Stereochemical Studies. XXXIX. A Novel Method for the Preparation of Optically Active (R)(+)-α-Cyclocitril, (S) (+)-Dehydrovomifoliol, and (S) (+)-Abscisic Acid

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It was found that direct hydrolysis of the crude oxazolidine derivatives (3a, b), prepared with dl-α-cyclocitril (dl-1a), or its 6-benzoxy derivative (dl-1b) and (S) (+)-prolinol ((S) (+)-4), with aqueous acetic acid, afforded (R) (+)-1a, 19% optically pure, and (S) (+)-6-hydroxy-α-cyclocitril ((S) (+)-2b), 63% optically pure, respectively. A merit of the resolution method is that optically active (R) (+)-1a or (S) (+)-2b can be obtained without any recrystallizations.

Some mechanistic studies and discussions on the hydrolysis were also examined. Optically active (S) (+)-2b, thus obtained, was successfully converted into (S) (+)-dehydrovomifoliol ((S) (+)-5) via (S) (+)-6-hydroxy-α-ionone ((S) (+)-9). By this chemical conversion, (S) (+)-abscisic acid could be formally synthesized from dl-1b.

Although there have been reported various methods including resolutions for preparation of optically active compounds, methods which are effective for producing optically active carbonyl compounds are quite limited.5,7

Recently, it was reported that the resolution of racemic aldehyde and ketone, which were key intermediates for prostaglandin synthesis, could be achieved by repeated recrystallizations of the diastereomeric mixtures of oxazolidines prepared with d-ephedrine. In the course of our effort for preparing optically active carbonyl compounds using optically active α-amino acid derivatives, the authors have found that the racemic aldehydes such as dl-α-cyclocitril (dl-1a) and dl-6-benzoxy-α-cyclocitril (dl-1b) can be readily converted into the corresponding optically active aldehydes ((R) (+)-1a and (S) (+)-2b) by the direct acidic hydrolysis of oily diastereomeric mixtures of the oxazolidines (3). Since 3 is obtained by the condensation of dl-1 with (S) (+)-prolinol ((S)-(+)-4),10 and moreover, since fairly high degrees of optical purity for (R) (+)-1a and (S) (+)-2b are obtained without any recrystallizations of 3, the method developed here, could be considered to be one of the effective methods for preparation of optically active aldehydes.

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3) Location: Hongo, Bunkyo-ku, Tokyo, 113, Japan.
9) For the cleavage of benzoyl group, see the later description.
This report deals with a full account of the novel resolution method and its successful application to the synthetic approach to naturally occurring (S) (+)-dehydrovomifoliol ((S) (+)-5)\(^{11}\) from which (S) (+)-abscisic acid ((S) (+)-6), a plant growth regulator, have been synthesized by many groups.\(^{11,12}\)

**Result and Discussion**

A. **Preparation of Optically Active (R) (+)-α-Cyclocitrinal ((R) (+)-1a) and (S) (+)-6-Hydroxy-α-cyclocitrinal ((S) (+)-2b)**

It has been already established that when secondary amino alcohols react with carbonyl compounds, stable oxazolidine derivatives are formed.\(^{13}\) Therefore, we first examined the applicability of (S) (+)-4 to the resolution of dl-1a\(^{14}\) by way of its oxazolidine derivative (3a).

Condensation of dl-1a with an equimolar amount of (S) (+)-4 in the presence of p-toluenesulfonic acid and Molecular Sieves 4A gave an almost quantitative yield of the crude oily 3a. As shown in Chart 2, presence of four diastereoisomers are theoretically possible for 3a due to the asymmetric center inherently present in dl-1a and to the newly created C₂-position of oxazolidine system. Moreover, it is probable that one of four possible pairs of the diastereoisomers\(^{15}\) was selectively formed in a manner similar to the case for the resolution in prosta-glandin synthesis\(^{16}\) if the oxazolidine formation proceeds stereoselectively concerning the C₂-position. However, attempted separation of one of the formed diastereoisomers as crystalline picrate or perchlorate\(^{16}\) turned out to be unpromising, and the relative ratio of the formed

