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Synthetic Studies on Anthracyclinones. XIV.[1] On the Conformational Aspects of Ring A of Daunomycinone: A Model Study

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A pair of stereoisomers of the ring A model for daunomycinone was synthesized. The stereochemistries of isomeric α-tetralol-type intermediates and of the target compounds were discussed on the basis of spectral evidences. For all of the synthetic *cis*-1,3-glycol systems related to ring A of daunomycinone were demonstrated a favorable di-axial conformation of the hydroxyls and the outside orientation of the O–H bond in the quasi-axial benzylic hydroxyl, while a quasi-equatorial conformation of the benzylic hydroxyl was found favorable for *trans*-1,3-glycol system of the stereoisomers epimeric at C_1.

Daunomycinone (I),[3] the aglycone of daunomycin, carries both an acetyl and a tertiary hydroxyl on C_9 and a benzylic hydroxyl group on C_7 of ring A. The conformation of these groups has been postulated, on the basis of the acetonide formation,[3d,3e,4] as a *cis*-glycol with di-axial hydroxyl orientation which is the common feature for anthracyclinones of tetrahydronaphthacenequinone system.[5] Recently, aklavinone-II,[6] the C_7-epimer of aklavinone, or α-rhodomycinone[7] has been reported to have a trans-1,3-glycol system where the C_7-hydroxyl has a pseudo-equatorial conformation. As an exploratory experiment on the PMR-spectral investigation of ring A of daunomycinone (I) and of the unknown C_7-epimer, we synthesized a model compound (II) and its isomer (III) and determined their conformations on the basis of PMR spectra.

Syntheses of the Ring A Model and the Epimer

1-Oxo-1,2,3,4-tetrahydro-3-naphthoic acid (IV)[8] was ketalized to give 1,1-ethylenedithio-1,2,3,4-tetrahydro-3-naphthoic acid (V), and followed by treatment with methyllithium in ether to give 1,1-ethylenedithio-1,2,3,4-tetrahydro-3-acetonaphthone (VI) in 89% yield. Oxidation of the methyl ketone (VI) with oxygen in the presence of sodium *t*-butoxide and triethyl phosphite gave 1,1-ethylenedithio-3-hydroxy-1,2,3,4-tetrahydro-3-acetonaphthone (VII) in 31% yield. The α-ketol (VII) was ketalized with 2,2-dimethyl-1,3-dioxolane in the

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2) Location: *Yamada-kami 133–1, Suita, Osaka, 565, Japan.*
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4) For the glycoside, daunomycin, a pseudo-axial conformation of the C_7-Olinkage was proposed on the proton magnetic resonance (PMR) spectral evidences: See ref. 3d. And the conformation in the solid state was proposed on the basis of X-ray analysis of N-bromoacetyl-daunomycin solvate. [R. Angiuli, E. Foresti, L. Riva di Sanseverino, N.W. Isaacs, O. Kennard, W.D.S. Motherwell, D.L. Wampler, and F. Arcamone, *Nature* (London), *New Biol.*, **234**, 78 (1971)].
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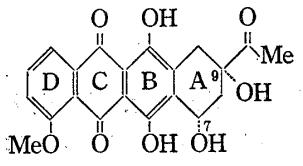

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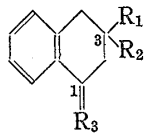
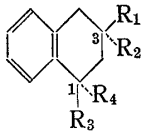


	R_1	R_2	R_3
IV	COOH	H	O
V	COOH	H	S,S
VI	COMe	H	S,S
VII	COMe	OH	S,S
VIII	$C(OCH_2CH_2O)Me$	OH	S,S
IX	$C(OCH_2CH_2O)Me$	OH	O
XIV	$C(SCH_2CH_2S)Me$	OH	S,S
XV	$C(SCH_2CH_2S)Me$	OH	O



