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SESQUITERPENES FROM *SEVERINIA BUXIFOLIA*

TIAN-SHUNG WU, MASATAKE NIWA and HIROSHI FURUKAWA

Faculty of Pharmacy, Meijo University, Tempaku, Nagoya 468, Japan

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Key Word Index—*Severinia buxifolia*; Rutaceae; sesquiterpene; α-santalen-11-one; α-santalene epoxide; dihydro-α-santalen-12-one; α-santalene; (*E*)-5-(2,3-dimethyl-3-nortricyclyl)pent-3-en-2-one; $\Delta^{13,14}$-iso-α-santalol; α-photosantalol A; ^{1}H NMR; ^{13}C NMR.

Abstract—Three new sesquiterpenes were isolated from *Severinia buxifolia*, and identified as α-santalen-11-one, dihydro-α-santalen-12-one, and 12,13-epoxy-α-santalene, respectively. α-Photosantalol A, $\Delta^{13,14}$-iso-α-santalol, α-santalene and (*E*)-5-(2,3-dimethyl-3-nortricyclyl)pent-3-en-2-one were also isolated and characterized.

INTRODUCTION

In a previous paper, we reported on the presence of several acridone alkaloids in the root-bark of *Severinia buxifolia* [1]. A further study on the constituents of the same plant has resulted in the isolation of three new sesquiterpenes having the same carbon skeleton as α-santalene (**6**), along with four known sesquiterpenes. The present paper describes the isolation and structure elucidation of the new sesquiterpenes.

RESULTS AND DISCUSSION

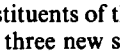
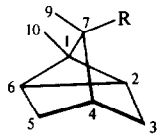
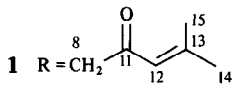
The hexane fraction obtained from the ethanolic extract of the root-bark of S. *buxifolia* [1] was rechromatographed over silica gel to give seven sesquiterpenes, **1**–**7**. **1** had a molecular formula of $C_{15}H_{22}O$ and its IR (1670 and 1610 cm^{-1}), UV (240 nm), ^{1}H NMR [δ 1.86 (3H, *s*), 2.11 (3H, *s*), 2.29 (2H, *s*) and 6.06 (1H, *s*)] and ^{13}C NMR [δ 20.5 (*q*), 27.6 (*q*), 47.9 (*t*), 125.4 (*d*), 153.5 (*s*) and 200.8 (*s*)] spectra together with a mass fragmentation ion peak at *m/z* 121 $[M-C_6H_9O]^+$ strongly suggested the presence of the partial structure  in **1**. The close resemblance of the ^{13}C NMR spectrum of **1** to that of the tricyclene (**8**) [2] (Table 1) indicated the presence of a tricyclene-type carbon skeleton in **1**. Treatment of **1** with sodium methoxide in MeOD gave a deuterio-compound, whose ^{13}C NMR spectrum showed no signals corresponding to those at δ 20.5 (*q*), 27.6 (*q*), 47.9 (*t*), and 125.4 (*d*) in the spectrum of **1**. Reduction of **1** with sodium borohydride in methanol afforded a colourless oil, which was found to be identical with α-photosantalol A (**2**) by comparison (IR, ^{1}H NMR, and $[\alpha]_D$) with an authentic sample [3]. On the basis of these results, **1** should be represented by the structure cor-

Table 1. ^{13}C NMR data of *Severinia* sesquiterpenes [25 MHz, $CDCl_3$ (**1**, **3**–**5**) or neat (**2**, **6**, **7**), TMS as int. standard]

