Studies on Coumarins from the Root of *Angelica decursiva* Fr. et Sav. II.[1] Stereostructures of Decursin, Decursidin, and Other New Pyranocoumarin Derivatives

Kiyonori Sano,[2a] Itiro Yosioka, and Isao Kitagawa[2b]

Research Institute for Wakan-Yaku, Toyama University[2a] and Faculty of Pharmaceutical Sciences, Osaka University[2b]

The stereostructures of pyranocoumarin derivatives named decursin (I), decursidin (II), AD-I (III), AD-II (IV) isolated from the root of the titled plant have been elucidated on the basis of chemical and physicochemical evidence. Decursin is expressed as 3'(S)-senecioyloxy-3',4'-dihydroxanthyletin (I) and decursidin as 3'(S), 4'(R)-disenecioyloxy-3',4'-dihydroxanthyletin (II).

AD-I has been revealed to be a mixture of two diastereoisomers being isomeric at C-4' and is expressed as 3'(S)-angeloyloxy-4'(R and S)-isovaleroyloxy-3',4'-dihydroxanthyletin (III). Finally, AD-II has been established to be 3'(S)-angeloyloxy-4'(R)-senecioyloxy-3',4'-dihydroxanthyletin (IV) and it has been suggested on the basis of close similarity of the physical properties of AD-II with those of andelin that the structure proposed for andelin by Avramenko, *et al.* might be revised.

In the previous paper,[1] we reported the isolation of two new coumarin derivatives (named decursin and decursidin) and a new non-crystalline coumarin derivative (now designated as AD-I) in addition to the isolation of known coumarins: nodakenetin and umbelliferone from the root of *Angelica decursiva* Fr. et Sav. (Japanese name: nodake, Umbelliferae), and also presented the chemical evidence which was in accord with the formulations I and II (stereochemistry at C-3' and C-4' undefined) for decursin and decursidin, respectively. The present paper deals with a full account of our further study on these pyranocoumarin derivatives which has led us to formulate the stereostructures of decursin and decursidin as 3'(S)-senecioyloxy-3',4'-dihydroxanthyletin (I) and 3'(S), 4'(R)-disenecioyloxy-3',4'-dihydroxanthyletin (II).[3] in addition, we wish to present the chemical evidence on the structure elucidation of other pyranocoumarin congeners designated as AD-I and AD-II (newly isolated) which supports their respective formulations as III (a mixture of 3'(S)-angeloyloxy-4'(R)-isovaleroyloxy- and 3'(S)-angeloyloxy-4'(S)-isovaleroyloxy-3',4'-dihydroxanthyletin) and 3'(S)-angeloyloxy-4'(R)-senecioyloxy-3',4'-dihydroxanthyletin (IV).[3]

Stereostructure of Decursin (I)

Sodium-amalgam reduction of decursinol (V)[1] yielded a product (VI), which on vacuum sublimation was converted to 3,4-dihydrodecursinol (VII). Benzoylation of either VI or VII with benzoic anhydride and pyridine gave a benzoate (VIII). It was anticipated on the basis of Dreiding model examination that if the C-3' configuration in VIII was S (either with β-*quasi*-axial (β-a) or with β-*quasi*-equatorial (β-e) benzoyloxy conformation), VIII would show a negative Cotton effect on referring to the benzoate sector rule,[4] while the Cotton effect would be reversed if the configuration was 3'(R) (either with α-*quasi*-axial (α-a) or with α-*quasi*-equatorial (α-e) benzoyloxy conformation (Fig. 1 and 2).

1) Part I: K. Hata and K. Sano, *Yakugaku Zasshi*, **89**, 549 (1969).
2) Location: a) *3190, Gofuku, Toyama*; b) *Toneyama, Toyonaka, Osaka.*
3) K. Sano, I. Yosioka, and I. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **21**, 2095 (1973) (Preliminary report).
4) N. Harada, M. Ohashi, and K. Nakanishi, *J. Am. Chem. Soc.*, **90**, 7349 (1968).

