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NEW BISABOLANE SESQUITERPENOIDS FROM THE RHIZOMES OF CURCUMA XANTHORRHIZA (ZINGIBERACEAE)

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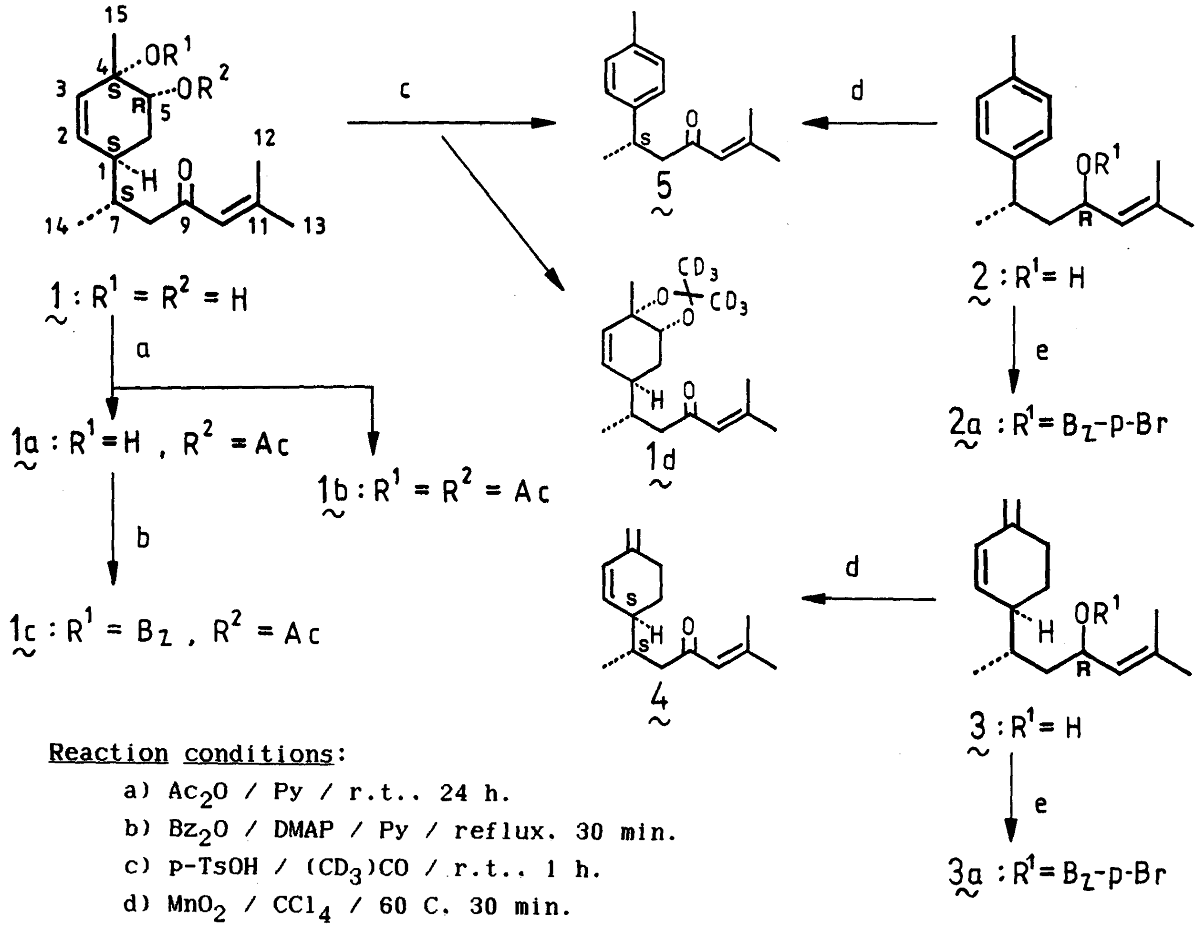
Three new bisabolane sesquiterpenoids, bisacurone (**1**), bisacumol (**2**) and bisacurol (**3**), and one kown compound, curlone (**4**), were isolated from the rhizomes of *Curcuma xanthorrhiza* (Zingiberaceae). The absolute structures of these new compounds were determined by spectroscopy, chemical conversions and the exciton chirality method for allylic alcohols.

KEYWORDS——*Curcuma xanthorrhiza*; Zingiberaceae; bisabolane sesquiterpenoid; bisacurone; bisacumol; bisacurol; curlone; CD; exciton chirality method; allylic alcohol

In our previous papers,[1,2] some bisabolane sesquiterpenoids and diarylheptanoids isolated from *Curcuma xanthorrhiza* (Zingiberaceae) were reported. Further investigation of the chloroform-soluble fraction of this plant afforded three new bisabolane sesquiterpenoids, named bisacurone (**1**), bisacumol (**2**) and bisacurol (**3**), and one already known compound, curlone (**4**).[3] We report here the absolute structures of these new compounds.

The methanol extract of fresh rhizomes of *C. xanthorrhiza* (collected in 1986, in Ciandur, Indonesia) were partitioned between $CHCl_3$ and water. The $CHCl_3$ fraction was chromatographed on a silica gel column and an ODS column to give **1**, **2**, **3** and **4**.

Compound **1**, colorless oil, $[\alpha]_D$ -19.2° (c = 0.15, MeOH). The molecular formula was judged to be $C_{15}H_{24}O_3$ on the basis of the ^{13}C-NMR data and high-resolution MS spectra [no molecular ion appeared (m/z: M^+-18 234.1621, Calcd. 234.1620)]. The UV and IR spectra displayed the characteristic absorptions for hydroxyl and an α,β-unsaturated ketone [IR (CCl_4): 3475, 1690 cm^{-1}, UV (MeOH): 239 nm]. The ^1H-NMR spectrum[4] (in $CDCl_3$) showed signals due to one secondary methyl (δ 0.91, d, J = 6.7 Hz, H-14), one tertiary methyl (δ 1.30, H-15), two vinyl methyls (δ 1.89, d, J = 1.2 Hz, H-13 and 2.14, d, J = 1.2 Hz, H-12), one oxygen bearing methine proton(δ 3.79, dd, J = 7.0, 3.2 Hz, H-5) and three olefinic protons (δ 5.64, 2H, s, H-2, H-3 and 6.07, 1H, qq, J = 1.2, 1.2 Hz, H-10). The presence of one secondary and one tertiary hydroxyl group [δ 73.0 (d) and 70.8 (s)], one disubstituted and one trisubstituted double bond [δ 124.0 (d), 131.4 (d), 132.8 (d) and 155.7 (s)] was established by the signals in its ^{13}C-NMR spectrum, together with the parameters of ^1H-NMR signals. The above spectral data and the molecular formula showed bisacurone to be monocyclic (bisabolane sesquiterpenoid), having a secondary and a tertiary



Reaction conditions:

a) Ac$_2$O / Py / r.t., 24 h.

b) Bz$_2$O / DMAP / Py / reflux, 30 min.

c) p-TsOH / (CD$_3$)CO / r.t., 1 h.

d) MnO$_2$ / CCl$_4$ / 60 C, 30 min.

e) (p-Br-Bz)$_2$O / Py / CH$_2$Cl$_2$ / r.t., 2 h.

Table I. ^{13}C-NMR Data for 1 - 5 (in CDCl$_3$)[4]

No.	1	2	3	4	5
1	37.0(d)	144.0(s)	40.8(d)	40.5(d)	143.7(s)
2	131.4(d)	126.9(d)	129.8(d)	130.1(d)	126.6(d)
3	132.8(d)	129.0(d)	134.7(d)	133.8(d)	129.1(d)
4	70.8(s)	135.1(S)	143.6(s)	143.4(s)	135.5(s)
5	73.0(d)	129.0(d)	30.4(t)	30.1(t)	129.1(d)
6	28.2(t)	126.9(d)	24.5(t)	25.0(t)	126.6(d)
7	33.4(d)	35.8(d)	33.6(d)	33.4(d)	35.3(d)
8	48.9(t)	46.0(t)	42.1(t)	48.7(t)	52.7(t)
9	201.0(s)	66.7(d)	67.3(d)	200.8(s)	199.7(s)
10	124.0(d)	128.8(d)	128.3(d)	124.1(d)	124.1(d)
11	155.7(s)	133.7(s)	135.6(s)	155.0(s)	154.9(s)
12	20.8(q)	18.0(q)	18.3(q)	20.7(q)	20.6(q)
13	27.7(q)	25.6(q)	25.8(q)	27.7(q)	27.6(q)
14	17.2(q)	23.0(q)	16.4(q)	16.6(q)	22.0(q)
15	23.5(q)	20.9(q)	110.1(t)	110.3(t)	20.9(q)

hydroxyl. From homo spin decoupling experiments in the ^{1}H-NMR, the position of two hydroxyls were assigned to C-4 and C-5 and the disubstituted double bond was located at C-2 - C-3.

Acetylation of **1** afforded monoacetate (**1a**) and diacetate (**1b**). Further, **1** gave (+)-ar-turmerone (**5**)$^{5)}$ along with the acetonide (**1d**) of **1** when treated with p-TsOH / acetone-d_6. On the basis of these chemical and spectral data, the planar structure of bisacurone was proposed to be formula **1**.

The fact that **1** was dehydrogenated to give **5** indicated that the absolute configuration at C-7 was *S*. The C-4 and C-5 α-glycol system was cis because the acetonide (**1d**) of **1** was formed readily and the H-5 (δ 4.05, ddd, J = 3.0, 2.0, 1.5 Hz) of **1d** showed a large NOE (14%) in ^{1}H-NMR (in CD_3OD) when the methyl protons at H-15 (δ 1.26) was irradiated. The configuration of H-5 of **1d** was deduced as equatrial due to the small couplings (2.0 and 3.0 Hz) with the protons at H-6 [H-6_{ax}(δ 1.48, ddd, J = 14.0, 11.8, 2.0 Hz), H-6_{eq}(δ 2.00, dddd, J = 14.0, 5.0, 3.0, 1.4 Hz)] and the W-type long-range coupling (1.5 Hz) with H-3 (δ 5.47, ddd, J = 10.0, 2.5, 1.5 Hz) in ^{1}H-NMR. On the other hand, the diheadral angle between H-1 and H-2 of **1d** was about 90° since the H-1 (δ 2.33, m) showed a small coupling (1.5 Hz) with H-2 (δ 5.55, ddd, J = 10.0, 1.5, 1.4 Hz), an allylic coupling (2.5 Hz) with H-3, and a large ax.-ax. coupling (11.8 Hz) with H-6_{ax}. On the basis of these couplings of **1d**, the relative configuration of H-1 and H-5 of **1** was considered to be trans.

The absolute configuration of C-4 was examined by application of the CD exciton chirality method for determining the allylic alcohols.$^{6)}$ **1a** was converted into the benzoate (**1c**). The CD spectrum (in MeOH) of **1c** showed a positive first Cotton effect at 229 nm ($\Delta\varepsilon$ = +6.9), the sign of which is in accordance with the positive chirality between the benzoate and double bond chromophores. Therefore, it was apparent that the absolute configuration of C-4 was determined to be *S*. Consequently, the stereochemistry of C-5 and C-1 were unequivocally determined to be *R* and *S*, respectively.

Compound **2**, colorless oil, $[\alpha]_D$ +13.9°(c = 0.42, EtOH), $C_{15}H_{22}O$ (m/z: M^+ 218.1688, Calcd. 218.1671). IR (CCl_4): 3630 cm^{-1}. The ^{1}H-NMR spectrum (in $CDCl_3$) showed signals due to one secondary methyl (δ 1.23, d, J = 7.0 Hz, H-14), two vinyl methyls (δ 1.53, d, J = 1.3 Hz, H-13 and 1.67, d, J = 1.3 Hz, H-12), one aromatic methyl (δ 2.32, s, H-15), one methine proton adjacent to the hydroxyl group (δ 4.16, ddd, J = 8.5, 8.5, 6.0 Hz, H-9), one olefinic proton (δ 5.15, dqq, J = 8.5, 1.3, 1.3 Hz, H-10) and disubstituted benzene ring (4H, δ 7.10, s). The analysis of ^{1}H- and ^{13}C-NMR spectra allowed the identification of **2** as a sesquiterpenoid of bisabolane type. When the ^{13}C-NMR spectrum of **2** was compared with that of **5**, the C-9 signal at δ 199.7 (s) was found to be shifted highfield to δ 66.7 (d) in **2**. Further, oxidation of **2** with active MnO_2 gave **5** and, conversely, reduction of **5** with $LiAlH_4$ (in ether) gave **2** and its epimer$^{6)}$ (epi-**2**). On the basis of these chemical and spectral data, the planar structure of bisacumol is represented by formula **2**.

From the fact that oxidation of **2** gave **5**, the absolute configuration of C-7 was determined to be *S*. On the other hand, the absolute configuration of C-9 was examined by the CD exciton chirality method for acyclic allylic alcohols.$^{8)}$ **2** and epi-**2** were converted into the p-bromobenzoates (**2a** and epi-**2a**). The CD specta (in $CHCl_3$) of **2a** and epi-**2a** respectively showed a first negative maximum at 251 nm (

$=\Delta\varepsilon$-2.3) and a first positive maximum at 247 nm ($\Delta\varepsilon$ = +6.3) in the region of p-bromobenzoate transition. Consequently, the absolute configuration of C-9 of 2 was concluded to be R.

Compound 3, colorless oil, $[\alpha]_D$ -8.6° (c = 0.33, MeOH), $C_{15}H_{24}O$ (m/z: M^+ 220.1834, Calcd. 220.1827). IR (CCl_4): 3625, 2930, 880 cm^{-1}. The ^{1}H-NMR spectrum ($CDCl_3$) showed signals due to one secondary methyl (δ 0.85, d, J = 6.5 Hz, H-14), two vinyl methyls (δ 1.70, d, J = 1.5 Hz and 1.73, d, J = 1.5 Hz, H-12, 13), one methine proton adjacent to the hydroxyl group (δ4.45, ddd, J = 9.0, 8.0, 7.0 Hz, H-9), and five olefinic protons [(δ 4.74 (2H, br s, H-15), 5.12 (1H, dqq, J = 9.0, 1.5, 1.5 Hz, H-10), 5.65 (1H, d, J = 10.0 Hz, H-3) and 6.15 (1H, dd, J = 10.0, 2.5 Hz, H-2)]. The ^{1}H- and ^{13}C-NMR spectra identified of 3 as a sesquiterpenoid of bisabolane type, having a hydroxyl and terminal methylene. When the ^{13}C-NMR spectrum of 3 was compared with that of 4, the C-9 signal of 4 at δ 200.8 (s) was found to be shifted highfield to δ 67.3 (d) in 3. Further, oxidation of 3 with active MnO_2 gave 4 ($[\alpha]_D$ -10.5°). On the basis of these chemical and spectral data, the planar structure of bisacurol is represented by formula 3.

From the fact that oxidation of 3 gave 4, the absolute configuration of C-1 and C-7 were determined to be S and S, respectively. Moreover, the absolute configuration of C-9 was determined in the same way that 2. 3 was converted into the p-bromobenzoate (3a). The CD spectrum (in $CHCl_3$) of 3a showed a first negative maximum at 251 nm ($\Delta\varepsilon$ = -1.1). Therefore, the absolute configuration of C-9 was concluded to be R.

Compound 4, colorless oil, $[\alpha]_D$ -13.8° (c = 0.77, MeOH), $C_{15}H_{22}O$ (m/z: M^+ 218.1651, Calcd. 218.1671) was identified as curlone, which had already been isolated from Curcuma longa,[3] by comparing its spectral and chemical data with those of an authentic specimen. IR (CCl_4): 2950, 1690, 1630, 885 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ : 0.88 (3H, d, J = 6.5 Hz, H-14), 1.88 and 2.14 (each 3H, d, J = 1.3 Hz, H-12 and H-13), 4.75 (2H, br s, H-15), 5.67 (1H, d, J = 10.0 Hz, H-2), 6.07(1H, qq, J = 1.3 Hz, H-10), 6.16 (1H, dd, J = 10.0, 2.5 Hz, H-3).

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