Synthesis of Analogs of Optically Active α -Ionylideneacetic Acid

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The Wittig reaction of (–)- α -ionone (VIa) with carbethoxymethylenetriphenylphosphorane afforded (–)-ethyl α -ionylideneacetate (VIIa). *tert*-Butyl chromate oxidation of the above ester (VIIa) gave (–)-ethyl 4'-keto- α -ionylideneacetate (VIIIa). Selenium dioxide oxidation of (–)- α -ionone (IVa) in ethanol afforded (–)-1'-hydroxy- α -ionone (X), which reacted with carbethoxymethylenetriphenylphosphorane to give (–)-ethyl 1'-hydroxy- α -ionylideneacetate (XI). *tert*-Butyl chromate oxidation of the hydroxy-ester (XI) gave (–)-ethyl abscisate (XII) and ethyl 3'-keto- β -ionylideneacetate (XIII). The sensitized photooxidation of ethyl dehydro- β -ionylideneacetate (XVI) using chlorophyll was attempted.

It has already been reported that analogs of ($\pm$)-2-*cis*,4-*trans*- α -ionylideneacetic acid (I),¹⁾ i.e., ($\pm$)-2-*cis*,4-*trans*-4'-keto- α -ionylideneacetic acid (II),¹⁾ ($\pm$)-2-*cis*,4-*trans*-1'-hydroxy- α -ionylideneacetic acid (III),²⁾ have similar activity to (+)-abscisic acid (IV), a plant hormone capable of accelerating abscission. The absolute stereochemistry of (+)-abscisic acid has been deduced as (*S*)-configuration (IVa) by Cornforth *et al.*,³⁾ applying Mills' empirical rule. However, Burden *et al.*⁴⁾ showed that either the structure of (+)-abscisic acid (IVa) or Violaxanthin (V) had to be reversed by the conversion of V to (+)-abscisic acid (IV). The authors have already described the absolute configuration of analogs of optically active α -ionylideneacetic acid, and showed that natural (+)-abscisic acid has the opposite configuration (IVb) to (–)- α -ionone (VIa).⁵⁾ Here, we describe syntheses of optically active α -ionylideneacetic acid and (–)-ethyl abscisate (XII) from VIa in detail.

Resolution of ($\pm$)- α -ionone via the (–)-menthylhydrazone gave (–)- α -ionone (VIa), $[\alpha]_D^{25} = -400^\circ$ ($c=0.5$ in EtOH) and (+)- α -ionone (VIb), $[\alpha]_D^{25} = +260^\circ$ ($c=0.6$ in EtOH) by the method of Sobotka *et al.*⁶⁾ The absolute configuration of VIa has already been elucidated by Eugster *et al.* in 1969.⁷⁾ The Wittig reaction of VIa with carbethoxymethylenetriphenylphosphorane gave (–)-ethyl-2-*cis*

and *trans*,4-*trans*- α -ionylideneacetates (VIIa), which consisted of 2-*cis* isomer (36%) and 2-*trans*-isomer (64%) by gas chromatographical analysis (10% silicone SE-30, AW-DMCS). Alkaline hydrolysis of VIIa gave (–)-2-*trans*,4-*trans*- α -ionylideneacetic acid (VIIc), mp 75~76°C, $[\alpha]_D^{18} = -415^\circ$ ($c=1$ in EtOH) as first crystals from acetonitrile. The mother liquor of the acid, subjected to preparative TLC (thin-layer chromatography) with silica-gel and crystallization from acetonitrile, gave (–)-2-*cis*,4-*trans*- α -ionylideneacetic acid (VIIc), mp 58~59°C, $[\alpha]_D^{18} = -430^\circ$ ($c=1$ in EtOH). Similarly, the reaction of VIb with carbethoxymethylenetriphenylphosphorane gave (+)-ethyl 2-*cis* and *trans*,4-*trans*- α -ionylideneacetates (VIIb). $[\alpha]_D^{18} = +200^\circ$ ($c=0.5$ in EtOH).

tert-Butyl chromate oxidation⁸⁾ of VIIa, followed by silica-gel column chromatography, afforded (–)-ethyl 2-*cis* and *trans*,4-*trans*-4'-keto- α -ionylideneacetates (VIIIa), $[\alpha]_D^{18} = -230^\circ$ ($c=0.8$ in EtOH), consisting of 2-*cis* isomer (35%) and 2-*trans* isomer (65%). Similarly, oxidation of VIIb with *tert*-butyl chromate gave (+)-ethyl 2-*cis* and *trans*,4-*trans*-4'-keto- α -ionylideneacetates (VIIIb), $[\alpha]_D^{18} = +160^\circ$ ($c=1.5$ in EtOH).