![Chemical structures](image)

**Chart 1**

- 1: dl-1a (R=H)
- 2: dl-1b (R=OCOC₆H₅)
- 3: 3a (R=H)
- 4: (S) (+)-4
- 5: (S) (+)-5
- 6: (S) (+)-6

**Chart 2**

- 3aA
- 3aB
- 3aC
- 3aD

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14) Optically active (R) (+)-1a was recently synthesized by the asymmetric synthesis, and could be converted into optically active (R) (+)-trans-α-damascone, a famous perfume due to its fragrant odor (see ref. 7).

15) These pairs are as follows: 3aA and 3aB, 3aA and 3aD, 3aC and 3aB, and 3aC and 3aD.

16) In ref. 13, some oxazolidine derivatives are reported to give well-crystalline picrates or perchlorates.
isomers could not be determined. The structure of 3a was definitely confirmed by the following spectral data: IR (film): 1200, 1140, and 1050 cm\(^{-1}\) (oxazolidine ring); \(\delta\) 4.50—4.30 (1H, multiplet, \(\mathrm{C}_2\) proton of the oxazolidine ring).

Since oxazolidine is expected to be readily hydrolyzed to aldehyde by acidic treatment, the direct hydrolysis of crude 3a was next undertaken.

A two layer solution of benzene containing crude 3a, and 10\% aqueous acetic acid, was stirred at room temperature for 0.5 hr, regenerating oily (\(R\)) (+)-1a, \([\alpha]_D^2 +112.0^\circ\) (ethanol), in 28\% yield from \(dl\)-1a after extractive isolation and purification by column chromatography. The optical purity of this oil could be calculated as 19\%, based on the assumption that (\(R\)) (+)-1a showing \([\alpha]_D^2 +594.5^\circ\) (ethanol) was optically pure.\(^7\) Kinetic difference of the hydrolysis rates of diastereoisomers might explain the observed result. However, inspection of the stereo-structures of four diastereoisomers (3aA-D) using Dreiding model could not elucidate the reason why 3aA and/or 3aC were hydrolyzed preferentially to the others (3aB and/or 3aD).

When the hydrolysis time was changed, the optical purity of (\(R\)) (+)-1a varied as was shown in Table I. It is clear that the optical purity of (\(R\)) (+)-1a reaches at a maximum after 0.5 hr hydrolysis and gradually decreased with increase of the chemical yield of (\(R\)) (+)-1a at longer hydrolytic treatment. These phenomena are clearly compatible with the speculation that the optical activity observed in (\(R\)) (+)-1a is due to kinetic difference of the hydrolysis rates of diastereoisomers.

Next, we applied the above-mentioned method to the resolution of \(dl\)-1b, aiming to synthesize optically active dehydrovomilfoliol (\(R\)) (-)-5 or (S) (+)-5.

As shown in Chart 3, preparation of \(dl\)-1b was readily accomplished by the treatment of \(dl\)-\(\alpha\)-cyclocitril-\(\alpha\)-pyrrolidine enamine (7) with benzoyl peroxide.\(^{15}\) The benzyloxylation also afforded \(dl\)-4-benzyoxy-\(\beta\)-cyclocitril (\(dl\)-8) as a byproduct, but it could be easily separated from the desired \(dl\)-1b by column chromatography.

Condensation of \(dl\)-1b with (S) (+)-4 was carried out under a similar condition to that for \(dl\)-1a except for the relative amount of (S) (+)-4 (3.0 equivalents) and refluxing time (75 hr).\(^{18}\) Sequential extraction of the reaction mixture afforded crude \(dl\)-1b in 54\% recovery from the neutral fraction, and benzoic acid in 23\% yield from the acidic fraction. From the basic fraction,\(^{19}\) crude oily 3b was obtained as a mixture of diastereoisomers.\(^{20}\) Separation of

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one of the possible diastereoisomers and determination of the formation ratio of four isomers were again unsuccessful. However, the structure of $3b$, that is, exclusive cleavage of the benzoyl group during oxazolidine formation, was ascertained by its spectral data.