In the circular dichroism (CD) spectrum of VIII, a negative Cotton effect ($[\theta]_{228}$—29500) was observed, and therefore the 3′(S) configuration in VIII has been established. As for the preferred conformation in solution (MeOH) of the C-3′ benzoyloxy function of VIII, the β-*quasi*-axial conformation (β-a, Fig. 2) would be presumed probably due to its less skew interaction against the C-2′ geminal dimethyl functions, and the signal pattern of 3′-H in the proton magnetic resonance (PMR) spectrum of VIII (t., J=5 Hz, in CDCl₃) supports the assumption although the applied solvents are not the same.[5] Since the C-3′ configuration was preserved during the derivation from decursin to the benzoate (VIII), the stereostructure of decursin is expressed as 3′(S)-senecioyloxy-3′,4′-dihydroxanthyletin (I). The conclusion is in good agreement with the proposal of Lemmich and Nielsen[6] who elucidated the absolute
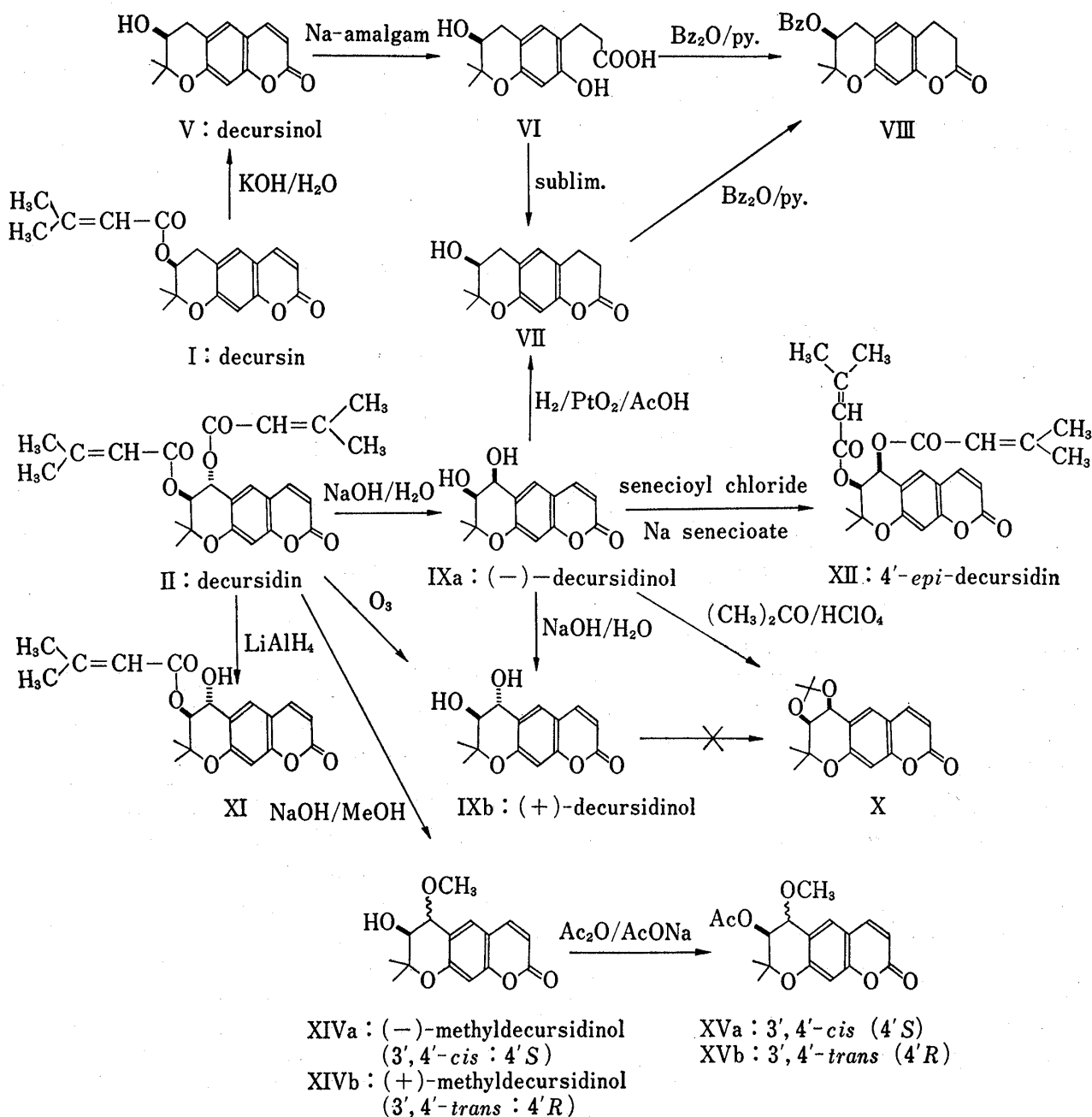

Chart 1

5) The large negative θ value in the CD spectrum of VIII would also support the assumption (Fig. 1, β-a).
6) J. Lemmich and B.E. Nielsen, *Tetrahedron Letters*, 1969, 3.

configuration of 3'(R)-angeloyloxy-3',4'-dihydroxanthyletin, which was isolated from the root of *Seseli libanotis* (L.) Koch subsp. *eu-libanotis* (Umbelliferae), on the basis of ozone degradation of its desangeloyl derivative: 3'(R)-hydroxy-3',4'-dihydroxanthyletin, $[\alpha]_D^{23}$—11° (CHCl$_3$), $[\alpha]_D^{23}$—102° (pyridine), being antipodal to decursinol (V): $[\alpha]_D^{26}$+10.8° (CHCl$_3$), $[\alpha]_D^{17}$ +103.8° (pyridine).

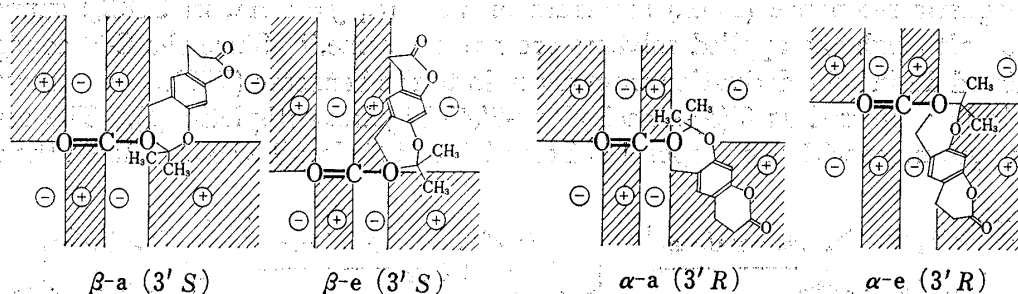β-a (3' S) β-e (3' S) α-a (3' R) α-e (3' R)

Fig. 1.   Benzoate Sector Projection of Four Conformers for VIII
if having 3'S or 3'R Configuration

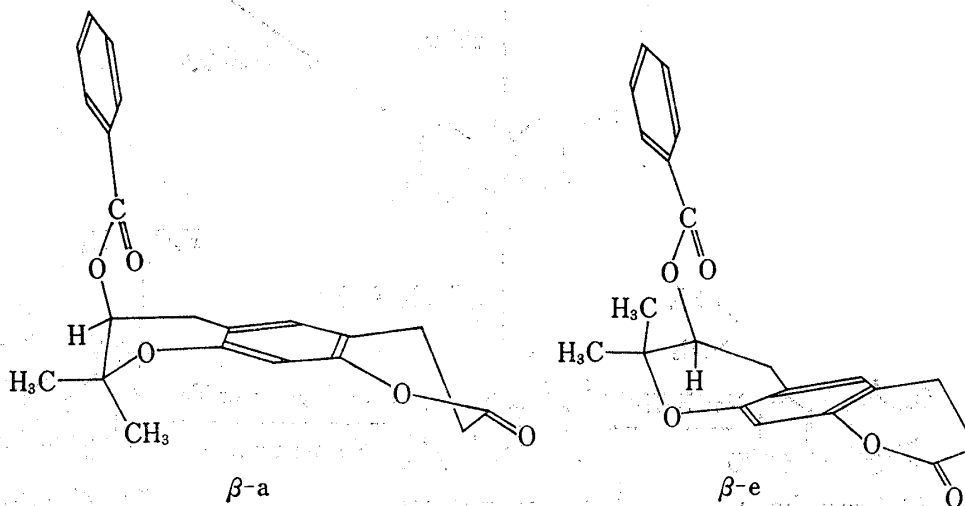β-a β-e

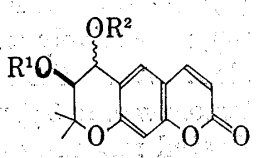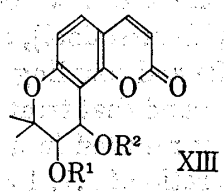Fig. 2.   Perspective Figures of VIII having 3'S Configuration

