CHAPTER - I

CONCISE TOTAL SYNTHESIS
OF

cis, trans-ABSCISIC ACID
Throughout the history of organic chemistry, it has been observed that the study of millions of natural products has frequently provided the impetus for great advances. As a sequel, a great deal of understanding of the intricate reactions and mechanisms involved in the biological systems has clearly emerged from this study. The major constituent part of the study has always been the total synthesis of naturally occurring and biologically active compounds where one consistently desires to construct highly complex molecules as well as the simple ones. This has indeed led to the demonstration of the organic chemist’s utmost ingenuity in the design of routes using established reactions besides discovering new methods and/or new reagents in order to achieve a specific goal. During the evolution of organic synthesis, certain classes of compounds have been well recognized at each stage of its progress. A vast group of organic chemists have been indulging in the synthesis of these molecules and some of the best and elegant chemistry has been generated during this period. These molecules have generated immense interest mainly because of their wide spectrum of biological activities.

We were interested in the total synthesis of plant growth hormone, cis, trans-Abscisic acid 1, which is biologically active. The reason is, that isolation from natural sources by itself is a tedious procedure and yields infinitesimally small quantities.

\[ \text{cis, trans-ABSCISIC ACID} \]
Plant hormones function as general growth stimulators or inhibitors. Unlike animal hormones, plant hormones are not produced in definite organs, do not have specific target tissues, and are not regulators of homeostasis. They are chemically produced in minute quantities and transported to other locations, where they elicit specific responses.

**CLASSIFICATION**

Plant hormones can be classified into two broad groups:

1. Growth stimulators which include auxins, gibberellins and cytokinins.
2. Growth inhibitors or antagonists to the known growth stimulators include abscisic acid and ethylene.

Charles and Francis Darwin first observed the action of auxins in the phototropic responses of seedling to light. Later experiments identified a chemical substance concentrated on the non-illuminated side of the seedling tip; this compound migrated from the light side to the dark side and had an elongating effect on the cells causing the tip to bend towards light. The only naturally occurring auxin is Indoleacetic acid (IAA), a compound synthesized from Tryptophan. It is produced in the shoot apex and diffuses downward to the base of the plant. It acts primarily by increasing the plasticity of young cell walls. Synthetic auxins are used as weed killers, to promote flowering, fruiting and prevent fruit drop.

Cytokinins promote cell division and differentiation of callus tissue in plant cell culture. They are chemically derived from adenine, produced in the
roots, and transported throughout a plant. Antagonistic to auxins, they promote growth of lateral branches and inhibit formation of lateral roots. Gibberellins were first observed in abnormally tall plants infected with a fungus, they are produced in the apical regions of stems and roots. They promote internodal elongation and accelerate seed germination. Brassinosteroids have only recently been classified as plant hormones. They have a wide range of physiological effects, that include elongation, cell division, membrane polarization, stem bending, vascular and reproductive tissue development and delayed senescence. Ethylene gas suppresses root and stem elongation and hastens fruit ripening. Natural ethylene production is often increased after exposure to adverse conditions like toxic chemicals and ozone.

**MULTIDIMENSIONAL NATURE OF HORMONE RESPONSE**

As more research was focused on plant hormones, it became apparent that not only hormones cause many responses but the responses depend on: Species, plant part, developmental stage, hormone concentration, interactions between hormones and various environmental factors.

**THE CONCEPT OF DIFFERENTIAL SENSITIVITY**

The concept states that the sensitivity of a plant or tissue within a plant to a certain hormone is more important than the hormone concentration. This was one of the first concepts on how plants respond to hormones. As it turns out, it is both concentration and sensitivity that give hormones the ability to induce responses.
Plant hormones represent an important mechanism by which the environment interacts with the genome to control phenotype\textsuperscript{21}. Again, this response of gene activation from plant hormones is most likely due to the mechanism of the hormone binding to a receptor and then causing a signal transduction cascade. Most likely when a hormone binds to a receptor, it induces many responses, one of which is gene activation, another could be the phosphorylation of an ATPase.

**HORMONE INTERACTION**

Cytokinin: Indole Acetic Acid ratio (CK: IAA ratio)

One example of hormones having an influence on the phenotype of the plant is the ratio of auxin to cytokinin. When there is a high ratio of auxin to cytokinin there will be root formation. When there is a high ratio of cytokinin to auxin there will be shoot formation.

**CLASSIFICATION OF GROWTH INHIBITORS**

They are divided into three groups:

1. Phytohormones e.g.: Abscissic acid (ABA)
2. Natural plant compounds (not hormones) that inhibit growth at high concentrations. e.g.: Phenolics and Benzoic acid derivatives.
3. Synthetics (from the chemical industry) applied to alter plant growth. e.g.: Reduce internode elongation; coordinate tiller growth rate. Proper use involves critical timing with plant growth stage. Requires high level of crop management.
AGRICULTURAL USES OF GROWTH INHIBITORS

1. Shorten internode length to prevent lodging in small grain cereals to allow greater fertilization. 2. Reduce late season vegetative growth of interminate legumes and favours photosynthesize partitioning to the fruit. 3. Defoliants applied to cotton. 4. Axillary bud suppression. Maleic hydrazide is used on all Tobacco after topping.

ABSCISIC ACID

Abscisic acid (ABA) is a common hormone present in nearly all plant tissues\textsuperscript{20}. Most of the ABA in plants occurs indirectly by degradation of certain carotenoids present in plastids. Its production in plants can be regulated in two ways: 1) Attachment of ABA to a glucose molecule and 2) oxidation of ABA. The phytohormone ABA plays regulatory role in a host of physiological processes in all higher as well as in lower plants\textsuperscript{11-14}. ABA mediates stress tolerance responses in higher plants, is a key signal compound that regulates stomatal aperture\textsuperscript{15} and is concerted with other plant signaling compounds. It is implicated in mediating responses to pathogens and wounding.

In 1963, ABA\textsuperscript{18} was first identified and characterized by Frederick Addicott\textsuperscript{1b} and his associates. They were studying the compounds responsible for the abscission of fruits (cotton). Two components were isolated and called abscisin I and abscisin II. The latter is presently called Abscisic Acid (ABA). Two other groups at about the same time discovered the same compound; one group headed by Philip wareing\textsuperscript{2,32} was studying bud dormancy in woody plants and the other group led by Van Steveninck\textsuperscript{3} was studying abscission of flowers and fruits from
lupine. Plant physiologists agreed to call the compound "Abscisic acid" (Salisbury and Ross, 1992).

ABA has been shown to be a constituent of sycamore, birch, willow\textsuperscript{22} and cabbage leaves as well as cotton balls, potatoes, avocado seeds and lemons. It has also been established that it has hormonal activity in these plants. This activity in most cases, is related to leaf and flower abscission or to dormancy\textsuperscript{4}. ABA has been shown to be present in trees in larger amounts during short-day periods than during long-days\textsuperscript{5} which is consistent with the hypothesis that ABA is important in the regulation of dormancy. Cotton fruits became a suitable source for the isolation to elucidate the chemical structure and was confirmed from lupine seeds\textsuperscript{6}. Mass spectrometry method was developed for the quantification of ABA in crude plant extracts without derivatization\textsuperscript{7}.

