Stereochemical Studies of Monoterpene Compounds. X.[1] Intramolecular Interaction of Oxirane and Cyclopropane Rings with a Hydroxyl Group[2]

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The intramolecular interaction of oxirane and cyclopropane rings with a hydroxyl group in the alicyclic α,β-epoxy-, β,γ-epoxy-, and cyclopropyl alcohols was investigated by means of the infrared spectroscopy. *cis*-α,β-Epoxyalcohols (II, IV and V) showed a free hydroxyl band, an interacted hydroxyl band with a C–O bond of the oxirane ring, and/or a band due to a O–H···O hydrogen bond, whereas *trans*-epoxyalcohols (I and III) showed only a free hydroxyl band. The interaction between the hydroxyl group and a C–C bond of the oxirane ring was likely to be absent. β,γ-Epoxyalcohols revealed a hydroxyl band interacting with lone-pair electrons of the oxirane oxygen, in addition to a free hydroxyl band. The O–H··· cyclopropane interaction was found with 2-(1-methylcyclopropyl)-5-methylcyclohexanols (VII and VIII). The correlation of the infrared spectra with the conformation of the interacting groups is also discussed.

A hydroxyl group interacts with the π-electrons of a double bond and a carbonyl group.[4–6] Cyclopropane and oxirane rings are known to show properties like those of the π-electron system. It seemed, therefore, that it would be interesting to investigate the intramolecular interaction between the hydroxyl group and the oxirane and cyclopropane rings. For acyclic epoxyalcohols, the interaction between the hydroxyl group and the oxirane ring can be created by using electrons of the C–O bond, and it is favored when the hydroxyl group approaches not from the top, but from the plane of the ring.[7] However, the correlation of the infrared spectrum with the geometry of the interacting groups has not yet been clarified for cyclic compounds, in which the approach of the hydroxyl group can be regulated both in site and in direction. This paper will report on the intramolecular interaction of the hydroxyl group with the oxirane and cyclopropane rings in cyclic monoterpene alcohols, such as *trans*- and *cis*-1,2-epoxy-*p*-menth-8-en-6-ols (I and II), *trans*- and *cis*-4,8-epoxy-*p*-menthan-3-ols (III, IV, and V), 8,9-epoxy-*p*-menthan-3-ol (VI), and 2-(1-methylcyclopropyl)-5-methylcyclohexanols (VII and VIII).

Results and Discussion

The structure and the infrared (IR) spectral data of α,β- and β,γ-epoxyalcohols are collected in Chart I.

We will first deal with the interaction between the hydroxyl group and the oxirane ring of the α,β-epoxyalcohols. The hydroxyl stretching absorption of *trans*-1,2-epoxy-*p*-menth-8-en-6-ol (I) showed only one peak, at 3635 cm^{-1}, which corresponds to the free, secondary hydroxyl group. The *trans*-epoxyalcohol I, therefore, takes a conformation in which the hydroxyl group is unable to interact with the oxirane ring, as is shown in Chart I. Now, the IR spectrum of *cis*-epoxy-*p*-menth-8-en-6-ol (II), an isomer of I in respect of the hydroxyl group, showed three bands, at 3629, 3594, and 3572 cm^{-1} (Fig. 1). The highest-frequency band is similar in position to the free hydroxyl absorption band of the isomer I. The remaining peaks are, thus, due to the intramolecularly-interacting hydroxyl group. The nuclear magnetic resonance (NMR) spectrum of the C-6 proton revealed the hydroxyl group to take an axial orientation, as is shown in Chart I. The molecular models suggest, then, that the interaction between an axial hydroxyl group and an oxirane ring would be possible in three cases, shown as A, B, and D in Chart