Stereostructure of Decursidin (II)

Treatment of decursidin (II) with aqueous 10% sodium hydroxide primarily furnished a (—)-diol[3] (now named (—)-decursidinol, IXa), which, upon prolonged heating under the same reaction conditions, was converted to a diastereoisomer (+)-diol[3] (named (+)-decursidinol, IXb). The both diols showed the resembled physical properties (infrared (IR) and PMR spectra) but the raise of melting-point was observed on admixture of both. Significant difference noticed in the both PMR spectra is a fact that the coupling constant between 3'-H and 4'-H in (—)-decursidinol is 4.2 Hz while that in (+)-decursidinol is 9.0 Hz. On the PMR spectra of khellactone (=3',4'-dihydroxy-3',4'-dihydroseselin) derivatives (XIII), it was reported that the J values of the signals due to *cis* 3'-H and 4'-H were found nearly *ca.* 5 Hz whereas those due to *trans* 3'-H and 4'-H were observed to vary in a range of 3.0 and 7.0 Hz.[7] The observation has been ascribed to an inference that the dihedral angles of 3'-H and 4'-H in the *trans* isomers change depending upon the kind of C-3' and C-4' substituents but those in the *cis* isomers are unchanged irrespective of the substituents. Since a similar trend is also expected in the J values of 3'-H and 4'-H in the present *cis* and *trans* 3',4'-di-hydroxy-3',4'-dihydroxanthyletin derivatives, (—)-decursidinol and (+)-decursidinol are assumed respectively to be *cis*-3',4'-dihydroxy (IXa) and *trans* 3',4'-dihydroxy (IXb) derivatives (Table I).

7) J. Lemmich, E. Lemmich, and B.E. Nielsen, *Acta Chem. Scand.*, 19, 2497 (1965).

In addition, as has been noticed by Hata in the PMR spectra of khellactone derivatives,[8] the signals due to 4'-H in the *trans* isomers always appear at higher field than those in the corresponding *cis* isomers, probably due to *quasi*-axial character of 4'-H in the former which is therefore more shielded by the neighboring aromatic ring: the bulky C-4' substituent occupying the *quasi*-equatorial conformation. This is the case in the present 3',4'-dihydroxy-3',4'-dihydroxanthyletin derivatives: for example, the signals due to 4'-H in IXa is observed at τ 4.80 whereas that in IXb at τ 4.94 (Table I).

TABLE I. PMR Data of 4'-H in 3',4'-*cis* and 3',4'-*trans* Derivatives
(Chemical Shifts are in τ Values and *J* Values in Parentheses are in Hz)

Compound	Relation of 3'-H/4'-H		Compound	Relation of 3'-H/4'-H	
	cis	*trans*		*cis*	*trans*
(−)-Decursidinol (IXa)	4.80(4.2)	—	3'(S)-khellactone^a) (R¹=R²=H)	4.80	5.00
(+)-Decursidinol (IXb)	—	4.90(9.0)			
Decursidin (II)	—	4.08(6.0)	3'(R)-ethylkhellactone^a,b) (R¹=H, R²=Et)	5.17	5.33
4'-*epi*-Decursidin (XII)	3.86(4.2)	—			
(−)-Methyldecursidinol (XIVa)	5.50(4.0)	—	3'(S)-ethylkhellactone^a,b) (R¹=H, R²=Et)	5.15	5.32
(+)-Methyldecursidinol (XIVb)	—	5.63(7.5)			
XVa	5.49(4.2)	—	3'(S)-acetylethylkhel-lactone^a) (R¹=Ac, R²=Et)	5.05	5.45
XVb	—	5.77(5.0)			
AD-II (IV)	—	4.01(6.6)	3'(S)-diacetylkhel-lactone (R¹=R²=Ac)	3.42	3.73

a) K. Hata, M. Kozawa, and Y. Ikeshiro, *Chem. Pharm. Bull.* (Tokyo), 14, 94 (1966).
b) K. Hata, M. Kozawa, and K.Y. Yen, *Chem. Pharm. Bull.* (Tokyo), 14, 422 (1966); K. Hata, M. Kozawa, Y. Ikeshiro, and K.Y. Yen, *Yakugaku Zasshi*, 88, 513 (1968)

On treatment of (−)-decursidinol with acetone containing perchloric acid, an acetonide (X) was obtained in an excellent yield, however (+)-decursidinol was unaffected on the same treatment. Therefore, the *cis* 3',4'-diol moiety in (−)-decursidinol has been proved chemically. Catalytic hydrogenation of (−)-decursidinol over Adams catalyst in acetic acid furnished a reduction product which was found identical with 3,4-dihydrodecursinol (VII) described above in all respects including the specific rotation. Consequently, the absolute configuration at C-3' in (−)- and (+)-decursidinol has been established as *S*, the same as in decursin (I), and the absolute configurations of (−)-decursidinol and (+)-decursidinol are expressed respectively as 3'(S), 4'(S) (IXa) and 3'(S), 4'(R) (IXb).

