Absolute Configurations of Asperlin, a Metabolite of *Aspergillus nidulans*, and Its Related Compounds

Keiichi FUKUYAMA,* Yukiteru KATSUBE, Akihiro NODA,**
Takashi HAMASAKI,** and Yuichi HATSUDA**
Faculty of Engineering, Tottori University, Koyama, Tottori 680
***Faculty of Agriculture, Tottori University, Koyama, Tottori 680*
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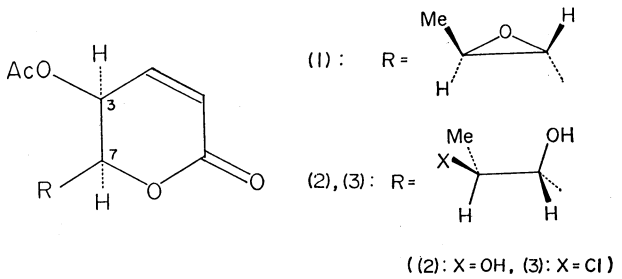
The structures of asperlin (**1**) $C_{10}H_{12}O_5$ and asperlinol (**2**) $C_{10}H_{14}O_6$, isolated from *Aspergillus nidulans*, and a chloro derivative of asperlin (**3**) $C_{10}H_{13}O_5Cl$ have been studied by the X-ray diffraction method. The absolute configuration of **3** has been determined by the Bijvoet method by utilizing the anomalous scattering of chlorine atom for Cu $K\alpha$ radiation. The present analysis has verified the configurations of the atoms in an $\alpha\beta$-unsaturated δ-lactone ring as suggested by spectroscopy. In each compound, the acetoxyl group occupies a quasi-axial and the three-carbon side chain a quasi-equatorial position on the lactone ring. All the crystals are orthorhombic, space group $P2_12_12_1$ with $Z=4$. The cell dimensions are $a=26.536$, $b=5.955$, $c=6.973$ Å for **1**, $a=25.496$, $b=7.097$, $c=6.329$ Å for **2**, and $a=26.050$, $b=5.899$, $c=7.548$ Å for **3**. The structures of **1**, **2**, and **3** were refined by the block-diagonal least-squares method to $R=0.068$ for 1084 reflections, $R=0.056$ for 1127 reflections, and $R=0.051$ for 831 reflections, respectively.

Extensive investigations have been made on the structures[1-4] and biosynthesis[5,6] of various kinds of lactone derivatives isolated from the genus *Aspergillus*. Although the configurations at the C(3) and C(7) atoms in asperlin (**1**), a metabolite isolated from *Aspergillus nidulans*, have been suggested by spectroscopy,[1,3] the whole stereochemistry has not yet been established. Recently we have isolated a new compound $C_{10}H_{14}O_6$ (**2**), named asperlinol, from *Aspergillus nidulans* together with asperlin. Asperlinol (**2**) was suggested to be one of the hydrated compounds of asperlin on the basis of spectroscopic evidence, but a definitive structure remained to be determined because of its instability in solution. For the establishment of the absolute configurations of these compounds, the chloro derivative (**3**) was prepared from asperlin to utilize the anomalous scattering of the chlorine atom for X-radiation. In this paper we report the results of the X-ray analyses of **1**—**3**.



Experimental

Isolation of Asperlin (1) and Asperlinol (2). *Aspergillus nidulans* Wint. IFO 6390 was grown on malt extract medium in stationary culture at 24 °C for three weeks. The culture filtrate was adsorbed on activated carbon at pH 2—3 adjusted by hydrochloric acid. The carbon was extracted with acetone. Chloroform-soluble fraction of the acetone extract was concentrated, and chromatographed on a column of silicic acid. **1** was eluted with benzene, and **2** subsequently with benzene–acetone (9:1 v/v). **1** was recrystallized with ether to give colorless plates, which had physical constants identical with those for asperlin. **2** was further subjected to silicic acid column chromatography. The fraction eluted with benzene–acetone (4:1 v/v) yielded a colorless solid, which was recrystallized from an acetone–hexane solution to give colorless prisms (49 mg), mp 117—118 °C. Found: C, 52.38; H, 6.14%. Calcd for $C_{10}H_{14}O_6$: C, 52.18; H, 6.13%. $[\alpha]_D^{18}=220°$ ($c=0.9$, EtOH), λ_{max} (EtOH) 205(9200), ν_{max} (KBr) 3500, 3000, 2950, 1750, 1720, and 1640 cm^{-1}, δ(DMSO-d_6, 60 MHz) 7.07 (1H, dd, $J=6$ and 10 Hz), 6.12 (1H, d, $J=10$ Hz), 5.25 (1H, dd, $J=2.5$ and 6 Hz), 5.03 (1H, d, $J=5$ Hz), 4.48 (1H, d, $J=5$ Hz), 4.36 (1H, dd, $J=2.5$ and 9 Hz), 3.5—4.0 (2H, m), 2.01 (3H, s), and 1.03 (3H, d, $J=6$ Hz).

