Oxidation of l-Dihydrocarveol and its Acetate with Selenium Dioxide

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It was previously reported that in the oxidation of β-terpineol[1] and its acetate[2] with selenium dioxide at room temperature (about 30°C), the use of *tert*-butyl alcoholic solution of the oxidant as an oxidizing agent appeared to be favorable both as to yield and as to quality of product. In this paper *l*-dihydrocarveol and its acetate were taken up as the sample and oxidized with selenium dioxide in a manner similar to that in the case of β-terpineol. A solution of selenium dioxide dissolved in *tert*-butyl alcohol by heating to 70~75°C under stirring was used as an oxidizing agent. The conditions and the results in oxidations are shown in Table I.

In the case of *l*-dihydrocarveol, the active methyl group of C_9 position outside the ring was oxidized mainly. The reaction products, in Exp. 1, consisted of 8(9)-*p*-menthen-2,10-diol (I), 8(9)-*p*-menthen-2-ol-10-al (II) and a small amount of dihydrocarvone (III) which was produced by the oxidation of the secondary alcohol group of the sample. In Exp. 2, I and II were obtained.

In the case of *l*-dihydrocarvyl acetate. the active methylidyne group of C_4 position in the ring was oxidized mainly, and the conjugated diene compound was obtained as the result of dehydration of the tertiary alcohol formed[3]. As the reaction products, in Exp. 3, *trans*-8(9)-*p*-menthen-2,4-diol (IV) monoacetate and a small amount of II-acetate were obtained. In addition to these compounds, 3,8(9)-*p*-menthadien-2-ol (V) was identified in the saponified reaction mixture. In Exp. 4, the reaction mixture was saponified, and IV and V were identified. Excepting III these four products are new compounds. In each oxidation the total yield of crude materials was about 6~9% to the sample used, and unchanged samples was recovered in amounts ranging from 60 to 70%.

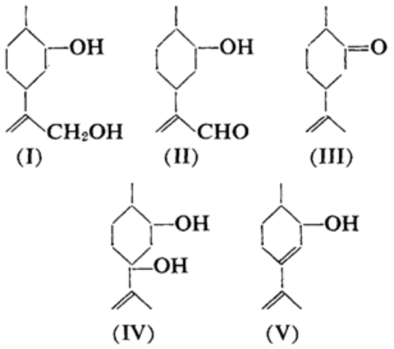

Fig. 1

Each reaction product was identified by the following procedures.

(8)9-*p*-Menthen-2, 10-diol.—In Exp. 1 and 2, crystals melting at 66°C were obtained. It was previously observed that the infrared spectrum of (8)9-*p*-menthen-1, 10-diol showed, in addition to the band due to a bonded hydroxyl group at 3275 cm^{-1}, characteristic bands due to the endmethylene group[1]. That is to say, the band based on the -C=C- stretching vibrations was at 1650 cm^{-1}, normal region, but the band

TABLE I. CONDITIONS AND RESULTS IN OXIDATION OF DIHYDROCARVEOL AND ITS ACETATE

Exp.	Sample g.	CH_3COOH g.	$(CH_3CO)_2O$ g.	SeO_2 g.	*t*-BuOH g.	Benzene g.	Temp.* °C	Time hr.	Reacton product**	Yield*** %
1	26	50	50	9.3	77	70	R.T. 45	15	I II III	8
2	31	50	/	12.0	90	90	40~43 R.T.	4 20	I II	9
3	Acetate 39 〃	50	50	12.0	90	90	45~47 R.T.	4 20	II IV V	6
4	66	/	/	18.5	148	/	48~50	8	IV V	8

* R. T.: Room temperature
** I—V are shown ın Fig. 1.
*** Yields represent wt% to sample used.

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[1] Y. Sakuda, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **82**, 117 (1961).

[2] Y. Sakuda, ibıd., **81**, 1891 (1960).

