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SYNTHESIS OF CHIRAL ACETYLENIC ANALOGS OF THE PLANT HORMONE ABSCISIC ACID

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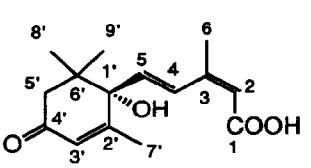
Abstract

Syntheses of optically active acetylenic analogs of abscisic acid are described. The key step involves the diastereoselective alkylation of the (2S,3S)-butanediol ketal of oxoisophorone, which produces a 3:1 mixture of separable diastereoisomers. The absolute stereochemistry of the analogs was established by conversion to a known derivative and by correlation of ORD data.

INTRODUCTION

Optically active analogs of (S)-(+)-abscisic acid (ABA, 1) are becoming increasingly useful tools for probing the stereochemical requirements of plants' recognition responses to the growth regulator ABA. This remarkable plant hormone has pleitropic effects in all higher plants, and is involved in regulating such diverse functions as transpiration, embryo maturation, seed germination and resistance to abiotic stress[1]. In a model study on receptors, optically active analogs were used as probes to define the stereochemical requirements of monoclonal antibodies raised against ABA[2]. Also recently, an array of chiral analogs was used to determine the sub-set of ABA-inducible genes that are involved in regulating germination of dormant wheat seeds[3].

We are constructing arrays of enantiomerically pure analogs with systematic changes to the functional groups of ABA, for the purpose of establishing structure/activity relationships to the different physiological actions of ABA. We wished to expand our library of compounds to include optically active analogs with a triple bond replacing the trans double bond of the sidechain. Previous work had shown the racemic acetylenic ABA analogs to be highly active in a number of ABA assays[4]. For example, racemic acetylenic alcohol **2** had been shown to exhibit antitranspirant activity in conifer seedlings[5], while the corresponding aldehyde **3** proved to be a powerful germination inhibitor and antitranspirant[4]. The biological activity associated with the enantiomerically pure compounds in these systems remains to be investigated.



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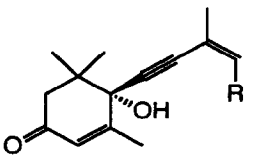


2 R = CH_2OH
3 R = CHO
4 R = CO_2CH_3
5 R = CO_2H

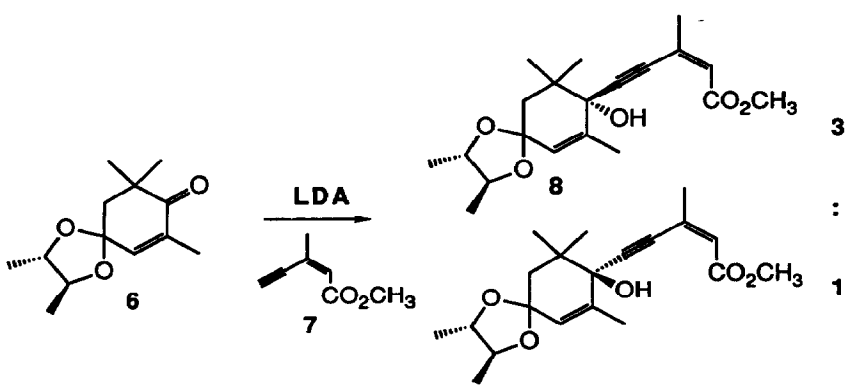
We were unable to separate the racemic mixture of the methyl ester **4** by chiral hplc, a procedure which worked well for the separation of (+)- and (-)- methyl ABA[6], as well as for several other analogs we had previously prepared. Therefore, we sought to develop a versatile synthesis which would lead us to the entire series of optically active compounds **2-5**. The key step was based on the production of diastereoisomers by alkylation of the (2S, 3S)-butanediol ketal of oxoisophorone.