Large scale of ABA is extracted from carotenoids. It has been found to be a ubiquitous plant hormone in vascular plants. It has been detected in mosses but appears to be absent in liver worts. Several genera of fungi make ABA as a sea metabolite. In algae\textsuperscript{17} and liver worts\textsuperscript{19}, a compound similar to ABA was found and named lunularic acid appears to play a physiological role similar to that of ABA in higher plants. Within the plant, ABA has been detected in every major organ or living tissue from the root cap to the apical bud. ABA is identical with a substance that causes bud dormancy in wooden perennial plants. It was therefore at first also called ‘dormin’. In maple and birch buds causes the change from long day to short day conditions a marked increase in the activity of dormin (ABA) and consequently stops the growth of buds. ABA is a single compound, unlike the auxins, gibberellins and cytokinins. The name ABA was coined by a compromise between the two groups (Abscissin-II and dormin). Though ABA generally is thought to play mostly inhibitory role, it has many promoting functions as well. ABA is known to have numerous hormonal functions and uses shown in the figure.
In summary, the importance of the ABA effect can be interpreted as an effector that has the ability to close down certain parts of the plant metabolism for a period of time. Since ABA is easily removed from the tissues, its effect is reversible; an example is the inhibition of seed germination in berries (like tomatoes). The germination does not occur even though the seeds are in humid surroundings. The failure of the inhibition of seed germination leads usually to vivipary.

It is a sesquiterpenoid (15-carbon) which is partially produced via the mevalonic pathway in chloroplasts and other plastids. The production of ABA is accentuated by stress such as water loss and freezing temperature. It is believed that the biosynthesis occurs indirectly through the production of carotenoids. Violaxanthin carotenoid is converted into xanthonin which is unstable and spontaneously changed to ABA-aldehyde, which on further oxidation results in ABA.
STRUCTURE AND ISOMERS

J.W. Cornforth, B.V. Milborrow and G. Ryback had confirmed the structure of Abscisin II by synthesis. Kazuhiko, Ohkuma, Nippon Nogei, Kegaku Kaishi prepared the chemical structure and calculated the molecular formula as C_{15}H_{20}O_{4}. The IUPAC name of ABA is 2,4-pentadienoic acid-5-(1-hydroxy-2,6,6-trimethyl-4-oxo-2-yl)-3-methyl.

In ABA the (2Z,4E)-diene side chain system as shown by Gedye constantino is constructed with a high stereospecificity. Natural ABA is cis-isomer, dextro rotatory but the unnatural levorotatory compound has equal inhibitory activity. In ABA a cis-trans isomerisation interaction with the positioning of the moiety in the aromatic ring and methyl at C-4 was best positioned for the activity. Xanthoin which has the analogous hormonal activities in a plant and was shown to be a precursor of ABA.

PHYSICAL PROPERTIES

MW : 264.3
Mp : 188-191°C

ABA is a weak acid with a Pka of 4.7 and its dissociation depends on the pH of each cellular compartment. Distribution of ABA between different compartments depends on their pH values. The more alkaline a compartment, the more ABA it accumulates. Because of these properties, ABA concentration in the chloroplast increases in the light, whereas the apoplast concentration increases in the dark. The chemical structure of ABA determines its physiological activity.

The structure of ABA resembles the terminal portions of some carotenoid molecules. The fifteen carbon atoms of ABA configure an aliphatic ring with one double bond, two methyl groups and an unsaturated chain with a terminal carboxyl group. The position of the protons at C-2 and C-4 and the ensuing orientation of
the carboxyl group at C-2 determines the cis and trans isomers of ABA. In addition, ABA also has an asymmetric carbon atom at position 1 in the ring, resulting in the (+) and (-) or S and R enantiomers. The (+) enantiomer is the natural form, and commercially available. Synthetic ABA is a mixture of approximately equal amount of (+), (-) form. The (+) enantiomer is only one active in fast responses to ABA, such as stomatal closure. In long term responses such as changes in protein synthesis both enantiomers are active. In contrast to the cis and trans isomers, the (+) and (-) ones can not be interconverted in the plant tissues. Some of the features shown to be essential for biological activity include the carboxyl group, the tertiary -OH group, and the 2-cis and ring double bonds. Catabolic products of ABA present in the tissue which are devoid of any of these groups were biologically inactive.

In view of the growing interest in this highly biological active plant growth hormone, it was felt worthwhile to draw a synthetic programme. Before presenting our details, a brief account of the work done on the construction of Abscisic acid by other research groups is discussed below.

WORK CARRIED OUT BY OTHER RESEARCH GROUPS

Kunikazu's Approach:

Preparation of optically active 2 was known to be obtained easily from mesityl oxide and ethyl acetoacetate in five steps via chiral induction of Sharpless epoxidation. The key reaction of the epoxy aldehyde 2 with 3-(bromomethyl)-crotonates (E:Z=1:1, R=Me or Et) in the presence of Zn powder gave a mixture of four products, i.e., two hydroxy esters 3a & 3b and isomeric mixture of cyclized
lactones 4a & 4b. All of these four intermediates gave the single diene product 5 by treatment with alkoxide respectively. The conversion of the diene 5 to cis, trans-ABA 1 (Scheme-1) was performed in one-pot conveniently by treatment with dilute HCl to effect deacetalization followed by the spontaneous enone formation by epoxy ring opening. Control of the acid treatment conditions using dilute perchloric acid gave the deacetalized product 6 which yield 1 also by following treatment with dilute HCl.

Scheme-1

Reagents and Conditions:

a) 3-(Bromomethyl)crotonate (R = Me or Et), Zn powder, I₂ cat/THF, rt, 0.5h;
b) KOMe, MeOH, 60°C, 2h; c) KOMe, MeOH, rt, 18h; d) 0.2M HCl, MeOH, water (4:1), rt, 18h; e) 10% HClO₄, THF-water (1:1), 0°C, 2 min.; f) dil.HCl.

Mauricio's Approach²⁸:

Allylic oxidation of the commercial alcohol 7 afforded the aldehyde, subsequent oxidation of aldehyde in the presence of cyanide ion and methanol gave the desired ester 8. Treatment of isophorone 9 with ethylene glycol and acid in toluene afforded ketal which, on oxidation with KMnO₄ in neutral medium and
further dehydration of the intermediate formed, with methane sulphonyl chloride in refluxing pyridine to afford the enone 10. Reaction of the lithium salt of 8 with enone 10 (-78°C to -30°C) afforded 11. Subsequent reduction of 11 with chromium (II) sulphate resulted in a complex mixture of products from which the methyl ester of racemic abscisic acid 12 (Scheme-2) was isolated. Saponification of 12 afforded racemic abscisic acid 13 as a white crystalline solid.

Scheme-2

Reagents and Conditions:
1) MnO2, CHCl3, rt, 3h; 2) MnO2, NaCN, MeOH, AcOH, rt, 24h; 3) Ethylene glycol, H+, toluene; 4) KMnO4, pH-7; 5) Methane sulphonyl chloride, pyridine, rt, 24h & reflux, 4h; 6) LDA, -78°C, 2h; 7) CrSO4, DMF-water, rt, 24h; 8) NaOH, MeOH:H2O (v/v, 1:1), rt, 1h.