[3] A. Guillemonat, *Ann. chım.*, **11**, 143 (1939).

based on the =C–H bending vibrations shifted slightly to higher frequency than in 1,4-diol, and was at 900 cm^{-1}. The infrared spectrum of the crystals melting at 66°C (Fig. 2) has similar bands at 900, 1646 and 3280 cm^{-1}. Moreover, in the oxidation of β-terpineol with selenium dioxide, the methyl group of C_9 position was oxidized mainly, but in the case of its acetate, the methylidyne group of C_4 position was oxidized[1]. In the oxidation of dihydrocarveol and its acetate, the same phenomenon is observed. By analogy with these facts, it is assumed that the crystal melting at 66°C is 8(9)-*p*-menthen-2, 10-diol.

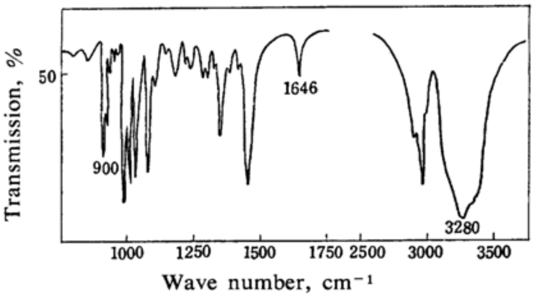

Fig. 2 Infrared spectrum of 8(9)-*p*-Menthen-2, 10-diol (KBr).

8(9)-*p*-Menthen-2-ol-10-al.—In Exps. 1 and 2, in addition to I, the carbonyl compound was obtained as the main product. The infrared spectrum of the carbonyl compound (Fig. 3) shows the bands at 900, 1621 and 3092 cm^{-1} attributable to the conjugated endmethylene group[4], at 1689 cm^{-1} to the unsaturated carbonyl group, and at 3405 cm^{-1} to the hydroxyl group. The ultraviolet spectra of derivatives of the carbonyl compound, semicarbazone gives $\lambda_{\max}^{\text{alc}}$ 262 mμ and 2,4-dinitrophenylhydrazone gives $\lambda_{\max}^{\text{alc}}$ 372 mμ which are identical with the absorption maxima of those of 8(9)-*p*-menthen-1-ol-10-al[1]. The carbonyl compound is easily oxidized with silver oxide to give the corresponding carboxylic acid. From these facts it seems that the carbonyl compound is 8(9)-*p*-menthen-2-ol-10-al.

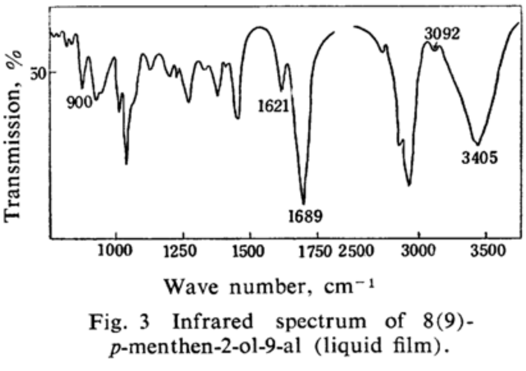

Fig. 3 Infrared spectrum of 8(9)-*p*-menthen-2-ol-9-al (liquid film).

***trans*-8(9)-*p*-Menthen-2, 4-diol.** — In the oxidation of *l*-dihydrocarvyl acetate, Exps. 3 and 4, the crystal melting at 128°C was obtained.

