

SYNTHESIS OF OPTICAL ACTIVE ABSICISIC ACID AND ITS ANALOGS\*

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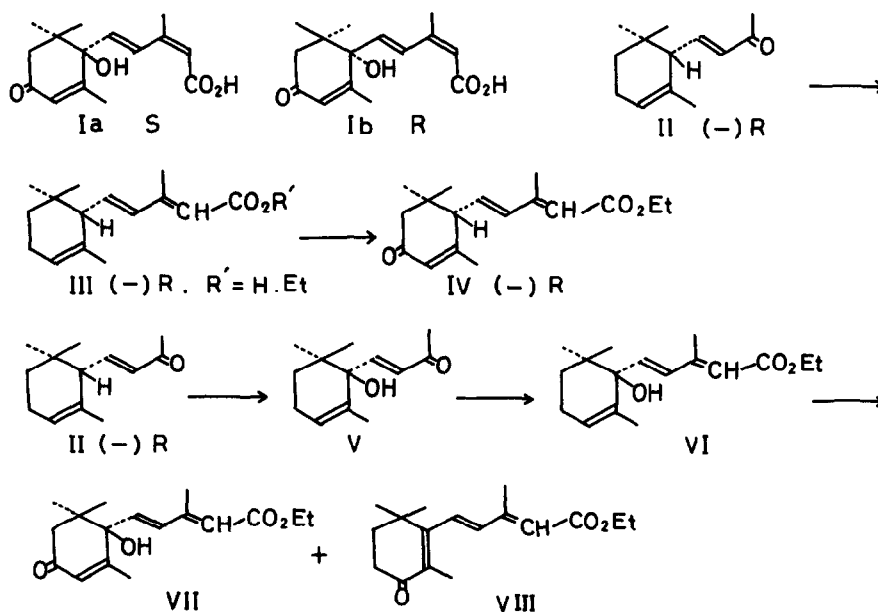
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The absolute stereochemistry of (+)-abscisic acid<sup>1)</sup> has been deduced as the (S)-configuration (Ia) by applying Mills' empirical rule by Cornforth et al<sup>2)</sup> in 1967. But, Burden et al<sup>3)</sup> reported that violaxanthin could be converted to (+)-abscisic acid by chemical transformation and either of the both structures had to be reversible. The authors think that the application of Mills' rule to the diol-esters derived from optical active abscisic acid first need the condition applying the rule of optical superposition<sup>4)</sup> and these diol-esters don't provide the condition. The determination of the configuration of (+)-abscisic acid only by the application of Mills' empirical rule may not be proper. Here, we synthesized (-)-ethyl abscisate (VII) from (-)-(R)- $\alpha$ -ionone(II) and suggest that (+)-abscisic acid has the (R)-configuration (Ib) by the measurement of the CD values of its analogs as follows.

The configurational nomenclature of (-)- $\alpha$ -ionone with the structural formula (II) was presented by the (S)-symbol<sup>5)</sup>, but, is corrected to the (R)-symbol by Sequence rule: the supplementary rule of Ligancy<sup>6)</sup>. The Wittig reaction of II with carbethoxymethylenetriphenylphosphorane gave (-)-(R)-ethyl  $\alpha$ -ionylideneacetate (III, R' = Et),  $[\alpha]_D^{18} = -330^\circ$  (C = 0.5 in EtOH), consisted of 2-cis isomer (36 %) and 2-trans isomer (64 %) by g. l. c. (SE-30). Alkaline hydrolysis of III (R' = Et) gave (-)-(R)-2-cis- $\alpha$ -ionylideneacetic acid (III, R' = H), mp 58-59°  $[\alpha]_D^{18} = -430^\circ$  (C = 1 in EtOH) and (-)-(R)-2-trans- $\alpha$ -ionylideneacetic acid (III, R' = H), mp 75-76°,  $[\alpha]_D^{18} = -415^\circ$  (C = 1 in EtOH). The tert-butyl chromate oxidation of III (R' = Et) afforded (-)-(R)-ethyl 4'-keto- $\alpha$ -ionylideneacetate (IV)<sup>7)</sup>,  $[\alpha]_D^{12} = -230^\circ$  (C = 0.8 in EtOH), consisted of 2-cis isomer (35 %) and 2-trans isomer (65 %). Selenium dioxide oxidation<sup>8)</sup> of II in ethanol gave