RESULTS AND DISCUSSION

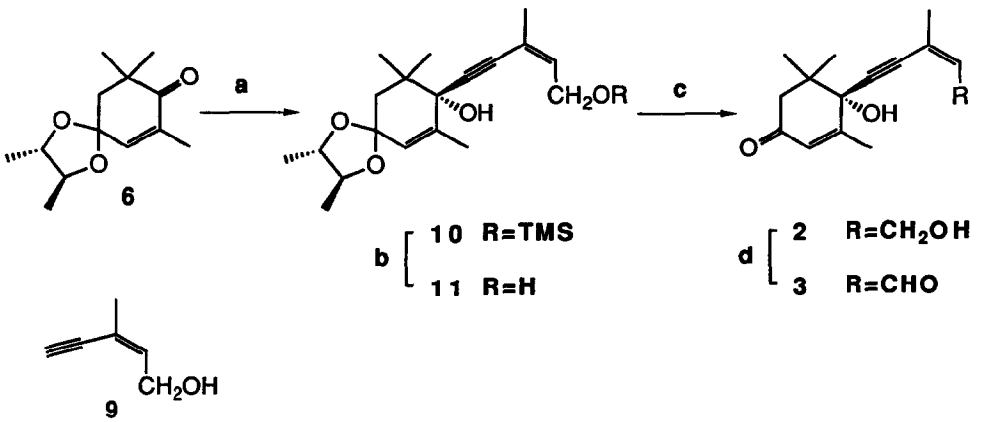
Acetylenic analogs

A high degree of optical purity could be introduced into the acetylenic compounds through the diastereoselective alkylation of the (2S,3S)-butanediol ketal of oxoisophorone **6**. The alkylation of this compound showed a 3:1 facial selectivity. Formation of **6** was high yielding giving complete regioselectivity at the less hindered carbonyl. The major diastereoisomer formed from alkylation of **6** with two different lithium acetylids had the same configuration at C-1' as natural (S)-ABA, (see below). [As expected, alkylation of the (2R,3R)-butanediol ketal of oxoisophorone gave a similar ratio of products, yielding predominantly the diastereoisomer having the same configuration at C-1' as (R)-ABA].

Alkylation of **6** with the lithium anion of cis 5-carbomethoxy-3-methyl-3-penten-1-yne[7] (**7**) produced a 3:1 mixture of diastereoisomers in 71% yield. These were separated with some difficulty by flash chromatography. The major isomer **8** was purified to greater than 99 % as determined by gc. Acetylenic ester **4** was formed by removal of the ketal from **8**, and base hydrolysis gave the acetylenic acid **5**.



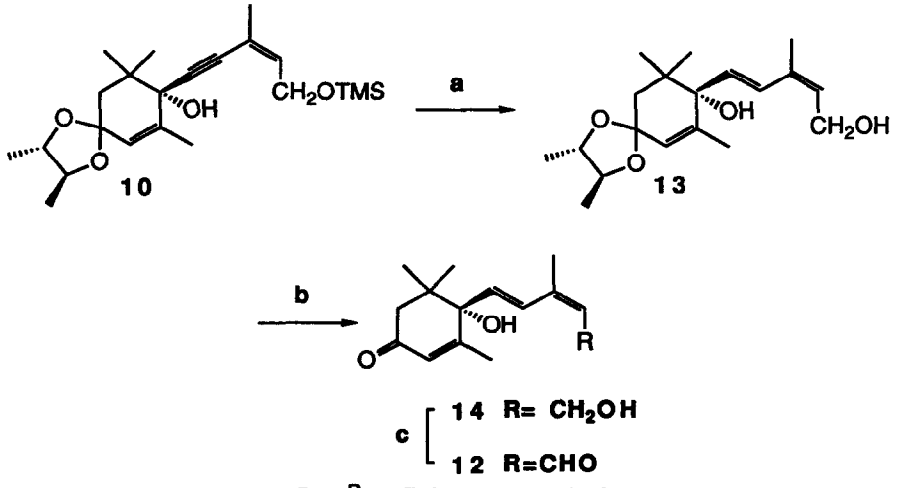
By using a side chain with a lower oxidation level i.e. **9**, we were able to synthesize analogs with either an alcohol or aldehyde at the C-1 position. Alkylation of **6** with the lithium dianion of cis 5-hydroxy-3-methyl-3-penten-1-yne **9**[8] produced a 3:1 mixture of separable diastereoisomers, with the major diastereoisomer **10** having the configuration at C-1' of natural ABA. Compound **10** could be purified to greater than 99% purity as shown by gc. Removal of the protecting silyl group with tetrabutylammonium fluoride generated compound **11** and subsequent deketalization gave the acetylenic analog of abscisyl alcohol, **2**. Oxidation to the aldehyde level was carried out using manganese dioxide, thus affording the acetylenic analog of abscisyl aldehyde **3**, optically pure.



a. nBuLi, **9**; b. Bu_4NF c. pTsOH, acetone; d. MnO_2

Determination of Stereochemistry

The stereochemistry of the C-1' position of compound **10** was determined through conversion to the known compound (+)-abscisyl aldehyde, a synthetic precursor to (S)-(+)-abscisic acid[9].



a. Redal^R; b. pTsOH, acetone; c. MnO_2

The synthesis follows the earlier work of Mayer[10]. Diastereoisomer **10** was modified to (+)-abscisyl aldehyde **12** in 3 steps. Reduction of the double bond using Redal^R (with concurrent removal of the protecting silyl group) produced the diene **13** in 65% yield. Removal of the ketal group to produce abscisyl alcohol **14** was carried out under mildly acidic conditions followed by formation of the aldehyde through a manganese dioxide oxidation. Spectroscopic data for the aldehyde produced compared favourably with that reported previously for (+)-abscisyl aldehyde[9], thus confirming the stereochemistry at the C-1' position of the alkylation product **10**.