Preparation of Chloro Derivative (3). Asperlin (950 mg) was treated with hydrochloric acid (6 M, 10 ml) in diethyl ether (12 ml) at room temperature. Slow evaporation of ether gave colorless crystals from the aqueous solution, which were filtered and washed with water. Recrystallization with methanol gave chloro derivative (**3**) as colorless needles (440 mg), mp 187—189 °C. Found: C, 48.37; H, 5.46; Cl, 14.00%. Calcd for $C_{10}H_{13}O_5Cl$: C, 48.30; H, 5.27; Cl, 14.26%. $[\alpha]_D^{18}=280°$ ($c=0.9$, EtOH), λ_{max} (EtOH) 205 (10300), ν_{max} (KBr), 3450, 2980, 2925, 1750, 1720, and 1640 cm^{-1}, δ(DMSO-d_6, 60 MHz), 1.43 (3H, d, $J=6.5$ Hz), 2.02 (3H, s), 3.97 (1H, m, $J=2$, 6, and 10 Hz), 4.25 (1H, dq, $J=2$ and 6.5 Hz), 4.50 (1H, dd, $J=2.5$ and 10 Hz), 5.26 (1H, dd, $J=2.5$ and 6 Hz), 5.85 (1H, d, $J=6$ Hz), 6.15 (1H, d, $J=10$ Hz), and 7.08 (1H, dd, $J=6$ and 10 Hz).

Crystal Data. (a) Asperlin (**1**), $C_{10}H_{12}O_5$, $M=212.2$, orthorhombic, $P2_12_12_1$, $a=26.536(6)$, $b=5.955(4)$, $c=6.973(4)$ Å, $V=1101.9$ Å^3, $Z=4$, $D_x=1.279$ g cm^{-3}, $\mu=8.9$ cm^{-1} (for Cu $K\alpha$). (b) Asperlinol (**2**), $C_{10}H_{14}O_6$, $M=230.2$, orthorhombic, $P2_12_12_1$, $a=25.496(6)$, $b=7.097(4)$, $c=6.329(4)$ Å, $V=1145.2$ Å^3, $Z=4$, $D_x=1.335$ g cm^{-3}, $\mu=9.6$ cm^{-1} (for Cu $K\alpha$). (c) Chloro derivative of asperlin (**3**), $C_{10}H_{13}O_5Cl$, $M=248.7$, $a=26.050(7)$, $b=5.899(5)$, $c=7.548(5)$ Å, $V=1159.9$ Å^3, $Z=4$, $D_x=1.424$ g cm^{-3}, $\mu=29.9$ cm^{-1} (for Cu $K\alpha$).

Crystallographic Measurements. Preliminary photographic investigation showed all these crystals to be orthorhombic with the systematic absences uniquely characterizing $P2_12_12_1$. The approximate crystal size used for intensity measurement was $0.2\times0.4\times0.1$ mm^3 for **1**, $0.2\times0.3\times0.1$ mm^3 for **2**, and $0.2\times0.5\times0.2$ mm^3 for **3**. Each crystal was mounted with the b axis parallel to the ϕ axis of the diffractometer.