	R_1	R_2	R_3	R_4
II	COMe	OH	H	OH
III	COMe	OH	OH	H
X	$C(OCH_2CH_2O)Me$	OH	H	OH
XI	$C(OCH_2CH_2O)Me$	OH	OH	H
XII	COMe	OAc	H	OAc
XIII	COMe	OAc	OAc	H
XVI	$C(SCH_2CH_2S)Me$	OH	H	OH
XVII	$C(SCH_2CH_2S)Me$	OH	OH	H

Chart 1

presence of *p*-toluenesulfonic acid to give 3-(1,1-ethylenedioxyethyl)-1,1-ethylenedithio-1,2,3,4-tetrahydro-3-naphthol (VIII) in 81% yield. Oxidative hydrolysis of the naphthol (VIII) with mercuric chloride in aqueous methanol gave 3-(1,1-ethylenedioxyethyl)-3-hydroxy-3,4-dihydro-1(2H)-naphthalenone (IX) in 75% yield. Reduction of the tetralone (IX) with sodium borohydride in methanol gave a mixture of isomeric 3-(1,1-ethylenedioxyethyl)-3-hydroxy-1,2,3,4-tetrahydro-1-naphthol (X and XI). The yields of X and XI were 44% and 40%, respectively. Compound X was deketalized with *p*-toluenesulfonic acid in acetone to give, unexpectedly, a mixture of isomeric 1,3-dihydroxy-1,2,3,4-tetrahydro-3-acetonaphthone (II and III). The yields of the ring A model (II) and its C_1-epimer (III) were 56% and 27%, respectively. Analogously, compound XI also gave II and III in 34% and 56% yields, respectively. The results indicate a ready isomerization of the benzylic hydroxyl in II or in III by acid catalysis. Treatment of III with acid actually gave II in 32% yield with 65% recovery of III. The glycols (II and III) were rather less stable and characterized as the acetates (XII and XIII), respectively.

In order to avoid the isomerization by acid, (II and III) were synthesized *via* the alternative pathway involving no acid treatment in the deketalization step of the 1-tetralol-type intermediates. Compound VII was ketalized with ethanedithiol in the presence of *p*-toluenesulfonic acid in acetic acid to give 3-(1,1-ethylenedithioethyl)-1,1-ethylenedithio-1,2,3,4-tetrahydro-3-naphthol (XIV) in 77% yield. Selective deketalization of XIV with mercuric chloride in aqueous methanol gave 3-(1,1-ethylenedithioethyl)-3-hydroxy-3,4-dihydro-1(2H)-naphthalenone (XV) in 60% yield. Reduction of XV with sodium borohydride gave a mixture of isomeric 3-(1,1-ethylenedithioethyl)-3-hydroxy-1,2,3,4-tetrahydro-1-naphthol (XVI and XVII). The yields of *cis*-diol (XVI) and *trans*-diol (XVII) were 43% and 49%, respectively. Compound XVI was deketalized with mercuric acetate in aqueous methanol to give II in 91% yield without any isomer formation. Compound XVII gave III in rather low yield (55%) in the

same treatment, but no trace of the epimer (II) was obtained. Thus the alternative synthesis of II and III was found to involve no isomerization of the benzylic hydroxyl.

Stereochemistries

The coupling constants ($J_{AX}+J_{BX}$) of the benzylic carbinol protons in PMR spectra were 7 Hz for X and 16 Hz for XI, respectively. The difference in coupling constants of the benzylic protons means that the conformation of the hydroxyl on C_1 is not the same between X and XI, and accordingly suggests that C_3-substituents in X and XI should have the same conformation where the larger substituent, 1,1-ethylenedioxyethyl, serves as a conformational anchor. Consequently, the isomer (X) with a quasi-axial benzylic hydroxyl should be a *cis*-glycol, and another isomer (XI) with a quasi-equatorial one a *trans*-glycol. The assignments of the *cis*-diol (II) with quasi-axial benzylic hydroxyl, the ring A model, and of *trans*-diol (III) with quasi-equatorial one were achieved in the similar manner. And it is now evident that the quasi-axial conformation of the benzylic hydroxyl corresponds to the *cis*-1,3-glycol system in the ring A model. The C_7-hydroxyl of daunomycinone (I) can be assigned as quasi-axial from its reported PMR data,[3e] the feature being a spectral evidence for its *cis*-glycol system.

