= 7.8 Hz), 8.36 (t, 1 H, H-2, $J_{1,2} = J_{2,3} = 6.9$ Hz), 8.26 (d, d, 2 H, H-7,10, $J_{7,8} = J_{9,10} = 7.8$ Hz, $J_{6,7} = J_{10,11} = 8.0$ Hz).

Registry No. $2^+ \cdot BF_4^-$, 99706-25-9; **3**, 35438-63-2; **4**, 99706-18-0; **5**, 99706-19-1; **6**, 99706-20-4; **7**, 99706-21-5; **8**, 99706-22-6; **9**, 99706-23-7; perylene, 198-55-0; *N*-methylformanilide, 93-61-8; diethyl malonate, 105-53-3; β-naphthalenesulfonic acid, 120-18-3; triphenylmethyl tetrafluoroborate, 341-02-6.

An Efficient Synthesis of (±)-Abscisic Acid

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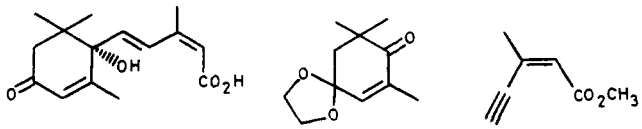
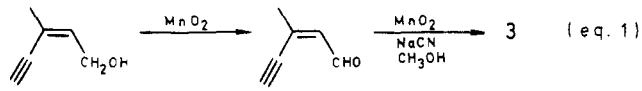
Abscisic acid **1** is a natural product extensively distributed in higher plants and has the important function of regulating the plants' dormancy state, permitting survival in adverse conditions.[1]



1 **2** **3**

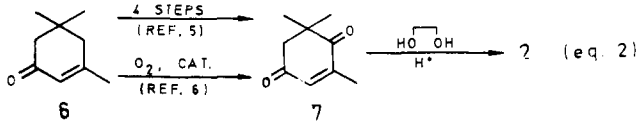
Several syntheses of **1** have been described previously.[2] The observed low to moderate yields are presumably attributable to the highly functionalized molecule. We describe herein an efficient synthesis of (±)-**1** from intermediates **2** and **3** as outlined below.

Allylic oxidation of the commercial alcohol **4** (eq 1) afforded aldehyde **5**.[3] Subsequent oxidation of **5** in the presence of cyanide ion and methanol[4] gave the desired ester **3**.[5]



4 **5** (eq. 1)

A five-step synthesis of compound **2** from isophorone **6** (eq 2) has been described by Marx and Sondheimer.[6] A direct conversion of isophorone to intermediate **7** by air oxidation has also been reported.[7] However, this latter

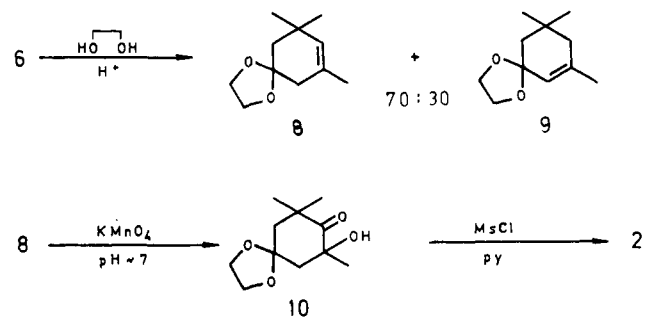


6 **7** (eq. 2)

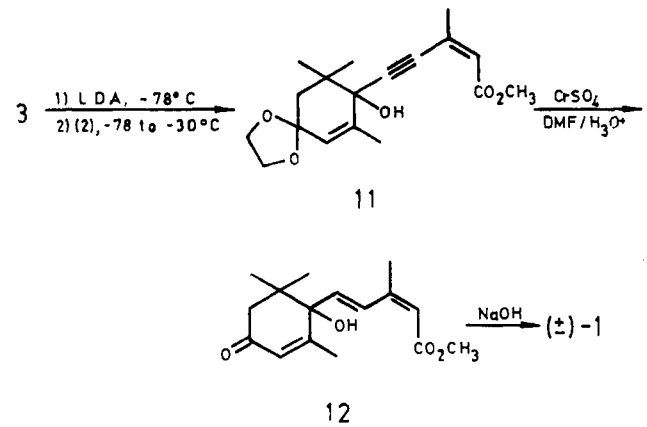
route could not be effected in our hands without extensive polymerization, leading to low yields of **7**. An alternate three-step synthesis of **2** from isophorone was realized as projected in Scheme I.