Having correlated compound **10** to the known compound (+)-abscisyl aldehyde, the stereochemistry of the acetylenic analogs **2-5** was determined by synthesizing acetylenic ester **8** from the protected acetylenic alcohol **10**. This required only three steps: initial removal of the silyl protecting group with tetrabutylammonium fluoride; a manganese dioxide oxidation; and finally, a Corey oxidation to the methyl ester **8**. Comparison of the optical rotations of compound **8** generated through the two different routes showed that the major diastereoisomer from the alkylation of ketal **6** with either alkyne **7** or **9** has the same configuration at C-1' as (+)-(S)-ABA.

A further proof of stereochemistry came from correlation of the ORD spectra of both enantiomers of methyl ABA and the corresponding acetylenic methyl esters. (+)-(S)-MeABA showed a large, positive Cotton effect as did the (+) form of the acetylenic ester **4**, whereas both (-)-enantiomers showed the corresponding negative Cotton effects. ORD data should prove useful for predicting the absolute stereochemistry of analogs which cannot be chemically transformed into known compounds.

We have developed a route to optically active acetylenic analogs of ABA which should prove to give us considerable insight into the role of ABA as a plant hormone. Tests on the biological activity of these compounds are underway and will be reported elsewhere.

EXPERIMENTAL

General. Melting points were determined with a microscope hot stage apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AM-360-WB (360 MHz) spectrometer, employing $CDCl_3$ as solvent with $CHCl_3$ as reference. For clarity, the conventional ABA numbering system is employed in assignments of peaks in the ^{1}H NMR spectra. IR spectra were obtained with a Perkin Elmer 237B instrument. Optical rotations were obtained from a Perkin-Elmer 141 Polarimeter and were carried out in MeOH. Flash column chromatography was performed using E. Merck silica gel 60 (230 - 400 mesh). E. Merck silica gel 60 F254 plates (0.2 mm) with alumninium sheet backing were used in analytical TLC. Preparative tlc was also performed on the Chromatotron (Harrison Research) with circular glass plates precoated with silica gel F254 (1, 2, or 4 mm), where the radial flow of eluent and sample were centrifugally accelerated. Analysis by gc was carried out using a DB-5 column, 180-240°C @10° / min. GC/MS were obtained by using a DB-5 column (60 m) in a Finnigan 4000 E instrument operated in the electron impact (EIMS) mode or the chemical ionization (CIMS) mode. High resolution electron impact (HREIMS) mass spectra were recorded with a VG 70-250SEQ double-focusing hybrid spectrometer. Mass spectra are reported in mass to charge units (*m/z*).

(2S, 3S)-2,3,7,9,9-pentamethyl-1,4-dioxaspiro[4.5]dec-6-en-8-one, **6**

Oxoisophorone (Fluka, 3.9 g, 25.6 mmol), (2S,3S)-(-)-2,3-butanediol (Aldrich, 3.0 g, 33.3 mmol), p-toluenesulfonic acid monohydrate (150 mg) and benzene (25 ml) were combined and refluxed 4 h using a Dean-Stark trap. The solution was cooled and a saturated $NaHCO_3$ solution was added. The benzene layer was removed and the aqueous layer was washed with ether. The combined organics were washed with brine, dried over Na_2S0_4 and evaporated to afford the crude product. Flash chromatography on silica (ether-hexane, 30:70) afforded compound **6** (5.26 g, 91%). $[\alpha]_D^{20}$ = - 15.7 [MeOH, c 1.24]; HREIMS: [M+] at *m/z* 224.1433 ($C_{13}H_{20}O_3$ requires 224.1412); IR υ_{max} cm^{-1}: 1680 (C=O); ^1H NMR: δ 6.30 (*s*, 1H, C=CH), 3.64 (*m*, 2H, CH-O), 2.10 (*d*, 1H, *J* = 14 Hz, CHH), 2.03 (*d*, 1H, *J* = 14 Hz, CHH), 1.77 (*d*, 3H, *J* = 1Hz, =CCH_3), 1.27 (*d*, 6H, *J* = 5Hz, $OCCH_3$), 1.20 (*s*, 3H, CH_3), 1.15, (*s*, 3H, CH_3); ^{13}C NMR: δ 204.3 (C=O), 141.7 (C=), 135.2 (=C), 102.9, 78.4, 47.5, 42.0, 26.8, 26.2, 16.2, 16.7, 16.6, 16.1.