Next, the direct chemical correlation of decursidin (II) with (+)-decursidinol (IXb) was accomplished by the following derivation. Thus, ozone oxidation of II under ice-cooling followed by silica gel chromatography furnished IXb as a sole bis-dessenecioyl derivative and it should be mentioned that, although IXa was subjected to the same purification procedure as a blank test, no isomerization of IXa to IXb occurred. Therefore, it has been concluded that decursidin possesses *trans* 3'(S), 4'(R)-disenecioyloxy function as depicted in II. Lithium aluminium hydride reduction of II afforded, though in a lesser yield, a 4'-dessenecioyl derivative (XI), whose PMR spectrum showed a doublet at τ 5.31 (*J*=8 Hz) ascribable to 4'-H. Here

8) Private communication from Prof. K. Hata, Osaka College of Pharmacy.

again, the coupling constant between 3′-H and 4′-H was in accord with the assignment (3′-H, 4′-H: *trans*) as described above. Furthermore, 4′-*epi*-decursidin (XII) prepared by senecioylation of (—)-decursidinol (IXa) showed a 4′-H doublet at τ 3.86 ($J=4.2$ Hz) in its PMR spectrum (Table I). The finding indicates the presence of the *cis* 3′,4′-disenecioyloxy function in XII on the basis of above discussion (4′-H in II: 4.08).

All the accumulated evidence corroborates the formulation of decursidin as 3′(*S*),4′(*R*)-disenecioyloxy-3′,4′-dihydroxanthyletin (II). Based on the present knowledge, two diastereoisomers: (—)-methyldecursidinol and (+)-methyldecursidinol and their acetates which were derived from decursidin (II) by 10% methanolic sodium hydroxide treatment and subsequent acetylation[1] are now formulated as XIVa (4′(*S*): (—)-methyldecursidinol), XIVb (4′(*R*): (+)-methyldecursidinol), and XVa (4′*S*), XVb (4′*R*), respectively on the basis of their 4′-H chemical shifts and coupling patterns as listed in Table I. As for the correlation of XIVa and XIVb, it was found that treatment of either one diastereoisomer in 5% methanolic sodium hydroxide at reflux resulted in a formation of an equilibrated mixture of XIVa and XIVb with approximate ratio of 1.7: 1 as revealed by PMR examination.

Stereostructures of AD-I (III) and AD-II (IV)

In the previous paper,[1] AD-I was reported as an oily substance and was assumed to be a derivative of 3′,4′-dihydroxy-3′,4′-dihydroxanthyletin which was esterified with angelic and isovaleric acids. On a 10% methanolic sodium hydroxide treatment under reflux, AD-I gave, along with angelic and isovaleric acids, two methoxyl derivatives (isomeric each other at C-4′ configuration)[1] being respectively identical with XIVa and XIVb which were obtained from decursidin (II) under the same reaction conditions.

In the PMR spectrum of AD-I, the aromatic proton signal due to 5-H was found at τ 2.71 and 2.77 (combined intensity: one proton) and the signal due to 3′-H was also observed as two doublets at τ 4.71 and 4.78 (total intensity: one proton). It was presumed therefore that AD-I was a mixture of two diastereoisomeric angeloyl-isovaleroyl derivatives (approximate ratio=1: 1) whose C-3′ configuration was the same as that of II but C-4′ configuration differed each other, however, all the effort for separation of each component was without success.

Treatment of AD-I with 1% methanolic sodium hydroxide at room temperature afforded a methoxyl-angelate and isovaleric acid. The PMR spectrum of the methoxyl-angelate showed the presence of a singlet at τ 2.52 (due to 5-H), a pair of doublets at τ 4.67 ($J=4.8$ Hz, 3′-H) and τ 5.65 ($J=4.8$ Hz, 4′-H) in addition to other signals (see Experimental section) which are consistent with its formulation as XVI (configuration at C-4′ undefined). Therefore, AD-I has been elucidated to be a mixture of two diastereoisomers (isomeric at C-4′) and is formulated as III in which an angeloyloxy group connects at C-3′ (*S*) and an isovaleroyloxy at C-4′ (*R*+*S*).

Another new pyranocoumarin derivatives designated as AD-II was obtained as a glassy substance. The physical properties of AD-II along with its chemical behavior are quite similar to those of decursidin (II). It differs from II by the possession of an angeloyl and a senecioyl in contrast to the presence of two senecioyl functions in II. The PMR spectrum of AD-II, which assured uniformity of the substance, showed a pair of doublets at τ 4.76 ($J=$ 6.6 Hz) and τ 4.01 ($J=6.6$ Hz) ascribable to 3′-H and 4′-H, and other signals similar to those in II.

On treatment of AD-II with 10% methanolic sodium hydroxide under reflux, two aforementioned methoxyl derivatives (XIVa and XIVb) were obtained along with angelic and senecioic acids. On the other hand, mild alkaline treatment of AD-II as for AD-I (III) resulted in a formation of XVI as from AD-I, thus the location of angeloyloxy moiety being defined at C-3′. Finally, ozone oxidation of AD-II as for decursidin (II) furnished a diol as a sole isolable product which was identical with IXb obtained from decursidin under the same treatment. Therefore, AD-II is now formulated as 3′(*S*)-angeloyloxy-4′(*R*)-senecioyloxy-3′,4′-dihydroxanthyletin (IV).