Masato’s Approach:

Hydrogenation of peroxide 14 by Lindlar’s catalyst gave in quantitative yield, the dl-cis-diol 15 (Scheme-3) which was converted into the diastereomeric MTP ester 16 & 17 with (+)-MTP acetyl chloride. The more polar MTP ester 16 was likewise hydrolysed to the cis-α-diol 18, which was oxidized using Jones’s reagent in acetone for 30 min. Finally, it was converted into a mixture of trans and cis esters 19 & 21 by a wittig reaction further hydrolysis led to cis, trans-ABA 1 and trans, trans-ABA 20.
Reagents and Conditions:

a) Lindlar's catalyst; b) MTP acetyl chloride; c) KOH, H₂O-MeOH, rt;
d) Jones's reagent (CrO₃-H₂SO₄), acetone, rt, 0.5h; e) Wittig reaction;
f) KOH, H₂O-MeOH, rt, 5h.

Takayuki's Approach:

Selenium dioxide oxidation of α-ionone 22 in ethanol gave (-)-1'-hydroxy-
α-ionone 23. The reaction of 23 with carbethoxymethylene triphenylphosphorane afforded (-)-ethyl-1'-hydroxy-α-ionylidene acetate 24 (Scheme-4), consisted of
two isomers (cis and trans). The t-butyl chromate oxidation of 24 gave isomeric
mixture of ethyl abscisate 25 in 5.6% yield.
Reagents and Conditions:

a) SeO₂, EtOH, reflux, 2h; b) Carbethoxy methylene-triphenylphosphorane, toluene, reflux, 5h; c) t-Butyl chromate, t-butanol, reflux.

Donald's Approach³¹:

Oxidation of α-ionone 22 with t-butyl chromate in refluxing t-butanol solution yielded a mixture of 26 & 27. The wittig reaction of 26 with carbethoxymethylene triphenylphosphorane refluxed at 140-170°C for 1 h afforded a mixture of cis, trans and trans, trans – ethyl esters of abscisic acid 25 (Scheme-5) which, on treatment with alcoholic base provided a mixture of cis, trans and trans, trans isomers of abscisic acid 13. The two isomers were readily separated by slow crystallization from ether.
Reagents and Conditions:

a) t-Butyl chromate, t-butanol, reflux, 5h; b) Carbethoxy methylene triphenylphosphorane, toluene, reflux, 5h; c) KOH, MeOH, rt, 24h.

Cornforth's Approach:

3-Methyl-5-(2,6,6-trimethylcyclohexa-1,3-dienyl)-cis,trans-2,4-pentadienoic acid 28 in benzene-ethanol was irradiated with visible light in an atmosphere of oxygen in presence of eosin as a photosensitizer. The crystalline epidioxide 29 so formed, was heated at 100°C for 7.5 min in 0.07N aqueous sodium hydroxide, rearrangement occurred and racemic abscisin 13 (Scheme-6) was isolated after acidification.

Reagents and Conditions:

a) Benzene-EtOH, eosin, visible light, O₂ atm; b) 0.07N NaOH solution, 100°C, 7.5 min.
**Milan’s Approach**

Compound 30 on protection with isopropenyl methyl ether, pyridinium-p-toluene-sulphonate in THF at room temperature for 10 min yielded the compound 31 which, on coupling with 32 in presence of n-BuLi, THF at -45°C for 1 h followed by the reaction with sodium dihydro-bis(2-methoxyethoxy)aluminate in methanol and by the reaction with pyridinium-p-toluene-sulphonate afforded a mixture of C_{15}-dil-aldehyde 33 & 34. cis, trans-isomer of 34, on oxidation with MnO₂, chloroform, room temperature for 2 h, provided the ABA-aldehyde 35 (Scheme-7) which, on further oxidation in presence of NaClO₂, sodium dihydrogen-orthophosphate in water at room temperature for 1 h resulted the cis, trans-Abscisic acid 1.

**Scheme-7**

Reagents and Conditions:

a) Isopropenyl-methyl ether, pyridinium-p-toluene-sulphonate, THF, rt, 10 min; b) n-BuLi, THF, -45°C, 1h; c) Sodium dihydro bis(2-methoxyethoxy) aluminate, MeOH, 45 min; d) THF-H₂O, pyridinium-p-toluene-sulphonate; e) MnO₂, CHCl₃, rt, 2h; f) NaClO₂, NaH₂PO₄, 2H₂O, H₂O, rt, 1h.
Hans's Approach:\(^\text{34}\):

Reaction of the derivative of the cis isomer 7 (formed by the condensation of methyl vinyl ketone with acetylene followed by the anionotropic rearrangement of the intermediate 3-methyl-pent-1-en-4-yn-3-ol) with the ketone 10 derived from isophorone gave the expected 2-cis compound 36. This, on reduction with sodium bis(2-methoxyethoxy)aluminium hydride furnished the 2-cis-4-trans-diene-diol 37 which, without purification was treated with acid to give the dihydroxy ketone 38. Allylic oxidation of the primary hydroxyl group with manganese dioxide gave the aldehyde 39 (Scheme-8) which, on further oxidation with silver oxide yielded racemic abscisic acid 13.

\begin{center}
Scheme-8
\end{center}

\begin{center}
Reagents and Conditions:
\begin{enumerate}
  \item \text{Lithium, ferric nitrate, liq.ammonia, rt, 16h;}
  \item \text{Sodium bis(2-methoxyethoxy)aluminium hydride, benzene, THF, rt, 5h;}
  \item \text{Acetone, 1N H}_2\text{SO}_4, \text{rt, 1h;}
  \item \text{MnO}_2, \text{THF, rt, 18h;}
  \item \text{NaOH, AgNO}_3\cdot\text{H}_2\text{O, MeOH, -5°C, 0.5h.}
\end{enumerate}
\end{center}
Our main aim for this novel synthesis was to standardize the appropriate yields and to scale up the process for industrial use.

The retro synthetic analysis of cis, trans-Abscisic acid 1 (Scheme-9) revealed that β-ionone 41 was the key synthon in the synthesis which was obtained from acetone 44 after several transformations.