Selenium dioxide oxidation⁹⁾ of VIa in ethanol afforded (–)-1'-hydroxy- α -ionone (X), mp 87~88°C, $[\alpha]_D^{18} = -55^\circ$ ($c=2$ in EtOH). Recrystallization of the ketone (X) from *n*-hexane gave X with a higher optical rotation,

SCHEME 1.

SCHEME 2.

FIG. 1. ORD and CD Curves of (—)- α -ionone (VIa) and (—)-1'-Hydroxy- α -ionone (X) in EtOH. 15~150 μ g/ml, 25°C, 1~10 mm path length.

mp 90~91°C, $[\alpha]_D^{12} = -260^\circ$ ($c=0.6$ in EtOH). ORD and CD curves of X are very similar to those of VIa, as shown in Fig. 1, and ORD curves have already been used as evidence for identification of the stereochemistry of steroids without the interaction of introduced groups in the molecules.¹⁰⁾ The retention of configuration in the case of selenium dioxide oxidation in ethanol has been postulated to proceed through SN 2'-type solvolysis.¹¹⁾ However, Bhalerao *et al.*¹²⁾ recently reported that the solvolysis of the allylic selenite ester is best explained as SN i and SN l types of solvolysis. Therefore, it was considered that the retention of configuration in the above oxidation probably occurred by SN i-type solvolysis via the intermediate (IXb) rather than SN 2'-type via IXa.

The reaction of X with carbethoxymethyl-enetriphenylphosphorane afforded (—)-ethyl 2-*cis* and *trans*,4-*trans*-1'-hydroxy- α -ionylideneacetates (XI), $[\alpha]_D^{12} = -280^\circ$ ($c=0.8$ in EtOH), consisting of 2-*cis* isomer (38%) and 2-*trans* isomer (62%). *tert*-Butyl chromate oxidation of XI, followed by separation by means of preparative TLC, gave ethyl 2-*cis* and *trans*,4-*trans*-3'-keto- β -ionylideneacetates (XIII) (57.0% yield) and (—)-ethyl 2-*cis* and *trans*-abscisates

(XII) (5.6% yield).

As shown in Fig. 2, the ORD of (—)-ethyl abscisate (XII) showed a curve opposite to that of (+)-abscisic acid, and the latter curve is very similar to the ORD curve of (+)-ethyl 4'-keto- α -ionylideneacetate (VIIIb) as in the case of the relation of VIa and X.

Further, it is apparent that the differences between the 2-*cis* and *trans* isomers or between the ethyl ester and free acid in analogs of the same optically active α -ionylideneacetic acid do not invert their Cotton effects.⁵⁾ This shows that natural (+)-abscisic acid¹³⁾ has the absolute configuration (IVb). Therefore, it is obvious that the metabolite C¹⁴⁾ and phaseic acid¹⁴⁾ have the configurations (XIV) and (XV), respectively.

On the (*R*, *S*) nomenclature of analogs of abscisic acid there is the ambiguity that the (*S*)-symbol⁷⁾ for (—)- α -ionone with structure (VIa) did not coincide with the (*S*)-symbol⁸⁾ for abscisic acid with structure (IVa), as indicated by Cornforth *et al.* According to the sequence rule,¹⁵⁾ it is obvious that the highest priority is the 1'-OH group and the lowest is the C-5 side chain with regard to the molecular chirality at C-1' of IVa. In comparison between the second set atom at

FIG. 2. ORD Curves of Analogs of Optically Active α -Ionylideneacetic Acid: (–)-Ethyl α -Ionylideneacetate (VIIa) and (–)-Ethyl 1'-Hydroxy- α -ionylideneacetate (XI) in EtOH, (+)-Ethyl 4'-Keto- α -ionylideneacetate (VIIIb) and (–)-Ethyl Abscisate (XII) in 0.005 N- $\text{H}_2\text{SO}_4\text{MeOH}$, Natural (+)-Abscisic Acid (IVb) in 0.005 N- $\text{H}_2\text{SO}_4\text{EtOH}$.

15~150 $\mu\text{g/ml}$, 25°C, 1~10 mm path length.