Chart 2
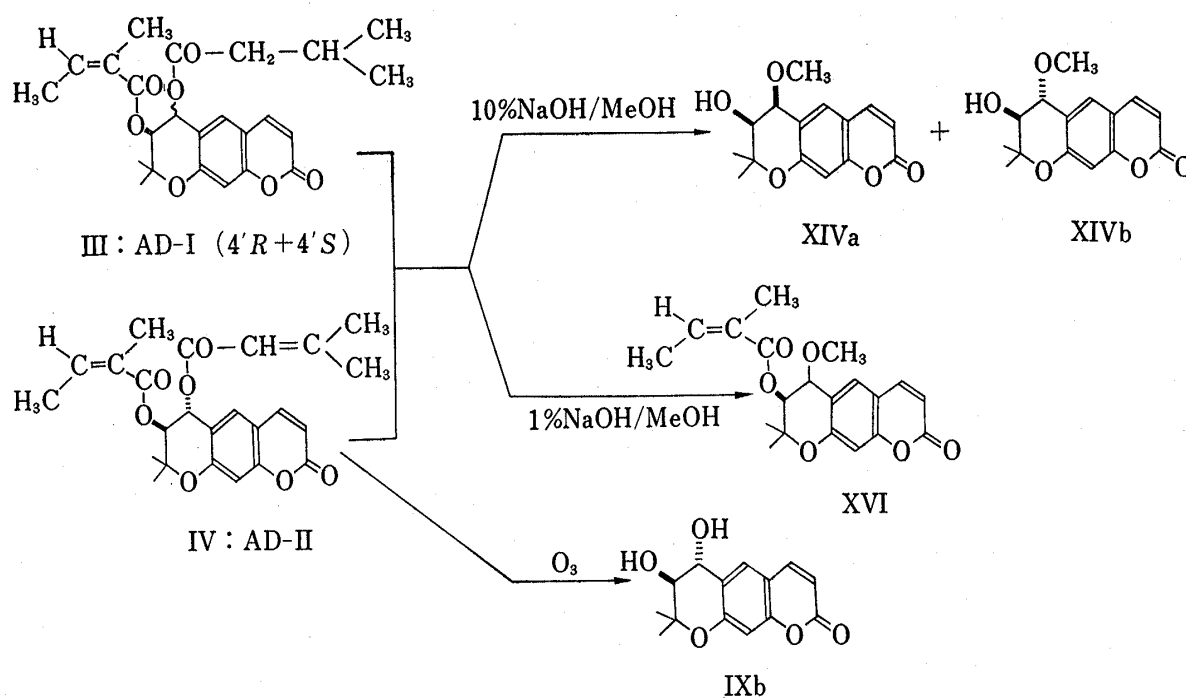
In 1970, Avramenko, *et al.* reported[9] the isolation of andelin from *Angelica decursiva*[10] and proposed its structure as 3'-senecioyloxy-4'-angeloyloxy-3',4'-dihydroxanthyletin (stereochemistry unknown). However, because of the similarity of the physical properties of AD-II (IV) with andelin, the structure of andelin might be revised although the direct comparison of both specimens has not yet been realized. Very recently, El-Antably and Soine reported[11] the syntheses of (+)-*cis*- and (+)-*trans*-3',4'-dihydroxy-3',4'-dihydroxanthyletin and their diesters and the PMR data cited therein especially concerning the 4'-H chemical shifts (higher τ values in the *trans* isomers) are in good accord with our present results.

It is worth to mention here that decursidin (II) and AD-II (IV) are the unprecedented examples possessing a *trans* 3',4'-diol system among the naturally occurring pyranocoumarin derivatives.

Experimental[12]

Na-Amalgam Reduction of Decursinol (V)——A solution of V (1.26 g)[1] in aq. 5% NaOH (50 ml) was adjusted weakly basic by treatment with dil. HCl and added with 5% Na-amalgam (75 g) under effective

9) L.G. Avramenko, G.K. Nikonov, and M.G. Pimenov, *Khim. Prir. Soedin*, 6, 190 (1970) [(*Chem. Abstr.*, 73, 87814 (1970)].
10) Judging from their description, the plant material used by them seems to be *Angelica decursiva* Fr. et Sav. forma *albiflora*.
11) S.M. El-Antably and T.O. Soine, *J. Pharm. Sciences*, 62, 1643 (1973).
12) The following instruments were used for obtaining the physical data. Melting points: Yanagimoto Micro-meltingpoint Apparatus (a hot-stage type) and recorded uncorrected; Specific rotations: Rex Photoelectric Polarimeter NEP-2 (1=1 dm); CD spectra: JASCO ORD/UV-5 Spectrometer; IR spectra: Hitachi IR Spectrometer EPI-2, EPI-G3, or JASCO IR Spectrometer IR-S; UV spectra: Hitachi UV Spectrometer EPS-3T; PMR spectra (tetramethylsilane as an internal standard): Hitachi R-22, Varian A-60, or JEOL JNM-C-60H NMR Spectrometer; Gas–liquid chromatography (GLC): Hitachi Gas Chromatograph K-23, with 20% silicone SE-30/chamelite CK in stainless tube 2 m × 3 mm, 150°, He gas (35.3 ml/min).
    For chromatography, silicic acid (Mallinckrodt, 100 mesh) or silica gel (Merck, 0.06—0.2 mm) which was activated by heating at 110° for 45 min before use, was used for column, and Silica Rider (Daiichi Kagaku KK.), which was activated at 120° for 40 min, was used for thin–layer chromatography (TLC); spots were detected by fluorescence under UV irradiation or by spraying aq. 10% H₂SO₄ followed by heating.

stirring and the total mixture was left standing at room temperature for 4 days and heated at 60—70° for one hr. Precipitated mercury was removed by decantation from a light yellow reaction mixture and an aqueous layer was acidified and extracted with AcOEt. The AcOEt extract was then washed with water, dried, and evaporated to yield a product, which was crystallized from ether–petr. ether mixture to give colorless needles of VI (1.19 g, 87%), mp 157.5°. *Anal.* Calcd. for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.25; H, 6.85. IR ν_{max}^{KBr} cm^{-1}: 3300 (OH), 1685 (COOH), 1615, 1510 (aromatic ring), 1195, 1095, 1050.

3,4-Dihydrodecursinol (VII)——Sublimation of VI at 150—160°, 1 mmHg, gave colorless fine needles of VII, mp 140—142°, $[\alpha]_D^{20}$ +29.7° (c=0.64, MeOH). *Anal.* Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.62; H, 6.69. UV λ_{max}^{MeOH} nm (log ε): 287 (3.48), λ_{min}^{MeOH} nm (log ε): 263 (2.91). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600— 3500 (OH), 1767 (lactone), 1628, 1593, 1491 (aromatic ring), 1448, 1383, 1370, 1340, 1140, 1110. PMR (CDCl$_3$) τ: 3.16 (1H, s, 5-H), 3.52 (1H, s, 8-H), 6.23 (1H, d.d, J_{AX}=4.5 Hz, J_{BX}=5.3, $>$CH–CH$_2$–), 7.05, 7.28 (1H, each, d.d, J_{AX}=4.5, J_{BX}=5.3, J_{AB}=18.0, $>$CH–CH$_2$–), 7.22 (4H, br, 3-H, 4-H), 7.93 (1H, OH), 8.67 (6H, s, $>$C(CH$_3$)$_2$). CD (c=0.0546, MeOH): $[\theta]_{281.5}$ +1090.