Chart 4

Cleavage of the benzoyl group is conceivably due to the result of intramolecular catalysis as is shown in Chart 4.\textsuperscript{21,22}

Hydrolysis of crude $3b$ was attempted by refluxing a two layer solution of benzene containing $3b$ and 10\% aqueous acetic acid for 5.0 hr. Extractive isolation and purification by preparative thin-layer chromatography (TLC) afforded (S) (+)-$2b$, $\alpha$\textsubscript{D}\textsuperscript{20} +472.4\textdegree (benzene), 63\% optically pure,\textsuperscript{23} in 14\% yield based on $dl$-$1b$ (in 26\% yield from $dl$-$1b$ when corrected for the recovered $dl$-$1b$). Infrared and nuclear magnetic resonance spectra (IR and NMR) of (S) (+)-$2b$ were identical with those of $dl$-$2b$ prepared independently from $dl$-$1b$.

Since the optical purity of (S) (+)-$2b$ was amazingly high when compared with that of (R) (+)-$1a$, the same hydrolysis as that mentioned above, was repeated two more times to check the reproducibility of the reaction. The following optical rotations, optical purities, and chemical yields based on $dl$-$1b$ were observed: $\alpha$\textsubscript{D}\textsuperscript{20} +362.7\textdegree (benzene), 49\% optically pure,\textsuperscript{23} 8\%; $\alpha$\textsubscript{D}\textsuperscript{20} +406.0\textdegree (benzene), 54\% optically pure,\textsuperscript{23} 10\%. The reason why the optical purity of (S) (+)-$2b$ was about three times higher than that of (R) (+)-$1a$ is obscure,\textsuperscript{24} but these results definitely discloses that the resolution method developed here, usually gives (S) (+)-$2b$ which is 50 to 60\% optically pure.

\textsuperscript{21} Similar intramolecular mechanism was presented for the ester cleavage of methyl o-formylbenzoate with secondary amine. See, M.L. Bender and M.S. Silver, \textit{J. Am. Chem. Soc.}, 84, 4589 (1962), and M.L. Bender, J.A. Reinstein, M.S. Silver, and R. Mikulak, \textit{ibid.}, \textbf{87}, 4545 (1965).

\textsuperscript{22} Refluxing a benzene solution of cyclohexyl benzoate and (S) (+)-$4$ for 25 hr under the same condition as that used for the preparation of $3b$ recovered cyclohexyl benzoate in a quantitative yield. This observation further supports the mechanism shown in Chart 4.

\textsuperscript{23} The optical purity and absolute configuration of (S) (+)-$2b$ were clearly established by converting (S) (+)-$2b$ into (S) (+)-$6$-hydroxy-$\alpha$-ionone ((S) (+)-$9$ (see Section B).

\textsuperscript{24} Although there is no experimental evidence, the preferential decomposition of one or two diastereoisomers of $3b$ leading to (R) (-)-$2b$, in addition to the selective hydrolysis of $3b$ similar to the case for $3a$, might significantly increase the optical purity of (S) (+)-$2b$. 
B. Preparation of Optically Active (S) (+)-Dehydrovomifoliol ((S) (+)-5)

In order to establish the optical purity and absolute configuration of (S)-2b, and moreover, to exploit the synthetic route to optically active 5,110 the chemical scheme shown in Chart 5 was studied.