C-2' (C,C,(C)) and those at C-6' (C,C,C), the authors considered that C-6' precedes C-2' by the phantom atom rule¹⁵⁾: preference of a true atom over a doubly represented atom, and indicated the (S)-symbol for structural formulas (X), (XII) and (IVa), as suggested by Cornforth *et al.*,³⁾ in previous reports.⁵⁾ However, according to IUPAC tentative rules for the nomenclature of organic chemistry (section E) (sequence preference table)¹⁶⁾ an *iso*-propenyl group probably precedes a *tert*-butyl group by subrule 1¹⁵⁾: a decision may be possible at the third set atoms at C-3' (C,(C),H) and C-5' (C,H,H) and C-2' may precede C-6'. This means that abscisic acid with structure (IVa) is indicated by the (R)-symbol, and therefore the (S)-symbol applies for natural (+)-abscisic acid (IVb) and structures (VIIa), (VIIIa), (VIa), as indicated by Eugster *et al.*⁷⁾

In addition, the authors attempted the sensitized photooxidation of methyl dehydro- β -ionylideneacetate (XVI) using chlorophyll and hemoglobin as natural photosensitizers to obtain optically active product. However, optically inactive methyl abscisate (XVII) was obtained in much lower yield than that ob-

tained using rose-bengal¹⁷⁾ as a photosensitizer. This means that natural (+)-abscisic acid (IVb) is probably not produced by sensitized photooxidation of dehydro- β -ionylidene-analogs in plants, as Wright¹⁸⁾ suggested that light is not involved in the biosynthesis of IVb from its unknown precursor. It seems probable that the oxidized product of natural (+)- α -carotene (XVIII) with the same configuration as (+)-abscisic acid (IVb) may be a biosynthetic precursor, besides violaxanthin (V).⁴⁾

EXPERIMENTAL

All mp's and bp's are uncorrected. IR spectra were recorded with a Model IR-E machine of Japan Spectroscopic Co., Ltd. NMR spectra were recorded at 60 MHz with TMS as an internal standard (Model JMN-MH-60-II, Japan Electron Optics Laboratory Co., Ltd.). Gas-liquid chromatography was carried out on a Yanagimoto Model GCG-550T. ORD and CD spectra were recorded at 25°C with a Model ORD/UV-5, Japan Spectroscopic Co., Ltd. and $[\alpha]_D$ values were measured with an Automatic Polarimeter, Model DIP-SL, Japan Spectroscopic Co., Ltd.

1) Optical resolution of (±)- α -ionone

(±)- α -Ionone-(–)-menthylhydrazone, mp 165~

166°C, prepared by the method of Sobotka *et al.*,⁶⁾ was recrystallized from 95% ethanol-acetone (1:1 v/v). Fractional recrystallization gave (+)- α -ionone-(−)-menthylhydrazone, mp 181~182°C, $[\alpha]_D^{18} = +140^\circ$ ($c = 0.5$ in EtOH) as first crystals. From the mother liquor (−)- α -ionone-(−)-menthylhydrazone was obtained, mp 184~185°C, $[\alpha]_D^{18} = -340^\circ$ ($c = 0.5$ in EtOH). Hydrolysis of the above menthylhydrazones using phthalic anhydride, followed by steam distillation, gave (+)- α -ionone (VIb), bp 95~100°C/4 mmHg, $[\alpha]_D^{18} = +260^\circ$ ($c = 0.6$ in EtOH) and (−)- α -ionone (VIa), $[\alpha]_D^{18} = -400^\circ$ ($c = 0.5$ in EtOH). ORD ($c = 0.005$ in EtOH): $[\phi]_{589} -769$, $[\phi]_{340} -1,240$, $[\phi]_{282} -30,770$ (trough), $[\phi]_{237} 0$, $[\phi]_{216} +34,610$ (peak). CD ($c = 0.005$ in EtOH): $[\theta]_{366} 0$, $[\theta]_{317} +3,810$, $[\theta]_{288} 0$, $[\theta]_{244} -50,820$, $[\theta]_{202} 0$.

