 (+), 39.8 (−), 51.7 (+), 74.7 (+), 128.2 (+), 132.3 (+), 180.0 (−); HRMS (FAB) calcd for $C_{18}H_{34}O_3SiNa$ [$(M + Na)^+$] 349.2175, found 349.2178.

(2*S*,3*S*)-2-(2-((1*S*,2R*S*,3*S*)-3-Hydroxy-2-((*Z*)-pent-2-en-1-yl)cyclopentyl)acetamido)-3-methylpentanoic acid (**29**)

According to the synthesis of the conjugate **10**, acid *ent*-**9** (50.0 mg, 0.153 mmol) was condensed with L-isoleucine (100 mg, 0.765 mmol) and the TES group was removed with HCO_2H (2 mL) to afford alcohol **29** (25.0 mg, 50%): $R_f = 0.33$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{25}$ +31 (*c* 0.21, $CHCl_3$); IR (neat) 3,346, 1,718, 1,647, 1,214 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, $J = 8$ Hz, 3 H), 0.95 (t, $J = 7$ Hz, 3 H), 0.97 (d, $J = 7$ Hz, 3 H), 1.11–1.72 (m, 4 H), 1.82–2.32 (m, 10 H), 2.56 (dd, $J = 14$, 3 Hz, 1 H), 4.22 (t, $J = 4$ Hz, 1 H), 4.60 (dd, $J = 8$, 4.5 Hz, 1 H), 5.33–5.50 (m, 2 H), 5.8 (br s, 2 H), 6.32 (dd, $J = 8$, 4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7 (+), 14.3 (+), 15.5 (+), 20.7 (−), 25.2 (−), 25.4 (−), 29.2 (−), 33.1 (−), 37.7 (+), 39.3 (+), 41.7 (−), 51.4 (+), 56.6 (+), 74.5 (+), 127.4 (+), 132.9 (+), 173.3 (−), 174.8 (−); HRMS (FAB) calcd for $C_{18}H_{32}NO_4$ [$(M + H)^+$] 326.2331, found 326.2326.

(*ent-epi*-Jasmonoyl)-L-isoleucine (**6**)

According to the synthesis of the conjugate **2a**, alcohol **29** (9.8 mg, 0.030 mmol) was oxidized with Jones reagent (2 drops, 4 M solution) to afford the title conjugate **6** (9.0 mg, 92%): $R_f = 0.42$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{23}$ +6 (*c* 0.18, $CHCl_3$); IR (neat) 3,410, 3,334, 1,646, 1,463 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.94 (t, $J = 7$ Hz, 3 H), 0.95 (t, $J = 7$ Hz, 3 H), 0.96 (d, $J = 7$ Hz, 3 H), 1.16–1.32 (m, 2 H), 1.44–1.56 (m, 1 H), 1.82–2.10 (m, 6 H), 2.18–2.44 (m, 5 H), 2.85–2.94 (m, 1 H), 4.64 (dd, $J = 8.5$, 5 Hz, 1 H), 5.30–5.50 (m, 2 H), 6.21 (d, $J = 8.5$ Hz, 1 H), 7.2 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7 (+), 14.2 (+), 15.6 (+), 20.8 (−), 23.0 (−), 25.2 (–), 25.5 (–), 29.8 (–), 35.3 (–), 35.8 (–), 36.1 (+), 37.6 (+), 53.1 (+), 125.6 (+), 133.6 (+), 172.1 (–), 175.4 (–), 219.8 (–); HRMS (FAB) calcd for $C_{18}H_{30}NO_4$ [$(M + H)^+$] 324.2175, found 324.2173.

2-((1*R*,2*R*,3*S*)-3-((Triethylsilyl)oxy)-2-((*Z*)-pent-2-en-1-yl)cyclopentyl)acetic acid (**31**)

A mixture of ester **30** (50.0 mg, 0.119 mmol, 98% ee) and 3 N NaOH (1 mL) in MeOH (1 mL) and THF (1 mL) was stirred at room temperature for 30 min and acidified with 1 N HCl. The mixture was extracted with EtOAc twice. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give the alcohol acid, which was used for the next reaction without further purification.

To an ice-cold solution of the above alcohol and imidazole (32.4 mg, 0.476 mmol) in DMF (6 mL), TESCl (0.060 mL, 0.36 mmol) was added. The solution was stirred at room temperature for 24 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with EtOAc twice. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to afford TES ether **31** (38.8 mg, 100%): $R_f = 0.37$ (hexane/EtOAc 3:1); $[\alpha]_D^{25}$ +69 (*c* 0.55, $CHCl_3$); IR (neat) 3,000, 1,709, 1,057, 1,005 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.58 (q, $J = 8$ Hz, 6 H), 0.95 (t, $J = 8$ Hz, 9 H), 0.96 (t, $J = 7.5$ Hz, 3 H), 1.20–1.42 (m, 2 H), 1.54–1.66 (m, 1 H), 1.68–1.82 (m, 1 H), 1.96–2.28 (m, 7 H), 2.52–2.66 (m, 1 H), 4.19 (dt, $J = 2.5$, 6 Hz, 1 H), 5.32–5.44 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.1 (−), 7.0 (+), 14.3 (+), 20.7 (−), 25.8 (−), 29.1 (−), 34.0 (−), 38.5 (+), 39.8 (−), 51.7 (+), 74.7 (+), 128.2 (+), 132.3 (+), 179.6 (−); HRMS (FAB) calcd for $C_{18}H_{34}O_3SiNa$ [$(M + Na)^+$] 349.2175, found 349.2172.