Base-catalyzed condensation of (S)-2b, [\(\beta\) +298.5° (benzene), 25] with acetone gave a 23% yield of (S)-6-hydroxy-\(\alpha\)-ionone ((S)-9), [\(\beta\) +103.7° (ethanol). The structure of (S)-9 was confirmed by comparing its spectral (IR and NMR) and chromatographic (TLC) behavior with those of the authentic racemic compound independently prepared from racemic \(\alpha\)-ionone.26 Since (S)-9 showing [\(\beta\) -260° (ethanol), was reported to be optically pure and to have (R)-configuration,26,27 (S)-9 obtained here was determined to have (S)-configuration and to be 40% optically pure. This conversion further elucidated that the absolute configuration and optical purity of (S)-2b, [\(\beta\) +298.5° (benzene) were (S)-configuration and 40% optically pure, and that the pure optical rotation of (S) (+)-2b could be calculated as [\(\beta\) +746.3 (benzene). Oxidation of (S) (+)-9, [\(\beta\) +103.7° (ethanol), with \(t\)-butyl chromate26b,26d yielded (S) (+)-5, [\(\beta\) +99.8° (chloroform), in 5% yield with a large amount of recovered starting material. Spectral (IR and NMR) and chromatographic (TLC) behavior of (S) (+)-5 were identical with those of the authentic racemic compound.28

As the conversion of (S) (+)-5 to (S) (+)-6 has been well documented,11.113 completion of the synthetic route to (S) (+)-5 means that (S) (+)-6 has been formally synthesized from dl-1b.

Experimental29,30

(S) (+)-Prolinol ((S) (+)-4)—Prepared from optically pure l-proline according to the reported procedure.29 This sample showed bp 87–89.5° (12 mmHg), and [\(\beta\) +2.8° (c = 2.046, EtOH), [\(\beta\) +0.446° (I = 0.1, neat) (lit.,29 bp 100–105° (9 mmHg)).

dl-\(\alpha\)-Cyclocitral (dl-1a)—This compound was prepared from commercially available citral (a mixture of cis- and trans-isomer whose ratio was ca. 5:6) by the reported procedure.3 The oily sample obtained showed a single spot on TLC analysis. RF value was ca. 0.5 (silica gel, solvent benzene: hexane 1:1)

Preparation of (R) (+)-\(\alpha\)-Cyclocitral ([R] (+)-1a) from dl-\(\alpha\)-Cyclocitral (dl-1a) via the Oxazolidine Derivative (3a)—Procedure which could afford (R) (+)-1a showing the highest optical activity, was given as an example.

25) This sample was prepared by combining several lots of (+)-2b accumulated during the study on the hydrolysis condition for 3b.
27) In ref. 26, (R) (–)-9 was erroneously expressed as (S) (–)-9 because of the misunderstanding of the 1966 Cahn-Ingold-Prelog convention (see G. Ryback, Chem. Comm., 1972, 1190).
29) All melting and boiling points are uncorrected. IR spectra measurements were performed with spectrometers, JASCO Infrared Spectrometer Model DS-402G and JASCO IRA-1 Grating Infrared Spectrometer. NMR spectra were recorded with spectrometers, JNM-PS100 and Hitachi R-24 High Resolution NMR Spectrometers. All signals are expressed by the ppm downfield from tetramethylsilane used as an internal standard. Following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). Optical rotations were determined with a Yanaco OR-50 Automatic Polarimeter. Mass spectra measurements were carried out using a JEOL JMS-OISG-2 Mass Spectrometer.
30) Extraction solvent used for the isolation of volatile compound was not completely evaporated in order to prevent a loss of the reaction product, so weight measurement at the stage of crude evaporation residue was not performed throughout this work.
Preparation of 3a from dl-1a: A solution of dl-1a (0.30 g, 2.0 mmole) and (S) (+)-4 (0.20 g, 2.0 mmole) in anhyd. benzene (10 ml) was heated at reflux for 25 hr in the presence of anhyd. p-toluenesulfonic acid (10 mg) and Molecular Sieves 4A (ca. 0.8 g) under nitrogen atmosphere. After filtration, the benzene layer was concentrated in vacuo, giving crude 3a as a pale yellow oil (0.44 g, 97% yield). IR νmax cm⁻¹: 1200, 1140, 1050 (O-C=N system of oxazolidine ring).¹⁹ NMR (in CCl₄): 4.50–4.30 (1H, m, O-CH=N), 5.37 (1H, broad s, =CH-). Mass Spectrum m/e: 234 ([M⁻]).