RETROSYNTHESIS:

Scheme-9

In accordance with the plan (Scheme-10), β-ionone 41 was synthesized starting from acetone 44. Compound 44 was reacted with sodium acetylide (from NaNH₂ and acetylene) at -70°C to form the acetylenic alcohol 45 in 87% yield. The reaction with sodium in ammonia instead of NaNH₂ gave moderate yield. But, when we used THF as solvent, yield was very poor because of the close boiling points of THF and compound 45 and isolation became difficult. The resulting acetylenic alcohol underwent partial reduction using Lindlar’s catalyst at room temperature, to afford the substituted allyl alcohol 46, which was confirmed by the PMR spectrum giving proton resonance at δ 4.95 (d), 5.15 (d) and 5.95 (dd) ppm
for olefinic protons, IR absorption at 3540 cm$^{-1}$ (OH) and the molecular ion peak at m/e 86 in Mass spectrum. The allylic rearrangement of compound 46 was carried out either by 37% HCl or 48% HBr at 0°C to obtain 47a or 47b respectively. The allyl chloride 47a underwent nucleophilic substitution with sodium acetate in presence of TEBA, a PTC for 4.5h to afford the acetate 48 in 96% yield. The PMR spectrum showed the characteristic chemical shift value at δ 2.05 (COCH$_3$) and 4.55 ppm (CH$_2$OAc), IR absorption of carbonyl group at 1720 cm$^{-1}$ and m/e value of 128 in EI mass confirmed the corresponding acetate. Our procedure for this conversion is more efficient compared to the earlier reports. Hydrolysis of acetate 48 with 10% NaOH solution under refluxed conditions gave allyl alcohol 43 in 95% yield, the PMR, IR and Mass values were in accordance with the spectral data. The alcohol 43 was subjected to allylic oxidation with MnO$_2$ in petroleum ether at room temperature, resulting in α,β-unsaturated aldehyde 49 (95% yield) and PMR spectrum confirmed the structure by the characteristic aldehyde peak as doublet at δ 9.95 ppm. It was further substantiated by the molecular ion peak m/e at 84 and odd m/e value at 83 in Mass spectrum. Oxidation with PDC, PCC also yielded moderate yields. Prenol 43 and prenal 49 refluxed at 200°C/40 atm afforded citral 42, which involved the claisen followed by cope rearrangement in 51% yield. The structure was characterized by all PMR, IR and Mass spectral data. Citral 42 underwent aldol condensation with acetone followed by dehydration resulted in pseudoionone 50, which was further subjected to smooth cyclization in conc.H$_2$SO$_4$ to give β-ionone 41, which was the key intermediate. All the spectral data (PMR, IR, Mass, $^{13}$C NMR and UV) were confirming the compound 41. β-Ionone on allylic bromination using NBS, in presence of light followed by dehydrobromination by adding sodium carbonate and DMF provided 3,4-dehydro-β-ionone 52 in 68% yield, showing the olefinic protons of cyclic ring which resonated at δ 5.85 ppm as singlet in PMR spectrum,
Scheme-10

Acetone

Reagents and Conditions:

a) Acetylene, NH₃, NaNH₂, at -70°C, 3h; b) H₂/Lindlar's catalyst, hexane, rt, 10h; c) 37% HCl, 0°C, 1h; or 48% HBr, 0°C, 0.5h; d) CH₃COONa, TEBA, reflux, 4.5h; e) 10% NaOH, reflux, 2.5h; f) MnO₂, pet-ether, rt, 7h; g) 200°C/40 mm, 1.5h; h) i) Acetone, NaOMe, -10°C to 0°C, 1h, ii) 5% NaHSO₃, reflux, 5h; i) 10% H₂SO₄, hexane, -10°C, 0.5h; j) NBS, CCl₄, hv, reflux, 2h; k) Na₂CO₃, DMF; l) m-CPBA, CH₂Cl₂, -78°C, 5h; m) Jones' reagent, acetone, 0°C, 1h, rt, 5h; n) 54a, PPh₃, benzene, reflux, 20h; o) 54b, PPh₃, benzene, rt, 5h; p) phenolphthalein, 10% NaOH solution till pH=14; q) Ylide 56, benzene, reflux, 8h; r) KOH, MeOH:H₂O (1:1), rt, 24h.
and was further confirmed by the Mass spectrum showing m/e at 190. 1,2-Epoxidation of 52 with m-CPBA in CH₂Cl₂ at -78°C resulted in the epoxide 53 which, on Jone's oxidation, yielded 1-hydroxy-4-keto-α-ionone 40 in 78% yield as yellow crystalline solid, whose melting point 110-112°C matched with the literature. The compound 40 was characterized by the spectral data, mainly the molecular ion peak at m/e 222 in EI-MS, IR absorption bands at 3461 cm⁻¹ for hydroxyl, 1738, 1692 and 1669 cm⁻¹ for carbonyl groups of C=O & COCH₃. Wittig coupling of the optically pure hydroxy-ketone 40 with stable ylide 56 by refluxing in benzene for 8h furnished a mixture of cis, trans and trans, trans- α,β-unsaturated ester 57, which was used as such for further hydrolysis. Wittig reaction using toluene as solvent gave very poor yield. The cis and trans esters were identified by PMR spectrum, in trans-isomer olefinic protons resonated at 6 6.05 (d) and 6.35 (d) ppm, whereas in cis isomer the resonance was observed at 6 6.10 (d) and 7.75 (d) ppm. Mixture of ester 57 were saponified with potassium hydroxide in aqueous-methanol (1:1) for 24 h at room temperature provided an isomeric mixture of abscisic acid (1 and 20), which was separated by recrystallisation from chloroform.

Desired cis-isomer 1 was less soluble in chloroform, and was obtained in yield 80% (m.p. 189°-191°C) by recrystallisation. The two isomers were differentiated by the olefinic protons in PMR spectroscopy. For cis-isomer, the olefinic protons were observed at 6 5.90 (s), 6.10 (d) and 7.80 (d) ppm and for trans-isomer at 6 5.80 (s), 6.05 (d) and 6.40 (d) ppm.

**CONCLUSION**

In conclusion, cis,trans-Abscisic acid 1 was synthesized by an unambiguous route compared with the various other syntheses. Our approach is simple, operationally novel and practical.
EXPERIMENTAL PROCEDURE FOR β-IONONE

3-Methyl-1-butyn-3-ol 45:

In a 5 L three necked round bottom flask, fitted with a cold finger, dropping funnel and a gas bubbler, was taken sodamide (273 g, 7 mol, 0.96 eq), ammonia (3 L) at -70°C and passed acetylene gas for half an hour. To this mixture, was added acetone (530 mL, 418.7 g, 7.22 mol, 1 eq) for 3 h at the same temperature. After the completion of addition, cooling bath was removed and kept at room temperature overnight. Stirring was continued for 30 min at 25°C, followed by quenching with 10% H₂SO₄ solution (5 L). The aqueous layer was extracted with dichloromethane, then organic layer concentrated under reduced pressure and distilled at 104-105°C to afford 45. Yield 533g (87.9%).

\[ \begin{align*}
\text{45} & \\
\text{OH} &
\end{align*} \]

\(^1\text{H NMR (400 MHz, CDCl₃) ppm: } & 8 1.55 (s, 6H, 2 x CH₃), 1.95 \\
& \text{(brs, 1H, OH, D₂O exchangeable), 2.40 (s, 1H, C=CH).} \\
\text{IR (Neat, } \nu_{\text{max}} \text{) cm}^{-1}: & 3385, 3302. \\
\text{MS-EI (m/e): } & 83 (M^+ -1), 69 (M^+ -CH₃), 67 (M^+ -OH). \\
\]

3-Methyl-1-butyn-3-ol 46:

Procedure I:

To a solution of compound 45 (70 g, 0.833 mol, 1 eq) in hexane (210 mL), was added Lindlar’s catalyst (7 g) and stirred at room temperature for 10 h under H₂ atmosphere. The reaction mixture was filtered and distilled over a column packed with glass beads at 97°C to provide 46. Yield 65.3 g (91.1%).