2) Optically active ethyl α -ionylideneacetates (VIIa and VIIb)

a) (−)-Ethyl 2-*cis* and *trans*, 4-*trans*- α -ionylideneacetates (VIIa). A mixture of 1.7 g of VIa and 3.5 g of carbethoxymethylenetriphenylphosphorane was heated at 170~180°C under nitrogen for 1 hr. After cooling, the reaction mixture was treated with *n*-hexane-ether to separate triphenylphosphine oxide and a residual oil was chromatographed on silica-gel. Elution with benzene gave (−)-ethyl 2-*cis*- and *trans*, 4-*trans*- α -ionylideneacetates (VIIa) as an oil (1.75 g). $[\alpha]_D^{18} = -330^\circ$ ($c = 0.7$ in EtOH). Gas chromatographic analysis using a 1.5 m $\times$ 3 mm column packed with 10% silicone SE-30 on Chromosorb G (AW-DMCS), column temp: 225°C isothermal, He flow rate: 15 cc/min (1.05 kg/cm²), retention time: 3.0 min (36%) (−)-ethyl 2-*cis*, 4-*trans*- α -ionylideneacetate and 3.8 min (64%) (−)-ethyl 2-*trans*, 4-*trans*- α -ionylideneacetate). ORD ($c = 0.01$ in EtOH): $[\phi]_{589} -865$, $[\phi]_{285} -19,960$ (trough), $[\phi]_{265} 0$, $[\phi]_{243} +21,660$ (peak). CD ($c = 0.01$ in EtOH): $[\theta]_{300} 0$, $[\theta]_{260} -50,160$, $[\theta]_{230} 0$. The above esters were hydrolyzed with 10% ethanolic sodium hydroxide at room temperature for 12 hr and the acid fraction obtained was recrystallized from *n*-hexane to give (−)-2-*trans*, 4-*trans*- α -ionylideneacetic acid (VIIc), mp 75~76°C, $[\alpha]_D^{18} = -415^\circ$ ($c = 1$ in EtOH). NMR (CCl₄) δ : 0.87, 0.91 (6H), 1.60 (3H, s), 2.32 (3H, s, 2-*trans*-3-CH₃), 5.40 (1H, s), 5.70 (1H, s). ORD ($c = 0.001$ in EtOH): $[\phi]_{589} -972$, $[\phi]_{278} -28,120$ (trough), $[\phi]_{256} 0$, $[\phi]_{230} +29,290$ (peak). CD ($c = 0.001$ in EtOH): $[\theta]_{300} 0$, $[\theta]_{260} -50,260$, $[\theta]_{230} 0$. From the mother liquor (−)-2-*cis*, 4-*trans*- α -ionylideneacetic acid (VIIc) was separated, mp 58~59°C, $[\alpha]_D^{18} = -430^\circ$ ($c = 1$ in EtOH), by preparative TLC with silica-gel (Merk PF 254), developing with benzene-ethyl acetate (10:1 v/v). NMR (CCl₄) δ : 0.87, 0.91 (6H), 1.60 (3H, s), 2.03 (3H, s, 2-*cis*-3-CH₃), 5.40 (1H, s), 5.60 (1H, s). ORD ($c = 0.015$ in EtOH): $[\phi]_{589} -1,010$, $[\phi]_{282} -24,080$ (trough), $[\phi]_{262} 0$, $[\phi]_{236} +28,890$ (peak).

CD ($c = 0.0015$ in EtOH): $[\theta]_{310} 0$, $[\theta]_{266} -52,970$, $[\theta]_{220} -7,950$.

b) (+)-Ethyl 2-*cis* and *trans*, 4-*trans*- α -ionylideneacetates (VIIb). Similarly, the reaction of VIb with carbethoxymethylenetriphenylphosphorane, followed by silica-gel column chromatography, gave (+)-ethyl α -ionylideneacetate (VIIb) as an oil. $[\alpha]_D^{18} = +200^\circ$ ($c = 0.5$ in EtOH).

3) Optically active ethyl 4'-keto- α -ionylideneacetates (VIIIa and VIIIb)