Hydrolysis of 3a: 10% Aqueous acetic acid (6 ml) was gradually added to a stirred benzene solution (6 ml) of crude 3a (0.44 g) in an ice-bath. The whole mixture was stirred at room temperature for 0.5 hr, then the upper benzene layer was separated. The residual aqueous layer was twice extracted with benzene. The combined benzene layers were washed with satd. NaHCO₃ and satd. NaCl solutions, then dried over anhyd. Na₂SO₄. Filtration followed by evaporation in vacuo afforded a yellow oil, which was purified by column chromatography (silica gel, solvent benzene: hexane 1:1), to give (R) (+)-1a as a pale yellow oil (79 mg, 26% yield based on dl-1a), [x]D +112.0° (c=0.866, EtOH). The optical purity of this sample could be calculated as 19%, by the assumption that (R) (+)-1a showing [x]D +594.5° (EtOH) was optically pure.³ Spectral (IR and NMR) and chromatographic (TLC) behavior were completely identical with those of the authentic sample.⁷

dl-6-Benzoxyl-α-cyclocotl (dl-1b) and dl-4-Benzoxyl-β-cyclocotl (dl-8) — A mixture of dl-1a (0.30 g, 2.0 mmole) and pyrrolidine (0.57 g, 8.0 mmole) in anhyd. benzene (10 ml) was heated at reflux for 25 hr in the presence of Molecular Sieves 4A (ca. 2.0 g) under nitrogen atmosphere. Filtration and evaporation in vacuo gave the crude ename (7) as a pale brown oil (0.42 g). IR νmax cm⁻¹: 1680, 1640, 1010 (olefinic double bonds). NMR (in CCl₄): 5.22 (1H, broad s, olefinic proton), 5.65 (1H, broad s, =CH-N). Crude 7 was immediately used for the next benzoxylolation.

A benzene solution (2 ml) of crude 7 (0.42 g) was added to a stirred solution of benzoyl peroxide (1.94 g, 8.0 mmole) in anhyd. benzene (8 ml) in an ice bath and under nitrogen atmosphere. The whole mixture was stirred at room temperature for 96 hr under nitrogen atmosphere and interception of light.¹⁹ The reaction was quenched by the addition of 10% aqueous acetic acid (10 ml) and potassium iodide (2.66 g, 16.0 mmole) to the mixture in an ice-bath, then the whole was stirred with stirring for 1.0 hr. After the upper benzene layer was separated, the lower aqueous phase was further extracted with stirring for 0.1 hr. Then the upper benzene layer was washed successively with satd. Na₂S₂O₅, satd. NaHCO₃, and satd. NaCl solutions, and finally dried over anhyd. Na₂SO₄. Filtration and evaporation in vacuo gave a brown viscous oil (1.44 g), which was chromagographed on silica gel column (solvent benzene: hexane 1:1) to afford dl-1b as a pale yellow solid (89 mg, 17% yield based on dl-1a). Repeated recrystallizations from hexane gave pure sample as colorless prisms, mp 96–98°. IR νmax cm⁻¹: 1733 (sh), 1725 (sh), 1712 (ester and aldehyde), 1285, 1150 (ester). NMR (in CCl₄): 1.05, 1.19 (6H, two s, =CH₂), 1.74 (3H, s, =C-Me), 1.50–2.40 (4H, m, =CH₂), 5.66 (1H, broad s, =CH-), 7.20–8.30 (5H, m, aromatic protons), 9.67 (1H, s, CHO). TLC analysis of this sample showed a single spot whose Rf value was ca. 0.4 (silica gel, solvent benzene: hexane 1:1). Anal. Calcd. for C₉H₈O₃: C, 74.97; H, 7.40. Found: C, 74.80; H, 7.39.