Treatment of isophorone with ethylene glycol and acid in toluene[8] afforded a 70:30 mixture of ketals **8** and **9** in 88.5% yield. The ketals were readily separated by fractional distillation. Potassium permanganate oxidation of **8** in neutral medium gave **10** (72.5%). Dehydration of **10** was accomplished with methanesulfonyl chloride in refluxing pyridine to afforded enone **2** (63%).

Scheme I



Scheme II



Reaction of the lithium salt of **3** (Scheme II) with enone **2** (−78 → −30 °C) afforded a quantitative yield of **11**. Subsequent reduction of **11** with chromium (II) sulfate[10] resulted in a complex mixture of products from which the methyl ester of (±)-abscisic acid **12** was isolated in 35% yield. Saponification of **12** afforded racemic abscisic acid (80%) as a white crystalline solid.

Experimental Section

Melting points were determined on a Reichert Kofler block melting point apparatus. All melting points and boiling points

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(8) The ketalization of isophorone was described by Babler, Malek, and Coghlan,[9] using a Dean–Stark trap to remove water. We found it preferable to distill out the azeotrope, water/toluene, or for larger amounts to use ethyl orthoformate. Ketal **9** can be converted into a mixture of **8** and **9** in the same original ratio (70:30) by simply stirring at room temperature in dry toluene with a catalytic amount of *p*-toluenesulfonic acid. This mixture can be treated as before to yield additional amounts of **8**.

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are uncorrected. ^{1}H NMR spectra were recorded at 60 or 90 MHz. Chemical shifts are reported in parts per million (δ) relative to Me_4Si as an internal standard, with conventional nomenclature for splitting and coupling constants. Analytical gas chromatography (GLC) separations were performed on a Varian 2800 gas chromatograph. High-performance liquid chromatography (HPLC) separations were performed on a Waters Prep LC/System 500-A, with PrepPAK-500 silica cartridges (5.7 × 30 cm).

2,6,6-Trimethyl-2-hydroxy-4,4-(ethylenedioxy)cyclohexanone (10). To a well-stirred mixture of compound 8[8] (910 mg, 5.0 mmol), water (500 mL), and magnesium sulfate (2.4 g), previously cooled to 4 °C, was added dropwise a solution of potassium permanganate (1.02 g, 6.6 mmol) in water (240 mL), maintaining the temperature of the reaction mixture below 6 °C. After the mixture was stirred for an additional 30 min, enough sodium sulfite was added to decolorize the solution, and the reaction mixture was filtered through Celite. The clear solution was extracted with ethyl ether in a liquid–liquid extractor. The resultant ethereal solution was dried (K_2CO_3) and evaporated to yield 870 mg (72.5%) of **10** as an oil after purification by Kugelrohr distillation: bp 80 °C (0.5 mm); IR (film) 3480, 1710, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.96 (m, 4 H), 2.18 (m, 2 H), 1.98 (m, 2 H), 1.42 (s, 3 H), 1.23 and 1.20 (2 s, 6 H); ^{13}C NMR ($CDCl_3$) δ 216.4 (s), 106.7 (s), 74.4 (s), 64.3 (t), 63.8 (t), 46.6 (t), 46.4 (t), 42.6 (s), 28.0 (q), 27.3 (q), 27.2 (q). Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.58; H, 8.88.