All the crystallographic measurements for **1** and **2** were

TABLE 1. FINAL ATOMIC COORDINATES WITH THEIR ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

	x	y	z
(a) Asperlin (**1**)			
C(1)	0.2725(1)	−0.1478(13)	−0.0629(8)
C(2)	0.3098(1)	−0.2441(8)	0.0732(6)
C(3)	0.3921(1)	−0.1955(6)	0.2042(5)
C(4)	0.4298(1)	−0.2999(7)	0.0759(6)
C(5)	0.4674(1)	−0.1797(7)	0.0055(6)
C(6)	0.4714(1)	0.0637(7)	0.0429(5)
C(7)	0.4151(1)	0.0027(6)	0.3076(5)
C(8)	0.3768(1)	0.1440(6)	0.4079(5)
C(9)	0.3842(1)	0.2173(8)	0.6081(6)
C(10)	0.3567(2)	0.4238(10)	0.6823(8)
O(1)	0.3063(1)	−0.4202(7)	0.1544(6)
O(2)	0.3510(1)	−0.1128(4)	0.0857(4)
O(3)	0.4978(1)	0.1892(6)	−0.0474(5)
O(4)	0.4416(1)	0.1511(4)	0.1799(4)
O(5)	0.3523(1)	0.0297(5)	0.5621(4)
H(C1)	0.271(1)	0.022(7)	−0.037(7)
H(C1)	0.240(2)	−0.205(11)	−0.046(10)
H(C1)	0.285(2)	−0.172(10)	−0.196(8)
H(C3)	0.378(1)	−0.317(6)	0.312(5)
H(C4)	0.428(2)	−0.462(8)	0.031(6)
H(C5)	0.494(2)	−0.263(8)	−0.083(8)
H(C7)	0.440(1)	−0.075(7)	0.410(7)
H(C8)	0.355(1)	0.244(7)	0.311(6)
H(C9)	0.417(2)	0.251(8)	0.659(6)
H(C10)	0.377(2)	0.547(8)	0.687(6)
H(C10)	0.350(2)	0.364(9)	0.822(8)
H(C10)	0.323(2)	0.447(8)	0.594(7)
(b) Asperlinol (**2**)			
C(1)	0.2575(2)	0.1821(6)	0.4569(9)
C(2)	0.2819(1)	0.2972(5)	0.6237(8)
C(3)	0.3593(1)	0.4672(5)	0.7188(6)
C(4)	0.3880(1)	0.3498(6)	0.8779(6)
C(5)	0.4389(1)	0.3168(6)	0.8586(7)
C(6)	0.4677(1)	0.3768(5)	0.6689(6)
C(7)	0.3971(1)	0.5887(4)	0.5940(6)
C(8)	0.3730(1)	0.6737(5)	0.3964(6)
C(9)	0.4105(1)	0.7974(6)	0.2761(6)
C(10)	0.4249(2)	0.9774(6)	0.3864(7)
O(1)	0.2627(1)	0.3484(5)	0.7884(6)
O(2)	0.3319(1)	0.3433(3)	0.5732(5)
O(3)	0.5117(1)	0.3212(4)	0.6304(4)
O(4)	0.4434(1)	0.4844(3)	0.5275(4)
O(5)	0.3286(1)	0.7784(4)	0.4677(4)
O(6)	0.3854(1)	0.8404(4)	0.0778(4)
H(C1)	0.273(2)	0.059(7)	0.471(8)
H(C1)	0.216(2)	0.171(6)	0.487(7)
H(C1)	0.262(2)	0.211(6)	0.310(7)
H(C3)	0.333(2)	0.542(6)	0.804(7)
H(C4)	0.364(2)	0.294(6)	1.015(7)
H(C5)	0.463(2)	0.249(6)	0.970(7)
H(C7)	0.408(1)	0.701(5)	0.693(6)
H(C8)	0.363(1)	0.561(5)	0.301(6)
H(C9)	0.443(1)	0.717(6)	0.245(6)
H(C10)	0.441(2)	0.952(6)	0.502(7)
H(C10)	0.387(2)	1.049(7)	0.420(8)
H(C10)	0.448(1)	1.043(6)	0.299(6)
H(O5)	0.300(2)	0.710(6)	0.408(7)
H(O6)	0.415(2)	0.872(6)	0.006(7)
(c) Chloro derivative (**3**)			
Cl	0.3820(1)	−0.1920(3)	0.6565(2)
C(1)	0.4820(3)	0.1991(16)	−0.0588(9)
C(2)	0.4616(2)	0.3926(14)	0.0516(9)
C(3)	0.3885(2)	0.4995(11)	0.2261(8)
C(4)	0.3574(2)	0.6575(12)	0.1156(9)
C(5)	0.3093(2)	0.6182(13)	0.0863(10)
C(6)	0.2849(2)	0.3978(12)	0.1373(9)
C(7)	0.3543(2)	0.3686(11)	0.3520(8)
C(8)	0.3817(2)	0.1696(11)	0.4424(8)
C(9)	0.3468(2)	0.0503(11)	0.5731(9)
C(10)	0.3296(3)	0.1926(14)	0.7308(9)
O(1)	0.4820(2)	0.5660(10)	0.0869(8)
O(2)	0.4146(1)	0.3373(8)	0.1125(5)
O(3)	0.2455(2)	0.3340(9)	0.0797(8)
O(4)	0.3108(1)	0.2676(7)	0.2564(6)
O(5)	0.4250(2)	0.2622(8)	0.5282(6)
H(C1)	0.476(3)	0.060(14)	−0.009(12)
H(C1)	0.517(3)	0.268(13)	−0.060(11)
H(C1)	0.468(3)	0.255(13)	−0.180(10)
H(C3)	0.413(3)	0.549(13)	0.304(10)
H(C4)	0.388(3)	0.775(14)	0.063(11)
H(C5)	0.288(3)	0.729(12)	0.023(9)
H(C7)	0.339(2)	0.501(11)	0.428(9)
H(C8)	0.393(3)	0.054(13)	0.333(10)
H(C9)	0.313(3)	−0.032(13)	0.500(11)
H(C10)	0.310(3)	0.100(12)	0.826(10)
H(C10)	0.361(3)	0.251(13)	0.790(11)
H(C10)	0.313(3)	0.348(13)	0.668(9)
H(O5)	0.455(3)	0.171(13)	0.497(11)

made under the same experimental conditions. The cell constants were determined by least-squares treatement of the angular settings of 13 reflections measured on a Rigaku computer-controlled four-circle diffractometer with Ni-filtered Cu $K\alpha$ radiation. The intensities were measured by the θ-2θ scan technique with a scan speed of 2° min^{-1} in θ. The scan width for each reflection was calculated with the formula; $\Delta(\theta)=1.0°+0.15°\tan\theta$. The background counts were taken for 8 s at each end of the scan range. Attenuators were inserted automatically to keep the counting rate below 10^4 cps. The intensities of 1085 and 1127 independent reflections were collected for **1** and **2** respectively in the range $0<\sin\theta/\lambda<0.58$.

The cell constants of **3** were determined from Bragg angles of the reflections of (h00), (0k0), and (00l). The intensities were measured in the left-handed coordinate system on a Rigaku tape-controlled four-circle diffractometer with Ni-filtered Cu $K\alpha$ radiation. The θ-2θ scan technique was used with the scan speed of 2° min^{-1} in θ. The scan width was 1.2° in θ for all reflections and the backgrounds were counted for 5 s at both sides of the scan. The intensities of 831 independent reflections were measured in the range 0<

