37. Katsumi Tanabe: The Structure of Alantolactone. II.\textsuperscript{1)}
The Conversion of Alantolactone into Dihydroeudesmol.

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Ukita and Nakazawa\textsuperscript{3)} isolated a monocarboxylic acid from the reaction mixture of catalytic hydrogenation of dihydroalantolactone (I) and identified the acid with 1,10-dimethyl-7-(2'-carboxyethyl)decalin (II), prepared by the oxidation of tetrahydrosequisilbenihiol (III). Katsura\textsuperscript{3)} previously reported that sesquibieniol (IV) on subjecting to ozonolysis followed by further oxidation with sodium hypobromite furnished the same tricarboxylic acid (VI) as had been obtained previously from the $\alpha$- and $\beta$-selinones.\textsuperscript{4)}

\[
\begin{array}{c}
\text{O} \\
\text{CO} \\
\begin{array}{c}
\text{H}_2 \\
\text{Pt or Pd}
\end{array} \\
\begin{array}{c}
\text{CH}_2\text{OH} \\
\text{O}
\end{array} \\
\text{H}_2\text{O} \\
\end{array}
\]

On the basis of the above informations we assumed alantolactone to have a \textit{trans}-decalin structure and discussed briefly the configurations of the lactone ring in the preceding paper.\textsuperscript{1)} However, some questions remained regarding the assumption made at that time concerning the decalin structure. The tricarboxylic acid (VI) had not been identified reliably with that derived from selinene by mixed fusion and the molecular rotation value was not also recorded, Katsura having reported merely that the melting point and analytical values were in good agreement. The two acids, therefore, cannot be considered as unequivocally identical.

Moreover, Katsura obtained the acid (VI) by oxidation of a ketocarboxylic acid (V), which possesses a carbonyl group at a position adjacent to the ring juncture, in an alkaline medium over a fairly prolonged period. Accordingly, the case must be taken into consideration where the decalin skeleton has already isomerized into a more stable \textit{trans}-fused system during this stage.

The configuration of the A/B ring juncture should be settled first and the present study is concerned with this problem.

Kavács, \textit{et al.}\textsuperscript{5)} stated that the glycol (VII), obtained by the action of lithium aluminum hydride on tetrahydroalantolactone (VII), when refluxed with $p$-toluenesulfonylic acid in benzene solution for 30 minutes, gave an unsaturated primary alcohol in a good yield. The author's result was, however, different from their's and the glycol was recovered unchanged nearly quantitatively under the above conditions. Either by a more prolonged heating or by replacing the solvent with toluene it was dehydrated to an unsaturated primary alcohol (IX) in a poor yield in addition to an oxide (X) having

\begin{itemize}
  \item [*] Nishi-shinagawa, Shinagawa-ku, Tokyo (니시신아가와, 신가와구, 도쿄).
  \item [2)] T. Ukita, S. Nakazawa: This Bulletin, 2, 239 (1954).
  \item [3)] S. Katsura: Nippon Kagaku Zasshi, 63, 1465 (1942).
  \item [4)] $\alpha$- and $\beta$-Selinenes belong to the \textit{trans}-decaline type, since they afford the same dihydrochloride as that derived from eudesmol.\textsuperscript{5)}
\end{itemize}
a tetrahydrofuran structure. The 6-7 position of the double bond in (IX) was assigned from its infrared absorption at 1670 and 808 cm\(^{-1}\) (trisubstituted olefin). The structure of (X) was based on the analytical values, absence of coloration with tetratinomethane, and on its ready elution from alumina (Brockmann grade II) with petroleum ether.\(^6\)

The oxide (X) was also obtained as a major product by treatment of (VII) with \(p\)-toluenesulfonyl chloride in pyridine, affording the expected ditosylate only in a poor yield. The reaction of phenylmagnesium bromide on tetrahydroalantolactone (VII) also gave the analogous oxide (XI), probably produced by the elimination of water from a phenyl-substituted glycol as an intermediate. Such a tendency of the hydroxyl group at 7 to cyclize readily to a tetrahydrofuran ring may give an evidence to our assumption that alantolactones belong to 7-O axial cis-lactone.\(^5\)