Procedure II:

The above procedure was followed, using compound 45 (52 g, 0.619 mol, 1 eq), Lindlar’s catalyst (4.6 g), quinoline (2.6 g, 0.020 mol, 0.03 eq), and petroleum ether (75 mL) to afford compound 46. Yield 52.71g (99%).
\[ \text{^1H NMR (400 MHz, CDCl}_3\text{) ppm: } \delta 1.30 (s, 3H, CH}_3\text{), 1.50 (s, 3H, CH}_3\text{), 2.50 (brs, 1H, OH, D}_2\text{O exchangeable), 4.95 (d, J = 7.40 Hz, cis-1H, CH}_2\text{), 5.15 (d, J = 14.80 Hz, trans-1H, CH}_2\text{), 5.95 (dd, J = 7.40, 14.80 Hz, 1H, CH).} \]

IR (Neat, \( \nu_{\text{max}} \)) cm\(^{-1}\): 3540.

MS-EI (m/e): 86 (M\(^+\)), 71 (M\(^+\)-CH\(_3\)), 69 (M\(^+\)-OH).

**1-Chloro-3-methyl-2-butene 47a:**

A precooled compound 46 (13 g, 0.1511 mol, 1 eq) was mixed with aqueous HCl (37%, 44.2 mL, 16.35 g, 0.448 mol, 2.96 eq) at 0°C and stirred at the same temperature for 1h. Organic layer was separated, washed with water (2 x 20 mL), dried (Na\(_2\)SO\(_4\)) and distilled at 109°C to give 47a. Yield 15.2 g (96.3%), \( R_f = 0.72 \) (Ethyl acetate-Petroleum ether (1:4), Stain-Anisaldehyde).

\[ \text{^1H NMR (200 MHz, CDCl}_3\text{) ppm: } \delta 1.75 (s, 3H, CH}_3\text{), 1.80 (s, 3H, CH}_3\text{), 4.05 (d, J = 7.78 Hz, 2H, CH}_3\text{), 5.45 (t, J = 7.78 Hz, 1H, CH).} \]

MS-EI (m/e): 105, 104 (M\(^+\)).

**1-Bromo-3-methyl-2-butene 47b:**

A precooled alcohol 46 (13.49 g, 0.1568 mol, 1 eq) was mixed with aqueous HBr (48%, 62.7 mL, 30.09 g, 0.3715 mol, 2.37 eq) and the resulting mixture was stirred for 30 min at the same temperature. Organic layer was separated and the aqueous layer was extracted with dichloromethane (2 x 50 mL). The combined extracts were dried (Na\(_2\)SO\(_4\)), filtered, concentrated under reduced
pressure and distilled at 59-60°C to afford 47b. Yield 21.03 g (90%), $R_f = 0.72$ 
[Ethyl acetate-Petroleum ether (1:4), Stain-Anisaldehyde].

![Chemical structure of 47b]

$^1$H NMR (200 MHz, CDCl$_3$) ppm: $\delta$ 1.70 (s, 3H, CH$_3$), 1.75 (s, 3H, CH$_3$), 3.95 (d, $J = 6.74$ Hz, 2H, CH$_2$Br), 5.50 (t, $J = 6.74$ Hz, 1H, CH).  
MS-EI (m/e): 150, 148 ($M^+$).

1-Acetoxy-3-methyl-2-butene 48:

A mixture of compound 47a (4.27 g, 0.0408 mol, 1 eq), sodium acetate (3.868 g, 0.0471 mol, 1.15 eq) and TEBA (0.4 g, 0.0017 mol, 0.043 eq) was heated for 4.5 h at 95-105°C. The mixture was extracted with dichloromethane (3 x 10 mL) and concentrated under vacuum. The crude product was distilled at 160°C/10 mm to afford 48. Yield 5.04 g (96.4%), $R_f = 0.70$ [Ethyl acetate-Petroleum ether (1:4), Stain-Anisaldehyde].

![Chemical structure of 48]

$^1$H NMR (200 MHz, CDCl$_3$) ppm: $\delta$ 1.75 (s, 3H, CH$_3$), 1.80 (s, 3H, CH$_3$), 2.05 (s, 3H, COCH$_3$), 4.55 (d, $J = 6.90$ Hz, 2H, CH$_2$OAc), 5.35 (t, $J = 6.90$ Hz, 1H, CH).  
IR (Neat, $v_{max}$) cm$^{-1}$: 3300, 1720.  
MS-EI (m/e): 128 ($M^+$), 127 ($M^+ -1$), 85 ($M^+ -C_2H_3O$).

3-Methyl-2-butenol 43:

A stirred solution of compound 48 (13.4 g, 0.1046 mol, 1 eq) and aq.NaOH (10%, 4.4 mL) were heated at 100°C for 2.5 h. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 x 250 mL). Organic layer and extracts were combined, dried (Na$_2$SO$_4$) and concentrated under reduced
pressure. The crude compound was distilled at 137°C to provide pure compound 43. Yield 8.6 g (95%), R_f = 0.40 [Ethyl acetate-Petroleum ether (1:4), Stain-Anisaldehyde].

\[ \text{1H NMR (200 MHz, CDCl}_3) \text{ ppm: } \delta 1.65 (s, 3H, CH}_3, 1.75 (s, 3H, CH}_3, 1.95 (brs, 1H, OH, D}_2\text{O exchangeable), 4.05 (d, J = 8.00 Hz, 2H, CH}_2), 5.35 (t, J = 8.00 Hz, 1H, CH). \]

IR (Neat, \nu_{max}) cm\(^{-1}\): 3332.

MS-EI (m/e): 86 (M\(^{+}\)), 71 (M\(^{+}\)-CH\(_3\)), 69 (M\(^{+}\)-OH).

3-Methyl-2-butenal 49:

To a solution of compound 43 (28.2 g, 0.327 mol, 1 eq) and petroleum ether (100 mL), was added MnO\(_2\) (71.2 g, 1.297 mol, 3.96 eq) and stirred at room temperature for 7 h. The reaction mixture was filtered and concentrated under reduced pressure gave crude product which was distilled at 132-133°C to afford pure compound 49. Yield 26.12 g (95%), R_f = 0.60 [Ethyl acetate-Petroleum ether (1:9), Stain-Anisaldehyde].

\[ \text{1H NMR (200 MHz, CDCl}_3) \text{ ppm: } \delta 1.95 (s, 3H, CH}_3, 2.20 (s, 3H, CH}_3, 5.85 (d, J = 9.37 Hz, 1H, CH), 9.95 (d, J = 9.37 Hz, 1H, CHO). \]

IR (Neat, \nu_{max}) cm\(^{-1}\): 1708, 1682.

MS-EI (m/e): 84 (M\(^{+}\)), 83 (M\(^{+}\)-1), 69 (M\(^{+}\)-CH\(_3\)), 55 (M\(^{+}\)-CHO).