Table 2. Results of Bijvoet measurements

h	k	l	B_{th}	B_{ex}	DEL
1	1	4	0.102	−0.076	−0.75
1	1	5	0.081	−0.072	−0.89
3	2	1	0.179	−0.150	−0.84
5	1	2	−0.140	0.159	−1.14
5	1	3	−0.071	0.055	−0.77
5	1	5	−0.078	0.107	−1.37
6	2	4	−0.089	0.075	−0.84
7	2	3	−0.108	0.149	−1.38
7	1	4	0.104	−0.102	−0.98
8	1	2	0.083	−0.042	−0.51
8	1	3	−0.117	0.087	−0.74
8	1	4	0.104	−0.083	−0.80
9	1	1	0.100	−0.039	−0.39
11	2	3	−0.100	0.113	−1.13
12	1	1	−0.116	0.197	−1.70
12	1	2	−0.095	0.169	−1.78
14	1	3	0.110	−0.036	−0.33
15	2	1	0.081	−0.058	−0.72

$DEL=B_{ex}/B_{th}$, $B=2.0(Q-1)/(Q+1)$, $Q=F(hkl)/F(\bar{h}\bar{k}\bar{l})$. B_{ex} is the mean value of two B's observed individually. B_{th} has been calculated from the parameters at the final stage of the refinement including anomalous dispersion terms of chlorine atom; $\Delta f'_{Cl}=0.348$ and $\Delta f''_{Cl}=0.702$.

$\sin\theta/\lambda<0.53$.

The intensities were corrected for the Lorentz and polarization factors, but were not corrected for absorption.

Structure Determination and Refinement. a): The structure of asperlin (**1**) was elucidated by MULTAN.[7] The 250 reflections with $|E|$ values greater than 1.2 were used for phase determination, and a set of phases of the highest figure of merit was chosen for the calculation of an E map. The map revealed the positions of all non-hydrogen atoms except the terminal methyl carbon atom; the atom was easily located by Fourier synthesis. The structure was refined by the block-diagonal least-squares method.[8] The atomic species and types of bonds were determined on the basis of temperature factors, and interatomic distances and angles as well as chemical information. The difference Fourier synthesis computed after the anisotropic refinement of the non-hydrogen atoms revealed the positions of hydrogen atoms. However, several minor residual peaks were found around the methyl gourp in the synthesis. The final refinement, including the contribution of these hydrogen atoms with isotropic temperature factors, reduced R to 0.068 for 1084 independent reflections ($R=0.052$ for non-zero reflections). The weighting scheme used in the final refinement was: $w=0.5$ for $F_o=0$ and $w=[\sigma^2(F_o)+0.004F_o^2]^{-1}$ for $F_o>0$, where the values of $\sigma(F_o)$ were calculated from counting statistics. However, zero weight was given for the strongest reflection, 601. The final atomic coordinates are given in Table 1(a).

b): The determination and the refinement of the structure of asperlinol (**2**) were made with the same way as that of asperlin. The final refinement, including the hydrogen atoms located in the difference Fourier synthesis with isotropic temperature factors, reduced R to 0.056 for 1127 independent reflections ($R=0.043$ for non-zero reflections). The weighting scheme used in the final refinement was $w=0.4$ for $F_o=0$ and $w=[\sigma^2(F_o)+0.03F_o]^{-1}$ for $F_o>0$.

Table 3. Bond lengths (Å) and angles (°) for non-hydrogen atoms with estimated standard deviations in parentheses

	1 (X=O(5))	**2** (X=O(6))	**3** (X=Cl)
Bond lengths			
C(1)-C(2)	1.485(9)	1.473(8)	1.510(13)
C(2)-O(1)	1.195(7)	1.208(6)	1.183(11)
C(2)-O(2)	1.348(6)	1.353(6)	1.348(10)
C(3)-C(4)	1.479(6)	1.497(6)	1.490(10)
C(3)-C(7)	1.511(5)	1.515(5)	1.515(9)
C(3)-O(2)	1.454(5)	1.454(5)	1.453(8)
C(4)-C(5)	1.323(6)	1.324(6)	1.294(10)
C(5)-C(6)	1.476(6)	1.471(6)	1.497(10)
C(6)-O(3)	1.202(6)	1.213(5)	1.177(9)
C(6)-O(4)	1.345(5)	1.330(5)	1.361(8)
C(7)-C(8)	1.493(5)	1.519(5)	1.534(9)
C(7)-O(4)	1.439(4)	1.455(4)	1.469(8)
C(8)-C(9)	1.475(6)	1.505(5)	1.516(9)
C(8)-O(5)	1.430(5)	1.428(5)	1.412(8)
C(9)-C(10)	1.521(8)	1.501(6)	1.523(11)
C(9)-X	1.438(6)	1.442(5)	1.812(7)
Bond angles			
C(1)-C(2)-O(1)	126.2(5)	127.8(5)	128.4(8)
C(1)-C(2)-O(2)	111.0(5)	111.3(4)	109.0(7)
O(1)-C(2)-O(2)	122.7(5)	120.9(5)	122.6(8)
C(4)-C(3)-C(7)	110.2(3)	110.9(3)	110.5(6)
C(4)-C(3)-O(2)	107.8(3)	108.9(3)	109.6(5)
C(7)-C(3)-O(2)	108.0(3)	108.7(3)	108.0(5)
C(3)-C(4)-C(5)	120.5(4)	121.0(4)	120.6(7)
C(4)-C(5)-C(6)	121.3(4)	120.9(4)	121.5(7)
C(5)-C(6)-O(3)	124.0(4)	122.1(4)	123.6(7)
C(5)-C(6)-O(4)	117.6(4)	118.8(3)	116.7(6)
O(3)-C(6)-O(4)	118.3(4)	118.9(4)	119.7(6)
C(3)-C(7)-C(8)	113.0(3)	113.4(3)	113.3(5)
C(3)-C(7)-O(4)	112.5(3)	112.2(3)	110.6(5)
C(8)-C(7)-O(4)	106.0(3)	107.0(3)	105.5(5)
C(7)-C(8)-C(9)	121.3(4)	113.0(3)	111.4(5)
C(7)-C(8)-O(5)	113.2(3)	105.5(3)	106.3(5)
C(9)-C(8)-O(5)	59.3(3)	111.1(3)	111.2(5)
C(8)-C(9)-C(10)	119.8(4)	114.6(3)	115.4(6)
C(8)-C(9)-X	58.8(3)	106.4(3)	106.8(5)
C(10)-C(9)-X	114.9(4)	109.5(3)	108.2(5)
C(2)-O(2)-C(3)	116.7(3)	116.7(3)	117.8(6)
C(6)-O(4)-C(7)	119.3(3)	118.4(3)	118.5(5)
C(8)-O(5)-C(9)	61.9(3)	—	—