3,4-Dihydrodecursinol Benzoate (VIII)——A solution of VII (589 mg) and Bz$_2$O (1.08 g) in pyridine (10 ml) was heated under reflux for 3 hr in an oil bath, treated with a few drops of water, and heated again for one hr. A residue obtained by evaporation of the solvent under reduced pressure was dissolved in ether and the ether solution was washed successively with aq. 2% NaOH, dil. HCl, and water, dried and evaporated to give a product which was purified by silica gel column chromatography eluting with n-hexane– AcOEt (2:1) followed by vacuum sublimation. Colorless fine crystals (VIII, 124 mg) thus obtained showed mp 54—56°, $[\alpha]_D^{19}$ +39.7° (c=1.24, MeOH). *Anal.* Calcd. for $C_{21}H_{20}O_5$: C, 71.58; H, 5.72. Found: C, 71.49; H, 5.79. UV λ_{max}^{MeOH} nm (log ε): 225 (4.30), 283 (3.57), 290 (3.52). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (lactone), 1720 (benzo- ate), 1632, 1598, 1496 (aryl C=C), 1455, 1390, 1373, 1343, 1275, 1145, 1115. PMR (CDCl$_3$) τ: 1.9—2.1 (2H), 2.4—2.6 (3H) (phenyl), 3.15 (1H, s, 5-H), 3.40 (1H, s, 8-H), 4.76 (1H, t, J=5 Hz, $>$CH–CH$_2$–), 6.85, 7.09 (1H, each, d.d, J=5.0 and 17.0, $>$CH–CH$_2$–), 7.15—7.25 (4H, 3-H, 4-H), 8.58, 8.62 (3H, each, s, $>$C(CH$_3$)$_2$). CD (c=0.0785, MeOH): $[\theta]_{305}$ 0, $[\theta]_{290}$ +2200 (sh), $[\theta]_{280}$ +3400 (pos. max), $[\theta]_{250}$ +1500 (pos. max), $[\theta]_{245}$ 0, $[\theta]_{228}$ −29500 (neg. max), $[\theta]_{210}$ −1900 (pos. max), $[\theta]_{206}$ −15000 (neg. max), $[\theta]_{201}$ 0, $[\theta]_{195}$ +85000.

Hydrolysis of Decursidin (II) with Aqueous NaOH——To a hot aq. 10% NaOH (20 ml) was added a solution of II (1.30 g) in a small amount of pyridine and the total mixture was refluxed for 1.5 hr. After cooling, the reaction mixture was acidified with 10% H$_2$SO$_4$ and extracted with AcOEt. The AcOEt solution was treated successively with satur. aq. NaHCO$_3$ solution, aq. NaCl solution, and dried, and evaporated to dryness. A residue was then purified by silica gel column chromatography eluting with n-hexane–AcOEt (3:1) followed by crystallization from MeOH to give colorless needles of (−)-decursidinol (IXa, 446 mg), mp 226—228°, $[\alpha]_D^{20}$ −43.8° (c=0.86, MeOH). *Anal.* Calcd. for $C_{14}H_{14}O_5$: C, 64.11; H, 5.38. Found: C, 64.37; H, 5.16. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430 (OH), 1730 (lactone), 1630, 1568, 1492 (aryl C=C), 1387, 1290, 1145, 1130. PMR (d_5-pyridine) τ: 2.06 (1H, s, 5-H), 2.37 (1H, d, J=9.0 Hz, 4-H), 3.15 (1H, s, 8-H), 3.77 (1H, d, J=9.0, 3-H), 3.87 (2H, s, OH), 4.80 (1H, d, J=4.2, 4′-H), 5.90 (1H, d, J=4.2, 3′-H), 8.28, 8.61 (3H, each, s, $>$C(CH$_3$)$_2$).

Conversion of (−)-Decursidinol (IXa) to (+)-Decursidinol (IXb)——A solution of IXa (297 mg) in aq. 2% NaOH (20 ml) was refluxed for 5 hr in an oil bath. After cooling, the reaction mixture was acidified with 10% H$_2$SO$_4$ and extracted with AcOEt. The AcOEt extract was then washed successively with satur. aq. NaHCO$_3$ solution, aq. NaCl solution, dried, and evaporated. A residue thus obtained was purified by passing through a silica gel column with an aid of n-hexane–AcOEt (1:1) mixture and crystallized from AcOEt–n-hexane mixture to give colorless needles of IXb (30 mg), mp 229—231°, $[\alpha]_D^{20}$ +144.2° (c=1.63, MeOH). *Anal.* Calcd. for $C_{14}H_{14}O_5$: C, 64.11; H, 5.38. Found: C, 64.10; H, 5.32. PMR (d_5-pyridine) τ: 2.02 (1H, s, 5-H), 2.23 (1H, d, J=9.5 Hz, 4-H), 3.23 (1H, s, 8-H), 3.71 (1H, d, J=9.5, 3-H), 4.94 (1H, d, J=9.0, 4′-H), 5.97 (1H, d, J=9.0, 3′-H), 7.51 (2H, OH), 8.32, 8.53 (3H each, s, $>$C(CH$_3$)$_2$).

Acetonidation of IXa and IXb——1) A solution of IXa (84 mg) in acetone (30 ml) was treated with aq. 60 % HClO$_4$ (1 ml) and the total mixture was stirred at room temperature for 6 hr. After addition of NaHCO$_3$ (1 g) and water (10 ml), the mixture was stirred for a while, evaporated *in vacuo*, diluted with water, and extracted with ether. The ether extract was then washed with water, dried, and evaporated to give a product, which was chromatographed on a silica gel column developing with n-hexane–AcOEt (4:1) to afford a color- less oily product (X, 81 mg), $[\alpha]_D^{28}$ −198.1° (c=0.86, MeOH). *Anal.* Calcd. for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.78; H, 6.19. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1733 (lactone), 1628, 1568, 1495 (aryl C=C), 1393, 1389, 1375, 1300, 1162, 1147. PMR (CCl$_4$) τ: 2.45 (1H, d, J=9.5 Hz, 4-H), 2.59 (1H, s, 5-H), 3.32 (1H, s, 8-H), 3.87 (1H, d, J=9.5, 3-H), 4.90 (1H, d, J=6.0, 4′-H), 5.87 (1H, d, J=6.0, 3′-H), 8.56, 8.66, 8.74, 8.92 (3H each, all s, $>$C(CH$_3$)$_2$×2). 2) A solution of IXb (52 mg) in acetone (30 ml) containing aq. 60% HClO$_4$ (1 ml) was treated as above, and only the starting material was recovered as shown by TLC (n-hexane–AcOEt (1:1)).

Catalytic Hydrogenation of IXa giving VII——A solution of IXa (96 mg) in glacial AcOH (30 ml) was hydrogenated over PtO$_2$ (60 mg) for 7 hr: totally 33.3 ml of hydrogen being consumed. After removing catalyst by filtration, the filtrate was evaporated and a product was purified by silica gel column chromato- graphy developing with n-hexane–AcOEt (2:1) and crystallized from AcOEt–n-hexane to give colorless needles (41 mg), mp 141—143°, $[\alpha]_D^{16}$ +22.6° (c=1.37, MeOH). *Anal.* Calcd. for $C_{14}H_{16}O_4$: C, 73;67. H, 6.50.

Found: C, 67.47; H, 6.56. The product was identified with 3,4-dihydrodecursinol (VII) prepared from decursinol (*vide supra*) in all respects.

Ozone Oxidation of Decursidin (II) giving IXb——An ice-cooled solution of II (861 mg) in CCl$_4$ (30 ml) was bubbled with a stream of ozone for 15 min. The solution was then evaporated and the residue was purified repeatedly by silica gel column chromatography developing with *n*-hexane–AcOEt (4:1) to give a product (85 mg), $[\alpha]_D^{20}$ +123.7° (c=1.07, MeOH), which was identified with (–)-decursidinol (IXb) by PMR and $[\alpha]_D$. The PMR examination of the chromatographic fractions containing substances having the same Rf value as IXa (also same as IXb) ascertained the absence of IXa in the total reaction products.

LiAlH$_4$ Reduction of II giving XI——To a stirred solution of LiAlH$_4$ (120 mg) in dry ether (20 ml) was added dropwise a solution of II (873 mg) in dry ether (30 ml) and the total mixture was kept stirring for 2 hr at room temperature, and treated with water and dil. H$_2$SO$_4$. The ether layer was separated and aqueous layer was extracted again with ether. The combined ether solution was treated in a usual manner to give a product which was purified by silica gel column chromatography eluting with *n*-hexane–AcOEt (4:1) and a viscous monosenecioate (XI, 26 mg) was obtained.[13] $[\alpha]_D^{20}$ +72.1° (c=1.11, MeOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (OH), 1720 (ester and lactone), 1625, 1560, 1492 (aryl C=C), 1445, 1385, 1144. PMR (CDCl$_3$) τ: 2.39 (1H, d, J=9.5 Hz, 4–H), 2.40 (1H, s, 5–H), 3.26 (1H, s, 8–H), 3.78 (1H, d, J=9.5, 3–H), 4.26 (1H, m, –CH= C(CH$_3$)$_2$), 4.96 (1H, d, J=8.0, 3'–H), 5.31 (1H, d, J=8.0, 4'–H), 7.81, 8.06 (3H, each, s, C=C(CH$_3$)$_2$), 8.57, 8.76 (3H each, s, >C(CH$_3$)$_2$).

4'-*epi*-Decursidin (XII)——A mixture of IXa (155 mg), sodium senecioate (1 g), and senecioyl chloride (2 ml) in a sealed tube was heated at 150—160° for 5 hr. After cooling, the mixture was dissolved in water and extracted with AcOEt. The AcOEt extract was then treated with satur. aq. NaHCO$_3$ solution and aq. NaCl solution, dried, and evaporated to dryness. The product was purified by silica gel column chromatography developing with *n*-hexane–AcOEt (4:1) to furnish a colorless oily substance (XII, 132 mg), $[\alpha]_D^{15}$ +44.5° (c=1.63, MeOH). *Anal*. Calcd. for C$_{24}$H$_{26}$O$_7$: C, 67.59; H, 6.15. Found: C, 67.33; H, 6.25. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1724 (ester and lactone), 1645, 1633, 1570, 1500 (aryl C=C), 1445, 1394, 1380, 1135, 1075, being very alike to decursidin (II). PMR (CCl$_4$) τ: 2.42 (1H, d, J=9.0 Hz, 4–H), 2.68 (1H s, 5–H), 3.23 (1H, s, 8–H), 3.84 (1H, d, J=9.0, 3–H), 3.86 (1H, d, J=4.2, 4'–H), 4.34 (2H, m, –CH=C(CH$_3$)$_2$×2), 4.61 (1H, d, J=4.2, 3'–H), 7.77, 7.88, 8.04, 8.10 (3H each, all s, C=C(CH$_3$)$_2$×2), 8.50, 8.57 (3H each s, >C(CH$_3$)$_2$).

AD-I (III)[1]——IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1732 (ester and lactone), 1631, 1565, 1498 (aryl C=C), 1465, 1392, 1375, 1295, 1130, 825. PMR (CCl$_4$) τ: 2.49 (1H, d, J=9.5 Hz, 4–H), 2.71, 2.77 (totally 1H, each s, 5–H), 3.36 (1H, s, 8–H), 3.91 (1H, d, J=9.5, 3–H), 3.8—4.2 (2H, 4'–H and C=CH–C), 4.71, 4.78 (totally 1H, each d, J=6.8, 3'–H), 7.80, 7.9—8.1, 8.12 (totally 9H, –CO–C(CH$_3$)=CH–CH$_3$, –CO–CH$_2$–CH<, –CO(CH$_3$)=CH–CH$_3$), 8.58 (6H, br. >C(CH$_3$)$_2$), 8.9—9.1 (6H, br.d, J=6.5, –CH(CH$_3$)$_2$).