Naves[5] and Simonsen[6] deduced that dihydrocarveol had each equatorial group of methyl at C_1, hydroxyl at C_2 and isopropenyl at C_4 in chair conformations, based on the known fact[7] that on hydrogenation the alcohol gave carvomenthol. If the conformation of dihydrocarveol is maintained during the oxidation procedure, it is expected that 2,4-diol formed from dihydrocarveol is a *trans*-compound with one equatorial hydroxyl group at C_2 and one axial hydroxyl group at C_4. The conformational assignment of 2,4-diol may be supported by the infrared spectrum. Pickering and Price[8] empirically assumed that in *cis*-4-*tert*-butylcyclohexanol having a pure axial C–OH, a strong absorption band based on the C–OH stretching vibrations was at 955 cm^{-1}; and in *trans*-4-*tert*-butylcyclohexanol having a pure equatorial C–OH, at 1062 cm^{-1}. Choe and Tsutsumi[9] assumed that in *cis*-1,2-cyclohexanediol having one axial and one equatorial hydroxyl group, absorption bands based on the axial and equatorial C–OH stretching vibrations were at 950 and 1075 cm^{-1} respectively. The infrared spectrum of the crystals melting at 128°C (Fig. 4) shows, in addition to the usual bands due to the endmethylene group at 895 and 1645 cm^{-1}, two bands characteristic of the hydroxyl groups. One, at 930 cm^{-1}, is attributed to the axial C–OH stretch, although it shifts slightly to lower frequency; and the other, at 1077 cm^{-1}, is attributed to the equatorial C–OH stretch. From these facts, the crystals melting at 128°C seem to be *trans*-8(9)-*p*-menthen-2, 4-diol.

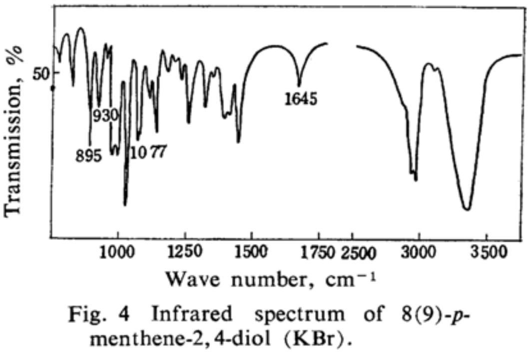

Fig. 4 Infrared spectrum of 8(9)-*p*-menthene-2, 4-diol (KBr).

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[4] E. R. Blout et al., *J. Am. Chem. Soc.*, **70**, 194 (1948).

[5] Y. R. Naves, *Bull. soc. chim. France*, **1956**, 1020.

[6] J. Simonsen, "The Terpenes", University Press, Cambridge, Vol. III, (1952), p. 520.

[7] R. G. Johnston and J. Read, *J. Chem. Soc.*, **1934**, 233.

[8] R. A. Pickering and C. C. Price, *J. Am. Chem. Soc.*, **80**, 4931 (1958).

[9] S. Choe and S. Tsutsumi, *J. Chem. Soc. Japan, Pure Chem. Sec.*, (*Nippon Kagaku Zasshi*), **81**, 785 (1960).

3, 8(9)-*p*-Menthadien-2-ol.—In Exps. 3 and 4, the ultraviolet spectrum of each reaction mixture gives $\lambda_{\max}^{\text{alc}}$ 233 mμ which is identical with the absorption maximum of 3, 8(9)-*p*-menthadien-1-ol[1]. The reaction mixture showing $\lambda_{\max}^{\text{alc}}$ 233 mμ reacts easily with maleic anhydride and the adduct is obtained.

Experimental

Materials and Reaction Procedure.—*l-Dihydrocarveol.*—*l*-Carvone was synthesized from *d*-limonene via limonene nitrosochloride and carvoxime[10]. *l*-Dihydrocarveol, the sample, was prepared by a reduction of carvone thus obtained with sodium and alcohol. The process is schematically shown in Fig. 5.

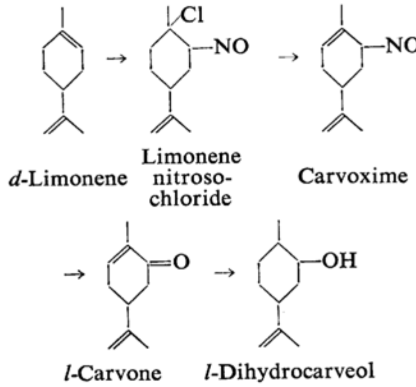

Fig. 5

The overall yield of *l*-dihydrocarveol is about 20% of the limonene used. As the crude *l*-dihydrocarveol thus obtained contained a small amount of non-reduced *l*-carvone, it was purified as follows. Crude *l*-dihydrocarveol was esterified with benzoyl chloride in a pyridine solution and the ester produced was steam-distilled. The remaining part of steam-distillation was saponified by 10% alcoholic sodium hydroxide solution. The saponification product was fractionated under reduced pressure. Rectified *l*-dihydrocarveol showed the following properties; b.p.$_6$ 95~97°C, n_D^{25} 1.4783, d_4^{25} 0.9296, $[\alpha]_D$ −33.2; 3,5-dinitrobenzoate m.p. 122°C, $[\alpha]_D$ −55.0 (in chloroform).