The final atomic coordinates are given in Table 1(b).

c): The structure of chloro derivative (**3**) was solved by the heavy-atom method, and refined by the block-diagonal least-squares method in the same way as described above. After the absolute configuration of this molecule was determined (see below), the anomalous scattering factor of chlorine atom was included in the refinement. The positions of all hydrogen atoms were assigned from the difference Fourier synthesis. The final refinement, including the contribution of the hydrogen atoms with isotropic temperature factors, reduced R to 0.051 for 831 independent reflections, where the following weighting scheme was used; $w=0.5$ for $F_o=0$, $w=1.0$ for $0<F_o\leqq15$, and $w=[1.0+0.4(F_o-15)]^{-1}$ for

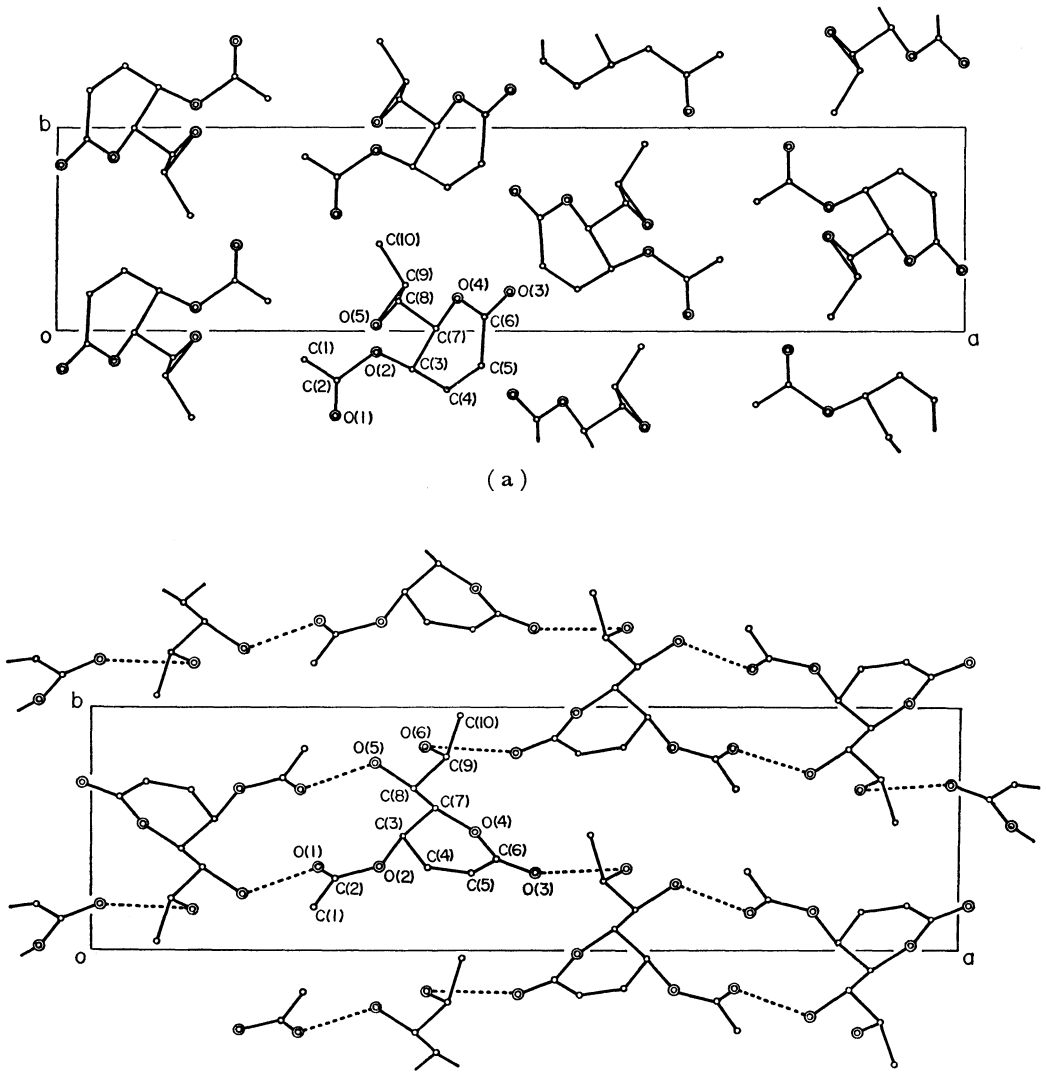


Fig. 1. (a) Projection of the crystal structure of asperlin (**1**). (b) Projection of the crystal structure of asperlinol (**2**). Broken lines indicate hydrogen bond. Hydrogen atoms are omitted for clarity.