Acetylenic analog 5

(+)-8(Z)-(2S, 3S, 8R)-8-(5-carbomethoxy-3-methylpent-3-en-1-ynyl)-2, 3, 7, 9, 9-pentamethyl-1,4-dioxaspiro[4.5]dec-6-en-8-ol **8** [and (2S, 3S, 8S)]

A solution of known ester **7**[7](440 mg, 3.6 mmol) in THF was added to a solution of lithium diisopropylamine (3.6 mmol) in THF at -78° and stirred for 10 min. A solution of ketal **6** (532 mg, 1.4 mmol) in THF was added. The temperature of the reaction mixture was allowed to rise to room temperature over 1 h. Saturated aqueous NH_4Cl was added and the product extracted into dichloromethane. The organics were washed with water, brine and dried over Na_2SO_4. Flash chromotography (50:50 ether / hexane) generated 586 mg (71% yield) of a mixture of two diastereoisomers in a GC ratio of 7:2. Further chromatography (15%ether / hexane) gave 308 mg of the major isomer **7** (in greater than 99% purity by GC) a mixed fraction and 55 mg of the minor isomer (95% purity by GC). The major compound showed the following spectral data: $[\alpha]_D^{20}$ = + 152.3 [MeOH, c 1.93]; HREIMS: [M+] at *m/z* 348.1949 ($C_{20}H_{28}O_5$ requires 348.1937); IR υ_{max} cm^{-1}: 3450 (br, O-H), 1700 (C=O); ^1H NMR: δ 5.92 (*m*, 1H-3'), 5.35 (*m*, 1H-2), 3.67 (*s*, 3H-1), 3.54 (*m*, 2H, CH-O), 2.68 (*br s*, 1H, OH), 2.03 (*d*, 1H-5', *J* = 14 Hz), 1.97 (*d*, 3H-6, *J* = 1 Hz), 1.89 (*d*, 3H-7', *J* = 1 Hz), 1.78 (*dd*, 1H-5', *J* = 1, 14 Hz) 1.20 (*d*, 3H, $OCCH_3$, *J* = 3 Hz), 1.18 (*d*, 3H, $OCCH_3$, *J* = 3 Hz), 1.15 (*s*, 3H-8'/9'), 1.07 (*s*, 3H-8'/9').
The minor isomer showed the following spectral properties: $[\alpha]_D^{20}$ = - 63.0 [MeOH, c 0.46]; HREIMS: [M+] at *m/z* 348.1946 ($C_{20}H_{28}O_5$ requires 348.1937); IR υ_{max} cm^{-1}: 3450 (br, O-H), 1710 (C=O); ^1H NMR: δ 5.95 (*s*, 1H-3'), 5.39 (*s*, 1H-2), 3.67 (*s*, 3H-1), 3.60 (*m*, 2H, CH-O), 2.50 (*br s*, 1H, OH), 1.99 (*d*, 3H-6, *J* = 1 Hz, overlapping 1H-5'), 1.93 (*d*, 3H-7', *J* = 1 Hz), 1.87 (*d*, 1H-5', *J* = 14 Hz), 1.21 (*d*, 3H, $OCCH_3$, *J* = 5 Hz), 1.18 (*d*, 3H, $OCCH_3$, *J* = 5 Hz), 1.15 (*s*, 3H-8'/9'), 1.12 (*s*, 3H-8'/9')

(+)-4(Z)-(4R)-4-Hydroxy-4-(5-carboxymethyl-3-methylpent-3-en-1-ynyl)-3, 5, 5-trimethylcyclohex-2-enone, **4**