l-Dihydrocarvyl acetate. — *l*-Dihydrocarvyl acetate was prepared by refluxing *l*-dihydrocarveol with acetic anhydride and anhydrous sodium acetate, and rectifying the product. The sample thus obtained showed the following properties; b.p.$_5$ 95~97°C, n_D^{25} 1.4611, d_4^{25} 0.9490, $[\alpha]_D$ −67.1, E. V. 286.5 (Calcd. for $C_{10}H_{17}OOCCH_3$: 285.9).

Oxidizing Agent. — Pulverized selenium dioxide was dissolved in *tert*-butyl alcohol by heating to 70~75°C under continuous stirring for two hours in a current of carbon dioxide. In exception of Exp. 4, the *tert*-butyl alcoholic solution of selenium dioxide was employed by diluting with benzene and drying with anhydrous sodium sulfate.

Reaction Procedure. — Under each condition as shown in Table I the solution of the oxidizing agent was added to the sample solution in one lot, and stirred from time to time. When the reaction was over, in Exp. 1, the reaction mixture was heated to 45°C and the solvent was removed in vacuo, and the remaining product was fractionated under reduced pressure. In Exps. 2—4, each reaction mixture was diluted with water and extracted twice with ether. The combined ether solution was treated with aqueous alkali and with water successively and dried. After removal of the solvent, the remaining product was fractionated under reduced pressure. The fractions thus obtained were treated by chromatography, and each reaction product was identified as follows.

Identification of the Reaction Products. — *Dihydrocarvone.* — The result of distillation of the reaction product obtained in Exp. 1 is shown in Table II.

TABLE II

Fraction	b. p., °C /3 mmHg	Yield, g.	n_D^{25}	d_4^{25}
1	73~ 78	2.0	1.4775	0.9293
2	78~ 80	8.0	1.4780	0.9285
3	80~ 83	3.0	1.4792	0.9314
4	83~ 85	1.7	1.4816	0.9381
5	85~106	1.5	1.4852	0.9500
6	106~119	2.6	1.4985	1.0367

Fraction 1 was chromatographed over 55 g. of silica gel. The column was eluted with petroleum ether-ethyl acetate (volume ratio 7 : 3). The initial elute gave 0.5 g. (n_D^{25} 1.4780, d_4^{25} 0.9274) of a faintly yellow oil possessing a carvone-like odor. The oil gave a semicarbazone, m.p. 188~189°C, $[\alpha]_D$ −14.6 (in chloroform).

Found: N, 20.25. Calcd. for $C_{11}H_{19}ON_3$: N, 20.27%. The ultraviolet spectrum of the semicarbazone gave $\lambda_{\max}^{\text{alc}}$ 228 mμ (log ε 4.14) which corresponded to the absorption maximum of that of the simple carbonyl compounds.

8(9)-p-Menthen-2-ol-10-al. — Fractions 5 and 6 of Table II were combined and chromatographed in the same way as in the case of fraction 1. A viscid yellow oil was obtained, which amounted to about 35% of these combined two fractions. The infrared spectrum of the oil (Fig. 3) showed the bands due to the conjugated carbonyl, endmethylene and hydroxyl groups.

Derivatives: Semicarbazone, m.p. 201~202°C; U. V. $\lambda_{\max}^{\text{alc}}$ 262 mμ, log ε 4.27.

