NEW BISABOLANE SESQUITERPENOIDS FROM THE RHIZOMES OF CURCUMA XANTHORRHIZA (ZINGIBERACEAE) II¹⁾Shin-ichi UEHARA,^a Ichiro YASUDA,^a Koichi TAKEYA,^b Hideji ITOKAWA*,^b and Yoichi IITAKA^c

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Four bisabolane sesquiterpenoids, named bisacurone epoxide (1), bisacurone A (2), bisacurone B (3) and bisacurone C (4), were isolated from the chloroform-soluble fractions of the rhizomes of Curcuma xanthorrhiza (Zingiberaceae). The absolute structures of these new compounds were determined on the basis of their spectral data, chemical conversions and X-ray crystallography. In the process of determining the absolute structure of 1, the stereochemistry reported for bisacurone (5) in our previous paper was revised.

KEYWORDS Curcuma xanthorrhiza; Zingiberaceae; bisabolane sesquiterpenoid; bisacurone epoxide; bisacurone A; bisacurone B; bisacurone C; bisacurone; X-ray crystallography

Recently, we reported three new bisabolane sesquiterpenoids, bisacurone (5) (1.2 g, 0.32 % from the CHCl₃ ext.), bisacumol and bisacurool, from the chloroform-soluble fractions of titled plants (collected in 1986, in Cianjur, Indonesia).¹⁾ Further investigation of the same polar chromatographic fractions have afforded four new bisacurone related compounds, named bisacurone epoxide (1) (25 mg, 0.007 %), bisacurone A (2) (15 mg, 0.004 %), bisacurone B (3) (13 mg, 0.003 %) and bisacurone C (4) (30 mg, 0.008 %). This paper is concerned with the identification of the stereochemistry of these new compounds.

1: colorless oil; $[\alpha]_D^{25} -11.6^\circ$ (c=0.61, MeOH); MS (m/z: M^+ , 268.170, Calcd. 268.167 for C₁₅H₂₄O₄); UV (MeOH): 237 nm (ϵ 9800); IR (CCl₄): 3650, 3570, 3475 (br), 1690, 1620 cm⁻¹; ¹H-NMR (CDCl₃) δ : 1.02 (3H, d, J=6.6 Hz, H-14), 1.36 (3H, s, H-15), 1.44-1.61 (2H, m), 1.89 (3H, d, J=1.0 Hz, H-13), 2.15 (3H, d, J=1.0 Hz, H-12 and 1H, m), 2.20-2.40 (2H, m), 2.62 (1H, dd, J=14.5, 4.0 Hz), 3.04 (1H, dd, J=4.0, 0.9 Hz, H-3), 3.37 (1H, dd, J=4.0, 2.3 Hz, H-2), 3.63 (1H, br dd, J=6.4, 3.5 Hz, H-5), 6.10 (1H, qq, J=1.0, 1.0 Hz, H-10). Its ¹H-NMR spectrum³⁾ is similar to that of 5 except that the signals of H-2 and H-3 of 1 appeared at δ 3.04 and 3.37 instead of the olefinic protons of 5 at δ 5.64. When the ¹³C-NMR spectrum of 1 was compared with that of 5, the signals due to oxygen bearing carbons appeared at δ 57.66 (C-2) and 58.07 (C-3) in place of at δ 131.43 (C-2) and 132.78 (C-3) in 5 (Table I). Further, the epoxidation of 5 with m-CPBA produced 1. Therefore, 1 was ascertained to be an epoxide of 5. The relative stereostructure of 1 was determined by X-ray crystallography of its monoacetate (1a)⁵⁾ (Fig. 2).

The fact that 5 was dehydrated to give (+)-ar-turmerone (6)^{1,2,5)} and the epoxidation of 5 gave 1 indicated that the absolute configuration of 1 was 1R, 2S, 3S, 4R, 5S, 7S. This also indicated that the absolute configuration of 5 was 1R, 4S, 5S, 7S, which was erroneously assigned as 1S, 4S, 5R, 7S in the previous paper.¹⁾ This apparently was due to the formation of acetone (8)⁵⁾ from 5 which occurred by inversion at C-4 via a carbocation mechanism. This was supported by the selective acetone (8) formation of 2, which has a C-4 and C-5 cis α -glycol system (see 2).