(-)-1'-hydroxy- $\alpha$ -ionone (V), mp 90-91 $^{\circ}$ ,  $[\alpha]_D^{12} = -260^{\circ}$  (C = 0.6 in EtOH). The reaction<sup>9)</sup> of V with carbethoxymethylenetriphenylphosphorane afforded (-)-ethyl 1'-hydroxy- $\alpha$ -ionylideneacetate (VI),  $[\alpha]_D^{12} = -280^{\circ}$  (C = 0.8 in EtOH), consisted of 2-cis isomer (38 %) and 2-trans isomer (62 %). The tert-butyl chromate oxidation of VI gave ethyl 3'-keto- $\beta$ -ionylideneacetate (VII)<sup>7)</sup> (57.0 % yield) and (-)-ethyl abscisate (VIII) (5.6 % yield), consisted of 2-cis and trans isomers.

The partial retention of configuration in the case of selenium dioxide oxidation in ethanol was already known about the oxidation of (+)-limonene<sup>10)</sup> and (+)-p-menth-3-ene<sup>11)</sup>. The ORD and CD curves of V and VI are very similar to those of II and III respectively, the ORD curve has been used as the proof for the identification of stereochemistry of steroids<sup>12)</sup> without the interaction for the introduced group in molecules. These facts suggest that V and VI have the (S)-configuration as shown in Scheme.



Scheme

Table 1. The Relation of CD and the Structures (A and B) in Analogs of Optical Active  $\alpha$ -Ionylideneacetic Acid

Compd.	Obs. UV $\lambda_{max}$ (nm)	CD Values		Structure (Head group)
		$\Delta \epsilon_1$ (nm)	$\Delta \epsilon_2$ (nm)	
(-)-(R)- $\alpha$ -Ionone (II)	228.5	-15.4 (244) +1.2 (317)		A (H)
(-)-1'-Hydroxy- $\alpha$ -ionone (V)	231.5	-12.2 (244) +0.2 (316)		A <sup>c</sup> (OH)
(-)-(R)-2-cis- $\alpha$ -Ionylideneacetic acid (III, R' = H)	265.5	-16.1 (265.5)		A (H)
(-)-(R)-2-trans- $\alpha$ -Ionylideneacetic acid (III, R' = H)	260	-15.2 (260)		A (H)
(-)-(R)-Ethyl $\alpha$ -ionylideneacetate (III, R' = Et)	268	-11.7 (268)		A (H)
(-)-Ethyl 1'-hydroxy- $\alpha$ -ionylideneacetate (VI)	268	-13.0 (267)		A <sup>c</sup> (OH)
(-)-(R)-Ethyl 4'-keto- $\alpha$ -ionylideneacetate (IV) a)	267	-20.2 (265) +10.1 (233) +1.7 (318)		A (H)
(-)-Ethyl absicisate (VII) b)	264	-7.6 (266)	+4.9 (232) +0.6 (318)	A <sup>c</sup> (OH)
(+)-Abscisic acid (Ib) <sup>14</sup> , b)	260.5	+39.5 (262) -34 (230) -2.5 (318)		B <sup>c</sup> (OH)

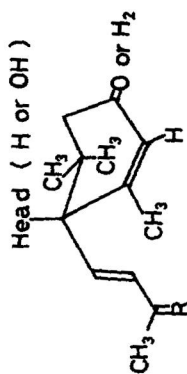
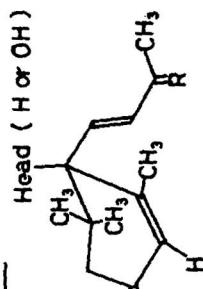
R = H, CHCO<sub>2</sub>H, CHCO<sub>2</sub>Et.

$\Delta \epsilon_1$  = CD values associated with chromophore in the cyclohexene ring.

$\Delta \epsilon_2$  = CD values associated with side-chain chromophore of the cyclohexene ring.

15-150  $\mu$ g/ml, 25°, 1-10 mm path length in EtOH. a) in 0.005 N-H<sub>2</sub>SO<sub>4</sub> EtOH.

b) in 0.005 N-H<sub>2</sub>SO<sub>4</sub> MeOH. c) Estimation.



As shown in Table 1, the CD of VII showed the opposite values to these<sup>13)</sup> of (+)-abscisic acid. And it is apparently that the difference of 2-cis and trans isomer or ethyl ester and free acid in analogs of the same optical active  $\alpha$ -ionylideneacetic acid don't invert their CD values. The above facts suggest that (+)-abscisic acid has the (R)-configuration (Ib).

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