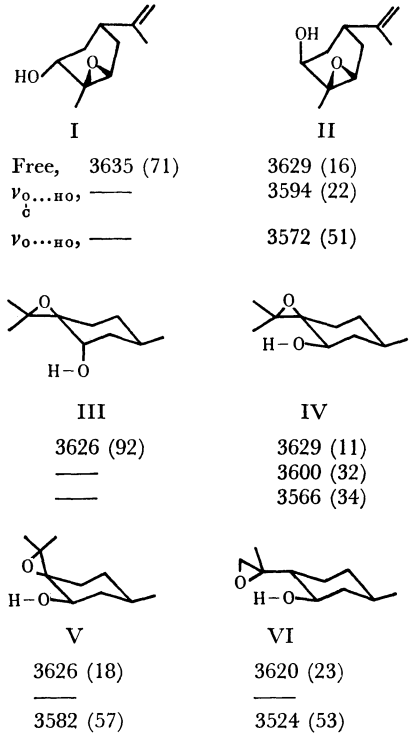

Chart I. Free and bonded peak positions of α, β- and β, γ-epoxyalcohols (I—VI), cm^{-1} (ε).

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[1] Paper IX of this series: T. Hirata and T. Suga, *J. Org. Chem.*, **36**, No. 3 (1971), in press.

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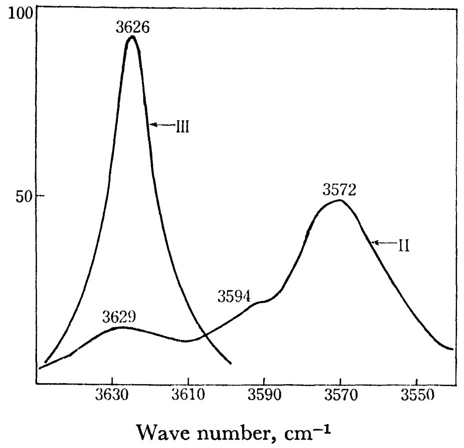


Fig. 1. IR spectra of epoxyalcohols (II and III) in a carbon tetrachloride solution.

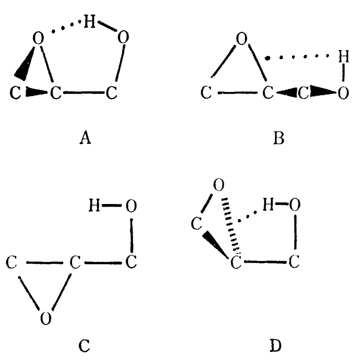


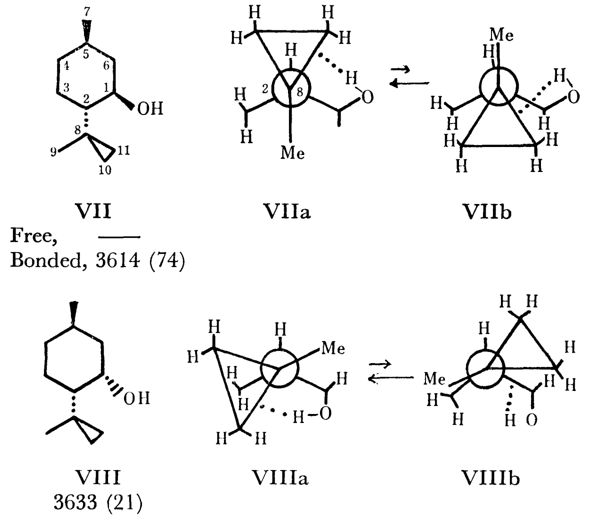
Chart II. Possible interactions between a hydroxyl group and an oxiran ring.

II. By comparison with the spectra of 2,3-epoxypropanols,[7] the peak at 3572 cm^{-1} ($\Delta\nu$=57 cm^{-1}) can be assigned to the interaction between the lone-pair electrons of an oxygen atom and the hydroxyl group which can approach the top of the oxirane ring surface; *cf.* A in Chart II. The other peak, at 3594 cm^{-1}, seems to be due to the hydroxyl group which interacts with electrons of the C–O bond in a plane of the oxirane ring; *cf.* B in Chart II.