(IX) was catalytically hydrogenated in acetic acid and the product, without further purification, was oxidized with sodium dichromate to a monocarboxylic acid (XIII), which was characterized as the amide of m.p. 139~140°, \([\alpha]_D^{20} +35.2°\). The same monocarboxylic acid (m.p. 70~72°) was isolated when the mixture of alantolactones, probably containing isoalantolactone, was subjected to hydrogenolysis in the presence of platinum oxide in acetic acid solution at 50°. The acid thus obtained can be considered as identical with the monocarboxylic acid (m.p. 65~67°; the amide, m.p. 138~140°, \([\alpha]_D^{20} +31.7°\) reported by Ukita, et al.\(^5\)

The methyl ester of (XIII) was treated with phenylmagnesium bromide and the reaction product was separated through alumina column into the corresponding tertiary alcohol (XIV), m.p. 140~141°, and its dehydrated product (XV), m.p. 109~110°, the former being easily dehydrated to the latter on heating with \(p\)-toluenesulfonic acid in benzene solution.

1,10-Dimethyl-7-acetyldecalin (XVI) was isolated in a pure state on regenerating its semicarbazone (m.p. 206~208°), which was produced from the ozonolysis reaction mixture of (XV). On treatment of (XVI) with methylmagnesium iodide, according to the procedure of Ruzicka, et al.,\(^7\) it afforded dihydrooedesmol (XVII), m.p. 84~85°, \([\alpha]_D^{20} +17.5°\), which was proved to be identical with the authentic specimen by mixed fusion and infrared spectra.

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Eudesmol was established by Riniker, et al. to have a trans-decalin structure by correlation with steroids, and, thus, alantolactone including isoa-lantolactone and dihydroisoalantolactone must have a trans-decalin structure and at the same time should be represented by (VIII) and not by its mirror image.

The present study was carried out under the kind guidance of Prof. K. Tsuda of the University of Tokyo for which the author is deeply grateful. The author wishes to express his appreciation to Prof. S. Shibata of the University of Tokyo for providing a sample of eudesmol, to Mr. M. Matsui, Director of this Laboratory, and to Dr. S. Yoshida and Dr. I. Iwai of this Laboratory for their kind encouragements. Thanks are due to Mr. T. Onoe, Miss C. Furukawa, and Miss H. Ohtsuka for microanalyses, and to Mr. H. Shindo and Mr. O. Amakasu for the infrared spectral measurement.

Experimental

Glycol (VIII)—Tetrahydroalantolactone(m.p. 142–143°, [α]₂⁰° +11.5°) was treated with LiAlH₄ in dehyd. ether and the product was recrystallized from hexane to give the glycol (VIII) in colorless needles, m.p. 112–113.5, [α]₂⁰° –8.1°(c=2). Anal. Calcd. for C₃₅H₇₀O₂: C, 74.56; H, 11.74. Found : C, 75.14; H, 11.90.

A solution of (VIII) (2.4 g.) and p-toluenesulfonyl chloride (5 g.) in pyridine (20 cc.) was set aside overnight at room temperature, the mixture was poured into ice-water, acidified with HCl and extracted with ether. The ether extract was washed with aq. NaHCO₃ solution, dried, and the solvent was removed. The residual oily substance (2.5 g.) was dissolved in hexane and stored in an ice-box overnight. The deposited crystalline precipitate was recrystallized from hexane to afford the ditosylate of (VIII) in colorless needles, m.p. 105°; yield, 146 mg. Anal. Calcd. for C₃₉H₆₅O₄S₂: C, 63.47; H, 7.35. Found : C, 63.82; H, 7.36.

The mother liquor separated from the ditosylate was passed through an alumina (Brockmann grade II) column and the column was eluted with petr. ether. Removal of the solvent gave an oily residue, which was distilled to give an oxide (X) as a colorless liquid, b.p. 128–128°, 1.1.4980; yield, 1.59 g. Anal. Calcd. for C₃₅H₇₀O₂: C, 81.02; H, 11.79. Found : C, 80.97; H, 11.47.