2-((1*R*,2*R*,3*S*)-3-Hydroxy-2-((*Z*)-pent-2-en-1-yl)cyclopentyl)-*N*-((2*R*,3*S*)-3-methylpentan-2-yl)acetamide (**32**)

According to the synthesis of the conjugate **10**, acid **31** (25.2 mg, 0.0772 mmol) was condensed with L-isoleucine (50.6 mg, 0.386 mmol) and the TES group was removed with HCO_2H (2 mL) to afford alcohol **32** (15.1 mg, 60%): $R_f = 0.36$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{24}$ +66 (*c* 0.41, $CHCl_3$); IR (neat) 3,313, 1,696, 1,458, 1,249 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, $J = 7.5$ Hz, 3 H), 0.97 (t, $J = 7.5$ Hz, 3 H), 0.98 (d, $J = 7.5$ Hz, 3 H), 1.10–1.74 (m, 6 H), 1.82–2.30 (m, 8 H), 2.55 (dd, $J = 14$, 4 Hz, 1 H), 4.1 (br s, 2 H), 4.23 (t, $J = 4$ Hz, 1 H), 4.60 (dd, $J = 8$, 5 Hz, 1 H), 5.34–5.52 (m, 2 H), 6.23 (d, $J = 8$ Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7 (+), 14.4 (+), 15.6 (+), 20.7 (−), 25.2 (−), 25.5 (−), 29.3 (−), 33.1 (−), 37.6 (+), 39.2 (+), 41.8 (−), 51.4 (+), 56.6 (+), 74.5 (+), 127.4 (+), 133.0 (+), 173.2 (−), 174.9 (−); HRMS (FAB) calcd for $C_{18}H_{32}NO_4$ [$(M + H)^+$] 326.2331, found 326.2324.

Jasmonoyl-L-isoleucine (**7**)

According to the synthesis of the conjugate **2a**, alcohol **32** (10 mg, 0.031 mmol) was oxidized with Jones reagent (2 drops, 4 M solution) to afford the title conjugate **7** (8.8 mg, 89%): $R_f = 0.43$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); mp 153–154°C; $[\alpha]_D^{21}$ –38 (*c* 0.26, MeOH); $[\alpha]_D^{27}$ +3 (*c* 0.22, $CHCl_3$); IR (neat) 3,313, 1,740, 1,701, 1,245 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.94–1.00 (m, 9 H), 1.16–1.28 (m, 2 H), 1.44–1.58 (m, 2 H), 1.88–2.28 (m, 7 H), 2.30–2.43 (m, 3 H), 2.67 (dd, $J = 14.5$, 4.5 Hz, 1 H), 4.62 (dd, $J = 8$, 4.5 Hz, 1 H), 5.29 (dt, $J = 7.5$, 11 Hz, 1 H), 5.46 (dt, $J = 11$, 7.5 Hz, 1 H), 5.6 (br s, 1 H), 6.12 (d, $J = 8$ Hz, 1 H); ^1H NMR (500 MHz, CD_3OD) δ 0.94 (t, $J = 7.5$ Hz, 3 H), 0.96 (d, $J = 7.5$ Hz, 3 H), 0.96 (t, $J = 7.5$ Hz, 3 H), 1.21–1.35 (m, 2 H), 1.48–1.60 (m, 2 H), 1.84–1.96 (m, 2 H), 2.00–2.12 (m, 2 H), 2.13–2.21 (m, 1 H), 2.26–2.41 (m, 5 H), 2.57–2.66 (m, 1 H), 4.36 (d, $J = 5.5$ Hz, 1 H), 5.28 (dt, $J = 6$, 11 Hz, 1 H), 5.43 (dt, $J = 11$, 6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7 (+), 14.2 (+), 15.6 (+), 20.7 (−), 25.2 (−), 25.8 (−), 27.2 (−), 37.6 (+), 37.8 (−), 38.8 (+), 41.1 (−), 54.1 (+), 56.5 (+), 125.3 (+), 134.1 (+), 171.8 (−), 175.5 (−), 219.6 (−); HRMS (FAB) calcd for $C_{18}H_{30}NO_4$ [$(M + H)^+$] 324.2175, found 324.2172.