The hydroxyl stretching absorption of *trans*-4,8-epoxy-*p*-menthan-3-ol (III), an exocyclic epoxide, showed only one peak, at 3626 cm^{-1} (Fig. 1); this peak is assignable to an absorption due to only the free secondary hydroxyl group. However, the hydroxyl group of III may interact with the C_4–C_8 bond in a plane of the oxirane ring, as in the case of C in Chart II; if any such interaction is present, however, it seems to be too little to detect by usual infrared measurements. *cis*-4,8-Epoxy-*p*-menthan-3-ol (IV), an isomer of III concerning the hydroxyl group, exhibited hereon three bands, at 3629, 3600, and 3566 cm^{-1}, which are similar in position to those of II. Thus, these were assigned to an absorption resulting from a free hydroxyl group and an interacted one, such as B and A (Chart II), respectively. On the other hand, epoxyalcohol V, an isomer of IV with respect to a methyl group, showed two bands, at 3626 and 3582 cm^{-1}, due to the free hydroxyl group and the intramolecular OH···O hydrogen-bonded hydroxyl group, shown in A, respectively. Although the hydroxyl group of V may approach the C–O bond from the top of the three-membered rings, as is shown in D, no such interaction was observed. This result indicates the impossibility of the interaction D for the epoxyalcohol V; this is in agreement with the literature.[7] The NMR spectrum of the C-3 proton of V showed double doublets (J_{vic}=10 and 6.5 Hz) at 3.88 ppm, which indicates the proton to be in a perfectly axial orientation. On the other hand, IV revealed the scarecely separated peak, suggesting some twisted conformations favorable for an approach of the hydroxyl group in a plane of the oxirane ring.

The IR spectrum of 8,9-epoxy-*p*-menthan-3-ol (VI) had two hydroxyl-stretching absorptions, at 3620 and 3524 cm^{-1}. The former was assigned to a free hydroxyl group, though the frequency of the band seems to be slightly low in comparison with a normal free secondary hydroxyl band; also, the hydroxyl proton may approach geometrically the C–O bond in a plane of the oxirane ring. On the other hand, the latter is shifted greatly from the free hydroxyl band. The extent of the shift is similar to that of *trans*- and *cis*-*p*-menthane-3,8-diols,[6] in which the hydroxyl group bonds intramolecularly with lone-pair electrons of the other hydroxyl oxygen atom. Thus, the band may be attributed to an intramolecular hydrogen bond between the hydroxyl group and the lone-pair electrons of an oxygen atom of the oxirane ring.

We now wish to deal with the interaction between the hydroxyl group and the cyclopropane ring of β,γ-cyclopropyl alcohols. The infrared spectral data are shown in Chart III. The spectrum of (−)-2-(1-methylcyclopropyl)-5-methylcyclohexanol (VII) has only one peak, at 3614 cm^{-1} (also Fig. 2). This shifted band was assigned on the basis of an internal O–H···cyclopropane interaction, since the free hydroxyl band of *l*-menthol[8] appears at 3628 cm^{-1}. Two conformers, VIIa and VIIb, can be considered for the preferred conformation of VII, because the preferred site for



Free, —
Bonded, 3614 (74)

VIII
3633 (21)
3618 (29)

Chart III. Free and bonded peak possitiosn of cyclopropylalconhols (VII and VIII), cm^{-1} (ε).

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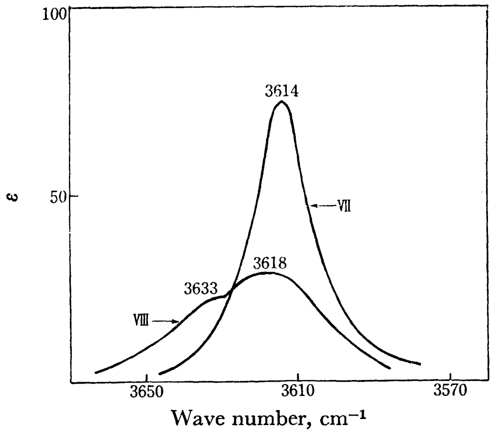