Dehydration of (VIII)—After refluxing a solution of (VIII) (6 g.) and p-toluenesulfonic acid (1 g.) in dehyd. benzene (150 cc.) for 2 hrs., the solvent was concentrated at an ordinary pressure to about 20 cc. and then at a reduced pressure to dryness. The residue was dissolved in hexane (30 cc.) and stored in an ice-box. The deposited crystalline mass was recrystallized from hexane to give unchang-ed glycol, m.p. 112–113°; yield, 4 g.

The filtrate separated from the glycol was chromatographed on alumina. The fraction eluted with petr. ether gave 1.1 g. of a colorless liquid, b.p. 148°, which proved identical with the oxide (X) described above by the comparison of their infrared spectra. The benzene eluate afforded 0.64 g. of an unsaturated alcohol (X) as a colorless viscous liquid, b.p. 140°(bath temperature). Anal. Calcd. for C₃₅H₇₀O₂: C, 81.02; H, 11.79. Found : C, 80.75; H, 11.57.

1,10-Dimethyl-7-(2’-carboxyethyl)decalin (XIII)—(a) A solution of (IX) (500 mg.) in AcOH was shaken in H₂ atmosphere with PT₀₅ absorbing about 1 mol. equiv. of H₂. After removal of the catalyst, a solution of Na₂Cr₂O₇·2 H₂O (250 mg.) in AcOH was added slowly to the filtrate and the mixture was set aside overnight at room temperature. The excess reagent was decomposed with EtOH and the solvent was removed under a reduced pressure. The residue was diluted with water and extracted with ether. The acidic portion was separated from the ether extract by shaking with 5% Na₂CO₃ solution, and converted to the amide by the usual procedure. The amide showed m.p. 139–140°, [α]₂⁰° +35.2°(c=2), after recrystallization from hyd. MeOH. Yield, 210 mg. Anal. Calcd. for C₃₅H₇₀ON : C, 75.89; H, 11.47; N, 5.90. Found : C, 75.86; H, 11.49; N, 5.94.

(b) A solution of 42 g. of a mixture of alantolactones (m.p. 120–130°) was shaken in AcOH with PtO₂ (5 g.) in H₂ atmosphere at 50°, ca. 1.8 moles of H₂ being consumed. After filtration of the catalyst, the filtrate was concentrated at a reduced pressure and the residue was dissolved in ether. The separated acidic substance (16 g.) from the ether solution was worked up as above and was recrystallized from hyd. MeOH to give 1,10-dimethyl-7-(2’-carboxyethyl)decalin (XIII) as colorless cubelets, m.p. 70–72°, [α]₂⁰° +37.1°(c=2). Anal. Calcd. for C₃₅H₇₀O₂: C, 75.58; H, 11.09. Found : C, 75.91; H, 11.14.

The amide showed m.p. 139–140°, [α]₂⁰° +35.7°(c=2), after recrystallization from hyd. MeOH, which was proved to be identical by mixed melting point and the infrared spectra with that obtained through the route described above.

9) Optical rotation was measured in CHCl₃.
The methyl ester of (XIII) was prepared with \(\text{CH}_2\text{N}_2\) and showed b.p., 92°; \(\eta^2_7\) 1.4835; \([\alpha]_{D}^{17} +42.5°\) (c=2).

**Grignard Reaction of the Methyl Ester of (XIII)**—A solution of the methyl ester (11 g.) of (XIII) in dehyd. ether (100 cc) was added dropwise with stirring and cooling into an ether solution of PhMgBr prepared from 23.5 g. of bromobenzene and 3.56 g. of Mg. After the addition was completed, the solution was refluxed for 1 hr. The cooled mixture was hydrolysed with 10% AcOH solution, the ether layer separated, washed with 5% NaHCO₃ solution, and dried. After removal of the solvent the residue was chromatographed on alumina (200 g.). The petr. ether eluate after evaporation of the solvent yielded 8.5 g. of an unsaturated hydrocarbon (XV), which was recrystallized from 95% EtOH to colorless needles, m.p. 109~110°. *Anal. Calcd. for C₉H₇₄: C, 90.44; H, 9.56. Found: C, 90.88; H, 9.47.*