a) (−)-Ethyl 2-*cis* and *trans*, 4-*trans*-4'-keto- α -ionylideneacetates (VIIIa). A mixture of 1.5 g of VIIa and 40 ml of *tert*-butyl chromate reagent was refluxed with stirring for 6 hr. After excess chromate was decomposed with aqueous oxalic acid, the resulting mixture was extracted with ether. The ether layer was washed with aqueous NaHCO₃ and dried over anhyd. MgSO₄. Evaporation of the ether gave a residual oil, which was chromatographed on silica-gel. Elution with benzene-ethyl acetate (9:1 v/v) afforded 200 mg of (−)-ethyl 2-*cis* and *trans*, 4-*trans*-4'-keto- α -ionylideneacetates (VIIIa) as an oil. $[\alpha]_D^{12} = -230^\circ$ ($c = 0.8$ in EtOH). NMR (CCl₄) δ : 1.01, 1.10 (6H), 1.30 (3H, t, $J = 7$ cps), 1.92 (3H, s), 2.05 (s, 35% of 2-*cis*-3-CH₃), 2.30 (s, 65% of 2-*trans*-3-CH₃), 4.12 (2H, q, $J = 7$ cps), 5.77 (s), 6.10 (s), 7.61 (d, $J = 15$ cps). IR $\nu_{\text{max}}^{\text{film}}$ cm^{−1}: 1720, 1670, 1630, 1370, 1230, 1160, 1045, 980, 880. ORD ($c = 0.0082$ in 0.005 N-H₂SO₄ EtOH): $[\phi]_{589} -636$, $[\phi]_{283} -40,440$ (trough), $[\phi]_{266} 0$, $[\phi]_{242} +60,800$ (peak), $[\phi]_{216} 0$, $[\phi]_{202} -15,200$. CD ($c = 0.0082$ in 0.005 N-H₂SO₄ EtOH): $[\theta]_{365} 0$, $[\theta]_{318} +5,610$, $[\theta]_{300} 0$, $[\theta]_{266} -66,660$, $[\theta]_{244} 0$, $[\theta]_{233} +33,330$.

b) (+)-Ethyl 2-*cis* and *trans*, 4-*trans*-4'-keto- α -ionylideneacetates (VIIIb). Similarly, *tert*-butyl chromate oxidation of 2.0 g of VIIb, followed by silica-gel column chromatography, afforded 300 mg of (+)-ethyl 4'-keto- α -ionylideneacetates (VIIIb) as an oily mixture of 2-*cis* and *trans* forms. $[\alpha]_D^{18} = +160^\circ$ ($c = 1.5$ in EtOH). Gas chromatographic analysis was carried out using the same column and column conditions as in 2), retention time: 6.2 min (35.1%) (+)-ethyl 2-*cis*, 4-*trans*-4'-keto- α -ionylideneacetate and 8.2 min (64.9%) (+)-ethyl 2-*trans*, 4-*trans*-4'-keto- α -ionylideneacetate. ORD ($c = 0.0015$ in 0.005 N-H₂SO₄ MeOH): $[\phi]_{589} +442$, $[\phi]_{283} +29,480$ (peak), $[\phi]_{266} 0$, $[\phi]_{242} -49,750$ (trough), $[\phi]_{212} 0$, $[\phi]_{204} +9,220$. CD ($c = 0.0015$ in 0.005 N-H₂SO₄ MeOH): $[\theta]_{370} 0$, $[\theta]_{318} -3,660$, $[\theta]_{300} 0$, $[\theta]_{266} +40,690$, $[\theta]_{232} -24,320$.

4) SeO₂ oxidation of (−)- α -ionone (VIa)

To a stirred solution of 1.7 g of (−)- α -ionone (VIa) in 100 ml of 95% ethanol was added dropwise an ethanolic SeO₂ solution (prepared from 780 mg of

SeO₂ and 150 ml of 95% ethanol) at room temperature for 6 hr and the mixture was refluxed for 16 hr. The reaction mixture was evaporated under reduced pressure and the mixture obtained was treated with active charcoal in ethanol to give a brown oil, which was chromatographed on silica-gel. Elution with *n*-hexane-ether (1:1 v/v) gave 400 mg of (–)-1'-hydroxy-*α*-ionone (X), mp 87~88°C (from *n*-hexane), $[\alpha]_D^{18} = -55^\circ$ (*c*=2 in EtOH). Recrystallization of the above ketone from *n*-hexane gave (–)-1'-hydroxy-*α*-ionone (X) with higher optical rotation as last crystals, mp 90~91°C (needles), $[\alpha]_D^{12} = -260^\circ$ (*c*=0.6 in EtOH). ORD (*c*=0.012 in EtOH): $[\phi]_{589} -542$, $[\phi]_{380} -1,458$ (trough), $[\phi]_{352} -1,187$ (peak), $[\phi]_{264} -24,300$ (trough), $[\phi]_{239} 0$, $[\phi]_{220} +26,040$ (a shoulder), $[\phi]_{202} +48,600$, CD (*c*=0.012 in EtOH): $[\theta]_{366} 0$, $[\theta]_{316} +528$, $[\theta]_{287} 0$, $[\theta]_{244} -40,260$.