Further elution of the silica gel column with the same solvent system as that used for dl-1b, followed by evaporation of the eluates, gave dl-8 as a yellow viscous oil (0.12 g, 22% yield based on dl-1a). IR νmax cm⁻¹: 1730 (ester), 1685 (α, β-unsaturated aldehyde), 1265, 1110 (ester). NMR (in CCl₄): 1.15, 1.23 (6H, two s, =C-Me), 2.05 (3H, s, =C-Me), 1.32–2.02 (4H, m, =CH₂), 5.42 (1H, t, J = 6 Hz, =CH-O), 7.12–8.12 (5H, aromatic protons), 10.02 (1H, s, CHO). Mass Spectrum m/e: 273 ([M+1]⁺). TLC analysis showed that this sample was completely homogeneous (Rf ca. 0.35, silica gel, solvent benzene: hexane 1:1).

dl-6-Hydroxy-α-cyclocotl (dl-2b) — A mixture of dl-1b (0.19 g, 0.70 mmole) and sodium ethoxide (0.12 g, 1.8 mmole) in absolute ethanol (8.8 ml) was stirred in an ice-bath for 1.5 hr. After ethanol was removed in vacuo below 0°, the yellow residue obtained was dissolved in H₂O (20 ml). The aqueous solution was extracted with benzene (3 times), and the combined benzene layers were successively washed with 10% aqueous acetic acid and NaCl solutions, then dried over anhyd. Na₂SO₄. Filtration and evaporation in vacuo afforded a yellow oil, which was purified by column chromatography (silica gel, solvent benzene: hexane 1:1) to give pure dl-2b as a colorless oil (80 mg, 68% yield). IR νmax cm⁻¹: 3520, 1140 (alcohol), 1720 (aldehyde), NMR (in CCl₄): 0.87, 0.96 (6H, two s, =C-Me), 1.44 (3H, broad s, =C-Me), 1.34–2.34 (4H, m, =CH₂), 3.38 (1H, broad s, OH), 5.71 (1H, broad s, =CH-), 9.51 (1H, s, CHO).

Preparation of (S) (+)-6-Hydroxy-α-cyclocotl ((S) (+)-2b) from dl-6-Benzoxyl-α-cyclocotl (dl-1b) via the Oxazolidine Derivative (3b) — Procedure which could afford (S) (+)-2b having the highest optical activity, was given as an example.

Preparation of 3b from dl-1b: A benzene solution (13 ml) of dl-1b (0.24 g, 0.90 mmole) and (S) (+)-4 (0.27 g, 2.7 mmole) was heated at reflux for 75 hr in the presence of anhyd. p-toluenesulfonic acid (30 mg) and Molecular Sieves 4A (ca. 0.9 g) under nitrogen atmosphere. After cooling, the Molecular Sieves 4A was filtered off, and washed with anhyd. benzene (13 ml). The combined filtrates were successively washed with 10% HCl (13 ml×1, then 4 ml×2), satd. NaHCO₃ (15 ml×2), and satd. NaCl (15 ml×2), and finally dried over anhyd. MgSO₄. Filtration and evaporation in vacuo recovered crude dl-1b as colorless plates (0.13 g,
54% recovery), [x]_D^25 ca. 0° (c = 1.074, benzene). Spectral (IR and NMR) and chromatographic (TLC) behavior were completely identical with those of the authentic racemic compound.

The combined sodium bicarbonate washings were acidified with 10% HCl, and extracted with ether (50 ml × 3). The combined ether extracts were washed with satd. NaCl (30 ml × 2), and dried over anhyd. MgSO_4. Filtration and evaporation in vacuo gave benzonic acid (25 mg, 23% yield) as a colorless solid. This solid was recrystallized from H_2O to give pure sample, mp 123—123.5°, which was identified with the authentic sample by comparing their spectral (IR and NMR) data and measuring the mixed melting point, mp 123.5—124°.