Found: N, 18.49. Calcd. for $C_{11}H_{19}O_2N_3$: N, 18.65%. 2,4-dinitrophenylhydrazone, m. p. 188°C; U. V. $\lambda_{\max}^{\text{alc}}$ 372 mμ, log ε 4.49.

Found: C, 54.87; H, 5.95; N, 16.00. Calcd. for $C_{16}H_{20}O_5N_4$: C, 55.16; H, 5.79; N, 16.08%.

Oxidation with Silver Oxide. — A solution of the carbonyl compound 0.13 g. (0.8×10^{-3} mol.) in 1 cc. alcohol was added dropwise under rapid stirring to a mixture of sodium hydroxide 0.5 g., water 5 cc. and silver oxide (0.6×10^{-3} mol. equiv.) which was newly prepared from silver nitrate 0.43 g. and sodium hydroxide 0.12 g. The combined mixture

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[10] E. E. Royals and S. E. Horne, *J. Am. Chem. Soc.*, **73**, 5856 (1951). C. Bordenca et al., *Ind. Eng. Chem.*, **43**, 1196 (1951).

was stirred at room temperature for 30 min. The reaction mixture was acidified with dilute hydrochloric acid and extracted repeatedly with ether. The combined extract was washed with water and dried. After removal of the solvent, it was distilled under reduced pressure, and 0.05 g. of a very viscid acidic material was obtained. The infrared spectrum thereof showed the bands due to the endmethylene group at 1621 cm^{-1} and that of the carboxylic acid group at 1690 cm^{-1}. From this oil *p*-bromophenacyl ester was prepared as white needles of m. p. 99~100°C.

8(9)-p-Menthen-2, 10-diol.—In the chromatography above described, the crystal was eluted after 8(9)-*p*-menthen*l*-2-ol-10-al as the final eluate. Recrystallization of the crystals from a mixed solvent of ethyl acetate and petroleum ether gave long white needles of m. p. 66°C.

Found: C, 67.22; H, 10.81. Calcd. for $C_{10}H_{18}O_2 \cdot 1/2H_2O$: C, 67.01; H, 10.68%.

Identification of the crystals has been described.

In Exp. 2, the reaction product was fractionated under reduced pressure, and was separated into four fractions. The fourth fraction, b. p.$_2$ 110~125°C, n_D^{25} 1.4990, d_4^{25} 1.0261, yield 6.2 g., was chromatographed in the same way as in the case of Exp. 1. 8(9)-*p*-Menthen-2-ol-10-al and 8(9)-*p*-menthen-2, 10-diol were yielded in about 50 and 5% of this fraction respectively.

TABLE III

Fraction	b.p.°C/ 2 mmHg	Yield g.	n_D^{25}	d_4^{25}	E.V.*
1	90~ 94	1.6	1.4640	0.9522	
2	94~ 95	19.8	1.4625	0.9490	
3	95~ 98	6.0	1.4630	0.9533	282.2
4	98~130	8.3	1.4704	1.0260	270.4

* E. V. calcd. for $C_{10}H_{16}(OH)OOCCH_3$: 265.0.

3, 8(9)-p-Menthadien-2-ol.—The results of distillation of the oxidation product of *l*-dihydrocarvyl acetate, in Exp. 3, is shown in Table III.

Fraction 4 was chromatographed over 350 g. of silica gel, and the column was eluted with petroleum ether-ethyl acetate (8 : 2), and the elutes were separated into five fractions. Saponification of the initial elute gave 1.2 g. of the oil. The ultraviolet spectrum of the oil gave $\lambda_{\max}^{\text{alc}}$ 233 mμ which corresponded to the absorption maximum of 3, 8(9)-*p*-menthadien[11]. The infrared spectrum of the oil showed the bands due to the endmethylene group at 887, 1643 and 3078 cm^{-1}, and that of the conjugated double bond[12] at 1609 and 1643 cm^{-1}, and that of the hydroxyl group at 3354 cm^{-1}. A solution consisting of 1.0 g. of the oil, 0.3 g. of maleic anhydride, a very small amount of hydroquinone and 3.0 g. of ether was refluxed for two hours. The ether solution was washed with water to remove the excess of maleic anhydride and was steam-distilled. The remaining part of the steam-distillation was recrystallized from 50% aqueous methyl alcohol. A colorless needle adduct, m. p. 190~191°C, was obtained.