TABLE 4. TORSION ANGLES (°)

	1 (X=O(5))	**2** (X=O(6))	**3** (X=Cl)		**1** (X=O(5))	**2** (X=O(6))	**3** (X=Cl)
C(7)-C(3)-C(4)-C(5)	−26.5	−19.7	−24.5	C(8)-C(7)-C(3)-O(2)	50.7	46.0	48.3
O(2)-C(3)-C(4)-C(5)	91.2	99.9	94.5	C(3)-C(7)-C(8)-C(9)	132.7	178.8	177.4
C(3)-C(4)-C(5)-C(6)	−3.6	−6.7	−9.5	O(4)-C(7)-C(8)-C(9)	−103.8	−57.0	−61.4
C(4)-C(5)-C(6)-O(4)	12.7	7.8	17.4	C(3)-C(7)-C(8)-O(5)	65.6	57.2	56.2
C(4)-C(5)-C(6)-O(3)	−163.6	−167.2	−162.3	O(4)-C(7)-C(8)-O(5)	−170.9	−178.6	177.4
C(5)-C(6)-O(4)-C(7)	12.1	20.1	12.1	C(7)-C(8)-C(9)-C(10)	157.2	−68.5	−64.1
O(3)-C(6)-O(4)-C(7)	−171.4	−164.7	−168.2	O(5)-C(8)-C(9)-C(10)	—	49.9	54.3
C(6)-O(4)-C(7)-C(3)	−42.8	−46.6	−45.3	C(7)-C(8)-C(9)-X	—	170.4	175.7
C(6)-O(4)-C(7)-C(8)	−166.7	−171.6	−168.1	O(5)-C(8)-C(9)-X	—	−71.2	−65.9
O(4)-C(7)-C(3)-C(4)	48.2	44.4	50.0	C(4)-C(3)-O(2)-C(2)	98.7	91.3	89.6
C(8)-C(7)-C(3)-C(4)	168.2	165.7	168.2	C(7)-C(3)-O(2)-C(2)	−142.3	−147.7	−149.9
O(4)-C(7)-C(3)-O(2)	−69.3	−75.3	−69.9				