Ketal **8** (272 mg, 0.78 mmol) was dissolved in 10 ml acetone and stirred with 15 mg of p-toluenesulfonic acid monohydrate overnight. The reaction mixture was quenched with water, extracted into dichloromethane, washed with brine and dried over Na_2SO_4. Purification using the Chromatotron (50% ether/hexane) gave 151 mg (70% yield) of keto ester **4**. $[\alpha]_D^{20}$ = + 238.3 [MeOH, c 1.26]; CIMS: $[M+1]^+$ at *m/z* 277 (15), $[M+18]^+$ at *m/z* 294 (33) ; IR υ_{max} cm^{-1}: 3400 (br, O-H), 1650, (C=O), 1720 (C=O); ^1H NMR: δ 6.01 (*d*, 1H-3', *J* = 1Hz), 5.83 (*d*, 1H-2, *J* = 0.5 Hz), 3.67 (*s*, 3H-1), 3.34 (*br s*, 1H, OH), 2.58 (*d*, 1H-5', *J* = 16 Hz), 2.38 (*d*, 1H-5', *J* = 16 Hz), 2.12 (*d*, 3H-7', *J* = 1 Hz), 2.00 (*d*, 3H-6, *J* = 1 Hz), 1.21 (*s*, 3H-8'/9'), 1.09 (*s*, 3H-8'/9').

(+)-4(Z)-(4R)-4-Hydroxy-4-(5-carboxy-3-methylpent-3-en-1-ynyl)-3, 5, 5-trimethylcyclohex-2-enone, **5**

Ester **4** (106 mg, 0.38 mmol) was dissolved into a mixture of 5 ml of 2N NaOH and 5 ml of methanol. The mixture was stirred at room temperature for 2 h, at which time it was diluted with 10 ml H_2O and washed with CH_2Cl_2 (3x20 ml). The organic layer was discarded and the aqueous layer acidified with 1M HCl and then extracted into CH_2Cl_2 (3x20 ml). The combined organic extracts were washed with brine and dried over Na_2SO_4 to yield, after concentration, 83 mg (83% yield) of pure acid **5**. $[\alpha]_D^{20}$ = + 283.5 [MeOH, c 0.45]; HREIMS: [M+] at *m/z* 262.1216 ($C_{15}H_{18}O_4$ requires 262.1205); IR υ_{max} cm^{-1}: 3300 (br, O-H), 1650, (C=O); ^1H NMR: δ 6.03 (*d*, 1H-3', *J* = 1Hz), 5.86 (*s* , 1H-2), 2.63 (*d*, 1H-5', *J* = 16 Hz), 2.38 (*d*, 1H-5', *J* = 16 Hz), 2.10 (*d*, 3H-7', *J* = 1 Hz), 2.04 (*d*, 3H-6, *J* = 1 Hz), 1.21 (*s*, 3H-8'/9'), 1.09 (*s*, 3H-8'/9').

Acetylenic alcohol ***2*** *and aldehyde* ***3***

(+)-8(Z)-(2S, 3S, 8R)-8-(5-tert-Butyldimethylsiloxy-3-methylpent-3-en-1-ynyl)-2, 3, 7, 9, 9-pentamethyl-1,4-dioxaspiro[4.5]dec-6-en-8-ol **10** [and (2S, 3S, 8S)]

A solution of known alkyne **9**[8] (6.6 g, 31.7 mmol) in dry THF (100 ml) was cooled in a dry ice/acetone bath under an argon atmosphere. n-Butyllithium (Aldrich, 1.6 M in hexane, 18.6ml, 29.5 mmol) was added dropwise with stirring. The reaction solution was kept at -78°C for 1 h, warmed to -40°C for 10 min., then cooled to -78°C again. A solution of chiral ketal **6** (4.73 g, 21.1 mmol) in dry THF (40 ml) was added dropwise. After the addition was complete, the reaction solution was allowed to warm to -10°C (over 30 min.), quenched with water and extracted into ether. The pooled organics were washed with brine and dried over Na_2SO_4. Evaporation of solvents gave a 3:1 ratio of diastereoisomers in 97% yield (8.9 g) after initial flash chromatography. Separation by flash chromatography eluting with ether-hexane (1:9) gave the major compound **10** in >99% purity by GC (4.6 g, 51% yield).

Compound **10**, the major isomer showed the following spectral properties: $[\alpha]_D^{20}$ = + 28.9 [MeOH, c 1.03]; HREIMS: [M+] at *m/z* 434.2870 ($C_{25}H_{42}O_4Si$ requires 434.2852); IR υ_{max} cm^{-1}: 3480 (O-H); ^1H NMR: δ 5.76 (*dt*, 1H-7', *J* = 1, 6 Hz), 5.35 (*bs* , 1H-2), 4.32 (*dd*, 2H-1, *J* = 1, 6 Hz), 3.56 (*m*, 2H, OCH), 2.00 (*d*, 1H-5', *J* = 14 Hz), 1.88 (*d*, 3H-7', *J* = 1 Hz), 1.82 (*d*, 3H-6, *J* = 1 Hz, overlapping 1H-5'), 1.20 (*d*, 3H, $OCCH_3$, *J* = 5.5 Hz), 1.22 (*d*, 3H, $OCCH_3$, *J* = 5.5 Hz), 1.13 (*s*, 3H-8'/9'), 1.08 (*s*, 3H-8'/9'), 0.87 (*s*, 9H, Si^tBu), 0.044 (*s*, 6H, $Si(CH_3)_2$); ^{13}C NMR: δ 140.0 (C=), 137.5 (C=), 125.1 (C=), 117.8 (C=), 103.9, 94.5, 84.2, 75.0, 62.3, 45.6, 39.4, 25.9, 25.7, 22.8, 22.3, 18.6, 18.3, 16.7, 16.7.