5) *tert*-Butyl chromate oxidation of (+)-*α*-ionone (VIb)

A mixture of 2.8 g of (+)-*α*-ionone (VIb) and 40 ml of *tert*-butyl chromate reagent in 10 ml of *tert*-butanol was refluxed with stirring for 5 hr. After decomposition of excess chromate with aqueous oxalic acid, the reaction mixture was extracted with ether. The ether extract was washed with aqueous NaHCO₃ and dried over anhyd. MgSO₄. Evaporation of the ether gave a residual oil, which was chromatographed on silica-gel. Elution with benzene-ethyl acetate (1:1 v/v) gave 470 mg of (+)-4'-keto-*α*-ionone as an oil, $[\alpha]_D^{18} = +10^\circ$ (*c*=2.3 in EtOH), IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 1670, 1610, 1360, 1245, 1150, 1025, 980, and then almost racemized 1'-hydroxy-4'-keto-*α*-ionone, mp 110°C, $[\alpha]_D^{18} = +2.1$ (*c*=6 in EtOH).

6) (–)-Ethyl 2-*cis* and *trans*,4-*trans*-1'-hydroxy-*α*-ionylideneacetate (XI)

A mixture of 50 mg of (–)-1'-hydroxy-*α*-ionone (X) and 180 mg of carbethoxymethylenetriphenylphosphorane was heated under nitrogen at 150°C for 1.5 hr. After cooling, the reaction mixture was chromatographed on silica-gel. Elution with benzene-ethyl acetate (9:1 v/v) afforded 30 mg of (–)-ethyl 2-*cis* and *trans*,4-*trans*-1'-hydroxy-*α*-ionylideneacetates (XI) as an oil. $[\alpha]_D^{12} = -280^\circ$ (*c*=0.8 in EtOH). IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 3540, 1720, 1610, 1230, 1130, 1040, 980, 865, 830. Gas chromatographic analysis was carried out using the same column and column conditions described in 2), retention time: 4.6 min (38.3% (–)-ethyl 2-*cis*,4-*trans*-1'-hydroxy-*α*-ionylideneacetate) and 6.3 min (61.7% (–)-2-*trans*,4-*trans*-1'-hydroxy-*α*-ionylideneacetate). ORD (*c*=0.0015 in EtOH): $[\phi]_{589} -780$, $[\phi]_{284} -25,970$ (trough), $[\phi]_{265} 0$, $[\phi]_{240} +27,840$ (peak), $[\phi]_{216} +16,680$ (trough), $[\phi]_{204} +33,360$. CD (*c*=0.0015 in EtOH): $[\theta]_{310} 0$, $[\theta]_{267} -12,990$, $[\theta]_{230} 0$.

7) *tert*-Butyl chromate oxidation of (–)-ethyl 1'-hydroxy-*α*-ionylideneacetates (XI)

A solution of 25 mg of XI in 1 ml of benzene and

3.5 ml of *tert*-butyl chromate reagent in 10 ml of *tert*-butanol was stirred at 35~45°C for 2 hr. After decomposition of excess chromate with aqueous oxalic acid, the reaction mixture was extracted with ether. The ether extract was washed with aqueous NaHCO₃ and dried over anhyd. MgSO₄. Evaporation of the ether gave a residual oil. Preparative TLC with silica-gel (Merk PF 254), developing with benzene-ethyl acetate (10:1 v/v), afforded 11.4 mg (57.0% yield) of ethyl 2-*cis* and *trans*,4-*trans*-3'-keto-*β*-ionylideneacetates (XIII) as an oil, IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 1720, 1668, 1610, 1230, 1155, 1040, 970, 880, and then 1.4 mg (5.6% yield) of (–)-ethyl 2-*cis* and *trans*-abscisates (XII) as an oil. ORD (*c*=0.0028 in 0.005 N-H₂SO₄-MeOH): $[\phi]_{330} -1,623$, $[\phi]_{285} -11,910$ (trough), $[\phi]_{268} 0$, $[\phi]_{244} +28,850$ (peak), $[\phi]_{220} 0$, $[\phi]_{210} -3,250$. CD (*c*=0.0028 in 0.005 N H₂SO₄-MeOH): $[\theta]_{360} 0$, $[\theta]_{318} +1,620$, $[\theta]_{266} -27,060$, $[\theta]_{245} 0$, $[\theta]_{232} +9,636$, $[\theta]_{213} 0$. Selection of the best experimental condition for the above oxidation was attempted for (±)-ethyl 2-*cis* and *trans*-1'-hydroxy-*α*-ionylideneacetates, prepared from (±)-1'-hydroxy-*α*-ionone, on a larger scale than that described above. (±)-2-*Cis* and *trans*-abscisates and ethyl 2-*cis* and *trans*-3'-keto-*β*-ionylideneacetates were obtained in the same way. Gas chromatographic analysis of the former was carried out using the same column and column conditions described in 2), retention time: 9.2 min (38% ethyl 2-*cis*-abscisate) and 11.6 min (62% ethyl 2-*trans*-abscisate). Hydrolysis of (±)-ethyl 2-*cis* and *trans*-abscisates with 10% ethanolic sodium hydroxide, followed by recrystallization from benzene-ethyl acetate, gave (±)-2-*cis*-abscisic acid, mp 189~190°C and (±)-2-*trans*-abscisic acid, mp 151~152°C.