Citral 42:

A mixture of 3-methyl-2-butenol 43 (5 g, 0.0581 mol, 1 eq) and 3-methyl-2-butenal 49 (4.88 g, 0.0581 mol, 1 eq) were heated at 200°C at 40-42 mm pressure for 1.5 h. The crude compound obtained was distilled at 80-81°C/5 mm to
furnish pure compound 42. Yield 4.52 g (51.2%), \( R_r = 0.44 \) [Ethyl acetate-Petroleum ether (1:9), Stain-Anisaldehyde].

\[ \text{1H NMR (200 MHz, CDCl}_3\text{)} \text{ ppm: } \delta 1.60 \text{ (s, } 3\text{H, CH}_3\text{), 1.70 (s, } 3\text{H, CH}_3\text{), 2.00 (m, } 1\text{H, CH}_2\text{), 2.20, 2.25 (s, } 3\text{H, CH}_3\text{, two sets), 2.25 (m, } 2\text{H, CH}_2\text{), 2.60 (t, } J = 5.70 \text{ Hz, } 1\text{H, CH}_2\text{), 5.10 (brs, } 1\text{H, CH}, \text{ 5.85 (d, } J = 5.70 \text{ Hz, } 1\text{H, CH}, \text{ 9.75, 9.85 (d, } J = 5.70 \text{ Hz, } 1\text{H, CHO, two sets).} \]

\[ \text{IR (Neat, } \nu_{\text{max}} \text{) cm}^{-1}: 1706, 1677. \]

\[ \text{MS-EI (m/e): 152 (M\textsuperscript{+}), 137 (M\textsuperscript{+}-CH}_3\text{), 123 (M\textsuperscript{+}-CHO).} \]

**Pseudoionone 50:**

To a cooled solution of citral 42 (7.49 g, 0.0493 mol, 1 eq) and acetone (13 mL, 10.27 g, 0.1770 mol, 3.59 eq) at -10°C, added NaOMe (0.886 g, 0.0164 mol, 0.33 eq) slowly, maintaining the temperature below 5°C over a period of 30 min with continued stirring for 1 h at the same temperature. The reaction was quenched with aqueous tartaric acid (1.107 g of tartaric acid dissolved in 7.38 mL of water), extracted with ethyl acetate (3 x 30 mL), dried (Na\textsubscript{2}SO\textsubscript{4}) and concentrated. The residue was refluxed with sodium bisulphite solution (5%, 100 mL) for 5h, extracted with ethyl acetate (2 x 50 mL), dried (Na\textsubscript{2}SO\textsubscript{4}) and concentrated. Pure compound 50 was isolated by silica gel column using ethyl acetate-petroleum ether as eluent (1:19). Yield 8.70 g (92%), \( R_f = 0.65 \) [Ethyl acetate-Petroleum ether (1:4), Stain-Anisaldehyde].

\[ \text{1H NMR (200 MHz, CDCl}_3\text{)} \text{ ppm: } \delta 1.55 \text{ (s, } 3\text{H, CH}_3\text{), 1.60 (s, } 3\text{H, CH}_3\text{), 1.90 (s, } 3\text{H, CH}_3\text{), 2.15 (brs, } 4\text{H, 2 x CH}_2\text{), 2.25 (s, } 3\text{H, COCH}_3\text{), 5.00 (brs, } 1\text{H, CH}, \text{ 5.90 (d, } J = 8.00 \text{ Hz, cis-1H, CH}, \text{ 6.05 (d, } J = 16.00 \text{ Hz, trans-1H, CH}, \text{ 7.40 (dd, } J = \]
8.00, 16.00 Hz, 1H, CHJ).
IR (Neat, v_max) cm⁻¹: 1699, 1677.
MS-EI (m/e): 192 (M⁺), 124 (M⁺ -C₄H₄O), 109 (M⁺ -C₅H₈O),
69 (M⁺ -C₈H₁₁O).

β-Ionone 41:

A solution of hexane (3.6 mL) and H₂SO₄ (5.16 mL, 9.49 g, 0.0968 mol, 5.98 eq) were cooled to -10°C and stirred for 10 min. Then compound 50 (3.1 g, 0.0162 mol, 1 eq) in hexane (4 mL) was added within 15 min and stirring was continued for 30 min. The reaction mixture was neutralized with 18% NaOH solution till the pH=7 at -10°C. The reaction mixture was extracted with dichloromethane (2 x 25 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure. The crude compound was distilled at 138-140°C/10 mm to give 41. Yield 2.325 g (75%), Rf = 0.66 [Ethyl acetate-Petroleum ether (1:4), Stain-Anisaldehyde].

\[ \text{\textbf{41}} \]

\(^1\text{H NMR (200 MHz, CDCl₃)} \text{ ppm: } \delta \text{ 1.05 (s, 6H, 2 x CH₃),} \\
1.45 (m, 2H, CH₂), 1.60 (m, 2H, CH₂), 1.75 (s, 3H, CH₃), \\
2.05 (t, J = 7.50 Hz, 2H, CH₂), 2.25 (s, 3H, COCH₃), 6.05 \\
(d, J = 16.80 Hz, 1H, CH), 7.20 (d, J = 16.80 Hz, 1H, CH).} \\
\(^{13}\text{C NMR (75 MHz, CDCl₃)} \text{ ppm: } \delta \text{ 198.5, 142.9, 135.8,} \\
135.6, 131.2, 39.4, 33.8, 33.3, 28.5, 26.8, 21.4, 18.6.} \\
\text{IR (Neat, v_max) cm⁻¹: 1693, 1673.} \\
\text{MS-EI (m/e): 192 (M⁺), 178 (M⁺ +1 -CH₃), 177 (M⁺ -CH₃),} \\
123 (M⁺ -C₄H₈O). \\
\text{UV (MeOH, λ_max) nm: 294.5, 221.0.} \]
PMR, IR, Mass Spectra of Compound 45
PMR, IR, Mass Spectra of Compound 46
PMR, IR, Mass Spectra of Compound 48
PMR, IR, Mass Spectra of Compound 43
PMR, IR, Mass Spectra of Compound 49
PMR, IR, Mass Spectra of Compound 42
PMR, IR, Mass Spectra of Compound 50
PMR, IR, Mass Spectra of Compound 41
(β-Ionone)
$^{13}$C NMR, UV Spectra of Compound 41

(β-Ionone)
EXPERIMENTAL PROCEDURE FOR ABSCISIC ACID

3,4-Dehydro-β-ionone 52:

To a solution of β-ionone 41 (9.6 g, 0.05 mol, 1 eq) and CCl₄ (500 mL), was added N-bromo succinimide (11.5 g, 0.064 mol, 1.29 eq) and refluxed for 2 h in presence of light (500 w bulb) to give 3-bromo-β-ionone 51. The reaction mixture was cooled to room temperature, followed by the addition of Na₂CO₃ (12.5 g, 0.118 mol, 2.35 eq) and DMF (125 mL, 132.4 g, 1.81 mol, 36.2 eq). The excess CCl₄ was distilled under atmospheric pressure. The pasty mass was diluted with ethyl acetate (500 mL) and filtered. The filtrate was washed with aq.HCl (5%, 2 x 500 mL) and saturated NaCl solution (2 x 250 mL). The organic layer was dried (Na₂SO₄), filtered and concentrated. The crude compound was then subjected to silica gel column using ethyl acetate-petroleum ether (1:9) to isolate yellow oily compound 52. Yield 6.50 g (68.42%), Rᵣ = 0.57 [Ethyl acetate-Petroleum ether (3:17), Stain-Anisaldehyde].