The minor isomer showed the following spectral properties: $[\alpha]_D^{20}$ = - 82.8 [MeOH, c 1.16]; HREIMS: [M+] at *m/z* 434.2874 ($C_{25}H_{42}O_4Si$ requires 434.2852); IR υ_{max} cm^{-1}: 3480 (O-H); ^1H NMR: δ 5.75 (*m*, 1H-7'), 5.38 (*s* , 1H-2), 4.32 (*dd*, 2H-1, *J* = 1, 6 Hz), 3.56 (*m*, 2H, OCH_3), 1.90 (*d*, 3H-7', *J* = 1 Hz), 1.82 (*d*, 3H-6, *J* = 1 Hz), 1.22 (*d*, 3H, $OCCH_3$, *J* = 5 Hz), 1.20 (*d*, 3H, $OCCH_3$, *J* = 5 Hz), 1.12 (*s*, 3H-8'/9'), 1.10 (*s*, 3H-8'/9'), 0.87 (*s*, 9H, Si^tBu), 0.04 (*s*, 6H, $Si(CH_3)_2$); ^{13}C NMR: δ 139.4 (C=), 137.4 (C=), 125.3 (C=), 117.9 (C=), 103.9, 94.3, 84.5, 75.0, 62.4, 44.4, 39.1, 25.9, 25.6, 23.6, 22.9, 19.4, 18.3, 16.8, 16.7.

(+)-8(Z)-(2S, 3S, 8R)-8-(5-Hydroxy-3-methylpent-3-en-1-ynyl)-2, 3, 7, 9, 9-pentamethyl-1,4-dioxaspiro[4.5]dec-6-en-8-ol, **11**

To an ice-cooled solution of compound **10** (2.0 g, 4.6 mmol) in dry THF (30 ml) under argon, was added dropwise tetrabutylammonium fluoride (1.0 M in THF, 6.9 ml, 6.9 mmol). The reaction solution was allowed to warm to room temperature. After 1.5 h, water was added and the aqueous layer extracted with ether and chloroform. The pooled organics were dried over Na_2SO_4 and concentrated. Purification by flash chromatography eluting with ether-hexane

(75/25) afforded alcohol **11** (1.35 g, 92%). $[\alpha]_D^{20}$ = + 163.3 [MeOH, c 1.02]; HREIMS: [M+] at *m/z* 320.1959 ($C_{19}H_{28}O_4$ requires 320.1988); IR υ_{max} cm^{-1}: 3400 (br, O-H); ^1H NMR: δ 5.85 (*m*, 1H-3'), 5.34 (*s*, 1H-2), 4.23 (*d*, 2H-1, *J* = 6 Hz), 3.55 (*m*, 2H, OCH), 2.05 (*s*, 1H, OH), 2.02 (*d*, 1H-5', *J* = 14 Hz), 1.88 (*d*, 3H-7', *J* = 1 Hz), 1.84 (*d*, 3H-6, *J* = 1 Hz), 1.22 (*d*, 3H, $OCCH_3$, *J* = 6 Hz), 1.20 (*d*, 3H, $OCCH_3$, *J* = 6 Hz), 1.13 (*s*, 3H-8'/9'), 1.07 (*s*, 3H-8'/9'); ^{13}C NMR: δ 140.3 (C=), 136.1 (C=), 125.1 (C=), 120.6 (C=), 103.9, 94.7, 83.9, 75.0, 61.1, 45.7, 39.5, 25.7, 22.9, 22.1, 18.5, 16.7, 16.6.