8) Sensitized photooxidation of methyl dehydro-*β*-ionylideneacetates (XVI) using natural photosensitizers

a) *Using chlorophyll-Cu, Na salt.* A mixture of 2.0 g methyl dehydro-*β*-ionylideneacetates (XVI), a stereoisomeric mixture of 2-*cis* form (33%, retention time: 3.2 min by gas chromatographic analysis using the same column and column conditions described in 2)) and 2-*trans* form (67%, retention time: 3.6 min), and 1.0 g of chlorophyll-Cu, Na salt (Nakarai Chemicals, Ltd.) in 250 ml of methanol was shaken under oxygen while being illuminated with a 20 W fluorescent lamp at 5°C for 50 hr. After evaporation of the methanol, the residue was treated with basic alumina for 2 hr and chromatographed twice on alumina. Elution with benzene-ether afforded 80 mg of hydroxy-keto-esters as an oil, $[\alpha]_D^{12} = 0$ (*c*=0.25 in EtOH), IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 3510, 1720, 1660, 1610, which consisted of 9 products (*R_f*: 0.66, 0.55, 0.48, 0.41, 0.31, 0.24, 0.18, 0.12 (methyl 2-*cis*-abscisate), 0.07 (methyl 2-*trans*-abscisate) on TLC (Merk, silica-gel H), developing with benzene-ethyl acetate (10:1 v/v). Preparative

TLC with silica-gel (Merk PF 254), developing with benzene-ethyl acetate, afforded 14 mg of methyl 2-*cis* and *trans* abscisates (XVII). $[\alpha]_D^{25}=0$ (in EtOH).

b) *Using chlorophyll-Fe, Na salt.* Similarly, photosensitized oxygenation of XVI (2.0 g) using 1.0 g of chlorophyll-Fe, Na salt (Nakarai Chemicals, Ltd.) in 250 ml of methanol, followed by treatment with basic alumina, gave 196 mg of hydroxy-keto-esters as an oil, $[\alpha]_D^{13}=0$ ($c=0.6$ in EtOH), which consisted of 5 products (*Rf*: 0.55, 0.41, 0.31, 0.12, 0.07 in the same TLC as described in a). Preparative TLC afforded 16 mg of XVII. $[\alpha]_D^{25}=0$ (in EtOH).

c) *Using hemoglobin.* Similarly, sensitized photo-oxidation of 2.0 g of XVI using 1.0 g of hemoglobin (Tokyo Kasei Chemicals, Ltd.) afforded 115 mg of hydroxyketo-esters as an oil, $[\alpha]_D^{12}=0$ ($c=0.2$ in EtOH), which consisted of 7 products (*Rf*: 0.55, 0.41, 0.31, 0.24, 0.18, 0.12, 0.07 in the same TLC as described in a)). Preparative TLC gave about 10 mg of XVII. $[\alpha]_D^{25}=0$ (in EtOH). Photosensitized oxygenation of XVI (2.0 g) using rose-bengal (200 mg) in 250 ml of methanol for 24 hr, followed by treatment with basic alumina, gave XVII in 50% yield.

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Note Added in Proof. After our preliminary reports⁵¹ published, the same absolute configuration of natural (+)-abscisic acid was recently reported: G. Ryback, *Chem. Commun.*, **1972**, 1190.