The remaining 10% HCl washings were combined and made basic (pH>10) with 10% NaOH under ice-cooling. The basic aqueous solution was extracted with benzene (17 ml × 3). The combined benzene extracts were dried over anhyd. K_2CO_3. Filtration and evaporation in vacuo afforded crude 3b as a yellow oil (0.13 g). IR ν_{max} cm⁻¹: 3440 (alcohol), 1200, 1140, 1080, 1050 (alcohol and O-C-N system of oxazoline ring). NMR (in CCl_4): 4.45 (1H, s, O-CH=N), 5.30 (1H, broad s, s=CH–). This NMR spectrum clearly showed an almost complete absence of the signals due to aromatic and aldehyde protons.

Hydrolysis of 3b: 10% aqueous acetic acid (5 ml) was added to the solution of crude 3b (0.13 g) in benzene (5 ml) with stirring in an ice-bath. After the mixture was heated at reflux for 5 hr with stirring, the upper benzene layer was successively washed with satd. NaHCO_3 and satd. NaCl solutions, then dried over anhyd. MgSO_4. Filtration and evaporation in vacuo gave a yellow oil, which was purified by preparative TLC (silica gel, solvent hexane: ether 4:1) to give pure (S) (+)-2b as soft crystals (18 mg, 14% yield based on dl-1b or 26% yield from dl-1b when corrected for the recovered dl-1b), mp 40—52°, [x]_D^25 +472.4° (c = 0.362, benzene). The optical purity of this sample could be calculated as 63% since (S) (+)-2b showed [x]_D^25 +298.5° (c=1.150, benzene) gave (S) (+)-9, [x]_D^25 +103.7° (c=0.108, EtOH), and the pure optical rotation of (R) (−)-9 was reported to be [x]_D^25 −260° (c=0.6, EtOH) (vide infra). IR and NMR spectra of this sample were completely identical with those of the authentic racemic compound recorded in the same states. TLC analysis of this solid showed a single spot whose RF value was the same as that of the pure racemic compound.

**dl-6-Hydroxy-a-ionone (dl-9)** — The compound was prepared from commercially available dl-x-ionone by using selenium dioxide as an oxidizing agent. Recrystallization from hexane gave colorless needles, mp 86—87.5°. IR ν_{max} cm⁻¹: 1692 (sh), 1672 (a,β-unsaturated ketone), 1622 (double bond), 1110 (alcohol). NMR (in CDCl_3): 0.90, 0.93 (6H, two s, C-Me₂), 1.56 (3H, broad s, C-Me), 2.19 (3H, s, COMe), 1.30—2.30 (5H, m, −(CH₂)₂− and OH), 5.43 (1H, broad s, s=CH–), 6.24 (1H, d, J = 16 Hz, −CH=CH-CO), 6.04 (1H, d, J = 16 Hz, −CH=CH-CO). Anal. Calcd. for C₁₅H₁₄O₂: C, 74.96; H, 6.68. Found: C, 74.49; H, 10.03.

(S) (+)-6-Hydroxy-a-ionone ((S) (+)-9) — Sodium ethoxide (0.23 g, 3.4 mmole) in absolute ethanol (1.9 ml) was added to an acetone solution (1.9 ml) of (S) (+)-2b ([x]_D^25 +298.5° (c=1.150, benzene)) (58 mg, 0.34 mmole) under ice-cooling. The whole mixture was stirred for 3.5 hr in an ice-bath, then neutralized with 10% HCl. After addition of H_2O (7 ml), ethanol and acetone were evaporated in vacuo to give an aqueous solution, which was extracted with ether (x×3). The combined ether extracts were washed with satd. NaCl (x×2), and dried over anhyd. MgSO_4. Filtration and evaporation in vacuo gave an yellow oil (0.16 g), which was purified by preparative TLC (silica gel, solvent hexane: ether 7:3) to afford pure (S) (+)-9 as a colorless semisolid (16 mg, 23% yield), mp 78—86°, [x]_D^25 +103.7° (c=0.108, EtOH). Since optically pure (R) (−)-9 was reported to show mp 90—91° and [x]_D^25 −260° (c=0.6, EtOH), the optical purity of this semisolid could be calculated as 40%. IR and NMR spectra of this sample were superimposable on those of the authentic racemic compound measured in the same states. TLC analysis of this product showed a single spot whose RF value was the same as that of the authentic racemic compound (RF ca. 0.3, silica gel, solvent hexane: ether 7:3).