\[ \text{1H NMR (200 MHz, CDCl₃ ppm: } \delta \text{ 1.05 (s, 6H, 2 x CH₃),} \]
\[ \text{1.95 (s, 3H, CH₃), 2.10 (brs, 2H, CH₂), 2.30 (s, 3H, COCH₃), 5.85 (s, 2H, CH), 6.20 (d, J = 16.00 Hz, 1H, CH),} \]
\[ \text{7.35 (d, J = 16.00 Hz, 1H, CH).} \]

\[ \text{IR (Neat, ν_max) cm}^{-1}: 1723, 1669.} \]

\[ \text{MS-El (m/e): 190 (M⁺), 175 (M⁺-CH₃), 147 (M⁺-C₂H₅O),} \]
\[ \text{43 (M⁺-C₁₁H₁₅O).} \]

1,2-Epoxy-3,4-dehydro-β-ionone 53:

To a solution of 3,4-dehydro-β-ionone 52 (6.84 g, 0.0360 mol, 1 eq) and methylene chloride (200 mL) at -78°C, was added a solution of m-CPBA (9.31 g, 0.0540 mol, 1.5 eq) in CH₂Cl₂ (300 mL) slowly, during 30 min and stirred further
for 5 h. The mixture was warmed up to 0°C during 1 h. The precipitate was filtered and filtrate was successively washed with Na₂SO₃ solution (10%, 100 mL), NaOH solution (10%, 100 mL), and NaCl solution (100 mL), dried (Na₂SO₄) and concentrated to give crude product. The residue was purified over silica gel, using ethyl acetate-petroleum ether (1:49) to yield 4.70 g (63.50%), an isomeric mixture of compound 53 in the ratio of 1:4 confirmed by PMR spectrum, Rᵣ = 0.40 [Ethyl acetate-Petroleum ether (3:17), Stain-Anisaldehyde].

\[ \text{IR (Neat, } \nu_{\text{max}} \text{) cm}^{-1}: 1699, 1276.} \]

\[ \text{MS-EI (m/e): 206 (M⁺), 163 (M⁺-C₂H₃O), 123 (M⁺+1-C₃H₅O).} \]

**1-Hydroxy-4-keto-α-ionone 40:**

To the solution of compound 53 (5 g, 0.0242 mol, 1 eq) in acetone (500 mL) at 0°C was added Jones's reagent (CrO₃-H₂SO₄, 100 mL) slowly. The mixture was stirred for 1 h at the same temperature and 5 h at room temperature. The excess of acetone was removed under reduced pressure, diluted with water (50 mL), filtered and extracted with ethyl acetate (2 x 100 mL), dried (Na₂SO₄) and concentrated. The crude material was purified over silica gel, using ethyl acetate-petroleum ether (1:1) to afford pure yellow crystalline compound 40. Yield 4.20 g (78.0%), Rᵣ = 0.18 [Ethyl acetate-Petroleum ether (3:7), Stain-Anisaldehyde].
$^1$H NMR (200 MHz, CDCl$_3$) ppm: δ 1.05 (s, 3H, CH$_3$), 1.10 (s, 3H, CH$_3$), 1.90 (s, 3H, CH$_3$), 2.15 (s, 3H, COCH$_3$), 2.50 (m, 2H, CH$_2$), 2.60 (brs, 1H, OH, D$_2$O exchangeable), 5.95 (s, 1H, CH), 6.40 (d, J = 16.00 Hz, 1H, CH), 6.90 (d, J = 16.00 Hz, 1H, CH).

IR (KBr, $\nu_{max}$) cm$^{-1}$: 3461, 1738, 1692, 1669.

MS-EI (m/e): 222 (M$^+$), 139 (M$^+$ +1 -C$_2$H$_4$O).

Mp.: 110-112°C (lit$^{35}$, m.p: 112-113°C).

Carbethoxy methylene triphenyl phosphoryl chloride 55a:

To a solution of triphenylphosphine (74.2 g, 0.2832 mol, 1 eq) and benzene (50 mL), was added chloro ethyl acetate 54a (34.7 g, 0.2832 mol, 1 eq) slowly, during a period of 0.5 h at room temperature. The reaction mixture was refluxed for 20 h and left for solidification. The solid compound was filtered, washed with benzene (100 mL) and dried under vacuo provided 55a. Yield 70.661 g (64.88%).

Mp.: 125°C (lit$^{36}$, m.p: 130°C).

Carbethoxy methylene triphenyl phosphoryl bromide 55b:

To a stirred solution of triphenylphosphine (100 g, 0.381 mol, 1 eq) in benzene (458 mL), was added bromo ethyl acetate 54b (63.7 g, 0.381 mol, 1 eq) during a period of 0.5 h and stirred 5 h further at room temperature and left over night for the crystallisation. The solid was filtered, washed with benzene (100 mL) and dried under vacuum provided 55b in quantitative yield melted at 151°C (lit$^{36}$, m.p: 150°C).

Carbethoxy methylene triphenyl phosphorane (Wittig ylide) 56:

To the wittig salt (55a or 55b, 10 g) in water (100 mL), was added a pinch of phenalphpthalein indicator. The mixture was treated with NaOH solution (0.5N,
40 mL, 2 g in 100 mL) till the pink colour was observed. The mixture was extracted with benzene (2 x 100 mL), dried (Na₂SO₄), filtered and concentrated to give the ylide 56. Yield 7.8 g (96.3%).

\begin{center}
\begin{align*}
\text{Ph} & \quad \text{Ph} & \quad \text{Ph} \\
\text{P} & \quad \text{C=O} & \quad \text{OCH₂CH₃} \\
\text{CH} & \quad & \\
\end{align*}
\end{center}

\[\text{56}\]

\[1\text{H NMR (200 MHz, CDCl}_3\text{) ppm: } \delta 1.00 (\text{brs, } 3\text{H, CH}_3), 2.70 (\text{brs, } 1\text{H, CH}), 3.90 (\text{brs, } 2\text{H, CH}_2), 7.40 (\text{m, } 9\text{H, Ar-H}), 7.60 (\text{m, } 6\text{H, Ar-H}).\]

IR (KBr, \(\nu_{\text{max}}\) cm⁻¹): 1600.

MS-FAB (m/e): 349 (M⁺ +1).

