NEW BISABOLANE SESQUITERPENOIDS FROM THE RHIZOMES OF CURCUMA XANTHORRHIZA (ZINGIBERACEAE) II[1)]

Shin-ichi UEHARA,[a] Ichiro YASUDA,[a] Koichi TAKEYA,[b] Hideji ITOKAWA*,[b] and Yoichi IITAKA[c]
The Tokyo Metropolitan Research Laboratory of Public Health,[a] 24-1, Hyakunincho 3 chome, Shinjuku-ku, Tokyo 169, Department of Pharmacognosy, Tokyo College of Pharmacy,[b] Horinouchi 1432-1, Hachioji, Tokyo 192-03 and Faculty of Medicine, Teikyo University,[c] Ohtsuka 359, Hachioji, Tokyo 192-03, Japan

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 $CHCl_3$ ext.), bisacumol and bisacurol, 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; $[\alpha]_D$ -11.6° (c=0.61, MeOH); MS (m/z: M^+, 268.170, Calcd. 268.167 for $C_{15}H_{24}O_4$); UV (MeOH): 237 nm (ε 9800); IR (CCl_4): 3650, 3570, 3475 (br), 1690 , 1620 cm^{-1}; ^{1}H-NMR ($CDCl_3$)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 ^{1}H-NMR spectrum[3)] 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 ^{13}C-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 acetonide (8)[5)] from 5 which occurred by inversion at C-4 via a carbocation mechanism. This was supported by the selective acetonide (8) formation of 2, which has a C-4 and C-5 cis α-glycol system (see 2).

2: colorless oil; $[\alpha]_D$ -35.9° (c=0.9, MeOH); MS (m/z: M^+, 252.173, Calcd. 252.173 for $C_{15}H_{24}O_3$); UV (MeOH): 238.5 nm (ε 9800); IR (CCl_4): 3575, 3500 (sh), 1690, 1620 cm^{-1}; ^{1}H-NMR ($CDCl_3$) 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; $[\alpha]_D$ +9.5° (c=0.89, MeOH); MS (m/z: M^+-18, 234.165, Calcd. 234.162 for $C_{15}H_{22}O_2$); UV (MeOH): 238 nm (ε 10400); IR (CCl_4): 3620, 3563, 3500 (sh), 1690, 1620 cm^{-1}; ^{1}H-NMR ($CDCl_3$) 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

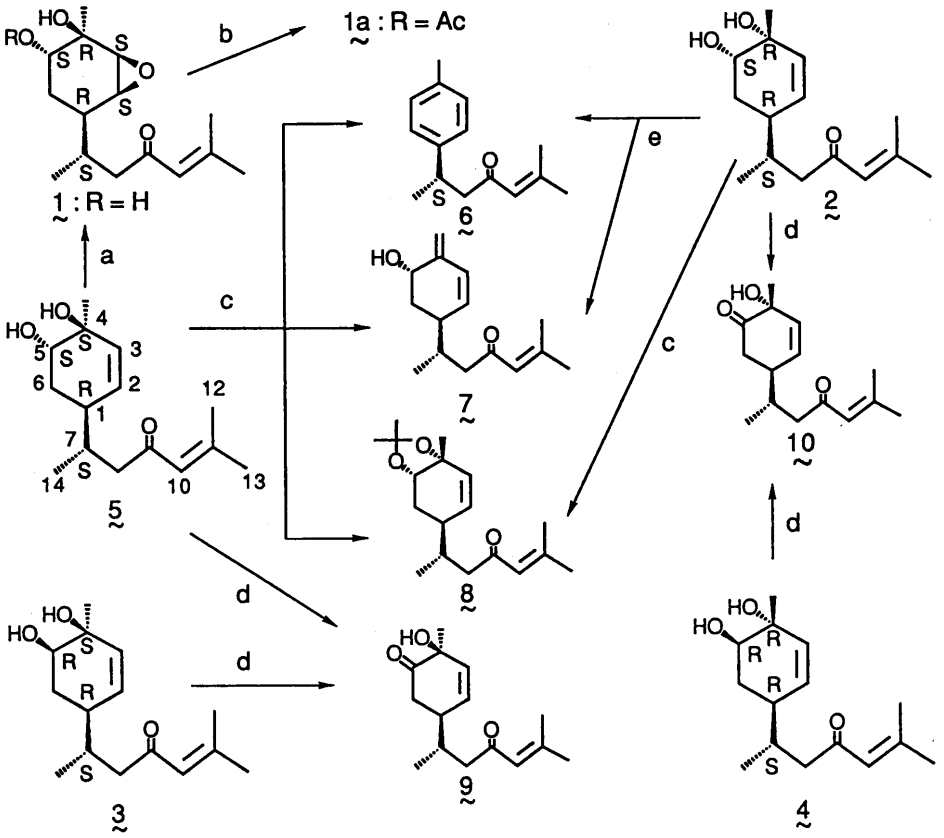

Fig. 1. Reaction conditions:
a: m-CPBA / Benzene / 7 °C, 1h.
b: Ac_2O / Pyridine / r.t., 12h.
c: p-TsOH / $(CH_3)_2CO$ / r.t., 1h.
d: PCC / CH_2Cl_2 / ice bath, 2h.
e: p-TsOH / CH_2Cl_2 / r.t., 1h.

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

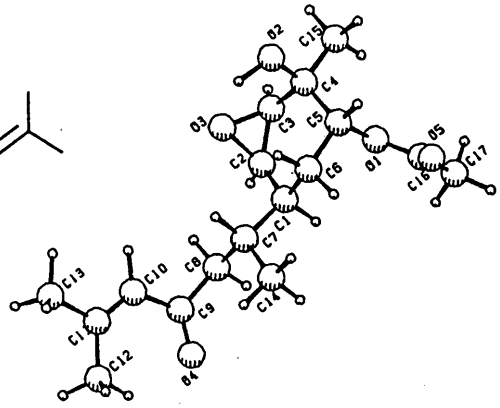

Fig. 2. Perspective View of 1a

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° (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}; ^{1}H-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 ^{1}H- 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 acetonide (8) when treated with p-TsOH / acetone, but 5 gave 8 accompanied by 6 and 7[5] 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.

ACKNOWLEDGEMENT We thank Mr. S. Hemmi, P.T.EISAI INDONESIA and Dr. K. Kagei, Tsukuba Research Laboratories, Eisai Co., Ltd. for the supply of C. xanthorrhiza.

REFERENCES AND NOTES

1) S.Uehara, I.Yasuda, K.Takeya and H.Itokawa, Chem.Pharm.Bull.,37, 237 (1989).

2) V.K.Honwad and A.S.Rao, Tetrahedron, 20, 2921 (1964).

3) The ^{1}H- and ^{13}C-NMR spectra were measured on a JEOL FX-270 NMR spectrometer.

4) 5: colorless oil; $[\alpha]_D$ -19.2° (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}; ^{1}H-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°(c=0.25, MeOH); IR (CCl_4): 1745 cm^{-1} ($\underline{COCH_3}$); ^{1}H-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° (c=0.55, MeOH); IR (CCl_4): 1690, 1620 cm^{-1} ; ^{1}H-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° (c=0.45, MeOH); IR (CCl_4): 900 cm^{-1}(=CH_2); ^{1}H-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° (c=0.30, MeOH); IR (CCl_4): 1690, 1620 cm^{-1}; ^{1}H-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° (c=0.49, MeOH); IR (CCl_4): 1720 cm^{-1}(-CO); ^{1}H-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°(c=0.13, MeOH); IR (CCl_4): 1726 cm^{-1}(-CO); ^{1}H-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).

(Received October 13, 1989)