2: colorless oil; $[\alpha]_D^{25} -35.9^\circ$ (c=0.9, MeOH); MS (m/z: M^+ , 252.173, Calcd. 252.173 for C₁₅H₂₄O₃); UV (MeOH): 238.5 nm (ϵ 9800); IR (CCl₄): 3575, 3500 (sh), 1690, 1620 cm⁻¹; ¹H-NMR (CDCl₃) δ : 0.87 (3H, d, J=6.6 Hz, H-14), 1.27 (3H, s, H-15), 1.61 (1H, ddd, J=14.0, 9.5, 2.1 Hz), 1.87 (1H, m), 1.89 (3H, d, J=1.0 Hz, H-13), 2.14 (3H, d, J=1.0 Hz, H-12), 2.16-2.45 (4H, m), 3.79 (1H, br d, J=5.5 Hz, H-5), 5.58 (2H, s, H-2 and H-3), 6.06 (1H, qq, J=1.0, 1.0 Hz, H-10).

3: colorless oil; $[\alpha]_D^{25} +9.5^\circ$ (c=0.89, MeOH); MS (m/z: M^+ -18, 234.165, Calcd. 234.162 for C₁₅H₂₂O₂); UV (MeOH): 238 nm (ϵ 10400); IR (CCl₄): 3620, 3563, 3500 (sh), 1690, 1620 cm⁻¹; ¹H-NMR (CDCl₃) δ : 0.87 (3H, d, J=6.6 Hz, H-14), 1.33 (3H, s, H-15), 1.38 (1H, ddd, J=12.0, 12.0, 12.0 Hz), 1.71 (1H, ddd, J=12.0, 4.5, 3.7 Hz), 1.89 (3H, d, J=1.3 Hz, H-13), 2.14 (3H, d, J=1.3 Hz, H-12), 2.15-2.31 (3H, m), 2.45 (1H, dd, J=14.0, 4.6

Crystal system: Monoclinic
 Space group: $P2_1$
 $z = 2$
 $a = 12.714 (7) \text{ \AA}$
 $b = 5.757 (4) \text{ \AA}$
 $c = 12.539 (8) \text{ \AA}$
 $v = 843.9 \text{ \AA}^3$
 $R = 0.04 \%$

Fig. 1. Reaction conditions:

- a: m-CPBA / Benzene / 7°C , 1h.
 b: Ac_2O / Pyridine / r.t., 12h.
 c: p-TsOH / $(\text{CH}_3)_2\text{CO}$ / r.t., 1h.
 d: PCC / CH_2Cl_2 / ice bath, 2h.
 e: p-TsOH / CH_2Cl_2 / r.t., 1h.

Fig. 2. Perspective View of 1a

Table I. ^{13}C -NMR Data for 1 - 5 (δ in CDCl_3)³⁾

C.No.	1	2	3	4	5
1	34.08(d)	35.79(d)	40.78(d)	40.84(d)	37.05(d)
2	57.66(d)	130.76(d)	132.55(d)	130.20(d)	131.43(d)
3	58.07(d)	132.61(d)	133.69(d)	133.93(d)	132.78(d)
4	69.72(s)	70.11(s)	68.99(s)	73.77(s)	70.84(s)
5	71.63(d)	72.69(d)	73.45(d)	75.65(d)	73.04(d)
6	25.81(t)	28.65(t)	29.27(t)	29.62(t)	28.21(t)
7	32.44(d)	32.82(d)	32.73(d)	32.79(d)	33.38(d)
8	48.70(t)	48.56(t)	48.47(t)	48.41(t)	48.91(t)
9	200.69(s)	200.57(s)	200.51(s)	200.42(s)	200.98(s)
10	124.06(d)	123.98(d)	124.03(d)	124.01(d)	124.03(d)
11	155.65(s)	155.59(s)	155.62(s)	155.68(s)	155.74(s)
12	20.78(q)	20.78(q)	20.78(q)	20.78(q)	20.81(q)
13	27.71(q)	27.68(q)	27.68(q)	27.71(q)	27.68(q)
14	17.70(q)	16.41(q)	16.32(q)	15.76(q)	17.17(q)
15	21.55(q)	27.01(q)	25.98(q)	21.87(q)	23.54(q)

Hz), 3.46 (1H, dd, $J=12.0$, 3.7 Hz, H-5), 5.62 (1H, ddd, $J=9.9$, 1.1, 0.8 Hz, H-2), 5.69 (1H, dd, $J=9.9$, 2.3 Hz, H-3), 6.07 (1H, qq, $J=1.3$, 1.3 Hz, H-10).