Although the *cis* relationship of the hydroxyls on ring A of daunomycinone was deduced, by the previous workers, from the acetonide formation under an acidic condition, it might be mentioned, from the present result, that the acetonide formation in an acidic medium is not always essential for the *cis*-glycol assignment of this system. The following spectral comparison between II and III leads the spatial orientation of the hydroxyl groups on the ring A model (II) to that depicted in Fig. 1.

1) The hydroxyl group absorption (3465 cm^{-1}) for II appears in the lower frequency region than that (3565 cm^{-1}) for III in high dilution infrared (IR) spectra, suggesting that the hydroxyl in II is intramolecularly hydrogen-bonded.

2) The chemical shift (in CCl_4 and in DMSO-d_6) of the benzylic carbinol proton for II (δ 4.70 and 4.55) appears at a higher field than that (δ 4.79 and 4.81) for III, the behaviour providing an example to the acetate rule.[9] The data indicate the outside orientation of the O–H bond of the axial benzylic hydroxyl in II under the acetate rule.

3) The coupling constant (6.6 Hz in DMSO-d_6) of the benzylic hydroxyl proton ($J_{\underline{H}OC\underline{H}}$) for II is smaller than that (6.9 Hz) for III, the difference suggesting that the quasi-axial conformation[10] of the hydroxyl in II is not changed even in dimethyl sulfoxide (DMSO) solution where an intramolecular hydrogen bonding, if any, of the hydroxyls should be destroyed owing to a strong hydrogen bonding with the solvent (DMSO). It is evident from this and above observation that the O–H bond of quasi-axial hydroxyl in II is directed to the outside of the ring in either polar or non-polar solvent.

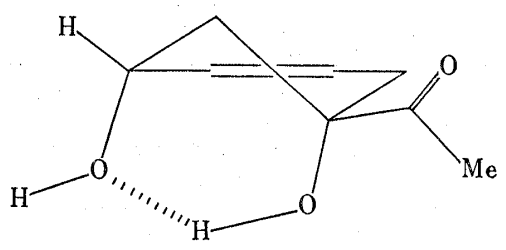


Fig. 1

Experimental

All the melting points are uncorrected. PMR spectra were obtained for the $CDCl_3$, CCl_4 or DMSO-d_6 solution with tetramethylsilane as an internal standard on Hitachi R-22 spectrometer. Chemical shifts are given on the δ scale. IR spectra were taken with a Hitachi EPI-G3 spectrometer. All organic extracts had been

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dried over Na_2SO_4 before evaporation. Column chromatography was effected using Mallinckrodt silicic acid. Thin-layer chromatography was performed on Merck Kieselgel 60 PF_{254}.

1,1-Ethylenedithio-1,2,3,4-tetrahydro-3-naphthoic Acid (V)——A mixture of 1-oxo-1,2,3,4-tetrahydro-3-naphthoic acid (IV)[8,11] (22.0 g), dry AcOH (220 ml), ethanedithiol (22.0 g) and BF_3–etherate (22.2 ml) was allowed to stand for 18 hr at room temperature, and poured onto ice water. The precipitates were collected, and dissolved in satd. $NaHCO_3$. After washing with benzene, the aqueous layer was acidified with conc. HCl to give colorless precipitates, which were collected, washed with water and dried to give 29.0 g of colorless crystals. Recrystallization from *n*-hexane–benzene gave 26.0 g (84.4%) of V as colorless cubes, mp 206—208°. *Anal.* Calcd. for $C_{13}H_{14}O_2S_2$: C, 58.61; H, 5.36. Found: C, 58.59, H, 5.31. IR ν_{max}^{KBr} cm^{-1}: 1705 (C=O).