Fig. 2. IR spectra of cyclopropyl alcohols (VII and VIII) in a carbon tetrachloride solution.

the O-H···cyclopropane interaction is the "edge" of a plane of the ring.[9,10] Of those two, the *gauche* conformer VIIa is energetically more favorable than the *eclipsed* one, VIIb. On the other hand, (+)-2-(1-methylcyclopropyl)-5-methylcyclohexanol (VIII), an isomer of VII in respect of the hydroxyl group, had two peaks, at 3633 (weak) and 3618 cm⁻¹ (*cf.* Fig. 2), attributable to the free hydroxyl group and the O-H··· cyclopropane interaction respectively. An interaction would be possible in both VIIIa and VIIIb. The ininteracted species may, then, be thought more populous in VII than in VIII, judging from the infrared spectra shown in Fig. 2. This may be interpreted as follows: a steric repulsion would be at a minimum in the *gauche* conformer VIIa, which is further stabilized by an internal O-H···cyclopropane interaction. On the other hand, the conformers, VIIIa and VIIIb, are favorable for the intraction, but are destabilized by the repulsion of the *eclipsed* groups. Therefore, both free and bonded hydroxyl absorptions appear in VIII.

Experimental

The IR spectra in the hydroxyl-stretching region were measured with a Perkin-Elmer Model 621 Infrared Spectrometer. A salt absorption cell (20 mm long) was used; the concentration of the carbon tetrachloride solution was 0.005 mol/*l*, at which concentration the association of the solute is negligible. The measurements were made at 25°C. The NMR spectra were recorded with a Hitachi Perkin-Elmer R-20 high-resolution spectrometer at 60 MHz, using tetramethylsilane as the internal standard. Gas-chromatographic analyses were made at 95—150°C, using a Hitachi Perkin-Elmer F6-D gas chromatograph with a flame ionization-type detector and a 3 mm×1 m column packed with 3%-polyethylene glycol on Celite. Compounds I and II were separated preparatively using a Shimadzu (Kyoto) GC-2B gas chromatograph with a thermal conductor-type detector and a 4 mm× 3 m column packed with 10%-diethylene glycol succinate on Diasolid L (80—100 mesh). Helium was used as the carrier gas.

trans- *and* cis-*1,2-Epoxy*-p-*menth-8-en-6-ols (I and II).* (−)-Carvone (78.0°C/4 mmHg; n_D^{25} 1.4944; d_4^{25} 0.9539; $[\alpha]_D^{25}$ −61.14° (neat)) was epoxydized with 6 N sodium hydroxide and 30% hydrogen peroxide in methanol to (+)-α,β-epoxycarvone (107—109°C/8 mmHg; n_D^{25} 1.4788; d_4^{25} 1.0282; $[\alpha]_D^{25}$ +79.44° (neat), lit:[9] $[\alpha]_D^{25}$ +87.60° (neat)), according to the published procedure.[11] A mixture of $NaBH_4$ (2.0 g) and 700 m*l* of 80% dioxane in water was added to a solution of (+)-α,β-epoxycarvone (10 g) in 200 m*l* of 80% dioxane in water. After the entire reaction mixture has been left to stand at room temperature for three days, it was worked up in the usual manner to give 8.0 g of a mixture of I and II. The fractionation of the mixture was carried out by gas chromatography, as has been described above (peak area, I: 65%, II: 35%). The first peak was II: n_D^{25} 1.4831; NMR (CCl_4), $-\overset{|}{\underset{|}{\mathrm{C}}}-\mathrm{CH_3}$, 1.38 ppm (singlet, 3H), $>\mathrm{C\underline{H}{-}OH}$ 3.70 (triplet, J=1.5 Hz, 1H), -OH 3.80 (broad singlet, 1H), $\mathrm{CH_2{=}}\overset{|}{\mathrm{C}}\mathrm{{-}C\underline{H}_3}$ 1.72 (triplet, J=1.1 Hz, 3H), $=\mathrm{CH_2}$ 4.69 (multiplet, 2H); ν_{max}^{liq} 889 cm⁻¹ ($=\mathrm{CH_2}$), 3413 (OH). The second peak was I: n_D^{25} 1.4878; mp 31.0—31.5°C; NMR (CCl_4), -OH 3.14 ppm (broad singlet, 1H), $>\mathrm{C\underline{H}{-}OH}$ 3.75 (double doublets, J_{vic}=11.0 and 6.0 Hz, 1H), $-\overset{|}{\underset{|}{\mathrm{C}}}-\mathrm{CH_3}$ 1.32 (singlet, 3H), $\mathrm{CH_2{=}}\overset{|}{\mathrm{C}}\mathrm{{-}C\underline{H}_3}$ 1.69 (triplet, J=1.1 Hz, 3H), $=\mathrm{CH_2}$ 4.68 (multiplet, 2H); ν_{max}^{liq} 888 cm⁻¹ ($=\mathrm{CH_2}$), 3448 (OH).

4,8-Epoxy-p-*menthan-3-ol (III, IV, and V).* Two isomers, A (mp 55°C) and B (mp 59°C), of pulegone oxide were prepared[12] by the epoxidation of pulegone in the same manner as used for carvone. The reduction of the isomer A by the procedure described above afforded a mixture (2.0 g) of III and IV, which was then fractionated into two eluates by column chromatography on silica gel with a mixture of petroleum ether and ethyl ether (1 : 1). The initial eluate (1.0 g) was IV: mp 24.5—25.0°C; bp 80.0—81.0°C/2 mmHg; n_D^{25} 1.4770; d_4^{25} 1.115; $[\alpha]_D^{25}$ −3.97° (neat); NMR ($CDCl_3$), $>\mathrm{CH{-}C\underline{H}_3}$ 1.05 ppm (doublet, J=6.0 Hz, 3H), -OH 1.61 (singlet, 1H), $>\mathrm{C\underline{H}{-}OH}$ 3.64 (broad singlet, 1H), $>\mathrm{C(CH_3)_2}$ 1.31 and 1.38 (each singlet, 6H); ν_{max}^{liq} 3441 cm⁻¹ (OH). The second eluate was III: mp 54.0—55.0°C; $[\alpha]_D^{25}$ +52.8° (*c* 6.66, $CHCl_3$); NMR ($CDCl_3$), $>\mathrm{CH{-}C\underline{H}_3}$ 0.91 ppm (doublet, J=6.0 Hz, 3H), -OH 1.61 (singlet, 1H), $>\mathrm{C\underline{H}{-}OH}$ 3.64 (broad singlet, 1H), $>\mathrm{C(CH_3)_2}$ 1.31 and 1.38 (each singlet, 6H); ν_{max}^{liq} 3394 cm⁻¹ (OH). The isomer B (3.0 g) was reduced as above to afford V (2.0 g): bp 83.5—84.0°C/0.5 mmHg; n_D^{25} 1.4672; d_4^{25} 1.0007; $[\alpha]_D^{25}$ +3.30° (neat); NMR ($CDCl_3$), $>\mathrm{CH{-}C\underline{H}_3}$ 1.04 ppm (doublet, J=6.0 Hz, 3H), $>\mathrm{C(CH_3)_2}$ 1.33 and 1.56 (each singlet, 6H), $>\mathrm{C\underline{H}{-}OH}$ 3.88 (double doublets, J_{vic}=10.0 and 6.0 Hz, 1H), -OH 2.38 (singlet, 1H); ν_{max}^{liq} 3438 cm⁻¹ (OH).