4: colorless oil; $[\alpha]_D -24.8^\circ$ ($c=0.37$, MeOH); MS (m/z : M^+ , 252.172, Calcd. 252.173 for $C_{15}H_{24}O_3$); UV (MeOH): 238.5 nm (ϵ 11800); IR (CCl_4): 3600, 3425 (br), 1690, 1620 cm^{-1} ; 1H -NMR ($CDCl_3$) δ : 0.83 (3H, d, $J=6.6$ Hz, H-14), 1.23 (3H, s, H-15), 1.36 (1H, ddd, $J=12.3$, 11.5, 10.0 Hz), 1.78 (1H, dddd, $J=10.0$, 6.0, 3.8, 1.4 Hz), 1.89 (3H, d, $J=1.2$ Hz, H-13), 2.14 (3H, d, $J=1.2$ Hz, H-12), 2.15-2.28 (2H, m), 2.31-2.47 (2H, m), 3.78 (1H, dd, $J=12.3$, 3.8 Hz, H-5), 5.41 (1H, ddd, $J=10.0$, 2.0, 1.4 Hz, H-2), 5.59 (1H, dd, $J=10.0$, 2.8 Hz, H-3), 6.06 (1H, qq, $J=1.2$, 1.2 Hz, H-10).

The spectral data of 2, 3 and 4 are similar to those of 5. Detailed studies of the 1H - and ^{13}C -NMR data for 2, 3, 4 and 5 indicated that they had the same planar structure as the bisabolane type, having a C-4 - C-5 α -glycol system.

The α -glycol of 2 was cis because 2 was preferentially converted to acetone (8) when treated with p-TsOH / acetone, but 5 gave 8 accompanied by 6 and 7⁵⁾ under the same condition. Moreover, dehydration of 2 with p-TsOH / CH_2Cl_2 gave 6 and 7. On the basis of this evidence, 2 and 5 are epimers with respect to C-4 and the absolute configuration of 2 is established as 1R, 4R, 5S, 7S.

Oxidation of both 3 and 5 with PCC gave 9.⁵⁾ Therefore, 3 and 5 are epimers with respect to C-5 and it is concluded that the absolute configuration of 3 is 1R, 4S, 5R, 7S. Similarly, oxidation of both 4 and 2 gave 10.⁵⁾ So, 4 and 2 are epimers with respect to C-5 and the absolute configuration of 4 is 1R, 4R, 5R, 7S.