1,1-Ethylenedithio-1,2,3,4-tetrahydro-3-acetonaphthone (VI)——A solution of MeLi which was prepared from MeI (15.0 g) and Li (1.8 g) in ether (100 ml) was added to a solution of V (6.0 g) in ether (500 ml) at 3°, and the mixture was stirred for 1 hr at room temperature. Water (500 ml) was added to the mixture, and the organic layer was separated. The aqueous layer was extracted with AcOEt (100 ml×3). The combined organic layer was washed with satd. $NaHCO_3$ and water, dried and evaporated. The crude product was recrystallized from isopropanol to give 5.3 g (89.1%) of VI as colorless needles, mp 89—91°. *Anal.* Calcd. for $C_{14}H_{16}OS_2$: C, 63.59; H, 6.10. Found: C, 63.43; H, 6.06. IR ν_{max}^{KBr} cm^{-1}: 1709 (C=O). PMR ($CDCl_3$) δ: 2.24 (3H, s, $COC\underline{H}_3$).

1,1-Ethylenedithio-3-hydroxy-1,2,3,4-tetrahydro-3-acetonaphthone (VII)——Sodium hydride (50% in mineral oil) (3.0 g) was dissolved in *t*-butanol (40 ml) and dimethyl formamide (DMF) (60 ml), and to the solution were added triethyl phosphite[12] (4 ml) and DMF (40 ml). Oxygen was passed through the mixture maintained at −25°, and a solution of VI (7.0 g) in tetrahydrofuran (THF) (60 ml) was added. Passage of oxygen was continued for 1 hr. After acidification with AcOH, the mixture was diluted with water and extracted with AcOEt (200 ml×3). The extract was washed with water, dried and evaporated. The residue (8.5 g) was chromatographed on silica gel (170 g) in $CHCl_3$. The later fraction gave 2.3 g (31.0%) of VII as colorless crystals (from ether), mp 105—107°. *Anal.* Calcd. for $C_{14}H_{16}O_2S_2$: C, 59.96; H, 5.75. Found: C, 59.96; H, 5.77. IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1699 (C=O). PMR ($CDCl_3$) δ: 2.29 (3H, s, $COC\underline{H}_3$), 2.55 (1H, dd, J=15 Hz, 2 Hz, C_2–$\underline{H}_{eq}$), 2.85 (1H, d, J=15 Hz, C_2–$\underline{H}_{ax}$), 2.88 (1H, dd, J=17 Hz, 2 Hz, C_4–$\underline{H}_{eq}$), 3.25 (1H, d, J=17 Hz, C_4–$\underline{H}_{ax}$), 3.55 (4H, m, $SC\underline{H}_2C\underline{H}_2S$), 3.88 (1H, s, O$\underline{H}$).

3-(1,1-Ethylenedioxyethyl)-1,1-ethylenedithio-1,2,3,4-tetrahydro-3-naphthol (VIII)——A mixture of the α-ketol (VII) (1.87 g), 2,2-dimethyl-1,3-dioxolane[13] (70 ml) and *p*-TsOH (150 mg) was allowed to stand for 4 days at room temperature. The mixture was washed with satd. $NaHCO_3$ and water, dried and evaporated to give 1.98 g of crystals. Recrystallization from cyclohexane gave 1.74 g (80.6%) of VIII as colorless needles, mp 124—125°. *Anal.* Calcd. for $C_{16}H_{20}O_3S_2$: C, 59.23; H, 6.21. Found: C, 59.32; H, 6.18. IR ν_{max}^{KBr} cm^{-1}: 3490 (OH). PMR ($CDCl_3$) δ: 1.38 (3H, s, $COC\underline{H}_3$), 2.62 (1H, s, O$\underline{H}$), 2.67 (2H, broad s, C_2–$\underline{H}_2$), 2.82, 3.08 (2H, each d, J=17 Hz, C_4–$\underline{H}_2$), 3.50 (4H, m, $SC\underline{H}_2C\underline{H}_2S$), 4.00 (4H, s, $OC\underline{H}_2C\underline{H}_2O$).