3-Methyl-5-(1-hydroxy-4-keto-2,6,6-trimethyl-2-cyclohexen-1-yl)ethyl-2,4-pentadienoate 57:

To a stirred solution of 1-hydroxy-4-keto-α-ionone 40 (4 g, 0.018 mol, 1 eq) in benzene (50 mL), was added ylide 56 (12.55 g, 0.036 mol, 2 eq) in benzene (15 mL) and refluxed for 8 h. The excess of benzene was distilled in \textit{vacuo} and the brown syrupy mixture was chromatographed over silica gel, using ethyl acetate-petroleum ether (1:4) as eluent to give a mixture of \textit{cis}, \textit{trans} and \textit{trans, trans} isomers 57, as pale yellow oil, 3.4 g (65%) used in next step without separation. The ratio of the \textit{cis}, \textit{trans} and \textit{trans, trans} isomers was determined by PMR spectrum and found to be 4:1, \(R_f = 0.60, 0.61\) [Ethyl acetate-Petroleum ether (2:3), Stain-Anisaldehyde].

\begin{center}
\begin{align*}
\text{O} & \quad \text{COOC₂H₅} \\
\text{57} & \quad & \text{CH₂OH} \\
\end{align*}
\end{center}

\[1\text{H NMR (200 MHz, CDCl}_3\text{) ppm: } \delta 0.95, 1.05 (\text{s, } 6\text{H, } 2 \times \text{CH}_3, \text{two sets}), 1.20 (\text{t, } J = 7.50 \text{ Hz, } 3\text{H, CH}_2-\text{CH}_3), 1.85, 1.90 (\text{s, } 3\text{H, CH}_3, \text{two sets}), 1.95, 2.25 (\text{s, } 3\text{H, CH}_3, \text{two sets}), 2.15, 2.30 (\text{s, } 1\text{H, CH, two sets}), 2.35, 2.40 (\text{d, } J = 4.00 \text{ Hz, } 1\text{H, CH,}}\]
two sets), 2.50 (brs, 1H, OH, D$_2$O exchangeable), 4.05, 4.10 (q, $J = 7.50$ Hz, 2H, CH$_2$-CH$_3$, two sets), 5.65, 5.70 (s, 1H, CH, two sets), 5.80 (s, 1H, CH), 6.05, 6.10 (d, $J = 15.20$ Hz, 1H, CH, two sets), 6.35, 7.75 (d, $J = 15.20$ Hz, 1H, CH, two sets).

IR (Neat, $\nu_{max}$) cm$^{-1}$: 1654.

MS-EI (m/e): 292 ($M^+$), 263 ($M^+ - C_2H_5$), 190 ($M^+ +$1

$-C_5H_{11}O_2$), 162 ($M^+ +3 -C_7H_{17}O_2$), 134 ($M^+$

$-C_9H_{18}O_2$), 117 ($M^+ -C_9H_{19}O_3$).

cis,trans-3-Methyl-5-(1-hydroxy-4-keto-2,6,6-trimethyl-2-cyclo-

hexen-1-yl)ethyl-2,4-pentadienoic acid [cis,trans-Abscisic acid] 1:

The mixture of ester 57 (3 g, 0.01 mol, 1 eq) was saponified by treatment
with potassium hydroxide (1.2 g, 0.021 mol, 2.1 eq) in aqueous methanol (5%, 12
mL) and stirred at room temperature for 24 h. The reaction mixture was diluted
with water and extracted with ethyl acetate (3 x 25 mL). The aqueous portion was
acidified to pH=2 with HCl (16%, 6 mL) and extracted with ethyl acetate (2 x 10
mL). The extracts were combined, dried (Na$_2$SO$_4$), filtered and concentrated. The
mixture of isomers were obtained in yield 1.7 g (63%), which were separated by
recrystallisation from chloroform to get cis,trans-isomer 1 (1.36 g, 80%) and
trans,trans-isomer 20 (0.34 g, 20%), $R_f = 0.35$, 0.37 [Ethyl acetate-Petroleum
ether (3:2), Stain-Anisaldehyde].

cis, trans-ABSCISIC ACID

$^1$H NMR (500 MHz, CDCl$_3$ + DMSO-d$_6$) ppm:

$\delta$ 1.00 (s, 3H, CH$_3$), 1.10 (s, 3H, CH$_3$), 1.25 (s,
1H, OH, D$_2$O exchangeable), 1.90 (s, 3H, CH$_3$),
2.00 (s, 3H, CH$_3$), 2.20 (d, $J = 17.80$ Hz, 1H,
CH$_2$), 2.40 (d, $J = 17.80$ Hz, 1H, CH$_2$), 3.60
(brs, 1H, COOH, D$_2$O exchangeable), 5.70 (s, 1H, CH), 5.90 (s, 1H, CH), 6.10 (d, $J = 17.60$ Hz, 1H, CH), 7.80 (d, $J = 17.60$ Hz, 1H, CH).

IR (KBr, $v_{max}$) cm$^{-1}$: 3431, 1677, 1654.

MS-EI (m/e): 278 ($M^+ + 2$Li), 264 ($M^+$), 208 ($M^+ - C_4H_8$), 190 ($M^+ - C_3H_6O_2$), 162 ($M^+ - C_4H_6O_3$), 134 ($M^+ + 2 - C_6H_{12}O_3$).

UV (MeOH, $\lambda_{max}$) nm: 252.0.

Mp.: 189-191°C (lit$^{28}$, m.p: 190-191°C).

$^1$H NMR (500 MHz, CDCl$_3$) ppm: $\delta$ 0.95 (s, 3H, CH$_3$), 1.00 (s, 3H, CH$_3$), 1.20 (s, 1H, OH, D$_2$O exchangeable), 1.80 (s, 3H, CH$_3$), 1.95 (d, $J = 17.60$ Hz, 1H, CH$_3$), 2.20 (s, 3H, CH$_3$), 2.40 (d, $J = 17.60$ Hz, 1H, CH$_3$), 4.00 (brs, 1H, COOH, D$_2$O exchangeable), 5.70 (s, 1H, CH), 5.80 (s, 1H, CH), 6.05 (d, $J = 17.24$ Hz, 1H, CH), 6.40 (d, $J = 17.24$ Hz, 1H, CH).

IR (KBr, $v_{max}$) cm$^{-1}$: 3431, 1677, 1654.

MS-EI (m/e): 264 ($M^+$), 208 ($M^+ - C_4H_8$), 190 ($M^+ - C_3H_6O_2$), 162 ($M^+ - C_4H_6O_3$), 134 ($M^+ + 2 - C_6H_{12}O_3$).

UV (MeOH, $\lambda_{max}$) nm: 252.0.

Mp.: 151-153°C (lit$^{28}$, m.p: 152-154°C).
PMR, IR, Mass Spectra of Compound 52
PMR, IR, Mass Spectra of Compound 53
PMR, IR, Mass Spectra of Compound 53
PMR, IR, Mass Spectra of Compound 40
PMR, IR, Mass Spectra of Compound 56
PMR, IR, Mass Spectra of Compound 57
PMR, IR, Mass Spectra of Compound 20

(trans, trans-Abscisic acid)
PMR, IR, Mass Spectra of Compound 1

*(cis, trans*-Abscisic acid)
UV Spectrum of Compound 20
\( (trans, trans\)-Abscisic acid)

UV Spectrum of Compound 1
\( (cis, trans\)-Abscisic acid)
References:


