A Series of Sesquiterpenes with a 7α-Isopropyl Side Chain and Related Compounds Isolated from *Curcuma wenyujin*

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Sesquiterpenoids possessing a 7α-isopropyl group, such as curcumol (1a), curdione (2a), curcumalactone (3), and a new epoxy germacrane, (1*R*,10*R*)-epoxy-(−)-1,10-dihydrocurdione (5a), were isolated from the essential oil of *Curcuma wenyujin*. Other related new sesquiterpenes, neocurdione (4) and (1*S*,10*S*),(4*S*,5*S*)-germacrone-1(10),4-diepoxide (6) were also isolated from this plant. The stereostructures and absolute configurations of these sesquiterpenes were established on the basis of spectroscopic and chemical data as well as X-ray crystallographic analyses.

Keywords *Curcuma wenyujin*; Zingiberaceae; curcumol; curdione; curcumalactone; germacrone-epoxide; neocurdione; germacrone-diepoxide

Of the eight Chinese species of the genus *Curcuma* (Zingiberaceae), the rhizomes of five have been used medicinally in China.[2)] In particular, the essential oil of *Curcuma wenyujin* is currently used as a clinical remedy for uterus cancer in China.[3)] Major constituents of the essential oil of this plant are found to be curcumol (**1a**)[4)] and curdione (**2a**),[5,6)] both of which are sesquiterpenes that were first isolated from *C. zedoaria*.[7)] However the stereochemistry of **1a** and **2a** has not been established.

In our continuing investigation of active constituents of *C. wenyujin*,[8)] we now wish to report in detail the absolute stereostructures of **1a**, **2a**, curcumalactone (**3**)[6)] and (1*R*,10*R*)-(−)-1,10-dihydrocurdione (**5a**).[9)] These sesquiterpenoids have a 7α-isopropyl side chain, which is uncommon among constituents of higher plants.[10)] Other related sesquiterpenes such as neocurdione (**4**)[11)] and (1*S*,10*S*),(4*S*,5*S*)-germacrone-1(10),4-diepoxide (**6**)[12)] were also isolated from this plant. The elucidation of their stereostructures and absolute configurations is also described.

Results and Discussion

Steam distillation of the rhizome of *C. wenyujin* gave an essential oil (1.2%). Silica gel chromatography of this oil eluting with petroleum ether–ether afforded curcumol (**1a**) (7.7%) and curdione (**2a**) (14.8%).

Other sesquiterpenes were isolated from this plant under the following mild extractive conditions. The air-dried rhizomes were soaked in ether for 5 d at about 5 °C. After evaporation of the solvent *in vacuo* at room temperature, the oil obtained was subjected to silica gel chromatography by using a gradient solvent system of petroleum ether and ether. After the separation of the major constituents, *i.e.* curdione (**2a**) and neocurdione (**4**), the fractions eluted with petroleum ether and ether (1 : 1) gave a crystalline compound. Recrystallization from the solvent mixture of petroleum ether and ether gave (1*R*,10*R*)-epoxy-(−)-1,10-dihydrocurdione (**5a**). The epoxy germacranoid compounds, *i.e.* (1*R*,10*R*)-epoxy-(−)-1,10-dihydrocurdione (**5a**),[9)] (4*S*,5*S*)-epoxy-(+)-4,5-dihydrogermacrone (**4b**),[13)] and (1*S*,10*S*),(4*S*,5*S*)-germacrone-1(10),4-diepoxide (**6**),[12)] were separated from the fractions eluted with petroleum ether and ether (4 : 5).

The physical data of **1a** accorded with those of curcumol isolated from *C. zedoaria*.[7)] Because the stereochemistry of curcumol had not been defined, the relative stereostructure of **1a** was determined by X-ray analysis as illustrated in Fig. 1.[4b)]

The absolute configuration was elucidated by examination of the circular dichroism (CD) spectrum of the ozonolysate.[4b)] This spectrum showed a negative Cotton effect ($[\theta]_{25}$ −1423, dioxane). Application of the octant rule suggested that the absolute structure of curcumol should be expressed as **1a** in Chart 1. The α-configuration

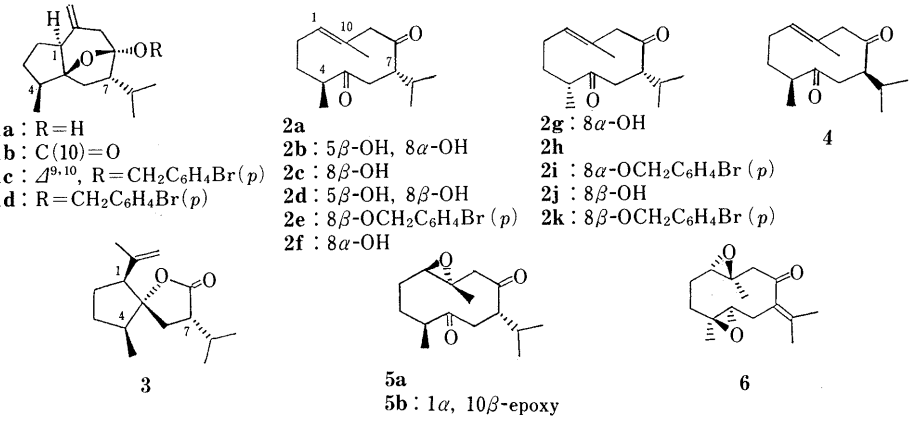

Chart 1

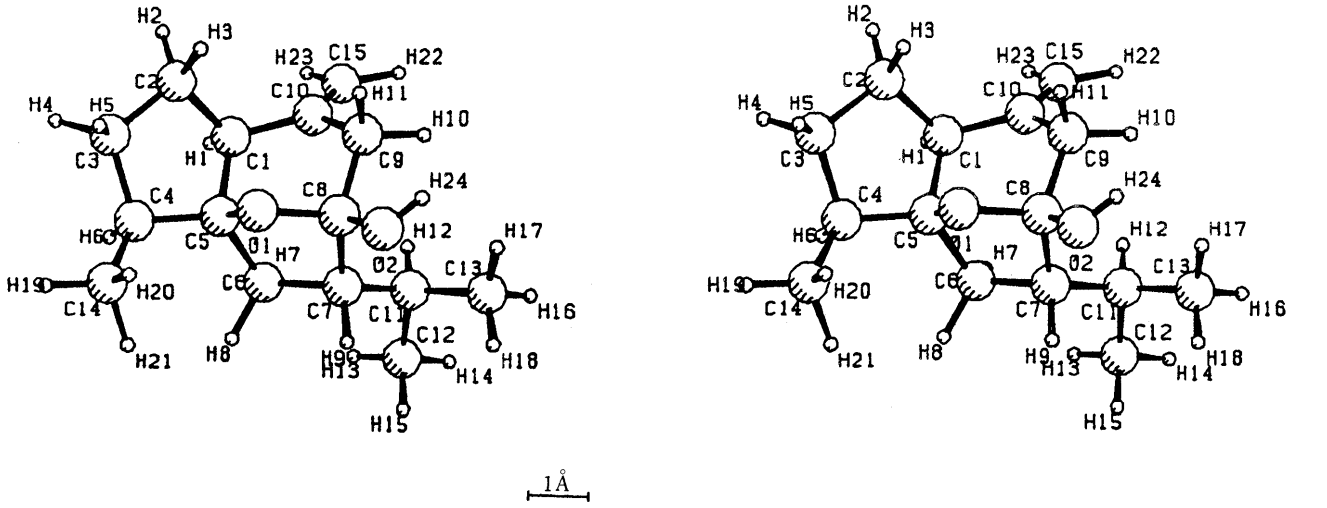

Fig. 1. Stereoview of Curcumol (**1a**)

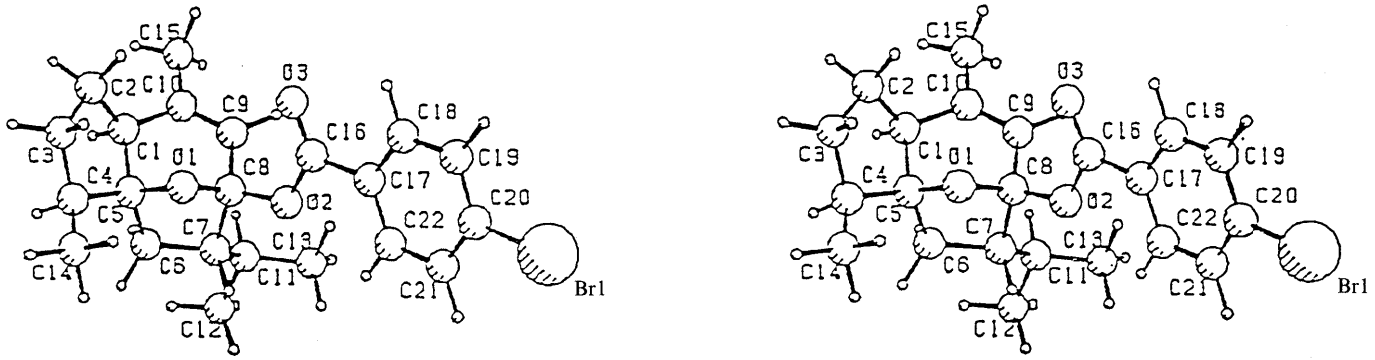

Fig. 2. Stereoview of the *p*-Bromobenzoate (**1c**) of the Δ^9-Isomer of **1a**

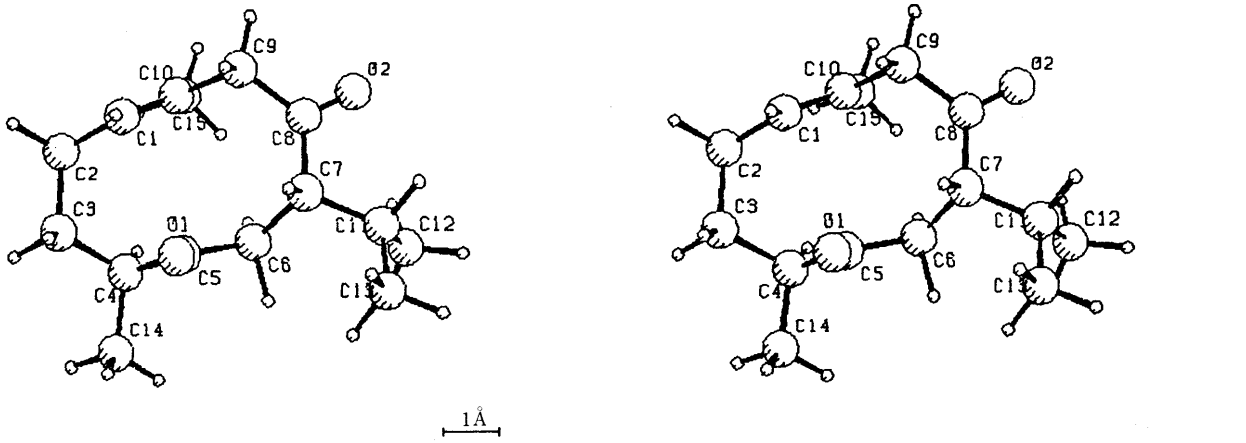

Fig. 3. Stereoview of Curdione (**2a**)

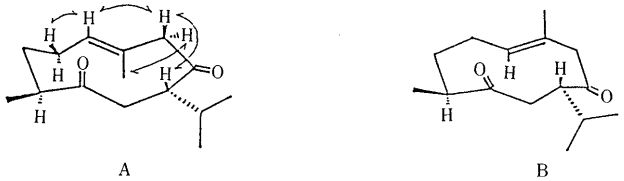

Chart 2. Conformer A and Conformer B of Curdione (**2a**)

of the isopropyl side chain seen in **1a** is not often found in higher plant constituents, for biogenetic reasons.[10] In order to obtain conclusive proof of the absolute structure of **1a**, its *p*-bromobenzoate (**1c**) was prepared and was submitted to X-ray crystal diffraction analysis. The absolute configuration of **1c** was determined from the anomalous dispersion of CuK_α radiation by the bromine-atom. The crystal data and the final atomic coordinates are given in the experimental section. The absolute structure and stereoview of **1c** are depicted in Chart 1 and in Fig. 2, respectively.

Thus, the absolute structure of curcumol must be expressed as **1a** and is in agreement with that deduced from the CD analysis.

Curdione (**2a**), a germacrane first isolated from *C. zedoaria*,[7] was also isolated from *C. wenyujin* by our group.[5b,6a] Physical data of **2a** were all coincident with those of curdione.[7] As the stereostructure of curdione had not been proved, we undertook the X-ray analysis of **2a** in order to determine its relative structure and conformation.[5b] The structure of **2a** is depicted in Fig. 3. Curdione (**2a**) exists in a chair–chair conformation, possessing a *trans* relationship between the C(4)-methyl group and C(7)-isopropyl side chain.

A variable temperature proton nuclear magnetic resonance (^{1}H-NMR) study of **2a** was performed to verify its conformation in solution. The spectrum showed a set of broad signals at $-30\,^\circ$C in spite of exhibiting sharp signals at room temperature. As the temperature was decreased below less than $-50\,^\circ$C, two sets of signals with an intensity ratio of approximately 5:1 (*e.g.* C(1)-H 5.06 and 5.63; C(10)-CH_3 1.76 and 1.48 ppm) were observed. These signals presumably arose from two chair–chair conformers, *i.e.* conformation A and conformation B (Chart 2), of which the latter takes the *syn*-arrangement of C(5)=O and C(10)-CH_3. Nuclear Overhauser effect (NOE) measurements of curdione (**2a**) at $-70\,^\circ$C also suggest that the major conformer is conformer A [C(5)=O/C(10)-CH_3: *anti*] and the minor one is conformer B [C(5)=O/C(10)-CH_3: *syn*].

Since curcumol (**1a**) was exclusively produced by heating of **2a** at 200 °C in ethanol (EtOH),[5] it seems that **2a** mainly existing in conformation A could transform *via* conformation B to **1a** with retention of the C(7) configuration.

In order to confirm the absolute configuration of **2a**, the bromobenzoate of 8αH-dihydrocurdione (**2c**) was prepared from **2a** and was subjected to X-ray diffraction analysis.

The stereoselective lithium aluminum hydride ($LiAlH_4$) reduction of **2a** afforded a ketol. This compound was treated with *p*-bromobenzoyl chloride (*p*-BrC_6H_4COCl)–dichloromethane (CH_2Cl_2) in the presence of 4-dimethylaminopyridine (DMAP) at room temperature to afford the *p*-bromobenzoate (**2e**).[6a] The absolute structure of **2e** was determined by the anomalous dispersion method and is shown in Fig. 4.

Curdione (**2a**) was converted to a cyclopentanolide (**3**) in quantitative yield in chloroform containing a catalytic amount of hydrochloric acid at room temperature. Compound **3** was identical with curcumalactone obtained from the essential oil of *C. wenyujin*. It is noteworthy that dehydrocurdione isolated from *C. zedoaria* was converted to a mixture of two dehydrocyclopentenolides[14] under

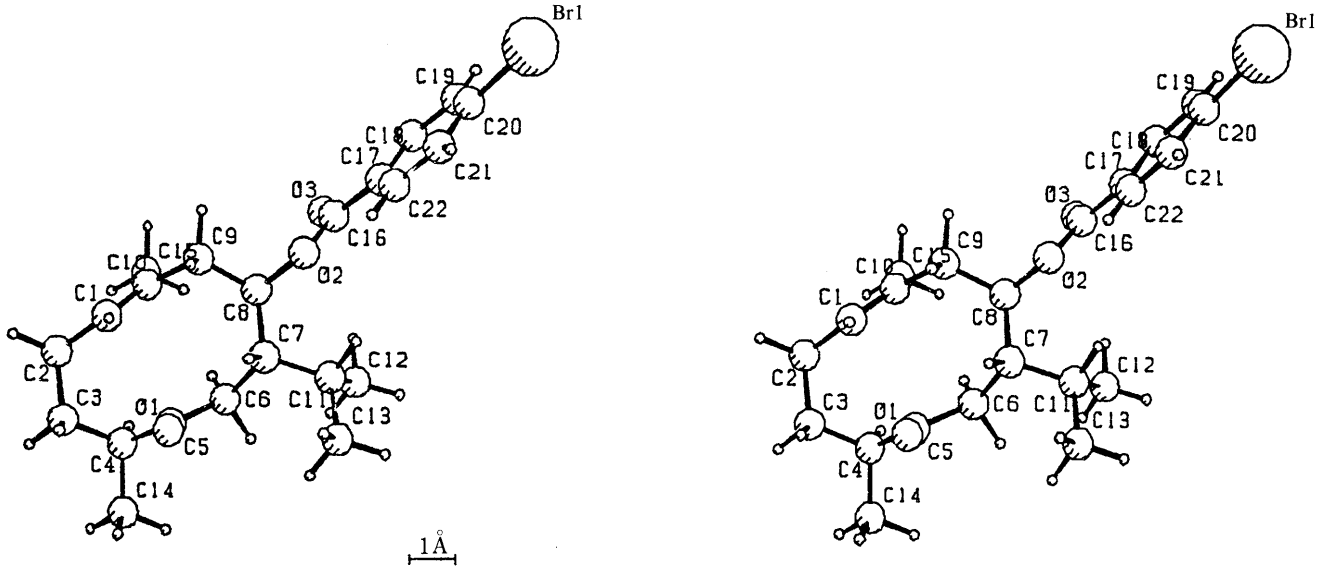

Fig. 4. Stereoview of the *p*-Bromobenzoate (**2e**) of 8αH-Dihydrocurdione (**2j**)

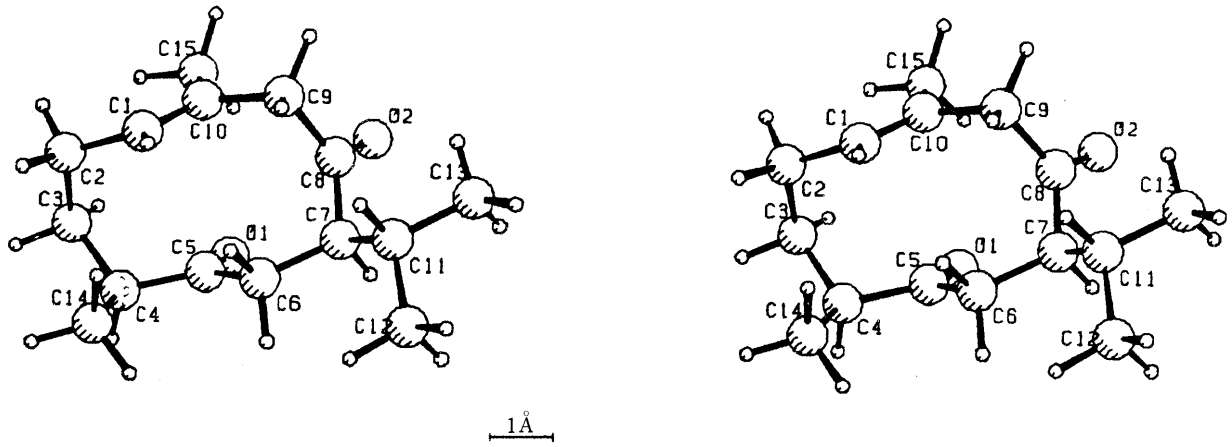

Fig. 5. Stereoview of Neocurdione (**4**)

acidic conditions.

Neocurdione (**4**)[8,11] was the second germacrane compound isolated from *C. wenyujin*. The very close similarity of the spectroscopic data of **4** to those of **2a** (^{1}H-NMR, infrared (IR) and mass (MS) fragmentation) and the opposite sign of the optical rotation and CD absorption suggested that **4** is an epimer of **2a** either at C(4) or at C(7). In order to solve the stereostructure of **4**, an X-ray diffraction analysis of **4** was carried out.[11b] The relative stereostructure is shown in Fig. 5. Neocurdione (**4**) was thus found to have an unusual twisted chair–boat conformation, wherein the C(10) and the C(5) substituents are on the same side of the average molecular plane (*syn*). It is of interest that **4** takes an unstable *syn* conformation of C(10)-CH_3/C(5)=O, in sharp contrast to curdione (**2a**), which possesses a rather stable *anti* conformation as described above. The low temperature ^{1}H-NMR study of **3** showed two sets of signals at $-60\,^\circ$C in the ratio of 26:74. A further NOE study at $-60\,^\circ$C suggested that the major conformation of **4** in solution is a chair–chair conformation, which is different from the one in the solid state. This observation prompted us to apply molecular mechanics calculations to these flexible germacranes, curdione (**2a**) and neocurdione (**4**).[15] The calculated ratios of conformations of *anti* and *syn* type [C(5)=O/C(10)-CH_3] are in reasonably good accordance with the ratios which were estimated from low temperature NMR studies.

In order to determine the absolute structure of **4**, the following chemical transformation was carried out. Compound **2a** was reduced with sodium borohydride ($NaBH_4$) in methanol (MeOH) at room temperature for 4 h to give a ketol, which was assigned as 8βH-dihydrocurdione (**2f**) by ^{1}H-NMR spectroscopy. This ketol was then treated with potassium *tert*-butoxide (*tert*-BuOK) in benzene to afford a 4:1 mixture of the starting material and its C(4)-epimer, *i.e.* 8βH-dihydro-4-epicurdione (**2g**). This epimer was oxidized with chromic anhydride (CrO_3) in pyridine to give 4-epicurdione (**2h**) ($[\alpha]_D$ $+65.9°$, $CHCl_3$). The physical properties of **2h** were identical with those of neocurdione (**4**) except for the optical rotation ($[\alpha]_D$ $-65.8°$) and the sign of CD Cotton effect {$[\theta]_{299.5}$ -36060; $[\theta]_{223}$ $+12368$ ($c=5.08$, MeOH)}. Neocurdione (**4**) is thus considered to be the antipode of 4-epicurdione (**2h**).

We decided to confirm the absolute structure of **2h**, since the availability of **4** was very limited. The first attempted preparation of *p*-bromobenzoate (**2i**) from the oily ketol (**2g**) gave no crystalline compound suitable for the X-ray diffraction study. When **2h** was rapidly treated with $LiAlH_4$ in tetrahydrofuran (THF), an oily ketol mixture was obtained. Separation of this mixture by silica gel chromatography as usual afforded 8βH- (**2g**) and 8αH-dihydro-4-epicurdione (**2j**) in yields of 80% and 8%, respectively. The latter crystalline ketol (**2j**) was converted to the corresponding crystalline *p*-bromobenzoate (**2k**) (*p*-BrC_6H_4COCl–pyridine–DMAP), which was suitable for X-ray crystallographic analysis. The absolute structure of **2k** was then determined from the anomalous dispersion of CuK_α radiation by the bromine atom. A stereoview of **2k** is shown in Fig. 6.

Since the absolute structure of 4-epicurdione (**2h**) was established, the absolute configuration of neocurdione (**4**) can be expressed as shown in Chart 1.

Heating of **4** in EtOH solution at 230 °C in a sealed tube afforded neocurcumol (**1b**) in 50% yield.[10] The stereostructure was deduced from the spectroscopic data and the analogy of the similar reaction of curdione (**2a**) to give curcumol (**1a**).

The third germacrane, (1*R*,10*R*)-epoxy-(−)-1,10-dihydrocurdione (**5a**), has the formula $C_{15}H_{24}O_3$. Both the IR spectrum (1705 cm^{-1}) and the ultraviolet (UV) absorption (288 nm) of **5a** suggest the presence of a saturated cyclic ketone. Its ^{1}H-NMR spectrum is similar to that of **2a** except that the signal of C(1)-hydrogen of **5a** appeared at δ 2.89, while that of **2a** was observed at δ 5.17 in the olefinic region. On the other hand, in the ^{13}C-NMR spectrum of **5a**, two signals appeared at δ 64.1 and 58.9, while in **2a** two olefinic carbon signals were observed at δ 131.6 and 129.9. This suggests that each of these two carbons is attached to oxygen in **5a**. As the IR spectrum of **5a** showed no hydroxyl absorption, **5a** was deduced to be the 1,10-epoxy derivative of either **2a** or its 7αH-epimer. No NOE was observed

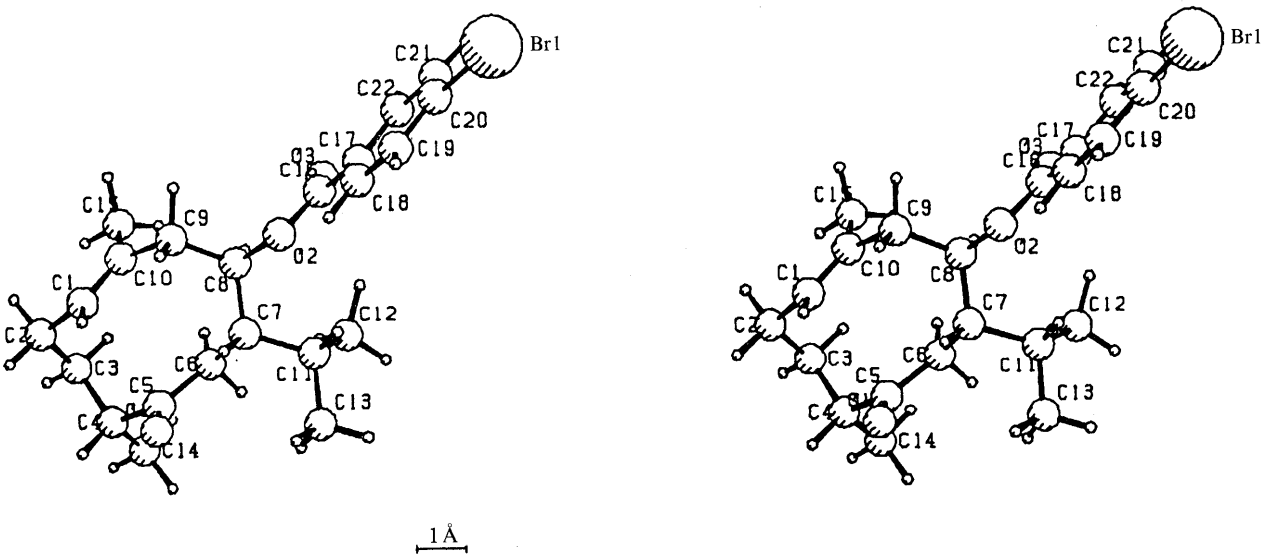

Fig. 6. Stereoview of the *p*-Bromobenzoate (**2k**) of 8αH-Dihydro-4-epicurdione (**2j**)

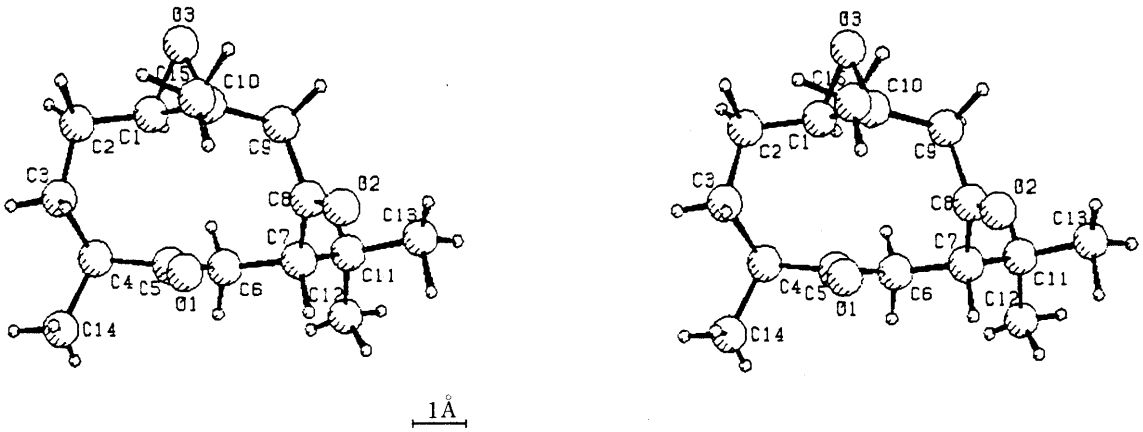

Fig. 7. Stereoview of (1*R*,10*R*)-Epoxy-(−)-1,10-dihydrocurdione (**5a**)

between the C(10)-CH_3 and C(4)-H. The relative stereostructure of **5a** was determined by X-ray analysis and is shown in Fig. 7.

In order to determine the absolute configuration of **5a**, epoxidation of **2a** was examined. Epoxidation of **2a** with *m*-chloroperbenzoic acid (MCPBA) afforded **5a** and its 1(10)-epoxy isomer in a ratio of 1.3 : 1. This conversion proved that the epoxy group in **5a** must have the same (4*S*,7*S*) configuration as that in **2a**. The ten-membered ring *trans*-fused with the oxirane group at C(1)–C(10) exists in a chair–boat conformation.[14,15] The C(4)-β-methyl and C(7)-α-isopropyl groups in **2a** and **5a** are on opposite sides of the average molecular plane.

The spectroscopic properties of the monoepoxide (**5c**) isolated from this plant were in accord with those of (4*S*,5*S*)-germacrone-4,5-epoxide isolated from *C. zedoaria*[13a] and *C. aromatica*.[13b] It is of interest from the biogenetic point of view that the enantiomer of **5c** was isolated from a higher plant, *Asarum caulescens* (Aristolochiacae).[16]

The next epoxy germacrane (**6**) (mp 84—86 °C) has the formula $C_{15}H_{22}O_3$. The physical and spectroscopic properties of **6** suggested that **6** has two epoxy rings and an α,β-unsaturated ketone moiety. From the ^{1}H- and ^{13}C-NMR spectral comparison between **6** and **5c**, compound **6** seemed to be a 1,10-epoxide of **5c**. The relative stereochemistry of the oxirane moieties of **6** was deduced to be *cis*, based on the observation of 3.6% NOE between the C(4)-Me and C(10)-Me. Epoxidation of **5c** with MCPBA (1 eq) in CH_2Cl_2 at room temperature afforded the diepoxide **6** in 86% yield. Thus the absolute structure of **6** was established to be (1*S*,10*S*),(4*S*,5*S*)-germacrone-1(10),4-diepoxide.[12]

A biogenetic hypothesis concerning sesquiterpenoids in *C. wenyujin*, including those described in this paper, will be presented elsewhere.[10]

Experimental

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-360 digital polarimeter, and IR spectra were obtained with a Hitachi EPI-G3 spectrometer. ^{1}H-NMR spectra were obtained with JEOL GSX-270 and GX-400 spectrometers at 270 and 400 MHz, respectively, using tetramethylsilane as an internal standard. Mass spectra such as electron impact (EI-), chemical ionization (CI-) and high resolution (HR-) were measured with a JEOL JMS-D300 spectrometer. Column chromatography was carried out on Kieselgel 60 (70—230 mesh).

Isolation of Curcumol (1a) and Curdione (2a) The air-dried rhizomes of *C. wenyujin* (7.5 kg) collected in Wechow (China) were powdered and submitted to steam distillation to yield 100 g of a dark brown essential oil. This oil was kept in a refrigerator several days to afford 25 g of a crystalline mixture of curcumol (**1a**) and curdione (**2a**). This mixture was subjected to silica gel column chromatography with a gradient solvent system of petroleum ether and ether. The fractions eluted with petroleum ether–ether (20 : 1) were collected and evaporation of the solvent yielded a crystalline material. Recrystallization of this from EtOH afforded 7.7 g of curcumol (**1a**) as white needles (0.1%). Curdione (**2a**) (14.8 g, 0.21%) was also isolated from the above mixture.

Curcumol (**1a**): $C_{15}H_{24}O_2$. mp 141—142 °C. $[\alpha]_D^{30}$ −32.26° (c=2.13, $CHCl_3$). HR-MS *m/z*: 236.1777 (Theor. 236.1770 for $C_{15}H_{24}O_2$). IR ν_{max}^{KBr} cm^{-1}: 3420 (OH), 3070, 1647, 882 (>C=CH_2). ^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, d, J=6.8, 4-CH_3), 1.00, 1.01 (3H×2, each d, J=6.8, 11-CH_3), 2.51, 2.57 (1H, ×2, each d, J=14.8, 9-H), 4.88 (2H, br s, 15-H).

Curdione (**2a**): $C_{15}H_{24}O_2$. mp 61—62 °C. $[\alpha]_D^{25}$ +26.0° (c=1.00, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1704 (C=O), 1667 (C=C). EI-MS *m/z*: 236 (M^+). HR-MS *m/z*: 236.1778 (Theor. 236.1770). ^{1}H-NMR ($CDCl_3$) δ: 5.17 (1H, s, 1-H), 3.07 (1H, d, J=11, 9α-H), 2.94 (1H, d, J=11, 9α-H), 2.85 (1H, ddd, J=8.8, 8.8, 2.2, 7β-H), 2.69 (1H, m, 6α-H), 2.40 (1H, dd, J=18, 2.2, 6β-H), 2.34 (1H, m, 4α-H), 2.09—2.15 (3H, br, 3α-H, 2α-H, 2β-H), 1.88 (1H, m, 12-H), 1.66 (3H, s, 10-CH_3), 1.57 (1H, m, 3α-H), 0.98 (3H, d, J=6.6, 4-CH_3), 0.88, 0.95 [3H×2, each d, J=6.6, 11-CH_3].

X-Ray Analysis of Curcumol (1a) A direct X-ray analysis of **1a** was carried out with a single crystal, a prism elongated along the *c* axis. The crystal data are: $C_{15}H_{24}O_2$; M.W. = 236; trigonal; space group $P3_2$; lattice constants: $a=b$=12.387(6), c=7.866(4) Å, $\alpha=\beta$=90°, γ=120°, U=1045 Å^3, Z=3, D_{calc}=1.125 g cm^{-3}. The intensity data were collected on a Philips PW1100 diffractometer using graphite monochromated CuK_α radiation. Of the total of 2323 reflections within the 2θ range of 6° through 156°, 1951 reflections observed above the 2σ(I) level were used for the X-ray analysis. The structure was solved by the direct method using a MULTAN program, and refined by the least-squares method with the block-diagonal matrix approximation. The final R value was 0.046 including 24 hydrogen atoms with isotropic temperature factors. The relative structure of curcumol (**1a**) is illustrated in Fig. 1.

X-Ray Analysis of Curdione (2a) The crystal data are: $C_{15}H_{24}O_2$; M.W. = 236; orthorhombic, space group $P2_12_12_1$; lattice constant: a=10.758(5), b=13.164(7), c=10.176(5) Å, U=1441.1 Å^3, Z=4, D_{calc}=1.0895 g cm^{-3}. The intensity data were collected on a Philips PW 1100 diffractometer using graphite monochromated CuK_α radiation and 1229 reflections up to 155° (2θ) were used. The structure was solved by the direct method using a MULTAN program and refined by the least-squares method with the block-diagonal matrix approximation. The final R value was 0.05 including 24 hydrogen atoms with isotropic temperature factors. The relative stereostructure of **2a** is shown in Fig. 2.

Ozonolysis of Curcumol (1a) A solution of **1a** (17 mg) in ethyl acetate (EtOAc) (6 ml) in an ice-salt bath was saturated with ozone. Water (1 ml), zinc powder (40 mg), $AgNO_3$ (trace) and hydroquinone (trace) were added to the reaction mixture. Then this mixture was refluxed for 1 h. Excess zinc powder was filtered off, the organic layer was washed with water and dried over anhydrous Na_2SO_4. After evaporation of the solvent at room temperature *in vacuo*, the residue was submitted to silica gel column chromatography to give 11 mg of the 14-norketone (**1b**) (65%).

TABLE I. Atomic Coordinates of Curcumol (**1a**)

No.	Atom	$x \cdot 10^4$	$y \cdot 10^4$	$z \cdot 10^4$	B_{eq} (Å^2)
1	C1	6123 (4)	−895 (4)	−714 (0)	3.76 (0.09)
2	C2	7065 (5)	−619 (5)	738 (7)	5.12 (0.12)
3	C3	8324 (5)	−185 (5)	−166 (8)	5.44 (0.13)
4	C4	8133 (5)	−35 (5)	−2081 (7)	4.55 (0.11)
5	C5	6943 (4)	41 (4)	−2113 (6)	3.43 (0.09)
6	C6	6236 (5)	−134 (4)	−3797 (6)	3.93 (0.10)
7	C7	5723 (4)	784 (4)	−3639 (6)	3.33 (0.09)
8	C8	6113 (4)	1303 (4)	−1814 (5)	3.24 (0.09)
9	C9	5224 (4)	555 (4)	−366 (6)	3.69 (0.09)
10	C10	5001 (4)	−770 (4)	−327 (6)	3.77 (0.09)
11	C11	4354 (4)	252 (5)	−4112 (6)	4.33 (0.10)
12	C12	4130 (6)	−234 (7)	−5948 (7)	6.67 (0.16)
13	C13	3948 (6)	1231 (7)	−3902 (8)	6.16 (0.15)
14	C14	9255 (5)	1068 (6)	−2934 (9)	5.83 (0.14)
15	C15	3881 (5)	−1748 (5)	−12 (6)	5.06 (0.11)
16	O1	7242 (3)	1272 (2)	−1554 (4)	3.09 (0.05)
17	O2	6405 (3)	2551 (3)	−1647 (4)	3.79 (0.06)

No.	Atom	$x \cdot 10^3$	$y \cdot 10^3$	$z \cdot 10^3$	B_{eq} (Å^2)
18	HCl	583 (4)	−181 (4)	−116 (5)	4.0 (1.0)
19	HC2	675 (5)	−138 (5)	161 (7)	7.0 (2.0)
20	H′C2	720 (5)	14 (5)	165 (6)	5.0 (1.0)
21	HC3	866 (5)	−88 (5)	1 (6)	6.0 (1.0)
22	H′C3	901 (5)	69 (5)	37 (6)	6.0 (1.0)
23	HC4	796 (5)	−90 (5)	−276 (6)	6.0 (1.0)
24	HC6	551 (5)	−109 (5)	−396 (7)	6.0 (1.0)
25	H′C6	688 (5)	10 (5)	−491 (6)	6.0 (1.0)
26	HC7	622 (5)	155 (5)	−454 (6)	6.0 (1.0)
27	HC9	433 (4)	54 (4)	−50 (5)	4.0 (1.0)
28	H′C9	561 (4)	104 (4)	72 (6)	5.0 (1.0)
29	HC11	386 (4)	−46 (4)	−343 (6)	4.0 (1.0)
30	HC12	437 (5)	−93 (5)	−613 (7)	7.0 (1.0)
31	H′C12	318 (5)	−55 (5)	−630 (6)	6.0 (1.0)
32	H″C12	467 (5)	50 (5)	−678 (7)	7.0 (1.0)
33	HC13	298 (6)	81 (5)	−427 (7)	8.0 (2.0)
34	H′C13	409 (5)	162 (5)	−270 (7)	7.0 (1.0)
35	H″C13	440 (6)	194 (6)	−473 (8)	8.0 (2.0)
36	HC14	1007 (6)	100 (6)	−289 (8)	9.0 (2.0)
37	H′C14	947 (5)	190 (5)	−242 (7)	6.0 (1.0)
38	H″C14	903 (5)	110 (5)	−435 (7)	7.0 (1.0)
39	HC15	310 (5)	−162 (5)	17 (7)	7.0 (1.0)
40	H′C15	373 (5)	−270 (5)	−2 (7)	7.0 (1.0)
41	HO2	593 (7)	266 (7)	−102 (9)	12.0 (2.0)

14-Norketocurcumol (**1b**): Colorless oil, $C_{14}H_{22}O_3$. $[\alpha]_D^{30}$ −62.76° (c=0.81, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3568 (OH), 3378 (br, OH), 1708 (C=O). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 2.78, 2.66 (each 1H, d, J=17, 9α, 9β-H), 1.05 (3H, d, J=6.8, 11-CH_3), 0.99 (3H, d, J=6.8, 11-CH_3), 0.91 (3H, d, J=6.4, 14-H).

Esterification of Curcumol (1a) A solution of **1a** (15 mg) and *p*-BrC_6H_4COCl (102 mg) in pyridine (2 ml) was refluxed for 17 h. Evaporation of the solvent and subsequent silica gel chromatography of the residue afforded 9 mg of curcumol *p*-bromobenzoate (**1d**), as a syrup and 5 mg of the *p*-bromobenzoate (**1c**) of the *Δ*^{9}-*endo* isomer of **1a** as crystals, the overall yield being 52%.

The *p*-Bromobenzoate (**1c**): $C_{22}H_{27}O_3Br$. mp 122.5—124.5 °C. $[\alpha]_D^{29}$ −7.42° (c=1.89, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1740 (C=O), 1594 (aromatic). CI-MS m/z: 419, 421 (each MH^+). EI-MS m/z: 418, 420 (each M^+). HR-MS m/z: 418.1137, 420.1112, (Theor. 418.3663 for $C_{22}H_{27}O_3Br$, 420.3643 for $C_{22}H_{27}O_3Br$). ^{1}H-NMR ($CDCl_3$) δ: 0.94 (3H, d, J=6.4, 14-H), 0.99, 1.01 (3H, each d, J=6.4, 13-H, 12-H), 1.74 (3H, d, J=1.2, 15-H), 5.65 (1H, s, 10H), 7.57, 7.90 (2H×2, each d, J=8.4, aromatic).

The *p*-Bromobenzoate (**1d**): $C_{22}H_{27}O_3Br$. $[\alpha]_D^{30}$ +46.2° (c=1.30, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3080 (C=C–H), 1742 (C=O), 1648 (C=C), 1595 (aromatic). CI-MS (isobutane) m/z: 419 (MH^+), 421 (MH^+). EI-MS m/z: 418, 420 (M^+). HR-MS m/z: 418.1159, 420.1110 (Theor. 418.3663 for $C_{22}H_{27}O_3Br$, 420.3643 for $C_{22}H_{27}O_3Br$). ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H,

TABLE II. Atomic Coordinates of the *p*-Bromobenzoate (**1c**) of the *Δ*^{9}-Isomer of **1a**

No.	Atom	$x \cdot 10^5$	$y \cdot 10^5$	$z \cdot 10^5$	B_{eq} (Å^2)
1	Br1	−23417 (6)	−19492 (7)	−6388 (6)	8.10 (0.01)

No.	Atom	$x \cdot 10^4$	$y \cdot 10^4$	$z \cdot 10^4$	B_{eq} (Å^2)
2	C1	2628 (5)	−3402 (5)	6383 (5)	6.54 (0.11)
3	C2	1986 (6)	−4225 (6)	6958 (7)	9.05 (0.16)
4	C3	1117 (7)	−3679 (7)	7574 (7)	10.35 (0.19)
5	C4	1275 (5)	−2570 (6)	7430 (5)	7.43 (0.13)
6	C5	1905 (4)	−2502 (5)	6349 (5)	5.64 (0.10)
7	C6	2461 (5)	−1523 (4)	6087 (5)	6.02 (0.10)
8	C7	2303 (4)	−1381 (4)	4789 (4)	4.69 (0.08)
9	C8	1861 (4)	−2416 (4)	4468 (4)	4.73 (0.08)
10	C9	2680 (4)	−3196 (4)	4318 (5)	5.02 (0.08)
11	C10	3081 (4)	−3642 (4)	5230 (5)	5.75 (0.10)
12	C11	3258 (4)	−1031 (4)	4172 (6)	5.57 (0.10)
13	C12	3703 (5)	−65 (5)	4684 (7)	7.47 (0.13)
14	C13	3046 (5)	−882 (5)	2912 (6)	7.12 (0.12)
15	C14	295 (5)	−1976 (7)	7477 (6)	8.93 (0.15)
16	C15	3941 (5)	−4376 (5)	5196 (7)	7.95 (0.14)
17	C16	755 (4)	−3085 (4)	3023 (4)	4.66 (0.08)
18	C17	82 (3)	−2765 (4)	2083 (4)	3.99 (0.07)
19	C18	−461 (4)	−3514 (4)	1516 (5)	4.94 (0.09)
20	C19	−1154 (4)	−3265 (4)	681 (5)	5.55 (0.09)
21	C20	−1306 (4)	−2283 (4)	423 (4)	5.07 (0.09)
22	C21	−761 (4)	−1525 (4)	939 (4)	4.92 (0.08)
23	C22	−59 (4)	−1779 (4)	1777 (4)	4.47 (0.08)
24	O1	1212 (3)	−2656 (3)	5394 (3)	4.92 (0.06)
25	O2	1231 (3)	−2281 (2)	3497 (3)	4.65 (0.05)
26	O3	858 (3)	−3930 (3)	3339 (4)	6.29 (0.07)

No.	Atom	$x \cdot 10^3$	$y \cdot 10^3$	$z \cdot 10^3$	B_{eq} (Å^2)
27	HC1	329 (4)	−322 (4)	697 (4)	7.0 (1.0)
28	HC2	167 (4)	−475 (4)	639 (5)	8.0 (2.0)
29	H′C2	244 (5)	−464 (4)	763 (5)	9.0 (2.0)
30	HC3	36 (4)	−391 (4)	715 (5)	9.0 (2.0)
31	H′C3	106 (5)	−388 (5)	845 (5)	10.0 (2.0)
32	HC4	171 (4)	−229 (4)	813 (4)	7.0 (1.0)
33	HC6	327 (4)	−160 (4)	629 (4)	6.0 (1.0)
34	H′C6	214 (4)	−93 (4)	663 (4)	7.0 (2.0)
35	HC7	173 (4)	−81 (4)	461 (4)	6.0 (1.0)
36	HC9	301 (4)	−338 (4)	347 (4)	7.0 (1.0)
37	HC11	388 (3)	−160 (3)	426 (4)	5.0 (1.0)
38	HC12	378 (4)	−16 (4)	561 (5)	7.0 (1.0)
39	H′C12	320 (4)	53 (4)	448 (5)	9.0 (2.0)
40	H″C12	447 (4)	9 (4)	433 (5)	8.0 (2.0)
41	HC13	253 (5)	−26 (3)	281 (4)	7.0 (1.0)
42	H′C13	374 (4)	−78 (4)	245 (4)	7.0 (1.0)
43	H″C13	265 (4)	−155 (4)	258 (4)	8.0 (2.0)
44	HC14	47 (4)	−115 (5)	736 (5)	9.0 (2.0)
45	H′C14	−13 (4)	−203 (5)	827 (5)	9.0 (2.0)
46	H″C14	−23 (4)	−216 (4)	678 (5)	9.0 (2.0)
47	HC15	372 (5)	−505 (4)	484 (5)	9.0 (2.0)
48	H′C15	456 (5)	−408 (5)	471 (5)	11.0 (2.0)
49	H″C15	422 (5)	−453 (4)	601 (5)	10.0 (2.0)
50	HC18	−31 (4)	−426 (4)	175 (4)	6.0 (1.0)
51	HC19	−161 (4)	−384 (4)	25 (4)	6.0 (1.0)
52	HC21	−86 (4)	−74 (4)	72 (5)	7.0 (1.0)
53	HC22	36 (4)	−120 (4)	220 (4)	6.0 (1.0)

Equivalent positions:

x	y	z
1/2−x	−y	1/2+z
1/2+x	1/2−y	−z
−x	1/2+y	1/2−z.

TABLE III. Atomic Coordinates of Curdione (**2a**)

No.	Atom	$x\cdot10^4$	$y\cdot10^4$	$z\cdot10^4$	B_{eq} (Å^2)
1	C1	1035 (4)	−1670 (3)	1295 (5)	4.92 (0.08)
2	C2	−8 (4)	−1019 (3)	1817 (6)	5.62 (0.09)
3	C3	288 (4)	116 (3)	1587 (5)	4.85 (0.07)
4	C4	1534 (3)	434 (3)	2198 (4)	3.54 (0.06)
5	C5	2624 (4)	33 (3)	1416 (4)	3.33 (0.05)
6	C6	3725 (3)	−394 (3)	2176 (4)	3.29 (0.05)
7	C7	4519 (4)	−1179 (3)	1404 (4)	3.51 (0.06)
8	C8	4190 (4)	−2264 (3)	1762 (5)	4.34 (0.07)
9	C9	2939 (4)	−2695 (3)	1331 (5)	5.24 (0.08)
10	C10	1839 (4)	−2198 (3)	2024 (5)	4.42 (0.07)
11	C11	5939 (4)	−973 (3)	1532 (5)	4.23 (0.07)
12	C12	6365 (4)	−833 (4)	2948 (5)	5.37 (0.08)
13	C13	6294 (5)	−73 (4)	662 (6)	6.08 (0.09)
14	C14	1647 (4)	1592 (3)	2255 (6)	5.55 (0.08)
15	C15	1770 (5)	−2347 (3)	3503 (5)	5.47 (0.08)
16	O1	2658 (3)	124 (3)	229 (3)	5.10 (0.05)
17	O2	4919 (3)	−2814 (2)	2319 (5)	7.50 (0.07)

No.	Atom	$x\cdot10^3$	$y\cdot10^3$	$z\cdot10^3$	B_{eq} (Å^2)
18	HC1	110 (4)	−158 (3)	15 (4)	5.1 (1.0)
19	HC2	−25 (4)	−109 (3)	305 (4)	6.8 (1.1)
20	H′C2	−86 (4)	−123 (3)	125 (5)	7.7 (1.3)
21	HC3	35 (4)	27 (3)	47 (4)	7.3 (1.2)
22	H′C3	−47 (4)	58 (3)	196 (4)	7.2 (1.2)
23	HC4	152 (3)	7 (3)	324 (4)	4.9 (0.9)
24	HC6	347 (3)	−68 (3)	315 (4)	4.5 (0.9)
25	H′C6	419 (3)	37 (3)	230 (4)	5.6 (1.0)
26	HC7	432 (4)	−111 (3)	34 (4)	5.0 (1.0)
27	HC9	292 (4)	−350 (3)	154 (4)	7.2 (1.2)
28	H′C9	282 (4)	−257 (3)	27 (4)	5.5 (1.1)
29	HC11	645 (4)	−164 (3)	113 (4)	6.1 (1.1)
30	HC12	738 (4)	−93 (3)	303 (5)	7.9 (1.3)
31	H′C12	617 (4)	−8 (3)	330 (4)	7.6 (1.2)
32	H″C12	595 (4)	−142 (3)	359 (4)	7.3 (1.3)
33	HC13	730 (4)	6 (4)	70 (4)	7.5 (1.2)
34	H′C13	603 (4)	−19 (3)	−34 (4)	5.7 (1.1)
35	H″C13	584 (4)	62 (3)	103 (4)	6.6 (1.2)
36	HC14	247 (4)	182 (3)	280 (5)	7.6 (1.3)
37	H′C14	173 (5)	191 (3)	121 (5)	8.4 (1.4)
38	H″C14	83 (4)	193 (3)	268 (5)	8.0 (1.3)
39	HC15	92 (5)	−200 (4)	393 (5)	10.1 (1.6)
40	H′C15	180 (5)	−312 (4)	380 (5)	9.4 (1.5)
41	H″C15	255 (5)	−193 (4)	401 (5)	9.9 (1.6)

Equivalent positions:

x	y	z
$1/2-x$	$-y$	$1/2+z$
$1/2+x$	$1/2-y$	$-z$
$-x$	$1/2+y$	$1/2-z$.

d, J=6.8, 14-H), 1.03, 0.99 (3H×2, each d, J=6.8, 12-H, 13-H), 2.62, 3.30 (1H×2, each d, J=14.4, 9-H), 4.91 (2H, br s, 15-H), 7.56, 7.79 (2H×2, each d, J=8.4, aromatic).

X-Ray Analysis of *p*-Bromobenzoate (1c) The absolute configuration of **1c** was determined from the anomalous dispersion of CuK_α radiation by the bromine atom. The crystal data are: $C_{22}H_{27}O_3Br$; mp 122.5—124.5 °C; M.W.=419.4; orthorhombic; space group $P2_12_12_1$; lattice constants: a=13.004(7), b=13.442(8), c=11.875(6) Å, U=2076 Å^3, Z=4, D_{calc}=1.342 g cm^{-3}. Intensity data were collected by using graphite monochromated CuK_α radiation, and of the total of 2311 reflections measured within the 2θ angle of 156°, 1908 that exceeded the 2σ(I) level were used for the structure determination. The structure was determined by the heavy atom method and refined by the least-squares method. Of the total of 76 Friedel pairs, 66 pairs clearly showed the absolute configuration. The final R value was 0.043 taking into account the contributions of 27 hydrogen atoms and dispersion corrections. The absolute configuration of **1c** is depicted in Chart 1 and in Fig. 3 (drawn by the PLUTO program).

Preparation of 5α,8βH-Tetrahydrocurdione (2b) A solution of $LiAlH_4$

TABLE IV. Atomic Coordinates of the *p*-Bromobenzoate (**2e**) of 8αH-Dihydrocurdione (**2j**)

No.	Atom	$x\cdot10^4$	$y\cdot10^4$	$z\cdot10^4$	B_{eq} (Å^2)
1	Br1	20107 (8)	100000 (0)	110893 (7)	10.24 (0.02)

No.	Atom	$x\cdot10^4$	$y\cdot10^4$	$z\cdot10^4$	B_{eq} (Å^2)
2	C1	−2765 (5)	8198 (16)	2604 (5)	4.7 (0.1)
3	C2	−3384 (6)	7564 (20)	1482 (6)	6.6 (0.2)
4	C3	−4434 (5)	7104 (19)	1274 (5)	5.9 (0.2)
5	C4	−4532 (4)	5211 (19)	2019 (4)	4.7 (0.1)
6	C5	−4178 (4)	6277 (16)	3115 (5)	4.5 (0.1)
7	C6	−3529 (4)	4625 (15)	4018 (4)	3.9 (0.1)
8	C7	−2878 (4)	6026 (12)	5026 (4)	3.2 (0.1)
9	C8	−1822 (4)	5923 (13)	5164 (4)	3.7 (0.1)
10	C9	−1602 (4)	7664 (13)	4440 (5)	3.8 (0.1)
11	C10	−2049 (5)	6870 (14)	3311 (5)	4.2 (0.1)
12	C11	−2981 (4)	5036 (16)	5984 (4)	3.6 (0.1)
13	C12	−2761 (6)	2292 (16)	6179 (6)	5.4 (0.2)
14	C13	−3991 (5)	5693 (16)	5911 (6)	5.3 (0.2)
15	C14	−5595 (5)	4450 (27)	1664 (6)	8.3 (0.2)
16	C15	−1622 (5)	4562 (18)	3083 (6)	5.8 (0.2)
17	C16	−427 (4)	5537 (16)	6789 (5)	4.4 (0.1)
18	C17	124 (4)	6599 (14)	7841 (5)	3.8 (0.1)
19	C18	1005 (4)	5542 (17)	8488 (5)	5.1 (0.1)
20	C19	1551 (5)	6502 (18)	9466 (5)	5.7 (0.2)
21	C20	1237 (5)	8541 (19)	9760 (5)	6.0 (0.2)
22	C21	361 (5)	9686 (20)	9148 (5)	5.5 (0.1)
23	C22	−184 (4)	8650 (16)	8174 (5)	4.8 (0.1)
24	O1	−4438 (3)	8262 (12)	3266 (4)	5.8 (0.1)
25	O2	−1223 (3)	6810 (9)	6218 (3)	3.8 (0.1)
26	O3	−178 (4)	3726 (12)	6477 (5)	7.4 (0.1)

No.	Atom	$x\cdot10^3$	$y\cdot10^3$	$z\cdot10^3$	B_{eq} (Å^2)
27	HC1	−297 (4)	993 (16)	286 (5)	5.0 (1.0)
28	HC2	−308 (5)	585 (17)	131 (6)	9.0 (2.0)
29	H′C2	−333 (5)	911 (17)	99 (7)	9.0 (3.0)
30	HC3	−487 (5)	651 (14)	49 (5)	6.0 (2.0)
31	H′C3	−473 (5)	880 (14)	140 (6)	7.0 (2.0)
32	HC4	−413 (4)	358 (13)	202 (5)	5.0 (2.0)
33	HC6	−398 (5)	325 (18)	416 (7)	9.0 (2.0)
34	H′C6	−310 (4)	337 (14)	375 (5)	6.0 (2.0)
35	HC7	−311 (4)	788 (13)	493 (5)	4.0 (1.0)
36	HC8	−164 (5)	393 (15)	505 (6)	8.0 (2.0)
37	HC9	−83 (5)	778 (16)	470 (6)	8.0 (2.0)
38	H′C9	−190 (4)	945 (14)	448 (5)	6.0 (2.0)
39	HC11	−247 (4)	597 (11)	663 (4)	4.0 (1.0)
40	HC12	−202 (5)	188 (16)	629 (6)	7.0 (2.0)
41	H′C12	−282 (5)	176 (15)	684 (6)	7.0 (2.0)
42	H″C12	−321 (5)	124 (17)	550 (7)	9.0 (2.0)
43	HC13	−456 (5)	483 (21)	521 (6)	9.0 (2.0)
44	H′C13	−406 (5)	495 (20)	660 (6)	8.0 (2.0)
45	H″C13	−410 (5)	770 (15)	588 (5)	6.0 (2.0)
46	HC14	−588 (5)	372 (17)	89 (7)	9.0 (3.0)
47	H′C14	−566 (6)	312 (21)	222 (8)	12.0 (3.0)
48	H″C14	−604 (6)	605 (10)	168 (7)	10.0 (3.0)
49	HC15	−168 (6)	308 (20)	353 (8)	11.0 (3.0)
50	H′C15	−195 (6)	400 (19)	231 (7)	11.0 (3.0)
51	H″C15	−90 (5)	474 (21)	334 (6)	9.0 (2.0)
52	HC18	122 (5)	419 (16)	828 (6)	8.0 (2.0)
53	HC19	215 (4)	574 (15)	988 (5)	7.0 (2.0)
54	HC21	16 (4)	1100 (14)	939 (5)	6.0 (2.0)
55	HC22	−77 (4)	934 (13)	773 (5)	5.0 (2.0)

Equivalent positions:

x	y	z
$-x$	$1/2+y$	$-z$.

(70 mg) in ether (5 ml) was added at 0 °C to a solution of **2a** (100 ml) in ether (2 ml), and the mixture was stirred for 1 h. The reaction mixture was worked up treated as usual. The residue thus obtained was subjected to silica gel column chromatography to afford 100 mg of colorless prisms (98%).

Compound **2b**: mp 107—109 °C. $[\alpha]_D^{19}$ 16.60° ($c=2.0$, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3309 (OH), 1660 (C=C). EI-MS *m/z*: 240 (M^+).

Preparation of 5α,8βH-Tetrahydrocurdione (2b) 8αH-Dihydrocurdione (2c) and 5α,8αH-Tetrahydrocurdione (2d) A mixture of $LiAlH_4$ (150 mg) and ether (5 ml) was added to a solution of **2a** (203 mg) in ether (5 ml). The solution was stirred for 10 min at room temperature. After the usual work-up, 206 mg of crude products was chromatographed on a silica gel column using a gradient solvent mixture of petroleum ether and ether to give successively 27 mg of 8αH-dihydrocurdione (**2c**) as needles, 100 mg of 5α,8βH-tetrahydrocurdione (**2b**) as prisms and 20 mg of 5α,8αH-tetrahydrocurdione (**2d**) as prisms.

8αH-Dihydrocurdione (**2c**): mp 162—163 °C. $[\alpha]_D^{24}$ +3.07° ($c=3.85$, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3474 (OH), 1698 (C=O). EI-MS *m/z*: 238 (M^+). CI-MS *m/z*: 239 (MH^+). HR-MS *m/z*: 238.1930 for $C_{15}H_{26}O_2$. ^{1}H-NMR: ($CDCl_3$) δ: 4.94 (1H, d, $J=8.3$, 1-H), 3.63 (1H, m, 8α-H), 2.53 (1H, d, $J=12.2$), 2.23—2.36 (2H, m), 2.05—2.19 (5H, m), 1.95 (1H, d, $J=11.7$), 1.76 (3H, s, 15-H), 1.57—1.61 (2H, m), 1.25 (1H, d, $J=6.3$), 0.96, 0.76 (3H × 2, each d, $J=6.83$, 12-H, 13-H), 0.85 (3H, d, $J=7.08$, 14-H).

5α,8αH-Tetrahydrocurdione (**2d**): mp 70—72 °C. $[\alpha]_D^{18}$ +13.66° ($c=0.85$, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3390, 3300 (br, OH). EI-MS *m/z*: 240 (M^+).

Esterification of 8αH-Dihydrocurdione (2c) A solution of **2c** (20 mg), *p*-BrC_6H_4COCl (40 mg) and pyridine (0.1 ml) in CH_2Cl_2 was stirred at room temperature for 3 h. After evaporation of the solvent at room temperature, the residue was submitted to silica gel column chromatography to give 27 mg of the *p*-bromobenzoate (**2e**) as needles (84%). Recrystallization from pentane afforded a single crystal suitable for X-ray analysis.

The *p*-Bromobenzoate (**2e**): mp 132—134 °C. $[\alpha]_D^{24}$ −23.52° ($c=0.77$, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1720 (C=O), 1595 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 6.21 (1H, ddd, $J=10$, 10, 4, 8α-H), 5.04 (1H, d, $J=10$, 1-H), 2.52—2.72 (2H, m), 1.96—2.48 (7H, m), 1.86 (3H, s, 15-H), 1.51—1.78 (2H, m), 1.01, 0.86, 0.67 (each 3H, d, $J=7$, 12-H, 13-H, 14-H).

X-Ray Analysis of the *p*-Bromobenzoate (2e) Crystal data for **2e** are as follows: $C_{22}H_{29}O_3Br$; M.W. = 421.4; monoclinic; space group $P2_1$; lattice constant: $a=15.394(8)$, $b=5.451(3)$, $c=14.225(8)$ Å, $\beta=115.61(6)$, $U=1076$ Å^3, $Z=2$, $D_{calc}=1.300$ g cm^{-3}. A single crystal of approximate dimensions $0.03\times0.01\times0.5$ mm was chosen for the X-ray study. Of the total of 2343 reflections observed within the 2θ range of 6° through 70°, 1620 reflections were crystallographically independent and 519 were Friedel reflections. The remaining 204 were equivalent reflections which agree with the original ones with an approximate $R'=\sum||F01(hkl)|-|F01(hkl)||/\sum|F01|$ of 0.03. The R' value for the Friedel reflections was 0.055. The structure was determined by the heavy atom method and refined by the block-diagonal matrix least-squares method to an R value of 0.06. All the hydrogen atoms were included with isotropic temperature factors. The absolute configuration was determined by the anomalous dispersion method allowing for the dispersion terms of Br, O and C atoms for CuK_α radiation. Of the total of 135 Friedel pairs, for which the value $=\sum||F_O(hkl)|-|F_O(h\bar{k}\bar{l})||$ was estimated to be greater than $2\delta(F_O)$, 120 pairs showed the same configuration as given in Fig. 4. The final refinement in which the dispersion corrections were adequately made, gave the R value of 0.053. Hence the absolute configuration of curdione (**2a**) was deduced to be as mentioned above.

Isolation of (1*R*,10*R*)-Epoxy-(−)-1,10-dihydrocurdione (5a) Air-dried rhizomes (75 g) of *C. wenyujin* were extracted with 4 l of ether at 5 °C for a week. After filtration, the solvent was evaporated off at room temperature. The residue obtained was chromatographed on a silica gel column using a gradient solvent system of petroleum ether and ether. The fractions eluted with petroleum ether–ether (10:8) were collected. Evaporation of the solvent afforded 200 mg of oil. Crystallization from petroleum ether and ether, subsequent repeated silica gel chromatography and final recrystallization from ether gave a pure sample of the (1*R*,10*R*)-epoxide (**5a**) (40 mg, 0.07%).

(1*R*,10*R*)-Epoxy-(−)-1,10-dihydrocurdione (**5a**): $C_{15}H_{24}O_3$. mp 133—134 °C. $[\alpha]_D^{24}$ −235.0° ($c=0.68$, $CHCl_3$). UV $\lambda_{max}^{CHCl_3}$ nm (ε): 288 (52). EI-MS *m/z*: 252 (M^+). CI-MS *m/z*: 253 (MH^+). HR-MS *m/z*: 252.1745 (Theor. 252.3528) for $C_{15}H_{24}O_3$. IR ν_{max}^{KBr} cm^{-1}: 1705 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 3.08 (1H, dd, $J=18.3$, 11.9, 6-H), 2.89 (1H, dd, $J=9.9$, 3.8, 1-H), 2.83 (1H, m, 4-H), 2.81 (1H, dd, $J=18.3$, 4.0, 6-H), 2.69 (1H, d, $J=11.2$, 9-H), 2.66 (1H, dd, $J=11.9$, 4.0, 7-H), 2.07 (1H, m, 2-H), 1.73 (1H, m, 11-H), 1.69 (1H, m, 2-H), 1.34 (1H, m, 3-H), 1.17 (3H, s, 15-H), 1.07 (3H, d, $J=6.8$, 14-H), 0.97 (3H, d, $J=6.6$, 13-H), 0.87 (3H, d, $J=6.6$, 12-H). ^{13}C-NMR ($CDCl_3$) δ: 213.1 (C-5), 208.9 (C-8), 64.1 (C-1), 58.9 (C-10), 56.0 (C-7), 50.9 (C-9), 44.5 (C-4), 42.5 (C-6), 30.1 (C-11), 29.6 (C-3), 24.8 (C-2), 21.1 (C-12), 20.6 (C-13), 18.9 (C-14), 16.1 (C-15).

TABLE V. Atomic Coordinates of Neocurdione (**4**)

No.	Atom	$x\cdot10^4$	$y\cdot10^4$	$z\cdot10^4$	B_{eq} (Å^2)
1	C1	1143 (3)	7651 (0)	5594 (6)	3.5 (0.0)
2	C2	−41 (3)	7071 (3)	4154 (7)	4.5 (0.1)
3	C3	321 (3)	6316 (3)	2188 (6)	4.2 (0.1)
4	C4	1584 (3)	5663 (3)	3129 (6)	3.4 (0.0)
5	C5	2808 (3)	6340 (3)	3281 (5)	2.8 (0.0)
6	C6	3837 (3)	6414 (2)	5724 (5)	2.8 (0.0)
7	C7	4839 (3)	7305 (3)	5810 (5)	3.1 (0.0)
8	C8	4221 (3)	8371 (3)	5080 (6)	3.5 (0.0)
9	C9	3127 (3)	8763 (3)	6278 (6)	3.9 (0.1)
10	C10	1793 (3)	8416 (3)	4750 (5)	3.4 (0.0)
11	C11	5736 (3)	7391 (3)	8519 (6)	4.0 (0.1)
12	C12	6476 (4)	6380 (4)	9305 (9)	7.1 (0.1)
13	C13	6709 (4)	8293 (4)	8707 (9)	7.4 (0.1)
14	C14	1558 (4)	5021 (3)	5461 (7)	4.5 (0.1)
15	C15	1349 (4)	8934 (3)	2218 (6)	4.8 (0.1)
16	O1	2981 (2)	6771 (2)	1402 (4)	3.7 (0.0)
17	O2	4625 (3)	8915 (2)	3595 (5)	5.3 (0.0)

No.	Atom	$x\cdot10^3$	$y\cdot10^3$	$z\cdot10^3$	B_{eq} (Å^2)
18	HC1	146 (3)	739 (3)	754 (6)	6.0 (1.0)
19	HC2	−46 (3)	661 (3)	551 (7)	6.0 (1.0)
20	H′C2	−78 (4)	761 (3)	325 (6)	6.0 (1.0)
21	HC3	47 (3)	677 (3)	56 (6)	6.0 (1.0)
22	H′C3	−48 (3)	576 (3)	154 (6)	6.0 (1.0)
23	HC4	164 (3)	506 (3)	169 (6)	5.0 (1.0)
24	HC6	333 (3)	651 (3)	724 (6)	5.0 (1.0)
25	H′C6	434 (3)	566 (3)	597 (6)	5.0 (1.0)
26	HC7	546 (3)	711 (3)	449 (6)	4.0 (1.0)
27	HC9	316 (4)	962 (3)	638 (7)	7.0 (1.0)
28	H′C9	328 (3)	845 (3)	822 (6)	5.0 (1.0)
29	HC11	511 (4)	755 (3)	989 (7)	6.0 (1.0)
30	HC12	502 (4)	571 (3)	922 (8)	8.0 (1.0)
31	H′C12	710 (4)	643 (3)	1120 (7)	7.0 (1.0)
32	H″C12	715 (4)	622 (4)	799 (8)	9.0 (1.0)
33	HC13	613 (3)	891 (3)	847 (6)	6.0 (1.0)
34	H′C13	739 (4)	829 (3)	1048 (8)	8.0 (1.0)
35	H″C13	724 (4)	820 (3)	718 (7)	8.0 (1.0)
36	HC14	147 (3)	555 (3)	702 (7)	6.0 (1.0)
37	H′C14	246 (4)	457 (3)	608 (7)	7.0 (1.0)
38	H″C14	72 (3)	449 (3)	513 (7)	7.0 (1.0)
39	HC15	127 (4)	970 (4)	244 (7)	8.0 (1.0)
40	H′C15	37 (4)	864 (4)	123 (7)	8.0 (1.0)
41	H″C15	204 (4)	877 (4)	104 (7)	7.0 (1.0)

Equivalent positions:

x	y	z
$-x$	$1/2+y$	$-z$.

X-Ray Analysis of (1*R*,10*R*)-Epoxy-(−)-1,10-dihydrocurdione (5a) The relative structure of **5a** was determined by X-ray analysis. The crystal data were as follows: $C_{15}H_{24}O_3$; M.W. = 252.4; orthorhombic; space group $P2_12_12_1$; lattice constants : $a=10.605(3)$, $b=13.503(1)$, $c=10.429$ (9) Å, $U=1493.4$ Å^3, $Z=4$, $D_{calc}=1.24$. The intensity data were collected on Philips PW 1100 diffractometer using graphite monochromated CuK_α radiation; 777 reflections up to 150° (2θ) were used. The crystal structure was determined by the direct method using the MULTAN program and refined by means of the block-diagonal least-squares method. The final R value was 0.051 including 24 hydrogen atoms with isotropic temperature factors. The crystal structure and relative stereostructure of **5a** were thus revealed to be as shown in Fig. 5.

Epoxidation of Curdione (2a) MCPBA (52 mg) in CH_2Cl_2 (1 ml) was added dropwise to a solution of **2a** (60 mg) in CH_2Cl_2 (1 ml) cooled in an ice-bath. The mixture was stirred for 2 h in the ice bath and for 3 h at

room temperature. Then it was washed with saturated aqueous Na_2CO_3 solution, dried over anhydrous Na_2SO_4 and evaporated to give 107 mg of crude products, which were separated by silica gel chromatography to afford 36 mg of (1*R*,10*R*)-epoxy-(−)-1,10-dihydrocurdione (**5a**) and (1*S*,10*S*)-epoxy-(+)-1,10-dihydrocurdione (**5b**) (27 mg). The overall yield was 98%.

(1*S*,10*S*)-Epoxy-(+)-1,10-dihydrocurdione (**5b**): $C_{15}H_{24}O_3$. mp 117—119°C. $[\alpha]_D^{24}$ +99.80° (c=0.95, $CHCl_3$). UV $\lambda_{max}^{CHCl_3}$ nm (ε): 288 (49). IR ν_{max}^{KBr} cm^{-1}: 1705 (C=O). EI-MS m/z: 252 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 2.91 (1H, dt, J=15.3, 8.9, 7-H), 2.81 (1H, d, J=10.3, 9-H), 2.80 (1H, dd, J=15.3, 8.9, 6-H), 2.70 (1H, dd, J=10.3, 2.2, 1-H), 2.48 (1H, dd, J=15.3, 1.8, 6-H), 2.44 (1H, m, 4-H), 2.26 (1H, d, J=10.3, 9-H), 2.24 (2H, m, 2-H, 3-H), 1.91 (1H, m, 11-H), 1.56 (1H, m, 3-H), 1.29 (3H, s, 15-H), 1.25 (1H, m, 2-H), 1.09 (3H, d, J=6.0, 14-H), 0.94 (3H, d, J=6.6, 13-H), 0.89 (3H, J=6.6, 12-H). ^{13}C-NMR ($CDCl_3$) δ: 214.3 (C-5), 212.0 (C-8), 62.5 (C-1), 58.5 (C-10), 55.6 (C-7), 55.9 (C-9), 46.8 (C-4), 42.4 (C-6), 30.4 (C-11), 29.1 (C-3), 35.8 (C-2), 21.2 (C-12), 20.2 (C-13), 18.2 (C-14), 17.3 (C-15).

Isolation of Neocurdione (4) Dried rhizomes of *C. wenyujin* (450 g) were cut into small pieces and the chips were percolated with ether for four days in a refrigerator. After the filtration of this ether extract, evaporation of the solvent *in vacuo* afforded 16.8 g of essential oil (3.7%), which was submitted to silica gel chromatography with *n*-hexane–ether. The fractions eluted with *n*-hexane–ether (1:1) were collected. Preparative thin layer chromatography (TLC) (*n*-hexane–ether) and finally recrystallization from *n*-pentane afforded 220 mg (1.3%) of neocurdione (**4**) as colorless prisms.

Neocurdione (**4**): $C_{15}H_{24}O_2$. mp 45—47°C. $[\alpha]_D^{22}$ −65.80° (c=1.20, $CHCl_3$). CD [θ] −36060 (300), +12368 (223). IR ν_{max}^{KBr} cm^{-1}: 1702 (C=O), 1662 (C=C). EI-MS m/z: 236 (M^+). CD [θ] (c=0.05, MeOH). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.91, 0.97 (6H, d, J=6.6, 12 or 13-H), 1.25 (3H, d, J=7.1, 14-H), 1.65 (3H, s, 15-H), 1.75 (1H, m, 3β-H), 1.91 (1H, m, 3α-H), 1.93 (1H, m, 11-H), 2.09 (1H, m, 2β-H), 2.16 (1H, m, 2α-H), 2.39 (1H, dd, J=14.9, 2.7, 6β-H), 2.88 (1H, d, J=12.5, 9α-H), 2.89 (1H, ddd, J=6.8, 3.2, 1.0, 7β-H), 3.04 (1H, d, J=12.5, 9β-H), 5.17 (1H, s, 1-H).

X-Ray Analysis of Neocurdione (4) The relative structure of neocurdione (**4**) was determined by X-ray analysis. The crystal data were as follows: $C_{15}H_{24}O_2$; M.W.=236.4; monoclinic; space group $P2_1$; lattice constants: a=10.446(7), b=12.785(7) Å, β=103.19(6)°, U=714 Å^3, Z=2, D_{calc}=1.099 g cm^{-3}. The intensity data were collected on a Philips PW 1100 diffractometer using graphite monochromated CuK_α radiation; 1387 reflections up to 156° (2θ) were used. The crystal structure was determined by the direct method using the MULTAN program, and refined by means of the block diagonal least squares method. The final R value was 0.04 including 24 hydrogen atoms with isotropic temperature factors.

Transformation of Curdione (2a) to 8βH-Dihydrocurdione (2f) Compound **2a** (28 mg) was dissolved in 2 ml of methanol. After addition of $NaBH_4$ (3.4 mg), the mixture was stirred for 3 h. After evaporation of the solvent, the residue was extracted with ether. Evaporation of the solvent afforded 28 mg of crude residue. This residue was submitted to silica gel column chromatography to yield 25 mg (89%) of 8βH-dihydrocurdione (**2f**) as colorless prisms.

Compound **2f**: $C_{15}H_{26}O_2$. mp 55—58°C. $[\alpha]_D^{19}$ +70.25° (c=2.10, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3460 (OH), 1695 (C=O). CI-MS m/z: 239 (MH^+). ^{1}H-NMR ($CDCl_3$) δ: 4.90 (1H, d, J=12.1, 1-H), 4.20 (1H, t, J=3.3, 8-H), 3.02 (1H, dd, J=18.0, 5.1), 2.41 (1H, m), 2.38 (1H, m), 2.18 (1H, dd, J=13.8, 3.7), 2.15 (1H, dd, J=13.9, 2.6), 1.90 (3H, s, 10-CH_3), 1.86—1.96 (2H, m), 1.60—1.68 (2H, m), 0.98 (3H, d, J=7.0, 14-CH_3), 0.95 (3H, d, J=6.6, 11-CH_3), 0.94 (3H, d, J=6.6, 11-CH_3).

Transformation of 8βH-Dihydrocurdione (2f) to 8βH-Dihydro-4-epicurdione (2g) Compound **2f** was dissolved in 2 ml of benzene and a catalytic amount of *tert*-BuOK was added. The reaction mixture was refluxed for 2 h, then the solvent was evaporated off. The residue was submitted to silica gel chromatography by using a *n*-hexane–ether gradient solvent system to afford 41 mg of 8βH-dihydrocurdione (**2f**) and 10 mg of 8βH-dihydro-4-epicurdione (**2g**) in the ratio of 4:1.

Compound **2g**: $C_{15}H_{26}O_2$. Oil. $[\alpha]_D^{20}$ −0.26° (c=3.82, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3470 (–OH), 1690 (C=O). EI-MS m/z: 238 (M^+), ^{1}H-NMR ($CDCl_3$) δ: 5.10 (1H, brs, 1-H), 4.15 (1H, brs, 8β-H), 3.07 (1H, dd, J=17.3, 5.4), 2.47 (1H, brs), 2.09 (1H, dd, J=13.4, 2.4), 1.83 (3H, s, 10-CH_3), 1.12 (3H, d, J=7.1, 14-CH_3), 1.12 (3H, d, J=7.1, 4-CH_3), 0.95 (3H, d, J=6.8, 11-CH_3), 0.94 (3H, d, J=6.6, 11-CH_3).

Transformation of 8βH-Dihydro-4-epicurdione (2g) to 4-Epicurdione (2h) Compound **2g** (10 mg) was dissolved in 1.5 ml of pyridine and CrO_3

TABLE VI. Atomic Coordinates of the *p*-Bromobenzoate (**2k**) of 8αH-Dihydro-4-epicurdione (**2j**)

No.	Atom	$x\cdot10^5$	$y\cdot10^5$	$z\cdot10^5$	B_{eq} (Å^2)
1	Br1	−43040 (6)	56556 (6)	−3610 (16)	9.88 (0.02)

No.	Atom	$x\cdot10^4$	$y\cdot10^4$	$z\cdot10^4$	B_{eq} (Å^2)
2	C1	3158 (5)	7854 (3)	−2103 (8)	4.5 (0.1)
3	C2	4251 (5)	8016 (3)	−2320 (9)	6.0 (0.1)
4	C3	4798 (4)	7400 (3)	−3119 (9)	5.0 (0.1)
5	C4	4472 (4)	7239 (3)	−4833 (8)	4.8 (0.1)
6	C5	3359 (4)	7079 (3)	−4986 (7)	4.1 (0.1)
7	C6	2965 (4)	6431 (3)	−4162 (7)	3.5 (0.1)
8	C7	1824 (4)	6433 (3)	−3922 (7)	3.3 (0.1)
9	C8	1568 (4)	6434 (3)	−2147 (7)	3.7 (0.1)
10	C9	1712 (4)	7147 (3)	−1300 (8)	4.4 (0.1)
11	C10	2777 (4)	7363 (3)	−1158 (8)	4.2 (0.1)
12	C11	1337 (4)	5820 (3)	−4853 (8)	4.3 (0.1)
13	C12	1674 (4)	5088 (3)	−4303 (10)	5.6 (0.1)
14	C13	1505 (5)	5900 (4)	−6671 (9)	6.2 (0.1)
15	C14	5069 (5)	6618 (4)	−5514 (11)	7.0 (0.1)
16	C15	3375 (5)	6974 (3)	105 (8)	5.5 (0.1)
17	C16	187 (4)	5767 (3)	−1099 (7)	4.1 (0.1)
18	C17	−910 (4)	5747 (3)	−996 (7)	3.9 (0.1)
19	C18	−1509 (4)	6203 (3)	−1833 (7)	3.9 (0.1)
20	C19	−2524 (4)	6179 (3)	−1666 (8)	4.7 (0.1)
21	C20	−2910 (4)	5696 (3)	−655 (9)	5.7 (0.1)
22	C21	−2345 (5)	5234 (4)	240 (11)	7.1 (0.1)
23	C22	−1324 (4)	5262 (3)	39 (10)	6.4 (0.1)
24	O1	2856 (3)	7446 (2)	−5832 (5)	5.5 (0.1)
25	O2	499 (3)	6306 (2)	−2015 (5)	4.1 (0.1)
26	O3	723 (3)	5357 (2)	−409 (6)	5.9 (0.1)

No.	Atom	$x\cdot10^3$	$y\cdot10^3$	$z\cdot10^3$	B_{eq} (Å^2)
27	HC1	271 (4)	814 (3)	−281 (8)	7.0 (2.0)
28	HC2	434 (5)	849 (3)	−302 (8)	9.0 (2.0)
29	H'C2	456 (5)	812 (3)	−117 (8)	8.0 (2.0)
30	HC3	467 (3)	692 (2)	−241 (6)	4.0 (1.0)
31	H'C3	556 (4)	751 (3)	−310 (7)	6.0 (1.0)
32	HC4	462 (5)	769 (3)	−555 (8)	8.0 (2.0)
33	HC6	319 (3)	599 (2)	−492 (6)	5.0 (1.0)
34	H'C6	332 (4)	621 (3)	−313 (7)	5.0 (1.0)
35	HC7	155 (3)	692 (2)	−445 (6)	4.0 (1.0)
36	HC8	199 (4)	603 (3)	−159 (7)	6.0 (1.0)
37	HC9	140 (4)	711 (3)	−10 (7)	6.0 (1.0)
38	H'C9	131 (4)	756 (3)	−192 (7)	5.0 (1.0)
39	HC11	56 (4)	585 (3)	−468 (7)	6.0 (1.0)
40	HC12	128 (5)	493 (3)	−317 (8)	7.0 (2.0)
41	H'C12	243 (5)	507 (3)	−400 (8)	7.0 (2.0)
42	H''C12	151 (5)	473 (3)	−516 (9)	9.0 (2.0)
43	HC13	227 (5)	584 (3)	−695 (9)	9.0 (2.0)
44	H'C13	129 (5)	642 (3)	−710 (8)	8.0 (2.0)
45	H''C13	113 (4)	550 (3)	−731 (7)	6.0 (2.0)
46	HC14	498 (4)	616 (3)	−477 (8)	8.0 (2.0)
47	H'C14	584 (4)	675 (3)	−560 (7)	6.0 (2.0)
48	H''C14	481 (5)	648 (3)	−674 (8)	8.0 (2.0)
49	HC15	335 (4)	644 (3)	−2 (8)	7.0 (2.0)
50	H'C15	311 (6)	709 (4)	130 (9)	11.0 (2.0)
51	H''C15	415 (5)	714 (3)	6 (10)	11.0 (2.0)
52	HC18	−123 (4)	655 (3)	−257 (7)	6.0 (2.0)
53	HC19	−294 (4)	650 (3)	−228 (7)	6.0 (2.0)
54	HC21	−264 (6)	486 (4)	93 (9)	10.0 (2.0)
55	HC22	−91 (4)	494 (3)	64 (7)	6.0 (1.0)

Equivalent positions:

x	y	z
1/2−x	−y	1/2+z
1/2+x	1/2−y	−z
−x	1/2+y	1/2−z.

(12 mg) was added. This mixture was stirred at room temperature for 4 h. After filtration and evaporation of the reaction mixture, the residue obtained was submitted to silica gel chromatography to afford 5 mg (50%) of 4-epicurdione (**2h**) as colorless prisms. The physical properties of this compound were in accord with those of neocurdione (**4**) except for the optical rotations.

4-Epicurdione (**2h**): $C_{15}H_{24}O_2$. mp 45—47 °C. $[\alpha]_D^{24}$ +65.88° (c=3.88, $CHCl_3$). CD (c=3.88, MeOH) [θ] (nm): +36100 (259). IR ν_{max}^{KBr} cm^{-1}: 1700 (C=O), 1663 (C=C). EI-MS m/z: 236 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 5.16 (1H, s, 1-H), 2.15 (1H, m, 2α-H), 2.09 (1H, m, 2β-H), 1.98 (1H, m, 3α-H), 1.76 (1H, m, 3β-H), 2.49 (1H, m, 4β-H), 2.69 (1H, dd, J=14.9, 2.7, 6β-H), 2.87 (1H, ddd, J=6.8, 2.7, 7-H), 2.88 (1H, d, J=12.5, 9α-H), 3.04 (1H, d, J=12.5, 9β-H), 1.05 (3H, d, J=7.1, 4-CH_3), 1.93 (1H, m, 11-H), 0.91 (3H, d, J=6.6, 11-CH_3), 0.97 (3H, d, J=6.6, 11-CH_3), 1.66 (3H, s, 10-CH_3).

Esterification of 8βH-Dihydro-4-epicurdione (2f) Compound **2f** (7 mg), p-BrC_6H_4COCl (30 mg) and DMAP (30 mg) were dissolved in 2 ml of pyridine. This mixture was stirred at room temperature for 2 d. After evaporation of the solvent *in vacuo*, the oil obtained was submitted to silica gel chromatography to yield 13 mg (quantitative yield, oil) of the benzoate (**2i**).

Compound **2i**: $C_{22}H_{29}O_3Br$. Oil. $[\alpha]_D^{20}$ +24.50° (c=0.53, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1720 (C=O), 1700 (benzoate ≻C=O), 1595 (arom.). CI-MS m/z: 423, 421 (MH^+).

Transformation of 4-Epicurdione (2h) to 8αH-Dihydro-4-epicurdione (2j) $LiAlH_4$ (5 mg) in dry THF (5 ml) was added to a solution of compound 2h (50 mg) in THF (5 ml). The reaction mixture was stirred for 10 min and worked up to afford 40 mg of oil. Silica gel chromatography of this oil afforded 4 mg (8%) of **2j** as colorless prisms and 40 mg (80%) of **2g**.

Compound **2j**: $C_{15}H_{26}O_2$. mp 102—103 °C. IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1682 (C=O). EI-MS m/z: 238 (M^+). CI-MS m/z: 239 (MH^+). HR-MS m/z: 238.1930 (Theor. 238.1928). ^{1}H-NMR ($CDCl_3$) δ: 5.07 (1H, br s, 1-H), 3.66 (1H, br s, 8α-H), 2.46 (1H, br s, 4-H), 1.76 (3H, s, 10-CH_3), 1.11 (3H, d, J=7.3, 4-CH_3), 0.83 (3H, d, J=7.1, 11-CH_3), 0.77 (3H, d, J=6.8, 11-CH_3).

Esterification of 8αH-Dihydro-4-epicurdione (2j) Compound **2j** (4 mg), p-BrC_6H_4COCl (15 mg) and DMAP (15 mg) were dissolved in 1 ml of pyridine, and the mixture was stirred overnight at room temperature. The solvent was evaporated off *in vacuo* to yield a colorless oil. This oil was submitted to silica gel chromatography. After usual work-up, 7 mg of the p-bromobenzoate (**2k**) was obtained as colorless prisms.

Compound (**2k**): $C_{29}H_{29}O_3Br$. mp 123—124 °C. $[\alpha]_D^{20}$ −11.36° (c=0.35, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1718 (C=O), 1700 (benzoate C=O), 1593 (arom.). EI-MS m/z: 220 ($M^+ - BrC_6H_4COOH$). ^{1}H-NMR ($CDCl_3$) δ: 7.90 (2H, d, J=7.0, arom.-H), 7.59 (2H, d, J=6.5, arom.-H), 5.13 (2H, br s, 1-H and 8α-H), 2.63 (1H, br s, 4-H), 1.86 (3H, s, 10-CH_3), 1.15 (3H, d, J=7.3, 4-CH_3), 0.83 (3H, d, J=6.8, 11-CH_3), 0.67 (3H, d, J=6.6, 11-CH_3).

X-Ray Analysis of Compound (2k) The absolute configuration of **2k** was determined from the anomalous dispersion of CuK_α radiation by the bromine atom. The crystal data are as follows: $C_{29}H_{29}O_3Br$; M.W. = 421.4; orthorhombic; space group $P2_12_12_1$; lattice constants: a=13.569(1), b=18.887(2), c=8.382(0) Å, $\alpha=\beta=\gamma=90°$, U=2151.4 Å^3, Z=4, D_{calc}= 1.289 g cm^{-3}. The intensity data of a total of 1720 reflections were collected within the 2θ angle of 156° by using graphite monochromated CuK_α radiation. The structure was determined by the heavy atom method and refined by the least-squares method as usual. The final R-value was 0.047.

Isolation of (1*S*,10*S*),(4*S*,5*S*)-Germacrone-1(10),4-diepoxide (6) Air-dried and chipped rhizomes of *Curcuma wenyujin* (875 g) were percolated with ether (4 l) at 5 °C for a week. Evaporation of the solvent *in vacuo* afforded 28.5 g, of essential oil. This oil was submitted to silica gel column chromatography with petroleum ether–ether solvent system to collect fifteen fractions. The eighth fraction (petroleum ether–ether; 5:4) was evaporated to give a residue (100 mg), which was purified by silica gel chromatography. Recrystallization of the oil from ether afforded 6 mg of (1*S*,10*S*),(4*S*,5*S*)-germacrone-1(10),4-diepoxide (**6**) as colorless needles.

(1*S*,10*S*),(4*S*,5*S*)-Germacrone-1(10),4-diepoxide (**6**): $C_{15}H_{22}O_3$. mp 84—86 °C. $[\alpha]_D^{23}$ +69.0° (c=0.51, $CHCl_3$). UV λ_{max}^{MeOH} nm (ε): 256 (1660), 315 (203). IR ν_{max}^{KBr} cm^{-1}: 1678, 1645 (enone). HR-MS m/z: 250.3524 for $C_{15}H_{20}O_3$(Theor. 250.3528). ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 3.02 (1H, d, J=11.6, 9-H), 2.94 (1H, dd, J=10.7, 1.1, 1-H), 2.88 (1H, dd, J=12.1, 1.8, 5-H), 2.67 (1H, dd, J=11.0, 2.0, 6-H), 2.66 (1H, d, J=11.6, 9-H), 2.30 (1H, dd, J=12.1, 11.0, 6-H), 2.22 (1H, m, 2-H), 2.08 (1H, m, 3-H), 1.88, 1.81 (each 3H, s, 11-CH_3), 1.46 (3H, s, 10-CH_3), 1.21 (3H, s, 4-CH_3). ^{13}C-NMR ($CDCl_3$) δ: 207.0 (C-8), 137.4 (C-11), 133.8 (C-7), 63.9 (C-5), 61.2 (C-1), 60.0 (C-4), 57.4 (C-10), 54.4 (C-9), 35.5 (C-3), 29.1 (C-6), 22.8 (C-2), 22.6 (C-12), 20.6 (C-13), 17.2 (C-15), 15.4 (C-6).

TABLE VII. Atomic Coordinates of (1*R*,10*R*)-Epoxy-(−)-1,10-dihydrocurdione (**5a**)

No.	Atom	$x\cdot10^4$	$y\cdot10^4$	$z\cdot10^4$	B_{eq} (Å^2)
1	C1	−54 (7)	−2716 (6)	−1980 (7)	4.6 (0.1)
2	C2	−325 (8)	−3575 (6)	−2830 (8)	5.3 (0.1)
3	C3	−1343 (8)	−4270 (6)	−2313 (7)	4.7 (0.1)
4	C4	−1283 (7)	−4480 (5)	−860 (7)	3.6 (0.1)
5	C5	−1792 (7)	−3578 (5)	−122 (7)	3.5 (0.1)
6	C6	−1033 (6)	−3164 (5)	980 (7)	3.6 (0.1)
7	C7	−1507 (7)	−2158 (5)	1472 (7)	3.4 (0.1)
8	C8	−1756 (7)	−1427 (5)	405 (7)	4.0 (0.1)
9	C9	−732 (7)	−1216 (5)	−610 (8)	4.4 (0.1)
10	C10	−850 (7)	−1807 (6)	−1833 (7)	4.4 (0.1)
11	C11	−566 (7)	−1725 (6)	2478 (8)	4.7 (0.1)
12	C12	−476 (9)	−2400 (7)	3645 (8)	6.5 (0.2)
13	C13	−957 (11)	−670 (7)	2870 (10)	8.3 (0.2)
14	C14	−2089 (9)	−5368 (6)	−515 (9)	6.1 (0.2)
15	C15	−2026 (9)	−1643 (6)	−2629 (9)	6.1 (0.2)
16	O1	−2821 (4)	−3230 (4)	−389 (5)	4.4 (0.1)
17	O2	−2742 (5)	−955 (4)	374 (5)	5.5 (0.1)
18	O3	324 (5)	−1785 (4)	−2571 (6)	5.9 (0.1)

No.	Atom	$x\cdot10^3$	$y\cdot10^3$	$z\cdot10^3$	B_{eq} (Å^2)
19	HC1	66 (6)	−285 (4)	−129 (6)	5.0 (2.0)
20	HC2	70 (9)	−396 (6)	−303 (8)	12.0 (3.0)
21	H′C2	−60 (9)	−328 (7)	−382 (9)	13.0 (3.0)
22	HC3	−227 (6)	−405 (5)	−254 (6)	6.0 (2.0)
23	H′C3	−130 (6)	−488 (4)	−273 (6)	5.0 (2.0)
24	HC4	−38 (5)	−466 (4)	−59 (5)	4.0 (1.0)
25	HC6	−2 (6)	−315 (5)	68 (6)	6.0 (2.0)
26	H′C6	−103 (6)	−371 (5)	172 (6)	5.0 (2.0)
27	HC7	−243 (5)	−235 (4)	194 (5)	3.0 (1.0)
28	HC9	13 (6)	−122 (4)	−17 (5)	4.0 (1.0)
29	H′C9	−85 (7)	−41 (5)	−85 (7)	8.0 (2.0)
30	HC11	59 (7)	−171 (6)	217 (7)	8.0 (2.0)
31	HC12	17 (8)	−205 (6)	441 (7)	10.0 (2.0)
32	H′C12	−13 (6)	−301 (5)	368 (6)	7.0 (2.0)
33	H″C12	−130 (6)	−232 (5)	401 (7)	5.0 (2.0)
34	HC13	−116 (8)	−21 (7)	222 (9)	10.0 (3.0)
35	H′C13	−43 (8)	−35 (6)	371 (8)	12.0 (3.0)
36	H″C13	−192 (8)	−88 (6)	336 (7)	9.0 (2.0)
37	HC14	−300 (8)	−515 (6)	−114 (8)	9.0 (2.0)
38	H′C14	−194 (8)	−558 (5)	27 (7)	9.0 (2.0)
39	H″C14	−168 (8)	−604 (6)	−82 (8)	10.0 (3.0)
40	HC15	−288 (8)	−177 (6)	−219 (7)	9.0 (2.0)
41	H′C15	−198 (8)	−203 (6)	−358 (8)	12.0 (3.0)
42	H″C15	−193 (7)	−89 (5)	−298 (7)	8.0 (2.0)

Equivalent positions:

x	y	z
1/2−x	−y	1/2+z
1/2+x	1/2−y	−z
−x	1/2+y	1/2−z.

Synthesis of (1*S*,10*S*),(4*S*,5*S*)-Germacrone-1(10),4-diepoxide (6) and (1*S*,10*S*),(4*S*,5*S*),(7ξ,11ξ)-(−)-1(10),4,7(11)-Triepoxide (7) from (4*S*,5*S*)-Germacrone-4,5-epoxide (5c) A mixture of (4*S*,5*S*)-germacrone-4,5-epoxide (**5c**) (500 mg) isolated from *C. wenyujin* and MCPBA (400 mg) in 4 ml of CH_2Cl_2 was stirred at room temperature for 24 h. The reaction mixture was washed twice with saturated Na_2SO_4. The organic layer was concentrated under reduced pressure, and the residue was subjected to a column chromatography over silica gel with a gradient solvent of petroleum ether and ether to afford 450 mg of **2a** (86%) and 20 mg of (1*S*,10*S*),(4*S*,5*S*),(7ξ,11ξ)-(−)-1(10),4,7(11)-triepoxide (**7**) (4%). **7**: $C_{15}H_{22}O_4$. mp 138—140 °C. $[\alpha]_D^{20}$ +228° (c=0.90, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1705 (C=O). CI-MS m/z: 267 (MH^+). EI-MS m/z: 266 (M^+). HR-MS m/z: 266.3595 for $C_{15}H_{22}O_4$ (Theor. 266.3522). ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 3.07 (1H, d, J=9.9), 3.04 (1H, d, J=10.6), 3.00 (1H, dd, J=10.3, 0.7), 2.43 (1H, d, J=10.6), 2.25—2.15 (2H, m), 2.10 (1H, dd,

J=13.9, 1.1), 1.98 (1H, dd, J=13.9, 2.0), 1.44, 1.42, 1.19, 1.14 (each 3H, s), 1.28—1.35 (2H, m).

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References and Notes

1) Visiting Research Associate of Keio University on leave from Dalian Institute of Medicinal and Pharmaceutical Sciences.
2) H.-J. Fang, J.-G. Yu, Y.-H. Chen and Q. Hu, *Acta Pharmaceutica Sinica*, **17**, 441 (1982).
3) H.-X. Xu, *Zhong Cao Yao Tong Xun*, **10**, 433 (1979).
4) *a*) H. Hikino, K. Meguro, Y. Sakurai and T. Takemoto, *Chem. Pharm. Bull.*, **27**, 275 (1979); *b*) S. Inayama, J.-F. Gao, K. Harimaya, T. Kawamata, Y. Iitaka and Y.-T. Guo, *ibid.*, **32**, 3783 (1984).
5) *a*) H. Hikino, K. Meguro, Y. Sakurai and T. Takemoto, *Chem. Pharm. Bull.*, **14**, 1341 (1966); *b*) S. Inayama, J.-F. Gao, K. Harimaya, Y. Iitaka, Y.-T. Guo and T. Kawamata, *ibid.*, **33**, 1323 (1985).
6) *a*) S. Inayama, J.-F. Gao, K. Harimaya, M. Hikichi, Y. Iitaka, Y.-T. Guo and T. Kawamata, *Chem. Pharm. Bull.*, **33**, 2179 (1985); *b*) J.-F. Gao, T. Ohkura, K. Harimaya, M. Hikichi, T. Kawamata, X.-Y. Wu, Y. Iitaka and S. Inayama, *ibid.*, **34**, 5122 (1986).
7) H. Hikino, Y. Sakurai, S. Takahashi and T. Takemoto, *Chem. Pharm. Bull.*, **15**, 1390 (1967).
8) *a*) T. Ohkura, J.-F. Gao, T. Nishishita, K. Harimaya, T. Kawamata and S. Inayama, *Shoyakugaku Zasshi*, **41**, 102 (1987); *b*) T. Ohkura, J-F. Gao, J.-H. Xie and S. Inayama, *ibid.*, **44**, 171 (1990).
9) J.-F. Gao, J.-H. Xie, Y. Iitaka and S. Inayama, *Shoyakugaku Zasshi*, **42**, 347 (1988).
10) T. Ohkura, J.-F. Gao, K. Harimaya and S. Inayama, *Shoyakugaku Zasshi*, submitted (1991).
11) *a*) T. Ohkura, J.-F. Gao, K. Harimaya, M. Hikichi, T. Kawamata, Y. Iitaka, X.-Y. Wu, T. Nishishita and S. Inayama, *Shoyakugaku Zasshi*, **40**, 352 (1986); *b*) T. Ohkura, J.-F. Gao, K. Harimaya, M. Hikichi, Y. Iitaka, T. Kawamata, M. Kuroyanagi, S. Fukushima and S. Inayama, *Chem. Pharm. Bull.*, **34**, 4435 (1986).
12) *a*) J.-F. Gao, J.-H. Xie, Y. Iitaka and S. Inayama, *Chem. Pharm. Bull.*, **37**, 233 (1989); *b*) J.-F. Gao, J.-H. Xie, K. Harimaya, T. Kawamata, Y. Iitaka and S. Inayama, *ibid.*, **39**, 854 (1991).
13) *a*) M. Yoshibara, H. Shibuya, E. Kitano, K. Yanagi and Y. Kitagawa, *Chem. Pharm. Bull.*, **32**, 2058 (1984); *b*) M. Kuroyanagi, A. Ueno, K. Ujiie and S. Sata, *ibid.*, **35**, 53 (1987). Note: (4*S*,5*S*)-germacrane-4,5-epoxide (**5c**) in ref. 15 should be better designated as (4*S*,5*S*)-germacrone-4-epoxide for comparison with compounds, *e.g.* (1*S*,-10*S*),(4*S*,5*S*)-germacrone-1(10),4-diepoxide-1(10),4-diepoxide (**6**) and (1*S*,10*S*),(4*S*,5*S*),(7ξ,11ξ)-germacrone-1(10),4,7(11)-triepoxide (**7**), in this paper.
14) See Note **10** in ref. 6*a* and ref. 14*c* in ref. 8*a* [Y. Shiobara, T. Iwata, M. Kodama, Y. Asakawa, T. Takemoto and Y. Fukazawa, *Tetrahedron Lett.*, **26**, 913 (1985)].
15) K. Harimaya, T. Ohkura, J.-F. Gao, Y. Iitaka, E. Osawa and S. Inayama, *Chem. Pharm. Bull.*, **35**, 3866 (1987).
16) *a*) J. Endo and M. Nagasawa, *Yakugaku Zasshi*, **94**, 1574 (1974); *b*) J. Endo, M. Nagasawa, H. Itogawa and Y. Iitaka, *Chem. Pharm. Bull.*, **27**, 275 (1979).