3-(1,1-Ethylenedioxyethyl)-3-hydroxy-3,4-dihydro-1(2H)-naphthalenone (IX)——A suspension of HgO (4.6 g) in a solution of $HgCl_2$[14] (4.6 g) and VIII (1.52 g) in MeOH (180 ml) and H_2O (14 ml) was stirred for 3 hr at room temperature. The suspension was evaporated *in vacuo*. The residue was extracted with ether (100 ml). The extract was washed with water, dried and evaporated to give colorless crystals. Recrystallization from isopropyl ether gave 0.87 g (75.2%) of IX as colorless needles, mp 124—125°. *Anal.* Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.91; H, 6.44. IR ν_{max}^{KBr} cm^{-1}: 3412 (OH), 1683 (C=O), 1599 (arom.). PMR ($CDCl_3$) δ: 1.40 (3H, s, $C\underline{H}_3$), 2.31 (1H, s, O$\underline{H}$), 2.84 (2H, broad s, C_2–$\underline{H}_2$), 3.01, 3.32 (2H, each d, J=18 Hz, C_4–$\underline{H}_2$), 3.99 (4H, s, $OC\underline{H}_2C\underline{H}_2O$).

3-(1,1-Ethylenedioxyethyl)-3-hydroxy-1,2,3,4-tetrahydro-1-naphthol, *cis*-Diol (X) and *trans*-Diol (XI)——A solution of $NaBH_4$ (240 mg) in MeOH (10 ml) was added to a stirred solution of IX (496 mg) in MeOH (14 ml) at 0°. The reaction mixture was stirred for 30 min at room temperature, poured onto ice water, and extracted with ether (20 ml×3). The extract was washed with water, dried and evaporated. The resulting viscous oil (487 mg) was chromatographed on silica thin-layer in ether. The fraction of a higher *Rf* value gave 221 mg (44.2%) of X. mp 101—103° (from *n*-hexane). *Anal.* Calcd. for $C_{14}H_{18}O_4$; C, 67.18; H, 7.25. Found: C, 66.96; H, 7.23. IR ν_{max}^{KBr} cm^{-1}: 3500, 3480 (OH). PMR ($CDCl_3$) δ: 1.40 (3H, s, $C\underline{H}_3$), 2.01 (1H, dd, J=4 Hz, 15 Hz, C_2–$\underline{H}_{ax}$), 2.35 (1H, dt, J=2 Hz, 2 Hz, 15 Hz, C_2–$\underline{H}_{eq}$), 2.76 (1H, s, O$\underline{H}$), 2.98 (2H, broad s, C_4–$\underline{H}_2$), 3.65 (1H, broad s, O$\underline{H}$), 4.04 (4H, s, $OC\underline{H}_2C\underline{H}_2O$), 4.80 (1H, dd, J=2 Hz, 4 Hz, C_1–$\underline{H}$). The fraction of a lower *Rf* value gave 201 mg (40.2%) of colorless crystals (XI), mp 113—115° (from benzene). *Anal.*

11) The procedure is essentially the same as that described by Gates and the co-worker [M. Gates and C.L. Dickinson, *J. Org. Chem.*, **22**, 1398 (1957)].
12) The procedure was first described by Gardner and the co-workers [J.N. Gardner, F.E. Carlon, and O. Gnoj, *J. Org. Chem.*, **33**, 3294 (1968)].
13) The procedure is essentially the same as that described by Dauben and the co-workers [H.J. Dauben jr., B. Löken, and H. J. Ringold, *J. Am. Chem. Soc.*, **76**, 1359 (1954)].
14) The procedure is essentially the same as that described by O.T. Dalley and R.J. McIlory [*J. Chem. Soc.*, 1949, 555].

Calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.11; H, 7.20. IR ν_{max}^{KBr} cm^{-1}: 3440, 3340 (OH). PMR ($CDCl_3$) δ: 1.38 (3H, s, C$\underline{H}_3$), 1.80 (1H, dd, J=10 Hz, 12 Hz, C_2-$\underline{H}_{ax}$), 2.19 (1H, s, O$\underline{H}$), 2.30 (1H, broad s, O$\underline{H}$), 2.31 (1H, dq, J=1.8 Hz, 6 Hz, 12 Hz, C_2-$\underline{H}_{eq}$), 2.75 (1H, dd, J=1.8 Hz, 16 Hz, C_4-$\underline{H}_{eq}$), 3.11 (1H, d, J=16 Hz, C_4-$\underline{H}_{ax}$), 4.00 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 4.95 (1H, dd, J=6 Hz, 10 Hz, C_1-$\underline{H}$).

3-(1,1-Ethylenedithioethyl)-1,1-ethylenedithio-1,2,3,4-tetrahydro-3-naphthol (XIV)——A mixture of VII (2.0 g) AcOH (6 ml), ethanedithiol (6 ml) and *p*-TsOH (400 mg) was allowed to stand for 2 hr at room temperature. The reaction mixture was poured into 1 N NaOH (120 ml) and extracted with $CHCl_3$ (30 ml×3). The extract was washed with water, dried and evaporated. The residue was recrystallized from toluene to give 1.95 g (76.8%) of XIV as colorless prisms, mp 163—165°. *Anal.* Calcd. for $C_{16}H_{20}OS_4$: C, 53.89; H, 5.65. Found: C, 53.93; H, 5.72.

3-(1,1-Ethylenedithioethyl)-3-hydroxy-3,4-dihydro-1(2H)-naphthalenone (XV)——A mixture of XIV (2.15 g), acetone (40 ml), H_2O (1 ml) and $HgCl_2$ (4.8 g) was stirred for 1 hr at room temperature. The reaction mixture was evaporated *in vacuo*. The residue was extracted with $CHCl_3$ (80 ml). The extract was washed with water, dried and evaporated to give 1.23 g of crystals. Recrystallization from MeOH gave 1.02 g (60.4%) of XV as colorless needles, mp 159—162°. *Anal.* Calcd. for $C_{14}H_{16}O_2S_2$: C, 59.96; H, 5.75. Found: C, 60.22; H, 5.84. IR ν_{max}^{KBr} cm^{-1}: 3405 (OH), 1655 (C=O), 1594 (arom.).

3-(1,1-Ethylenedithioethyl)-3-hydroxy-1,2,3,4-tetrahydro-1-naphthol, *cis*-Diol (XVI) and *trans*-Diol (XVII)——A solution of $NaBH_4$ (200 mg) in MeOH (10 ml) was added to a solution of XV (400 mg) in MeOH (18 ml) at 0°. The reaction mixture was stirred for 1 hr at room temperature, poured onto ice water and extracted with AcOEt (20 ml×3). The extract was washed with water, dried and evaporated. The residual oil was chromatographed on silica thin-layer in $CHCl_3$. The fraction of a higher *Rf* value gave 172 mg (43.0%) of XVI. mp 127—130° (from acetone-MeOH). *Anal.* Calcd. for $C_{14}H_{18}O_2S_2$: C, 59.53; H, 6.42. Found: C, 59.58; H, 6.47. IR ν_{max}^{KBr} cm^{-1}: 3480, 3430, 3370 (OH). PMR ($CDCl_3$) δ: 1.93 (3H, s, C$\underline{H}_3$), 2.20 (1H, dd, J=4 Hz, 15 Hz, C_2-$\underline{H}_{ax}$), 2.65 (1H, dt, J=2 Hz, 2 Hz, 15 Hz, C_2-$\underline{H}_{eq}$), 3.02 (2H, broad s, C_4-$\underline{H}_2$), 3.20 (1H, s, O$\underline{H}$), 3.35 (4H, s, SC$\underline{H}_2$C$\underline{H}_2$S), 3.58 (1H, s, O$\underline{H}$), 4.83 (1H, t, J=2 Hz, 4 Hz, C_1-$\underline{H}$). The fraction of a lower *Rf* value gave 195 mg (48.8%) of XVII. mp 134—135° (from benzene). *Anal.* Calcd. for $C_{14}H_{18}O_2S_2$: C, 59.53; H, 6.42. Found: C, 59.61; H, 6.23. IR ν_{max}^{KBr} cm^{-1}: 3380 (OH). PMR ($CDCl_3$) δ: 1.82 (1H, dd, J=10 Hz, 11 Hz, C_2-$\underline{H}_{ax}$), 1.90 (3H, s, C$\underline{H}_3$), 2.00 (1H, dt, J=2 Hz, 6 Hz, 11 Hz, C_2-$\underline{H}_{eq}$), 2.40 (2H, broad s, O$\underline{H}$×2), 2.95 (1H, dd, J=2 Hz, 18 Hz, C_4-$\underline{H}_{eq}$), 3.25 (1H, d, J=18 Hz, C_4-$\underline{H}_{ax}$), 3.35 (4H, s, SC$\underline{H}_2$C$\underline{H}_2$S), 5.00 (1H, q, J=6 Hz, 10 Hz, C_1-$\underline{H}$).