Partial Alkaline Methanolysis of AD-I (III) giving XVI——A solution of III (300 mg) in 1% NaOH– MeOH (10 ml) was kept stirring at room temperature for 10 min, acidified with 10% H$_2$SO$_4$, diluted with water, and extracted with ether. The ether extract was then washed with satur. aq. NaHCO$_3$ solution and water, dried, and evaporated to give a product, which was chromatographed on a silica gel column developing with *n*-hexane–AcOEt (4:1). A slightly discolored oily product (XVI, 109 mg), $[\alpha]_D^{20}$ +79.4° (c=1.70, MeOH) was obtained. *Anal*. Calcd. for C$_{20}$H$_{22}$O$_5$: C, 67.02; H, 6.19. Found: C, 67.26; H, 6.29. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1723 (ester and lactone), 1628, 1563, 1495 (aryl C=C), 1393, 1375, 1136, 934, 825. PMR (CCl$_4$) τ: 2.36 (1H, d, J=9.5 Hz, 4–H), 2.52 (1H, s, 5–H), 3.22 (1H, s, 8–H), 3.80 (1H, d, J=9.5, 3–H), 4.67 (1H, d, J=4.8, 3'–H), 5.65 (1H, d, J=4.8, 4'–H), 6.44 (3H s, OCH$_3$), 7.98, 8.10 (totally 6H, –C(CH$_3$)=CH–CH$_3$), 3.6—4.0 (1H, br, >C=CH–CH$_3$), 8.51, 8.60 (3H, each, s, >C(CH$_3$)$_2$). The NaHCO$_3$ soluble portion in the above procedure was acidified with 10% H$_2$SO$_4$ and distilled. A distillate was taken up with ether, methylated with ethereal diazomethane by keeping overnight, subjected to GLC and identified with methyl isovalerate.

Isolation of AD-II (IV)——Petr. ether insoluble portion (20 g) of an ether extract of the root[1] was chromatographed on a silicic acid column developing with *n*-hexane–AcOEt mixture: i) 3:1, ii) 2:1, and iii) 1:1, successively. The eluate (i) was chromatographed again on a silicic acid column developing with *n*-hexane–AcOEt (9:1) to give AD-I (III, 4.6 g), AD-II (IV, 1.5 g), and decursidin (II, 5.2 g). Crystallization of the eluate (ii) from ether–petr. ether and then from EtOH afforded decursin (I, 5.5 g). The eluate (iii) gave umbelliferone (0.14 g, crystallized from water), nodakenetin (70 mg, crystallized from EtOH), and a mixture of nodakenetin and marmesin (100 mg). AD-II (IV), being obtained as a colorless glassy substance by vacuum sublimation, $[\alpha]_D^{12}$ −24.2° (c=4.39, EtOH). *Anal*. Calcd. for C$_{24}$H$_{26}$O$_7$: C, 67.59; H, 6.15. Found: C, 67.71; H, 6.02. UV λ_{max}^{MeOH} nm (log ε): 221.5 (4.66), 256 (3.75, sh), 300 (4.10, sh), 325 (4.29); λ_{min}^{MeOH} nm (log ε): 214 (4.64), 264 (3.55). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1728 (ester and lactone), 1630, 1565, 1498 (aryl C=C), 1392, 1383, 1297, 1137, 1075, 852, 825. PMR (CCl$_4$) τ: 2.50 (1H, d, J=9.5 Hz, 4–H), 2.75 (1H, s, 5–H), 3.31 (1H, s, 8–H), 3.91 (1H, d, J=9.5, 3–H), 3.7—4.2 (1H, >C=CH–CH$_3$), 4.35 (1H, m, –CH=C(CH$_3$)$_2$), 4.01 (1H, d, J=6.6, 4'–H), 4.76 (1H, d, J=6.6, 3'–H), 7.80, 8.07, 8.14 (totally 12H, –CH=C(CH$_3$)$_2$. –C(CH$_3$)=CH–CH$_3$), 8.56, 8.63 (3H each, s, >C(CH$_3$)$_2$).

---

13) Although the purity of XI was assured by TLC and PMR, the elemental analysis did not give a satisfactory result.

Methanolic Alkaline Hydrolysis of AD-II (IV)——A solution of IV (664 mg) in 10% NaOH–MeOH (20 ml) was refluxed for one hour, cooled, acidified with 10% H_2SO_4, diluted with water, and extracted with ether. The ether extract was washed successively with satur. aq. $NaHCO_3$ solution and water, and worked up in a usual manner to give a slightly discolored crystalline product (352 mg), which was purified by silica gel column chromatography developing with *n*-hexane–AcOEt (4:1) to give XIVa (major) and XIVb (minor) as from II.[1] The $NaHCO_3$ soluble portion in the above procedure was acidified with 10% H_2SO_4 and distilled. A distillate was then dissolved in ether, methylated with ethereal diazomethane, and identified by GLC with authentic methyl angelate and methyl senecioate.

Partial Alkaline Methanolysis of IV——A solution of IV (233 mg) in 1% NaOH–MeOH (20 ml) was kept stirring at room temperature for 10 min, acidified with 10% H_2SO_4, diluted with water, and extracted with ether. The ether extract was washed with satur. aq. $NaHCO_3$ solution and water successively, and treated in a usual manner. A product thus obtained was purified by silica gel column chromatography eluting with *n*-hexane–AcOEt (4:1) to furnish XVI (137 mg). The above $NaHCO_3$ soluble portion was acidified with 10% H_2SO_4 and distilled and the distillate was dissolved in ether, treated with ethereal diazomethane, and identified with methyl senecioate by GLC.

Ozone Oxidation of AD-II (IV)——A cooled solution (−10°) of IV (715 mg) in CCl_4 (30 ml) was bubbled with a stream of ozone for 15 min and treated as for II to give IXb (66 mg), $[\alpha]_D^{20}$ +132.4° (*c*=0.94, MeOH).