Evaporation of the benzene eluate gave 1.6 g. of a diphenylcarbinol (XIV), which was recrystallized from 95% EtOH to colorless needles, m.p. 140~141°. *Anal. Calcd. for C₉H₈O: C, 86.11; H, 9.64. Found: C, 85.65; H, 9.59.*

After refluxing a solution of (XIV) (1.32 g.) and \(\rho\)-toluenesulfonic acid (0.15 g.) in benzene (60 cc.), the solution was washed with 5% Na₂CO₃ solution, dried, and the solvent was evaporated. The residue was recrystallized from 95% EtOH to (XV), m.p. 109~110°, which showed no depression of m.p. on admixture with that obtained above.

**1,10-Dimethyl-7-acetyldecaline (XVI)**—A solution of (XV) (4 g.) in CHCl₃ (100 cc.) at \(-10°\) was treated with ozonized oxygen until the solution gave no color with tetrinitromethane. The solvent was evaporated under a reduced pressure. After the addition of water the mixture was allowed to stand for 3 hrs. and extracted with ether. The ether extract after evaporation of the solvent gave 4.1 g. of a viscous liquid, which was distilled at a reduced pressure and the fraction of b.p., 140~160° was collected. The semicarbazone of (XVI) was prepared from this fraction in the usual way and was recrystallized twice from MeOH to colorless leaflets of m.p. 206~208°; yield, 1.9 g. *Anal. Calcd. for C₃H₇O₄N: C, 67.88; H, 10.26; N, 15.83. Found: C, 68.00; H, 10.10; N, 16.00.*

The semicarbazone (1.4 g.) was heated at 110° for 2 hrs. in saturated oxalic acid solution. The regenerated dimethyldacetyldicaline was collected with ether and distilled at a reduced pressure; b.p., 147~148°, \(\eta^2_7\) 1.4888; yield, 1.1 g.

**Dihydrodesmol (XVII)**—(a) To an ether solution of MeMgl, prepared from 2.15 g. of MeI and 0.36 g. of Mg, a solution of (XVI) (1 g.) in dehyd. ether (20 cc.) was added with stirring and cooling. After the addition was completed, the solution was allowed to stand overnight, poured into ice water, acidified with tartaric acid solution, and extracted with ether. The dried ether extract was evaporated to a crystalline mass, which was recrystallized from hydr. acetone to colorless needles. Dihydrodesmol thus obtained had m.p. 84~85° and \([\alpha]_{D}^{10} +17.5°\) (c=2), which proved identical with the authentic sample described below by mixed fusion and the infrared spectra. *Anal. Calcd. for C₃H₇O₄: C, 80.29; H, 12.58. Found: C, 80.10; H, 12.26.*

(b) Endosmol (m.p. 81~83°, \([\alpha]_{D}^{10} +30.5°\) was hydrogenated in EtOH in the presence of PtO₃, absorbing 1 mol. equiv. of H₂. The product was repeatedly recrystallized from hydr. acetone to give dihydrodesmol in colorless needles, m.p. 84~85°, \([\alpha]_{D}^{10} +17.0°\) (c=2).

**Reaction of Phenylmagnesium Bromide with Tetrahydroalantolactone**—A solution of tetrahydroalantolactone (2.36 g.) in dehyd. ether (150 cc.) was added dropwise into an ether solution of PhMgBr, prepared from bromobenzene (6.28 g.) and Mg (0.92 g.). After the addition was completed, the mixture was refluxed for 30 mins. On treatment in the usual way the product was chromatographed on alumina and the part (2.83 g.) eluted with petr. ether was recrystallized from 95% EtOH to (X) as colorless needles, m.p. 157~158°. *Anal. Calcd. for C₃H₈O: C, 86.58; H, 9.15. Found: C, 86.92; H, 9.46.*

Another part (0.45 g.) eluted with benzene proved to be the unchanged tetrahydroalantolactone, m.p. 142~143°, after recrystallization from hexane.

**Summary**

Alantolactone was converted to dihydrodesmol and it was confirmed that the alantolactone series belongs to the *trans*-fused decalin type.

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