2,6,6-Trimethyl-4,4-(ethylenedioxy)cyclohex-2-en-1-one (2). A solution of compound **10** (15.2 g, 71 mmol) in pyridine (100 mL) was added slowly to a solution of methanesulfonyl chloride (9.75 g, 85 mmol) in pyridine (180 mL) cooled to 4 °C. After being stirred overnight at room temperature, the reaction mixture was heated under reflux for 4 h. After cooling slightly the dark solution was treated with water (120 mL) and allowed to cool to room temperature with stirring. Water was added, and the reaction mixture was extracted with ethyl ether. The organic layer was washed with water, a 20% copper sulfate solution, water, and saturated brine and dried ($MgSO_4$). Evaporation of the solvent and subsequent purification by Kugelrohr distillation yielded 8.8 g (63%) of **2**: bp 65 °C (0.025 mm) [lit.[6] bp 76–80 °C (0.5 mm)]; ^{13}C NMR ($CDCl_3$) δ 203.3 (s), 139.3 (d), 134.8 (s), 103.3 (s), 64.1 (t), 45.7 (t), 41.4 (s), 25.9 (q), 15.6 (q).

Methyl (*Z*)-3-Methyl-2-penten-4-ynoate (3). To a mixture containing methanol (650 mL), activated manganese dioxide[11] (62 g), sodium cyanide (9 g), and glacial acetic acid (3.2 g) was added a solution of the aldehyde **5**[3] (5.1 g, 54 mmol) in methanol (100 mL). The reaction mixture was stirred overnight at room temperature and then filtered at reduced pressure. The solid cake was washed with a 1:1 mixture of methanol and water. The filtrate was diluted with water and extracted with ethyl ether in a continuous liquid–liquid extractor for 12 h. The ethereal solution thus obtained was washed with saturated brine, dried ($MgSO_4$), and evaporated. The residue was distilled under reduced pressure to yield 5.4 g (80%) of **3**: bp 92–93 °C (30 mm); IR (film) 3270, 2950, 2080, 1730, 1630, 1215, 1145, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.07 (m, 1 H), 3.77 (s, 3 H), 3.63 (s, 1 H), 2.08 (d, 3 H, J = 2 Hz); ^{13}C NMR ($CDCl_3$) δ 165.0 (s), 134.0 (s), 126.0 (d), 88.7 (d), 82.0 (s), 51.2 (q), 25.1 (q).

Methyl (*Z*)-3-Methyl-5-[1-hydroxy-2,6,6-trimethyl-4,4-(ethylenedioxy)-2-cyclohexenyl]-2-penten-4-ynoate (11). A solution of the ester **3** (3.7 g, 30 mmol) in tetrahydrofuran (50 mL) was added to a solution of lithium diisopropylamide (30 mmol) in tetrahydrofuran (500 mL) at −78 °C and stirred for 10 min. A solution of compound **2** (5.5 g, 28 mmol) in tetrahydrofuran (100 mL) was added. The temperature of the reaction mixture was allowed to rise slowly to −30 °C (about 45 min) and then maintained for another 45 min. The reaction mixture was quenched by addition of a saturated aqueous solution of ammonium chloride and the product was extracted with ethyl ether. The ethereal layer was washed with water and saturated brine, dried ($MgSO_4$), and evaporated to afford 9.5 g (100%) of crude **11**. Compound **11** was used in the next step without further purification. An analytical sample was prepared by purification through preparative HPLC using as an eluent a mixture of *n*-hexane and ethyl acetate (6:4): IR (film) 3400, 2200, 1710, 1615, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.95 (m, 1 H), 5.35 (br s, 1 H), 3.90 (s, 4 H), 3.75 (s, 3 H), 2.00 (d, 3 H, J = 1 Hz), 1.95 (d, 3 H, J = 1 Hz), 1.15 (s, 3 H), 1.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.0 (s), 140.1 (s), 134.4 (s), 125.6 (d), 123.1 (d), 104.6 (s), 101.4 (s), 85.3 (d), 74.5 (s), 63.9 (t), 63.7 (t), 51.0 (q), 43.3 (t), 39.0 (s), 25.2 (q), 24.7 (q), 22.3 (q), 18.6 (q).