Found: C, 67.41; H, 7.30. Calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24%.

In Exp. 4, the ultraviolet spectrum of the reaction product showed $\lambda_{\max}^{\text{alc}}$ 233 mμ. The reaction product was fractionated under reduced pressure, and the distillate was saponified. The oil thus obtained was treated with maleic anhydride in the same way as that described above, and the adduct of m. p. 191°C was obtained.

8(9)-p-Menthen-2-ol-10-al Acetate. — In chromatography of fraction 4 in Table III, a small amount of the carbonyl compound was obtained as the second eluate, and it gave 2, 4-dinitrophenylhydrazone as yellow needles of m. p. 183°C.

Found: N, 14.08. Calcd. for $C_{18}H_{22}O_6N_4$: N, 14.35%.

The ultraviolet spectrum of 2, 4-dinitrophenylhydrazone gave $\lambda_{\max}^{\text{alc}}$ 372 mμ, log ε 4.43, which was identical with the absorption maximum of that of 8(9)-*p*-menthen-2-ol-10-al. From this fact, it is assumed that the carbonyl compound is 8(9)-*p*-menthen-2-ol-10-al acetate.

trans-8 (9)-p-Menthen-2, 4-diol Monoacetate. — In the chromatography above described, the crystalline mass was obtained as the final eluate. Recrystallization of the mass from a mixed solvent of petroleum ether and ethyl acetate gave white crystals of m. p. 78°C. The infrared spectrum thereof showed the bands due to the acetate group at 1268 and 1705 cm^{-1}, and that of the hydroxyl group at 3478 cm^{-1}. Saponification of the crystals gave *trans*-8(9)-*p*-menthen-2, 4-diol mentioned next.

Found: C, 68.15; H, 9.75. Calcd. for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49%.

trans-8(9)-p-Menthen-2, 4-diol. — In the fractional distillation of the oxidation product obtained in Exp. 4, a very viscid residue having the following constants was obtained; b. p.$_7$ above 147°C, yield 8.5 g., n_D^{25} 1.4885, d_4^{25} 1.0593, E. V. 262.4 (Calcd. for $C_{10}H_{16}(OH)OOCCH_3$: 265.0). Saponification of the residue by 10% alcoholic sodium hydroxide solution gave 4.7 g. of the resinous mass. The mass was eluted through a column packed with silica gel using petroleum ether-ethyl acetate (55 : 45) as a moving phase. Recrystallizaton of the crystals thus obtained from ethyl acetate gave long white needles of m. p. 128°C. Identification of the crystals has been described.

Found: C, 70.36; H, 10.80. Calcd. for $C_{10}H_{18}O_2$: C, 70.58; H, 10.58%.

Summary

l-Dihydrocarveol and its acetate were oxidized with a solution of selenium dioxide dissolved in *tert*-butyl alcohol, in the range of 15~50°C. In the case of *l*-dihydrocarveol, the active methyl group of C_9 position outside the ring was oxidized mainly. As the reaction products, dihydrocarvone, 8(9)-*p*-menthene-2, 10-diol and 8(9)-*p*-menthen-2-ol-10-al were obtained. In the case of *l*-dihydrocarvyl

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[11] H. Pines and H. E. Eching, *J. Am. Chem. Soc.*, **77**, 6314 (1955).

[12] J. L. H. Allan et al., *J. Chem. Soc.*, **1955**, 1874.

acetate, the active methylidyne group of C_4 position in the ring was oxidized mainly. *trans*-(8)9-*p*-Menthen-2, 4-diol and its monoacetate, 8(9)-*p*-menthen-2-ol-10-al acetate and 3, 8(9)-*p*-menthadien-2-ol were identified. Excepting dihydrocarvone, these products are new compounds.

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