(−)-8,9-Epoxy-p-*menthan-3-ol (VI).* (−)-Isopulegol (15.4 g, 93.0°C/10 mmHg, n_D^{25} 1.4676, d_4^{25} 0.9052, $[\alpha]_D^{25}$ −22.27° (neat)) was added to a solution of monoperphthalic acid (22.0 g) in ether (127 m*l*) below 0°C. The mixture was allowed to stand overnight at room temperature; subsequently, an usual working-up of the mixture afforded a crude product (15.3 g). The purification of the product by column chromatography and subsequent recrystallization afforded VI: mp 53.5—54.0°C; $[\alpha]_D^{25}$ −15.6° (*c* 3.33, $CHCl_3$), lit:[13] α_D= −14.5°; NMR ($CDCl_3$), $>\mathrm{CH{-}C\underline{H}_3}$ 0.91 ppm (doublet, J=6.0 Hz, 3H), $>\mathrm{C\underline{H}{-}OH}$ 3.25 (broad singlet, 1H), $-\mathrm{O{-}CH_2{-}}$ 2.59 and 2.85 (each doublet, J=4.0 Hz, 2H), $-\mathrm{O}-\overset{|}{\underset{|}{\mathrm{C}}}-\mathrm{CH_3}$

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1.35 (singlet, 3H); $\nu_{\mathrm{max}}^{\mathrm{KBr}}$ 3523 cm^{-1} (OH).

(−)-2-(1-Methylcyclopropyl)-5-methylcyclohexanol (VII).[14] Methylene iodide (57.5 g) was added to a well-stirred suspension of anhydrous ether (125 m*l*), zinc-copper couple[15] (18.0 g), and iodine (0.1 g). To this gently-refluxing mixture, we then added a solution of (−)-isopulegol (15.4 g) in anhydrous ether (20 m*l*) over a period of 20 minutes. The mixture was stirred under reflux for an additional hour, and then it was worked up in the usual manner to yield VII (10.2 g): bp 105.0°C/15 mmHg; n_{D}^{25} 1.4696; d_4^{25} 0.9236; $[\alpha]_{\mathrm{D}}^{25}$ −33.07° (neat); the 3,5-dinitrobenzoate derivative, mp 130.0—130.5°C; NMR (CDCl$_3$) $>$CH-C$\underline{\mathrm{H}}_3$ 0.95 ppm (doublet, J=6.0 Hz, 3H), $-\overset{|}{\underset{|}{\mathrm{C}}}-\mathrm{CH}_3$ 0.99 (singlet, 3H), -OH 2.25 (singlet, 1H), $>$C$\underline{\mathrm{H}}$-OH 3.55 (triple doublets, J_{vic}=11 and 4 Hz, 1H), $-\mathrm{CH}_2-\mathrm{CH}_2-$ (cyclopropane ring) 0.08—0.81 (4H); $\nu_{\mathrm{max}}^{\mathrm{liq}}$ 3589 cm^{-1} (OH);

(+)-2-(1-methylcyclopropyl)-5-methylcyclohexanol (VIII). The oxidation of VII with a chromium trioxide-pyridine complex afforded a ketone, which was then reduced by the Meerwein-Ponndorf-Verley method. The purification of the reaction mixture by column chromatography on silica gel with a mixture of 30% *n*-hexane in ethyl acetate gave VIII: bp 80.0—85.0°C/7 mmHg; n_{D}^{25} 1.4720; d_4^{25} 0.9294; $[\alpha]_{\mathrm{D}}^{25}$ +28.72° (neat); mp 7.5—8.5°C; the 3,5-dinitrobenzoate derivative, mp 150.0—150.5°C; NMR (CDCl$_3$), $>$CH-C$\underline{\mathrm{H}}_3$ 0.88 ppm (doublet, J=6.0 Hz, 3H), $>$C$\underline{\mathrm{H}}$-OH 4.12 (multiplet, 1H), $-\mathrm{CH}_2\mathrm{CH}_2-$ (cyclopropane ring) 0.08—0.50 (4H), -OH 1.68 (singlet, 1H), $-\overset{|}{\underset{|}{\mathrm{C}}}-\mathrm{CH}_3$ 1.11 (singlet, 3H); $\nu_{\mathrm{max}}^{\mathrm{liq}}$ 3449 cm^{-1} (OH).

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