Methyl (2*Z*,4*E*)-3-Methyl-5-(1-hydroxy-2,6,6-trimethyl-4-oxo-2-cyclohexenyl)-2,4-pentadienoate (12). To a solution of **11** (1.0 g, ≃3.1 mmol) in a 2:1 mixture of dimethylformamide and water (375 mL), maintained under an oxygen-free nitrogen atmosphere, was added dropwise an aqueous solution of chromium (II) sulfate[10] until the blue color was no longer discharged. The reaction mixture was stirred at room temperature for 24 h. Water and solid ammonium sulfate were then added, and after being stirred for 30 min, the reaction mixture was extracted with ethyl ether. The organic layer was washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by preparative HPLC, eluting with *n*-hexane/ethyl acetate (4:6) and then with *n*-hexane/ethyl acetate (9:1) to yield 301 mg (35%) of **12**: IR (CCl_4) 3620, 2960, 1715, 1670, 1630, 1600 cm^{-1}; ^{1}H NMR (CCl_4) δ 7.81 (d, 1 H, J = 16 Hz), 6.15 (d, 1 H, J = 16 Hz), 5.83 (br s, 1 H), 5.67 (br s, 1 H), 3.68 (s, 3 H), 2.35 (d, 1 H, J = 17 Hz), 2.20 (d, 1 H, J = 17 Hz), 2.01 (d, 3 H, J = 1 Hz), 1.90 (d, 3 H, J = 1 Hz), 1.10 (s, 3 H), 1.00 (s, 3 H); mass spectrum, m/e (relative intensity) 278 (M^+, 1), 245 (2), 190 (100), 134 (50), 91 (40), 41 (20).

(±)-Abscisic Acid (1). Compound **12** (301 mg, 1.1 mmol) was treated with a solution of sodium hydroxide (12.0 g) in a 2:1 mixture of methanol and water (30 mL). The reaction mixture was stirred at room temperature for 1 h and then diluted with water and acidified with 0.1 N sulfuric acid. The product was extracted with ethyl ether, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was recrystallized from ethyl acetate and petroleum ether to afford 232 mg (80%) of **1** as a white crystalline solid: mp 183–184 °C (lit.[2a] mp 188–190 °C); IR (KBr) 3400, 3200–2300, 1680, 1645, 1625, 1600, 985 cm^{-1}; ^{1}H NMR ($CDCl_3/CD_3OD$) δ 7.73 (d, 1 H, J = 16 Hz), 6.11 (d, 1 H, J = 16 Hz), 5.91 (br s, 1 H), 5.74 (br s, 1 H), 2.41 (d, 1 H, J = 17 Hz), 2.25 (d, 1 H, J = 17 Hz), 1.99 (d, 3 H, J = 1.5 Hz), 1.89 (d, 3 H, J = 1.5 Hz), 1.07 (s, 3 H), 1.00 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 199.3 (s), 167.9 (s), 164.6 (s), 149.3 (s), 136.0 (d), 127.7 (d), 126.0 (d), 118.1 (d), 78.9 (s), 49.2 (t), 41.2 (s), 23.6 (q), 22.5 (q), 20.6 (q), 18.6 (q); mass spectrum, m/e (relative intensity) 264 (M^+, 2), 246 (5), 190 (83), 162 (60), 134 (74), 91 (100).

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Registry No. (±)-1, 14375-45-2; **2**, 14203-64-6; **3**, 99708-52-8; **4**, 6153-05-5; **5**, 52421-93-9; **6**, 78-59-1; **8**, 65339-06-2; **9**, 65339-07-3; (±)-**10**, 99708-51-7; (±)-**11**, 99708-53-9; (±)-**12**, 6901-96-8.

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Synthesis of (3*R*,4*R*)-3-(Benzyloxy)-4-(formyloxy)-1-nitro-1-cyclopentene, a Chiral Synthon for Prostaglandin Syntheses, from D-Glucose

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The conjugate addition of organometallic reagents to activated cyclopentenes has proven to be a potential strategy in the total synthesis of biologically active cyclopentanoid natural products, notably in the prostaglan-

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