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- 2) V.K.Honwad and A.S.Rao, Tetrahedron, **20**, 2921 (1964).
- 3) The 1H - and ^{13}C -NMR spectra were measured on a JEOL FX-270 NMR spectrometer.
- 4) 5: colorless oil; $[\alpha]_D -19.2^\circ$ ($c=0.15$, MeOH); MS (m/z : M^+ -18, 234.162, Calcd. 234.162 for $C_{15}H_{22}O_2$); UV (MeOH): 239 nm (ϵ 12700); IR (CCl_4): 3625, 3600, 3475 (br), 1690, 1620 cm^{-1} ; 1H -NMR ($CDCl_3$) δ : 0.91 (3H, d, $J=6.7$ Hz), 1.30 (3H, s), 1.72 (1H, ddd, $J=13.9$, 7.1, 6.4 Hz), 1.82 (1H, ddd, $J=13.9$, 7.0, 3.2 Hz), 1.89 (3H, d, $J=1.2$ Hz), 2.14 (3H, d, $J=1.2$ Hz), 2.23 (1H, m), 2.28 (2H, m), 2.46 (1H, dd, $J=14.8$, 4.5 Hz), 3.79 (1H, dd, $J=7.0$, 3.2 Hz), 5.64 (2H, s), 6.07 (1H, qq, $J=1.2$, 1.2 Hz).
- 5) 1a: colorless crystals (hexane); mp.85.5-86.0°C, $[\alpha]_D +15.4^\circ$ ($c=0.25$, MeOH); IR (CCl_4): 1745 cm^{-1} ($COCH_3$); 1H -NMR ($CDCl_3$) δ : 1.01 (3H, d, $J=6.3$ Hz), 1.31 (3H, s), 1.89 (3H, d, $J=1.0$ Hz), 2.05 (3H, s, $COCH_3$), 2.15 (3H, d, $J=1.0$ Hz), 3.03 (1H, dd, $J=4.1$, 1.8 Hz), 3.40 (1H, dd, $J=4.1$, 1.8 Hz), 4.73 (1H, br ddd, $J=5.5$, 3.0, 1.0 Hz), 6.07 (1H, qq, $J=1.0$ Hz). 6: colorless oil; $[\alpha]_D +70.4^\circ$ ($c=0.55$, MeOH); IR (CCl_4): 1690, 1620 cm^{-1} ; 1H -NMR ($CDCl_3$) δ : 1.24 (3H, d, $J=6.9$ Hz), 1.85 (3H, d, $J=1.3$ Hz), 2.10 (3H, d, $J=1.3$ Hz), 2.30 (3H, s), 2.60 (1H, dd, $J=15.8$, 8.1 Hz), 2.70 (1H, dd, $J=15.8$, 6.1 Hz), 3.29 (1H, ddd, $J=8.1$, 6.9, 6.1 Hz), 6.02 (1H, qq, $J=1.3$, 1.3 Hz), 7.10 (4H, s). 7: colorless oil; $[\alpha]_D -11.5^\circ$ ($c=0.45$, MeOH); IR (CCl_4): 900 cm^{-1} ($=CH_2$); 1H -NMR ($CDCl_3$) δ : 0.91 (3H, d, $J=6.3$ Hz), 1.88 (3H, d, $J=1.3$ Hz), 2.14 (3H, d, $J=1.0$ Hz), 4.43 (1H, br t, $J=3.5$ Hz), 4.96 (1H, br s), 5.06 (1H, br s), 5.76 (1H, br d, $J=10.0$ Hz), 6.06 (1H, qq, $J=1.3$, 1.0 Hz), 6.15 (1H, d br d, $J=10.0$, 2.0 Hz). 8: colorless oil; $[\alpha]_D -23.0^\circ$ ($c=0.30$, MeOH); IR (CCl_4): 1690, 1620 cm^{-1} ; 1H -NMR (CD_3OD) δ : 0.85 (3H, d, $J=6.5$ Hz), 1.26 (3H, s), 1.29 (3H, s), 1.33 (3H, s), 1.91 (3H, d, $J=1.0$ Hz), 2.12 (3H, d, $J=1.0$ Hz), 4.05 (1H, ddd, $J=3.0$, 2.0, 1.5 Hz), 5.47 (1H, ddd, $J=10.0$, 2.5, 1.5 Hz), 5.55 (1H, ddd, $J=10.0$, 1.5, 1.4 Hz), 6.19 (1H, qq, $J=1.0$, 1.0 Hz). 9: colorless oil; $[\alpha]_D -37.2^\circ$ ($c=0.49$, MeOH); IR (CCl_4): 1720 cm^{-1} ($-CO$); 1H -NMR ($CDCl_3$) δ : 0.84 (3H, d, $J=6.6$ Hz), 1.41 (3H, s), 1.88 (3H, d, $J=1.3$ Hz), 2.14 (3H, d, $J=1.3$ Hz), 3.44 (1H, br s, OH), 5.71 (1H, d br d, $J=10.0$, 3.1 Hz), 5.85 (1H, dd, $J=10.0$, 1.2 Hz), 6.03 (1H, qq, $J=1.3$, 1.3 Hz). 10: colorless oil; $[\alpha]_D +29.1^\circ$ ($c=0.13$, MeOH); IR (CCl_4): 1726 cm^{-1} ($-CO$); 1H -NMR ($CDCl_3$) δ : 0.94 (3H, d, $J=6.9$ Hz), 1.46 (3H, s), 1.90 (3H, d, $J=1.0$ Hz), 2.15 (3H, d, $J=1.0$ Hz), 3.58 (1H, br s, OH), 5.59 (1H, ddd, $J=10.2$, 2.0, 1.2 Hz), 5.79 (1H, dd, $J=10.2$, 2.6 Hz), 6.06 (1H, qq, $J=1.0$, 1.0 Hz).

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