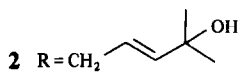
C	1	2	3	4	5	6	7	8 [2]
1	27.3 (*s*)	26.9 (*s*)	27.3 (*s*)	27.3 (*s*)	27.3 (*s*)	27.5 (*s*)	27.2 (*s*)	26.3 (*s*)
2	19.4 (*d*)*	19.6 (*d*)*	19.6 (*d*)*	19.8 (*d*)	19.5 (*d*)	19.8 (*d*)	19.6 (*d*)	20.6 (*d*)
3	31.4 (*t*)	31.2 (*t*)†	31.5 (*t*)†	31.4 (*t*)*	31.4 (*t*)*	31.7 (t)*	31.6 (t)*	31.3 (t)
4	38.6 (d)	38.4 (d)	38.2 (d)	38.2 (d)	38.1 (d)	38.5 (d)	38.7 (d)	41.8 (d)
5	31.4 (t)	31.1 (t)†	31.0 (*t*)†	31.0 (*t*)*	31.0 (*t*)	31.2 (*t*)*	31.2 (*t*)*	31.3 (*t*)
6	18.8 (*d*)*	19.6 (*d*)*	19.5 (*d*)*	19.8 (*d*)	19.5 (*d*)	19.8 (*d*)	19.6 (*d*)	20.6 (*d*)
7	46.1 (*s*)	46.3 (*s*)	45.5 (*s*)	45.5 (*s*)	45.6 (*s*)	46.0 (*s*)	46.6 (*s*)	43.1 (*s*)
8	47.9 (*t*)	37.1 (*t*)	28.3 (*t*)	29.8 (*t*)	30.6 (*t*)	23.6 (*t*)	37.6 (*t*)	19.4 (*q*)
9	18.1 (*q*)	17.4 (*q*)	17.3 (*q*)	17.3 (*q*)†	17.4 (*q*)	17.5 (*q*)†	17.6 (*q*)	19.4 (*q*)
10	10.7 (*q*)	10.8 (*q*)	10.6 (*q*)	10.7 (*q*)	10.6 (*q*)	10.8 (*q*)	10.6 (*q*)	9.4 (*q*)
11	200.8 (*s*)	123.0 (*d*)	36.0 (*t*)	29.8 (*t*)	24.3 (*t*)	34.8 (*t*)	132.9 (*d*)	
12	125.4 (*d*)	140.4 (*d*)	214.9 (*s*)	76.6 (*d*)	64.5 (*d*)	125.7 (*d*)	144.4 (*d*)	
13	153.5 (*s*)	70.2 (*s*)	40.8 (*d*)	147.4 (*s*)	57.8 (*s*)	129.9 (*s*)	195.9 (*s*)	
14	27.6 (*q*)	30.1 (*q*)	18.3 (*q*)	111.2 (*q*)	24.9 (*q*)	25.7 (*q*)	26.6 (*q*)	
15	20.5 (*q*)	30.1 (*q*)	18.3 (*q*)	17.5 (*q*)†	18.6 (*q*)	17.7 (*q*)†		

*,† Values with same superscript can be interchanged.
Numbering system used was according to ref. [7].





1 R = CH_2



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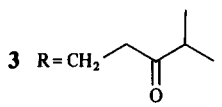

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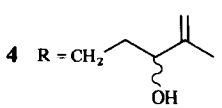
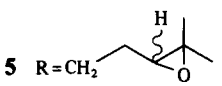
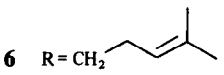


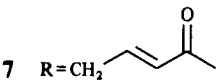
4 R = CH_2



5 R = CH_2

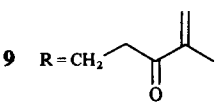


6 R = CH_2



7 R = CH_2

8 R = Me



9 R = CH_2

responding to α-santalen-11-one which was synthesized by Corey *et al.* in 1957 [4]. This is the first report of the occurrence of α-santalen-11-one (**1**) in Nature.

3 was also a tricyclic sesquiterpene with a molecular formula $C_{15}H_{24}O$. An IR absorption band at 1710 cm^{-1} was assignable to an isolated carbonyl group. The appearance of a mass fragment peak at *m/z* 121, as in **1**, coupled with the ^1H NMR [δ 0.80 (3H, *s*) and 1.01 (3H, *s*)] and ^{13}C NMR (Table 1) data suggested the carbon skeleton of **3** was the same as that of **1**. In the ^{13}C NMR spectrum of the base-catalysed deuterated compound of **3**, the absence of both signals at δ 36.0 (*t*) and 40.8 (*d*) found in the spectrum of **3**, showed that the carbonyl group was at C-12. Oxidation of $\Delta^{13,14}$-iso-α-santalol (**4**) [3, 5] with chromium trioxide in pyridine followed by catalytic hydrogenation using 10% Pd–C in methanol provided the corresponding saturated carbonyl compound, which was found to be identical with the natural sample of **3** (IR, ^1H NMR and MS).

*Stereochemistry at the carbon (C-12) bearing an oxirane ring remains unsettled.

5 was assigned to be a tricyclene type sesquiterpene, the same as **1** and **3**, from its spectral data. In addition, the presence of an epoxy group was indicated by the ^1H NMR and ^{13}C NMR spectra of this compound [δ_H 1.26 (3H, *s*), 1.30 (3H, *s*) and 2.66 (1H, *m*); δ_C 57.8 (*s*) and 64.5 (*d*)]. The structure of this compound was established by the identification with **5** prepared from α-santalene (**6**) with *m*-chloroperbenzoic acid in ether*.

In addition to these new sesquiterpenes, α-photosantalol A (**2**) [3], $\Delta^{13,14}$-iso-α-santalol (**4**) [3, 5], α-santalene (**6**) [3, 6], and (*E*)-5-(2,3-dimethyl-3-nortricyclyl)pent-3-en-2-one (**7**) [3, 6] were isolated and characterized by comparison with authentic samples.

EXPERIMENTAL

UV: MeOH; IR: $CHCl_3$, except where noted; ^1H NMR (100 MHz) and ^{13}C NMR (25 MHz): $CDCl_3$, unless otherwise stated, TMS as int. standard; MS: direct inlet system; $[\alpha]_D$: $CHCl_3$ at 23°c.

Extraction and separation. The *n*-hexane fraction obtained from the EtOH extract of the root-bark (4.2 kg) of *S. buxifolia* (Poir.) Tenore as described in the previous paper [1] was rechromatographed over silica gel, and eluted with *n*-hexane and then *n*-hexane–iso-Pr_2O (4:1) to give seven sesquiterpenes, **1** (4.5 g), **2** (6.3 g), **3** (0.2 g), **4** (0.3 g), **5** (0.1 g), **6** (2.4 g) and **7** (1.2 g).

α-Santalen-11-one (**1**). Colourless oil, $[\alpha]_D$ −47.8° (*c* 5.0) [lit. [4]: −47.6° (EtOH)]. (Found: $[M]^+$ 218.1675; $C_{15}H_{22}O$ requires 218.1669). UV λ_{max} 240 nm (log ε 4.10) [lit. [4]: 238 nm (log ε 4.05)]; IR ν_{max} cm^{-1}: 3040, 1670, 1610; ^1H NMR: δ 0.83 (3H, *s*), 1.02 (3H, *s*), 1.86 (3H, *s*), 2.11 (3H, *s*), 2.29 (3H, *s*), 6.06 (1H, *s*); MS *m/z* (rel. int.): 218 $[M]^+$ (3), 151 (26), 121 (12), 105 (23), 93 (18), 83 (100), 55 (34), 43 (18), 40 (21). The direct comparison of our compound with Corey's synthetic one has not been made.

α-Photosantalol (**2**). Colourless oil, $[\alpha]_D$ −20.7° (*c* 5.0). IR ν_{max} cm^{-1}: 3590, 3040, 1660 (w), 1370, 975; ^1H NMR: δ 0.80 (3H, *s*), 1.01 (3H, *s*), 1.31 (6H, *s*), 5.60 (2H, *m*); MS *m/z*: 220 $[M]^+$, 202, 121.

Dihydro-α-santalen-12-one (**3**). Colourless oil, $[\alpha]_D$ +3.7° (*c* 1.28). (Found: $[M]^+$ 220.1811; $C_{15}H_{24}O$ requires 220.1825). IR ν_{max} cm^{-1}: 3040, 1710, 850; ^1H NMR: δ 0.80 (3H, *s*), 1.02 (3H, *s*), 1.10 (6H, *d*, *J* = 7 Hz), 2.35 (2H, *m*), 2.60 (1H, *sept*, *J* = 7 Hz); MS *m/z* (rel. int.): 220 $[M]^+$ (13), 177 (12), 151 (11), 138 (21), 121 (63), 119 (37), 105 (36), 93 (100), 91 (47), 83 (36), 55 (34), 42 (94), 40 (64). This was found to be identical with **3** prepared from **9** by catalytic hydrogenation (see below).

$\Delta^{13,14}$-Iso-α-santalol (**4**). Colourless oil, $[\alpha]_D$ +0.5 (*c* 4.0). (Found: $[M]^+$ 220.1836; $C_{15}H_{24}O$ requires 220.1825.) IR ν_{max} cm^{-1}: 3340, 3040, 1645, 1450; ^1H NMR: δ 0.82 (3H, *s*), 1.00 (3H, *s*), 1.70 (3H, *s*), 2.28 (1H, *br s*, OH), 3.94 (1H, *t*, *J* = 6 Hz), 4.78 (1H, *br s*), 4.88 (1H, *br s*).