1,3-Dihydroxy-1,2,3,4-tetrahydro-3-acetonaphthone (*cis*-Diol (II) and *trans*-Diol (III))——a) From X: A mixture of X (100 mg), dry acetone (10 ml) and *p*-TsOH (10 mg) was allowed to stand for 24 hr at room temperature. The reaction mixture was poured onto ice water and extracted with ether (10 ml×3). The extract was washed with satd. $NaHCO_3$ and water, dried and evaporated to give a colorless oil, which was chromatographed on silica thin-layer in ether. The fraction of a higher *Rf* value gave 46 mg (55.8%) of II as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3460 (OH), 1716 (C=O). $\nu_{max}^{CCl_4}$ cm^{-1} (0.001 mol/liter): 3465 (OH). PMR ($CDCl_3$) δ: 2.25 (2H, broad d, J=3 Hz, C_2-$\underline{H}_2$), 2.34 (3H, s, C$\underline{H}_3$), 2.83, 3.25 (2H, each d, J=17 Hz, C_4-$\underline{H}_2$), 4.88 (1H, t, J=2 Hz, 4 Hz, C_1-$\underline{H}$). (CCl_4) δ: 2.07 (2H, broad s, C_2-$\underline{H}_2$), 2.21 (3H, s, C$\underline{H}_3$), 2.90, 3.15 (2H, each d, J=17 Hz, C_4-$\underline{H}_2$), 4.70 (1H, t, J=2 Hz, 4 Hz, C_1-$\underline{H}$). (DMSO-d_6) δ: 4.55 (1H, m, C_1-$\underline{H}$), 5.34 (1H, d, J=6.6 Hz, C_1-O$\underline{H}$). The fraction of a lower *Rf* value gave 22 mg (26.7%) of III as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580, 3475 (OH), 1715 (C=O), $\nu_{max}^{CCl_4}$ cm^{-1} (0.001 mol/liter): 3565 (OH). PMR ($CDCl_3$) δ: 2.21 (2H, m, C_2-$\underline{H}_2$), 2.28 (3H, s, C$\underline{H}_3$), 2.68, 3.29 (2H, each d, J=16 Hz, C_4-$\underline{H}_2$), 5.05 (1H, q, J=6 Hz, 10 Hz, C_1-$\underline{H}$), (CCl_4) δ: 2.11 (2H, m, C_2-$\underline{H}_2$), 2.23 (3H, s, C$\underline{H}_3$), 2.76, 3.18 (2H, each d, J=16 Hz, C_4-$\underline{H}_2$), 4.79 (1H, q, J=6 Hz, 10 Hz, C_1-$\underline{H}$), (DMSO-d_6) δ: 4.81 (1H, m, C_1-$\underline{H}$), 5.12 (1H, d, J=6.9 Hz, C_1-O$\underline{H}$).

b) From XI: A mixture of XI (100 mg), dry acetone (10 ml) and *p*-TsOH (10 mg) gave 28 mg (34.0%) of II and 46 mg (55.8%) of III in the same manner.