(+)-4(Z)-(4R)-4-Hydroxy-4-(5-hydroxy-3-methylpent-3-en-1-ynyl)-3, 5, 5-trimethylcyclohex-2-enone, **2**

Compound **11** (1.3 g), p-toluenesulfonic acid monohydrate (20 mg) and acetone (30 ml) were stirred at room temperature for 6 h. The reaction was then stored at -4° overnight. Solvent volume was reduced and the crude product was purified by flash chromatography eluting with ether-hexane (75/25) to give acetylenic alcohol **2** (550 mg, 55%). $[\alpha]_D^{20}$ = + 255.2 [MeOH, c 1.25]; HREIMS: [M+] at *m/z* 248.1400 ($C_{15}H_{20}O_3$ requires 248.1412); IR υ_{max} cm^{-1}: 3550 (br, O-H), 1665 (s, C=O); ^1H NMR: δ 5.90 (*m*, 1H-3'), 5.82 (*s*, 1H-2), 4.24 (*d*, 2H-1, *J* = 7 Hz), 2.47 (*d*, 1H-5', *J* = 16 Hz), 2.38 (*d*, 1H-5', *J* = 16 Hz), 2.10 (*s*, 3H-7'), 1.85 (*s*, 3H-6), 1.18 (*s*, 3H-8'/9'), 1.08 (*s*, 3H-8'/9'); ^{13}C NMR: δ 198.4 (C=O), 160.3 (C=), 136.8 (C=)m 126.0 (C=), 120.0 (C=), 92.8, 85.3, 74.7, 61.1, 49.2, 41.8, 25.2, 22.9, 21.9, 19.7.

(+)-4(Z)-(4R)-4-Hydroxy-4-(5-oxo-3-methylpent-3-en-1-ynyl)-3, 5, 5-trimethylcyclohex-2-enone, **3**

Compound **2** (230 mg, 0.93 mmol), manganese dioxide (1.5 g, 18.6 mmol) and acetone (20 ml) were stirred at room temperature in a round bottom flask fitted with a drying tube. After 3 h, the reaction mixture was filtered and the residual cake of MnO_2 washed with ether. The combined organics were evaporated and the crude product was purified using the chromatotron eluting with ether-hexane (75/25) to afford aldehyde **3** (462 mg, 54%). $[\alpha]_D^{20}$ = + 308.2 [MeOH, c 1.03]; HREIMS: [M+] at *m/z* 246.1235 ($C_{15}H_{18}O_3$ requires 246.1256); IR υ_{max} cm^{-1}: 3600 (w, O-H), 1675 (s, C=O); ^1H NMR: δ 9.93 (*d*, 1H-1, *J* = 1, 8 Hz), 6.21 (*dd*, 1H-2, *J* = 1.5, 8 Hz), 5.87 (*brd*, 1H-3', *J* =2Hz), 2.94 (*s*, 1H, OH), 2.45 (*d*, 1H-5', *J* = 2 Hz), 2.11 (*s*, 6H-6,7'), 1.21 (*s*, 3H-8'/9'), 1.11 (*s*, 3H-8'/9'); ^{13}C NMR: δ 197.5 (C=O), 191.7 (C=O), 154.6 (C=), 140.7 (C=), 136.1 (C=), 126.6 (C=), 98.9, 83.6, 75.0, 49.1, 42.0, 25.2, 24.7, 21.9, 19.7.

Synthesis of Abscisyl aldehyde, 12

(+)-8(2Z, 4E)-(2S, 3S, 8R)-8-(5-Hydroxy-3-methyl-2,4-pentadienyl)-2, 3, 7, 9, 9-pentamethyl-1,4-dioxaspiro[4.5]dec-6-en-8-ol, **13**

A solution of **10** (2.45 g, 5.6 mmol) in dry THF (100 ml) was cooled in an ice bath under an argon atmosphere. Sodium bis(2-methoxyethoxy) aluminium hydride (Redal^R, Aldrich, 3.4 M in toluene, 4.1 ml, 14 mmol) was added dropwise. After addition, the reaction solution was allowed to warm to room temperature. The reaction was monitored via tlc plates pretreated with 10% $AgNO_3$/ acetonitrile solution. After 2 h, water was carefully added, the THF layer removed and the aqueous layer extracted with ether. The pooled organics were washed with brine, dried over Na_2SO_4, and concentrated. Flash chromatography eluting with ether-hexane (75/25) afforded diene **13** (1.18 g, 65%). $[\alpha]_D^{20}$ = + 239.5 [MeOH, c 1.09]; HREIMS: [M+] at *m/z* 322.2094 ($C_{19}H_{30}O_4$ requires 322.2144); IR υ_{max} cm^{-1}: 3400 (br, O-H); ^1H NMR: δ 6.62 (*d*, 1H-5, *J* = 16 Hz), 5.69 (*d*, 1H-4, *J* = 16 Hz), 5.55 (*t*, 1H-2, *J* = 7 Hz), 5.40 (*s*, 1H-3'), 4.29 (*dd*, 1H-1, *J* = 7, 13 Hz), 4.24 (*dd*, 1H-1, *J* = 7, 13 Hz), 3.55 (*m*, 2H, CH-O), 1.90 (*d*, 1H-5', *J* = 14.5 Hz), 1.82 (*s*, 3H-6), 1.69 (*s*, 3H-7', overlapping 1H-5'), 1.23 (*d*, 3H, $CHCH_3$, *J* = 5.5 Hz), 1.20 (*d*, 3H, $CHCH_3$, *J* = 5.5 Hz), 1.06 (*s*, 3H-8'/9'), 0.87 (*s*, 3H-