**dl-Dehydrovomifoliol (dl-5)** — Preparation of the authentic dl-5 was carried out by the reported procedure. This sample showed 113.5—114° after recrystallizations from toluene (lit. mp 112—113°). IR ν_{max} cm⁻¹: 1665 (α,β-unsaturated ketones), 1625 (olefinic double bonds). NMR (in CDCl_3): 1.00, 1.07 (6H, two s, C-Me₂), 1.88 (3H, d, J = 1.5 Hz, s=CH–), 2.28 (3H, s, COMe), 2.15—2.60 (3H, m, −CH₂− and OH), 5.92 (1H, broad s, s=CH–), 6.42 (1H, d, J = 16 Hz, −CH=CH-CO), 6.82 (1H, d, J = 16 Hz, −CH=CH-CO). These spectral properties are the same as those reported. TLC analysis of this sample showed a single spot (RF ca. 0.1, silica gel, solvent ether: hexane 6:4).

(S) (+)-Dehydrovomifoliol ((S) (+)-5) — t-Butyl chromate solution was prepared by the successive addition of chromium trioxide (0.60 g, 6.0 mmole) and acetic anhydride (0.56 ml, 6.0 mmole) to t-butyl alcohol (0.8 ml) was gradually added to the stirred t-butyl chromate solution prepared above at room temperature. The

31) This sample was converted to (S) (+)-2b, [x]_D^25 +6.3° (c=1.052, benzene), according to the same method as that employed for the preparation of dl-2b from dl-1b. Since (S) (+)-2b, being 60% optically active, was found to exhibit [x]_D^25 +472.4° (c=0.362, benzene) (vide infra), the optical purity of the benzene showing [x]_D^25 ca. 0° (c=1.074, benzene) could be calculated as about 0%.
reaction mixture was stirred for 30 hr at room temperature. After evaporation of tert-buty1 alcohol in vacuo, H₂O (4 ml) was added to the residue. Then, 10% aqueous oxalic acid (15 ml) was added to the aqueous solution to decompose excess tert-buty1 chromate, and the whole solution was extracted with CHCl₃ (× 3). The combined chloroform extracts were successively washed with satd. NaHCO₃ (× 1), and satd. NaCl solutions (× 2), and dried over anhyd. MgSO₄. Filtration and evaporation in vacuo afforded a pale brown viscous oil (0.14 g), which was purified by preparative TLC (silica gel, solvent ether: hexane 6: 4) to give pure (S) (+)-5 (10 mg, 5%) as a colorless viscous oil, [α]D +99.8° (c=0.200, CHCl₃) 32) Spectral (IR and NMR) properties of this oil were identical with those of dl-5 recorded in the same states. This sample showed the identical Rf value with that of the authentic racemic compound on TLC analysis.

Separation with preparative TLC attempted here, recovered crude starting material (90 mg, 43% recovery) as a pale yellow viscous oil.

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32) Following optical rotations have been reported for (S) (+)-5 of natural origin, 11) [α]D +150° (CHCl₃), and [α]D +172° (CHCl₃), and that of chemical synthesis, 12) [α]D +266.3° (c=0.3, CHCl₃). The optical purity of this product could be calculated as 38% by the assumption that (S) (+)-5, [α]D +266.3° (c=0.3, CHCl₃), was optically pure.