Cf. lit. mp 155.5–156.5°C; $[\alpha]_D$ –39.7 (*c* 1.6, MeOH) (Fonseca et al. 2009).

2-((1*S*,2*S*,3*R*)-3-((Triethylsilyl)oxy)-2-((*Z*)-pent-2-en-1-yl)cyclopentyl)acetic acid (*ent*-**31**)

According to the synthesis of acid **31**, ester *ent*-**30** (50.3 mg, 0.120 mmol) was hydrolyzed with 3 N NaOH (1 mL) and the resulting alcohol was silylated with TESCl (0.060 mL, 0.36 mmol) to afford the TES ether *ent*-**31** (39.0 mg, 100%): $R_f = 0.37$ (hexane/EtOAc 3:1); ^1H NMR (300 MHz, $CDCl_3$) δ 0.52 (q, $J = 8$ Hz, 6 H), 0.93 (t, $J = 8$ Hz, 12 H), 1.20–1.40 (m, 2 H), 1.54–1.66 (m, 1 H), 1.68–1.81 (m, 1 H), 1.96–2.27 (m, 7 H), 2.54–2.66 (m, 1 H), 4.16–4.22 (m, 1 H), 5.12–5.44 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.5 (−), 6.9 (+), 14.3 (+), 20.7 (−), 25.8 (−), 29.1 (−), 34.0 (−), 38.5 (+), 39.7 (−), 51.7 (+), 74.7 (+), 128.2 (+), 132.3 (+), 179.2 (−); HRMS (FAB) calcd for $C_{18}H_{35}O_3Si$ [$(M + H)^+$] 327.2355, found 327.2359.

2-((1*S*,2*S*,3*R*)-3-Hydroxy-2-((*Z*)-pent-2-en-1-yl)cyclopentyl)-*N*-((2*R*,3*S*)-3-methylpentan-2-yl)acetamide (**33**)

According to the synthesis of the conjugate **10**, acid *ent*-**31** (39.3 mg, 0.120 mmol) was condensed with L-isoleucine (78.7 mg, 0.600 mmol) and the TES group was removed with HCO_2H (2 mL) to afford alcohol **33** (16.1 mg, 41%): $R_f = 0.36$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{25}$ –17 (*c* 0.68, $CHCl_3$); IR (Nujol) 3,312, 1,697, 1,602, 1,249 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89–1.00 (m, 9 H), 1.10–1.72 (m, 5 H), 1.82–2.30 (m, 9 H), 2.56 (dd, $J = 13$, 4 Hz, 1 H), 4.18–4.27 (m, 1 H), 4.60 (dd, $J = 10$, 5 Hz, 1 H), 5.30–5.60 (m, 2 H), 5.7 (br s, 2 H), 6.34 (d, $J = 8$ Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7 (+), 14.4 (+), 15.6 (+), 20.7 (−), 25.2 (−), 25.5 (−), 29.3 (−), 33.1 (−), 37.6 (+), 39.2 (+), 41.8 (−), 51.4 (+), 56.6 (+), 74.5 (+), 127.4 (+), 133.0 (+), 173.2 (−), 175.0 (−); HRMS (FAB) calcd for $C_{18}H_{32}NO_4$ [$(M + H)^+$] 326.2331, found 326.2332.

(*ent*-Jasmonoyl)-L-isoleucine (**8**)

According to the synthesis of the conjugate **2a**, alcohol **33** (11.6 mg, 0.0356 mmol) was oxidized with Jones reagent (2 drops, 4 M solution) to give the title conjugate **8** (10.3 mg, 89%): $R_f = 0.43$ ($CHCl_3$/EtOAc/HCO_2H 14:6:1); $[\alpha]_D^{25}$ +57 (*c* 0.43, $CHCl_3$); IR (Nujol) 3,316, 1,740, 1,696, 1,245 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92–1.00 (m, 9 H), 1.16–1.28 (m, 2 H), 1.44–1.58 (m, 2 H), 1.87–2.28 (m, 7 H), 2.32–2.44 (m, 3 H), 2.68 (dd, $J = 14$, 4 Hz, 1 H), 4.65 (dd, $J = 8.5$, 5 Hz, 1 H), 5.23–5.32 (m, 1 H), 5.42–5.50 (m, 1 H), 6.10 (d, $J = 8.5$ Hz, 1 H), 6.8 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7 (+), 14.2 (+), 15.6 (+), 20.7 (−), 25.2 (−), 25.6 (−), 27.1 (−), 37.7 (+), 37.8 (−), 38.6 (+), 41.3 (−), 54.2 (+), 56.5 (+), 125.1 (+), 134.2 (+), 171.8 (−), 175.5 (−), 219.7 (−); HRMS (FAB) calcd for $C_{18}H_{30}NO_4$ [$(M + H)^+$] 324.2175, found 324.2182.

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