8'/9'); ^{13}C NMR: δ 141.5 (C=), 134.8 (C=), 132.2 (C=), 128.4 (C=), 126.5 (C=), 125.5 (C=), 103.9, 79.3, 58.2, 46.2, 39.3, 24.9, 23.2, 20.6, 17.9, 16.7.

(+)-Abscisyl alcohol, **14**

Diene **13** (1.15 g), p-toluenesulfonic acid monohydrate (20 mg) and acetone (30 ml) were stirred at room temperature for 6 h. The reaction was then stored at -4° overnight. Solvent volume was reduced and the crude product was purified by flash chromatography eluting with ether-hexane (75/25) to give abscisyl alcohol (550 mg, 55%). $[\alpha]_D^{20}$ = + 72.5 [MeOH, c 1.25]; HREIMS: [M+] at *m/z* 250.1575 ($C_{15}H_{22}O_3$ requires 250.1569); IR υ_{max} cm^{-1}: 3600 (w, O-H), 1660 (C=O); ^1H NMR: δ 6.72 (*d*, 1H-5, *J* = 16 Hz), 5.89 (*s*, 1H-3'), 5.78 (*d*, 1H-4, *J* = 16 Hz), 5.60 (*m*, 1H-2), 4.27 (*d*, 2H-1, *J* = 5.5 Hz), 2.43 (*d*, 1H-5', *J* = 17 Hz), 2.24 (*d*, 1H-5', *J* = 17 Hz), 1.87 (*s*, 3H-7'), 1.84 (*s*, 3H-6), 1.67 (*bs*, 1H, OH), 1.07 (*s*, 3H-8'/9'), 0.98 (*s*, 3H-8'/9'); ^{13}C NMR: δ 198.0 (C=O), 162.9 (C=), 134.1 (C=), 130.7 (C=), 129.5 (C=), 127.0 (C=), 126.8 (C=), 79.6, 59.2, 58.3, 49.8, 41.4, 24.2, 23.0, 20.6, 18.9, 12.8.

(+)-Abscisyl aldehyde, **12**

Abscisyl alcohol (259 mg, 1.0 mmol), manganese dioxide (1.5 g, 18.6 mmol) and acetone (20 ml) were stirred at room temperature in a round bottom flask fitted with a drying tube. After 3 h, the reaction mixture was filtered and the residual cake of MnO_2 was washed repeatidly with ether. The combined organics were evaporated and the crude product was purified using the chromatotron eluting with ether-hexane (75/25) to afford abscisyl aldehyde, **12** (178 mg, 72%). $[\alpha]_D^{20}$ = + 451.7 [MeOH, c 1.38], lit. value[9] $[\alpha]_D^{20}$ = + 450.5 [EtOH]; HREIMS: [M+] at *m/z* 248.1399 ($C_{15}H_{20}O_3$ requires 248.1412); IR υ_{max} cm^{-1}: 3600 (w, O-H), 1665 (C=O); ^1H NMR: δ 10.16 (*d*, 1H-1, *J* = 8 Hz), 7.46 (*d*, 1H-5, *J* = 15.5 Hz), 6.18 (*d*, 1H-4, *J* = 15.5 Hz), 5.90 (*m*, 2H-2',3), 2.45 (*d*, 1H-5', *J* = 17 Hz), 2.31 (*d*, 1H-5', *J* = 17 Hz), 2.06 (*d*, 3H-6, *J* = 1 Hz), 1.89 (*d*, 3H-7', *J* = 1 Hz), 1.09 (*s*, 3H-8'/9'), 1.01 (*s*, 3H-8'/9'); ^{13}C NMR: δ 197.3 (C=O), 190.1 (C=O), 161.7 (C=), 153.0 (C=), 137.6 (C=), 129.3 (C=), 127.2 (C=), 126.0 (C=), 79.6, 49.7, 41.5, 24.3, 23.0, 21.5, 18.8.

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