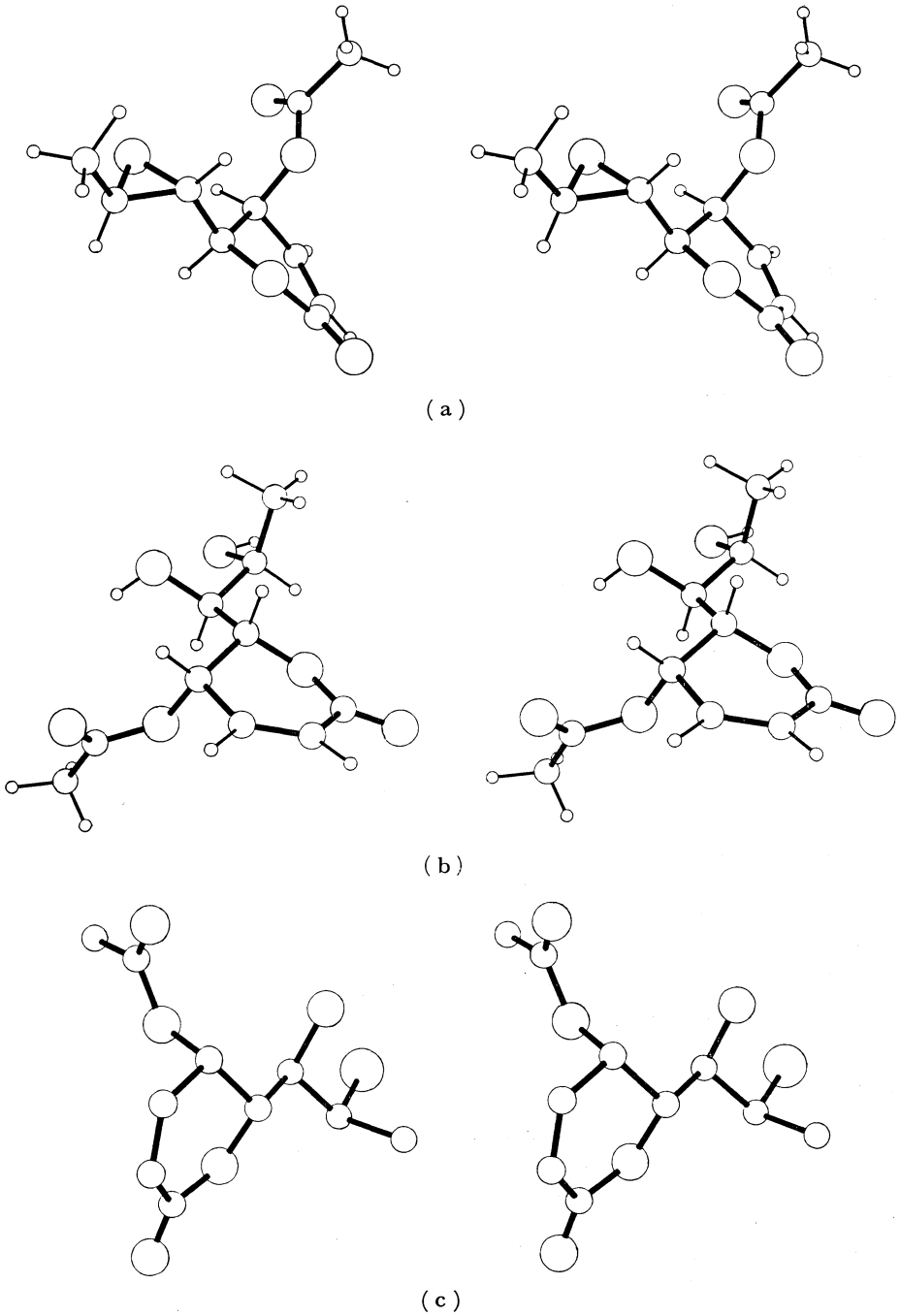


Fig. 2. (a) Stereoscopic view of asperlin (**1**). (b) Stereoscopic view of asperlinol (**2**). (c) Stereoscopic view of chloro derivative of asperlin (**3**). Each figure is drawn with the correct absolute configuration.

$15<F_o$. The final atomic coordinates are given in Table 1(c).

The temperature factors and the list of observed and calculated structure factors for each compound are kept as Document No. 7839 at the Chemical Society of Japan.

Absolute Configuration. The absolute configuration of **3** has been determined by the Bijvoet method.[9] The structure factors were calculated including anomalous scattering of chlorine atom for Cu $K\alpha$ radiation, and eighteen reflections sensitive to the choice of enantiomer were selected manually. The intensities of each pair of reflections, hkl and $h\bar{k}l$, were measured alternately twice. The experimental conditions for the Bijvoet measurement were the same as those for F_o-data collection previously described except the scan speed (1°/min in θ) and background counting time (10 s). The result of the Bijvoet measurement is given in Table 2. Since the measurement was made in a left-handed coordinate system, the absolute configuration of **3** is correctly represented by the atomic coordinates given in Table 1(c) referred to a right-handed coordinate system. Accordingly the absolute configurations of **1** and **2** have been established; the atomic coordinates in Table 1 in a right-handed coordinate system give the correct absolute configurations for **1** and **2**. The atomic scattering factors were taken from the International Tables for X-Ray Crystallography.[10]

TABLE 5. LEAST-SQUARES PLANES AND DEVIATIONS OF ATOMS FROM EACH PLANE

Each plane is represented by $lX+mY+nZ=p$, where X, Y, Z are Cartesian coordinates in Å, referred to the axes a, b, c.

	1	2	3
(a) Plane through the lactone group.			
l	0.730	0.356	0.482
m	−0.157	0.804	−0.456
n	0.665	0.476	−0.749
p	9.257	8.388	1.731
Deviation (Å)			
C(5)	0.006	0.008	−0.001
C(6)	−0.018	−0.025	0.002
O(3)	0.007	0.009	−0.001
O(4)	0.006	−0.009	−0.001
C(3)[a]	0.529	0.293	−0.523
C(4)[a]	0.296	0.223	−0.333
C(7)[a]	−0.210	−0.367	0.266
(b) Plane through the C(3)—C(6) atoms.			
l	0.568	0.242	0.303
m	−0.201	0.842	−0.434
n	0.798	0.482	−0.848
p	7.269	7.187	0.352
Deviation (Å)			
C(3)	−0.007	−0.012	0.009
C(4)	0.015	0.028	−0.048
C(5)	−0.015	−0.029	0.044
C(6)	0.007	0.013	−0.001
O(3)[a]	0.263	0.191	−0.221
O(4)[a]	−0.202	−0.049	0.224
C(7)[a]	−0.691	−0.590	0.751

a) Not included in least-squares calculations.