c) From XVI: A suspension of HgO (60 mg) in a solution of $Hg(OAc)_2$[15] (130 mg) and XVI (60 mg) in MeOH (6 ml) and H_2O (0.5 ml) was stirred for 5 hr at room temperature. The reaction mixture was filtered, and the filtrate was evaporated *in vacuo*. The residue was diluted with water (10 ml) and extracted with ether (3 ml×3). The extract was washed with water, dried and evaporated to give 40 mg (91.3%) of II as a colorless oil.

d) From XVII: A suspension of HgO (60 mg) in a solution of $Hg(OAc)_2$[15] (130 mg) and XVII (60 mg) in MeOH (6 ml) and H_2O (0.5 ml) was stirred for 10 hr at room temperature. The reaction mixture was filtered, and the filtrate was evaporated *in vacuo*. The residue was diluted with water (10 ml) and extracted with ether (3 ml×3). The extract was washed with water, dried and evaporated to give 48 mg of an oil, which was chromatographed on silica thin-layer in ether. The fraction of a higher *Rf* value gave a recovery of XVII (22 mg). The fraction of a lower *Rf* value gave 24 mg (54.5%) of III.

***cis*-1,3-Diacetoxy-1,2,3,4-tetrahydro-3-acetonaphthone (XII)**——A mixture of the *cis*-diol (II, 100 mg), Ac_2O (1 ml) and pyridine (2 ml) was allowed to stand for 15 hr at room temperature. The reaction mixture

15) The procedure is essentially the same as that described by G.P. Pollini, A. Barco, M. Anastasia, and G. Traverco, [*Farmaco, Ed. Sci.*, **23**, 405 (1968)].

was poured into 5% HCl and extracted with ether (10 ml×3). The extract was washed with water, satd. $NaHCO_3$ and water, dried and evaporated to give 125 mg of crystals. Recrystallization from ether gave 109 mg (77.3%) of XII as colorless prisms, mp 111—112°. *Anal.* Calcd. for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.17; H, 6.21. IR ν_{max}^{KBr} cm^{-1}: 1736, 1728 (OAc), 1714 ($COCH_3$). PMR ($CDCl_3$) δ: 2.05 (6H, s, Ac×2), 2.20 (3H, s, Ac), 2.65 (2H, m, C_2-$\underline{H}_2$), 3.08 (2H, broad s, C_4-$\underline{H}_2$), 6.18 (1H, q, J=2 Hz, 4 Hz, C_1-$\underline{H}$).

***trans*-1,3-Diacetoxy-1,2,3,4-tetrahydro-3-acetonaphthone (XIII)**——A mixture of the *trans*-diol (III, 90 mg), Ac_2O (1 ml) and pyridine (2 ml) gave 103 mg of an oil, which was chromatographed on silica gel (2.5 g) in $CHCl_3$ to give 77 mg (60.6%) of XIII as a colorless oil. *Anal.* Calcd. for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.15; H, 6.29. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1736 (OAc), 1719 (Ac). PMR ($CDCl_3$) δ: 2.03, 2.12, 2.18 (9H, each s, Ac×3), 2.20 (1H, m, C_2-$\underline{H}_{ax}$), 2.65 (1H, dq, J=2 Hz, 6 Hz, 15 Hz, C_2-$\underline{H}_{eq}$), 3.10, 3.62 (2H, each d, J=18 Hz, C_4-$\underline{H}_2$), 6.15 (1H, q, J=6 Hz, 10 Hz, C_1-$\underline{H}$).

Isomerization of III——A mixture of III (30 mg), AcOH (2 ml) and *p*-TsOH (5 mg) was allowed to stand for 24 hr at room temperature. The reaction mixture was poured into water and extracted with ether (2 ml×3). The extract was washed with satd. $NaHCO_3$ and water, dried and evaporated to give a colorless oil, which was chromatographed on silica thin-layer in ether. The fraction of a higher *Rf* value gave 6 mg (32.4%) of II as a colorless oil. The fraction of a lower *Rf* value gave 12 mg of III.

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