12,13-Epoxy-α-santalene (**5**). Colourless oil, $[\alpha]_D$ +2.4° (*c* 5.5). (Found: $[M]^+$ 220.1824; $C_{15}H_{24}O$ requires 220.1825.) IR ν_{max} cm^{-1}: 3040, 1230, 820; ^1H NMR: δ 0.82 (3H, *s*), 1.02 (3H, *s*), 1.26 (3H, *s*), 1.30 (3H, *s*), 2.66 (1H, *m*); MS *m/z* (rel. int.): 220 $[M]^+$ (3), 151 (23), 138 (40), 121 (60), 119 (33), 107 (25), 105 (51), 95 (38), 93 (100), 91 (50), 83 (81), 55 (47), 42 (71), 40 (74). This was found to be identical with **5** prepared from **6** (see below).

α-Santalene (**6**). Colourless oil, $[\alpha]_D$ +12.0° (*c* 5.0). IR ν_{max} cm^{-1}: 3040, 1575, 1450; ^1H NMR: δ 0.82 (3H, *s*), 0.99 (3H, *s*), 1.60 (3H, *s*), 1.67 (3H, *s*), 5.08 (1H, *m*).

(E)-5-(2,3-Dimethyl-3-nortricyclyl)pent-3-en-2-one (**7**). Colourless oil, $[\alpha]_D$ −25.8° (*c* 10.0). IR ν_{max} cm^{-1}: 3040, 1690, 1665, 1620, 1360; ^1H NMR: δ 0.86 (3H, *s*), 1.05 (3H, *s*), 2.23 (3H, *s*), 6.06 (1H, *d*, *J* = 15 Hz), 6.79 (1H, *dt*, *J* = 7.5, 15 Hz), 2.10 (2H, *d*, *J* = 7.5 Hz).

Deuteration of α-santalen-11-one (**1**). A soln of **1** (105 mg) in MeOD (7 ml) containing MeONa (81 mg) was heated under reflux for 5 hr and diluted with H_2O (15 ml), and extracted with *n*-hexane to give a colourless oil, which on prep. TLC (silica gel, C_6H_6) afforded a deuterated compound (39 mg). MS *m/z* 227 $[M]^+$. In the similar treatment of **1** in MeOH, the starting material was recovered.

Reduction of α-santalen-11-one (**1**). **1** (1.0 g) was treated with $NaBH_4$ (1.2 g) in MeOH (10 ml) for 2 hr. The usual work-up gave a colourless oil, which was chromatographed on silica gel ($CHCl_3$) to afford a colourless oil (0.65 g). This was found to be identical with α-photosantalol A (**2**) by comparison (IR, ^1H NMR and $[\alpha]_D$) with the authentic sample.

Deuteration of dihydro-α-santalen-12-one (**3**). **3** (20 mg) was treated with MeONa (10 mg) in MeOD (5 ml) under reflux for 5 hr, followed by dilution, extraction and concn to give the deuterated compound (19 mg). MS *m/z* 223 $[M]^+$. Similar treatment of **3** in MeOH gave the starting material.

Oxidation of $\Delta^{13,14}$*-iso-α-santalol* (**4**). A soln of **4** (30 mg) in pyridine (0.5 ml) was added to a soln of CrO_3 (0.1 g) in pyridine (2 ml) and stirred at room temp. for 1 hr. The usual work-up led to a pale brown oil, which was purified by prep. TLC (silica gel, C_6H_6–*n*-hexane, 1:1) to give **5** as a colourless oil (15 mg). UV λ_{max} 220 nm; IR ν_{max} cm^{-1}: 3040, 1670, 1630, 850; ^1H NMR: δ 0.82 (3H, *s*), 1.01 (3H, *s*), 1.85 (3H, *s*), 2.58 (2H, *m*), 5.74 (1H, *s*), 5.93 (1H, *s*); MS *m/z*: 218 $[M]^+$, 203, 121 (100%), 105, 93, 91, 81, 79, 69.

Catalytic hydrogenation of **9**. A mixture of **9** (15 mg) and 10% Pd–C (10 mg) in MeOH (5 ml) was stirred in H_2 at room temp. for 30 min, and then filtered. The filtrate was concd to give a **3** as a colourless oil (15 mg).

Epoxidation of α-santalene (**6**). A soln of **6** (50 mg) and *m*-chloroperbenzoic acid (55 mg) in Et_2O (10 ml) was stirred at room temp. for 3 hr. The Et_2O soln was successively washed with aq. 5% Na_2CO_3 and satd NaCl, dried and concd to give a colourless oil, **5** (45 mg).

Identification of known compounds, α-photosantalol A (**2**), $\Delta^{13,14}$-iso-α-santalol (**4**), α-santalene (**6**) and (*E*)-5-(2,3-dimethyl-3-nortricyclyl)pent-3-en-2-one (**7**) involved direct comparison with authentic samples.

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