TABLE 6. INTERMOLECULAR DISTANCES FOR NON-HYDROGEN ATOMS LESS THAN 3.8 Å

(a) Asperlin (**1**)			
O(5)···C(1)^{I}	3.526	O(5)···O(2)^{I}	3.749
C(8)···O(1)^{II}	3.655	C(10)···O(5)^{II}	3.706
O(3)···C(4)^{II}	3.641	C(10)···C(2)^{III}	3.590
C(10)···C(4)^{III}	3.742	C(10)···O(1)^{III}	3.672
O(5)···C(1)^{V}	3.496	O(3)···C(7)^{VII}	3.410
O(4)···C(5)^{VII}	3.414	O(3)···C(5)^{VIII}	3.415
(b) Asperlinol (**2**)			
C(3)···O(6)^{I}	3.552	C(4)···O(6)^{I}	3.705
C(7)···O(6)^{I}	3.557	C(10)···C(6)^{II}	3.525
C(10)···O(2)^{II}	3.710	C(10)···O(3)^{II}	3.638
C(10)···O(4)^{II}	3.737	O(5)···C(1)^{II}	3.391
C(1)···O(1)^{VI}	3.536	C(2)···O(1)^{VI}	3.481
C(8)···O(1)^{VI}	3.529	O(2)···O(1)^{VI}	3.721
O(5)···C(2)^{VI}	3.600	O(5)···O(1)^{VI}	2.739[a]
O(6)···C(1)^{VI}	3.725	C(9)···O(3)^{VII}	3.253
O(6)···O(3)^{VII}	2.940[a]	C(5)···O(3)^{IX}	3.796
C(6)···O(3)^{IX}	3.441	C(7)···O(3)^{IX}	3.342
C(10)···O(3)^{IX}	3.632	O(3)···C(5)^{IX}	3.735
O(4)···O(3)^{IX}	3.423		
(c) Chloro derivative (**3**)			
C(10)···C(5)^{I}	3.713	C(10)···C(6)^{I}	3.499
C(10)···O(2)^{I}	3.732	C(10)···O(3)^{I}	3.527
O(5)···C(1)^{I}	3.472	C(3)···Cl^{II}	3.727
C(7)···Cl^{II}	3.539	O(5)···Cl^{II}	3.544
C(4)···Cl^{IV}	3.634	C(9)···O(3)^{V}	3.304
Cl···O(3)^{V}	3.474	O(3)···C(6)^{VI}	3.779
O(3)···C(7)^{VI}	3.576	O(3)···C(10)^{VI}	3.596
C(1)···Cl^{VII}	3.675	C(2)···O(5)^{VII}	3.720
O(1)···C(1)^{VII}	3.766	O(1)···C(2)^{VII}	3.650
O(1)···C(8)^{VII}	3.611	O(1)···O(5)^{VII}	2.822[a]
O(5)···C(1)^{VII}	3.544		

a) Hydrogen bond.
Roman numeral superscripts refer to the following transformations of the coordinates:
(I) $x, y, 1+z$ (II) $x, 1+y, z$
(III) $x, 1+y, 1+z$ (IV) $x, 1+y, -1+z$
(V) $1/2-x, -y, 1/2+z$
(VI) $1/2-x, 1-y, -1/2+z$
(VII) $1-x, 1/2+y, 1/2-z$
(VIII) $1-x, 1/2+y, -1/2-z$
(IX) $1-x, 1/2+y, 3/2-z$

Results and Discussion

The crystal structures and the numbering scheme of atoms used in this paper are shown in Fig. 1, and a stereoscopic view of each molecule plotted by a local version of PLUTO[11] in Fig. 2. The bond lengths and angles for non-hydrogen atoms are listed in Table 3, the selected torsion angles in Table 4, the equations of the least-squares planes and deviations of atoms from each plane in Table 5, and intermolecular distances less than 3.8 Å in Table 6.

The present X-ray crystallographic analysis has verified the configurations at the C(3) and C(7) atoms suggested by spectroscopy.[3] The hydrogen atoms in the epoxide ring of **1** are *trans*, the configurations at the C(8) and C(9) atoms being *S* and *R*, respectively. The configuration of the C(9) atom in **1** is opposite to that in **2** and **3**. This fact is consistent with the known mechanism that Walden inversion occurs at the atom to which nucleophile attack to open the epoxide ring.[12] The conformations found in the $\alpha\beta$-unsaturated δ-lactone rings are similar to each other. The planes of the lactone ring and olefinic double bond are not coplanar; the dihedral angles for **1**, **2**, and **3** are 12.4, 6.9, and 11.8°, respectively. The C(7) and O(4) atoms deviate to the same side of the plane of the olefinic double bond by different amounts. Such features are also found in related compounds.[13,14] As suggested by spectroscopy,[1,3,4] the hydrogen atoms at C(3) and C(7) are quasi-equatorial and quasi-axial, respectively. Since the NMR spectrum is reasonably explained by the results from the present crystallographic analysis, it is almost certain that the conformation of the lactone ring in solution is the same as that in the crystalline state. Beecham discussed the relationship between the chirality in the system C=C-C=O in an $\alpha\beta$-unsaturated lactone and the sign of the Cotton effect in the CD spectrum; he suggested that right or left-handed chirality causes a negative or positive Cotton effect in the $n\rightarrow\pi^*$ transi-

tion respectively.[13] In asperlin (**1**), the chirality in the system C=C-C=O in the crystalline state is left handed with the torsion angle being −163.6°. This fact is, according to Beecham's idea, consistent with the positive Cotton effect of **1**.[13]

In the crystals of **2** and **3**, an intermolecular hydrogen bond between one of the hydroxyl group(s) and the acetyl group, O(5)–H(O5)···O(1), connects molecules related by a screw axis. The distance of H(O5)···O(1) is 1.81 Å for **2** and 1.87 Å for **3**, and the angle of O(5)–H(05)···O(1) is 163° for **2** and 166° for **3**, and that of H(O5)···O(1)–C(2) is 131° for **2** and 127° for **3**. The crystal structures of **2** and **3** are isotypic to each other (the b and c axes of **3** correspond to c and −b axes of **2** respectively), although **2** has an additional intermolecular hydrogen bond between the other hydroxyl group and the carbonyl oxygen atom of the lactone group, O(6)–H(O6)···O(3); the distance of H(O6)···O(3) is 2.08 Å, and the angles of O(6)–H(O6)···O(3) and H(O6)···O(3)–C(6) are 155° and 148° respectrively. There is no intramolecular hydrogen bond in the present three compounds. No abnormality in bond lengths and angles or in intermolecular distances is found in the crystals of **1**—**3**.

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