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# Structures of merrilactones B and C, novel anislactone-type sesquiterpenes from *Illicium merrillianum*, and chemical conversion of anislactone B to merrilactone A

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**Abstract**—Two new anislactone-type sesquiterpenes, merrilactones B (**1**) and C (**2**) were isolated from the pericarps of *Illicium merrillianum* along with anislactones A (**4**) and B (**5**). Their structures were elucidated by spectroscopic methods and chemical transformation and the structure of merrilactone C was established by X-ray crystallographic analysis of its methyl derivative. Merrilactone A (**3**), a unique anislactone-type sesquiterpene showing neurite outgrowth promoting activity, was effectively synthesized from anislactone B. 

## 1. Introduction

In 1989, Kouno reported the first isolation of anislactones A (**4**) and B (**5**) from *Illicium anisatum*.[1,2] Since then, no anislactone-type sesquiterepenes had been documented before we reported the isolation of 7-*O*-acetoxyanislactone B (**6**).[3] Anislactone-type sesquiterpenes have a unique carbon skeleton, which consists of the two consecutive five-membered ring framework fused with two γ-lactones. Certainly, they cannot be categorized to the previously known *seco*-prezizaane-type sesquiterpenes,[4] which commonly occur in *Illicium* species, and thus have been referred as chemical characteristics of the *Illicium* genus. The biosynthesis in *Illicium* species is not likely to prefer the accumulation of anislactone-type sesquiterpenes in light of the previous studies.[5–9] Recently, we have found that the pericarps of *I. merrillianum* A. C. Smith indigenous to southwestern China are rich in anislactone-type sesquiterpenes such as merrilactone A (**3**),[10] **4**, **5**, and **6** (Fig. 1). Thus, this plant has been shown to occupy a unique taxonomical place as the first *Illicium* plant producing an abundant of anislactone-type compounds as well as yielding a number of *seco*-prezizaane-type sesquiterpenes[11,12] including biosynthetically significant tashironin (**7**)[13,14] and 11-*O*-debenzoyltashironin (**8**).[14]

In this paper, we report the further studies on the structures of two novel anislactone-type sesquiterpenes named

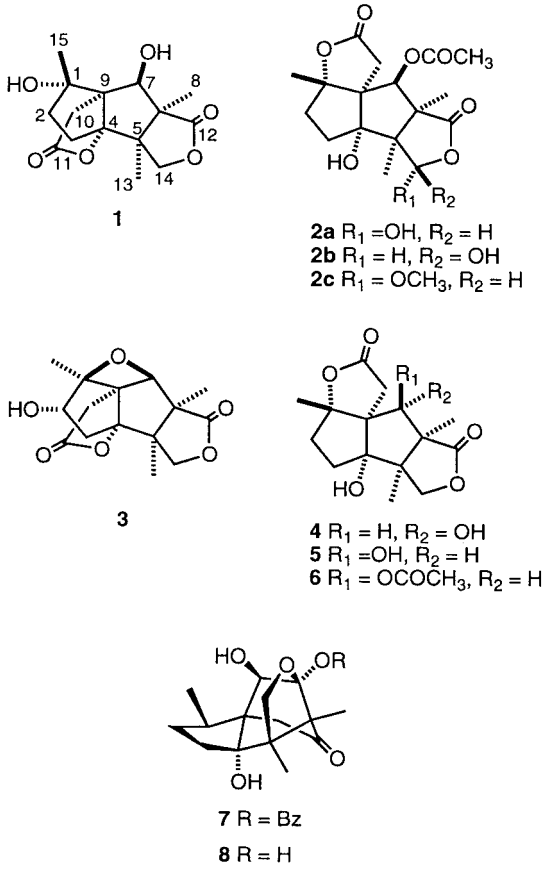


**Figure 1.**

*Keywords*: *Illicium*; sesquiterpene; structure; synthesis; anislactone; merrilactone.

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**Table 1.** $^1$H NMR spectral data of compounds **1**, **2a**, **2c** and **5**

| H | **1**[a] | **2a**[a] | **2c**[b] | **5**[c] |
|---|---|---|---|---|
| 2 | 1.89 dd (13.2, 7.2) | 1.99 ddd (14.6, 11.0, 8.8) | 2.14 m | 2.04 m |
| 2 | 2.19 ddd (13.2, 13.2, 7.8) | 2.32 ddd (14.6, 8.5, 2.5) | 2.51 m | 2.20 m |
| 3 | 1.96 dd (13.8, 7.8) | 1.78 ddd (14.0, 11.0, 8.5) | 2.26 m | 1.72 m |
| 3 | 2.03 ddd (13.8, 13.2, 7.2) | 2.45 ddd (14.0, 8.8, 2.5) | 2.53 m | 2.08 m |
| 7 | 4.03 s | 5.30 s | 5.69 s | 3.91 s |
| 8 | 1.22 s | 1.22 s | 1.39 s | 1.09 s |
| 10 | 2.33 d (19.2) | 2.89 d (16.8) | 3.15 d (16.8) | 2.73 d (16.6) |
| 10 | 3.15 d (19.2) | 3.05 d (16.8) | 3.45 d (16.8) | 2.97 d (16.6) |
| 13 | 1.14 s | 1.06 s | 1.33 s | 1.10 d (0.8) |
| 14 | 3.96 d (9.0) | 6.05 s | 5.67 s | 3.85 d (8.5) |
| 14 | 4.39 d (9.0) | | | 4.46 dd (8.5, 0.8) |
| 15 | 1.42 s | 1.38 s | 1.46 s | 1.58 s |
| $COCH_3$ | | 2.06 s | 2.15 s | |
| $OCH_3$ | | | 3.49 s | |

[a] 600 MHz, $CD_3OD$.
[b] 600 MHz, $C_5D_5N$.
[c] 300 MHz, $CD_3OD$.

merrilactones B (**1**) and C (**2**) isolated from *I. merrillianum* and an effective synthesis of merrilactone A from anislactone B, and wish to propose a plausible biosynthetic pathway leading to anislactone-type sesquiterpenes based on chemical transformation of **5**.

## 2. Results and discussion

### 2.1. Structure of merrilactones B (1) and C (2)

Merrilactones B (**1**) and C (**2**) were isolated from the methanol extract of the pericarps of *I. merrillianum* by a combination of various chromatographic methods.

Merrilactone B (**1**)[15] had the same molecular formula, $C_{15}H_{20}O_6$, as anislactones A (**4**) and B (**5**) established by high resolution FAB-MS. The $^1$H NMR spectrum (Table 1) of **1** showed the singlet signals at $\delta_H$ 1.14, 1.22 and 1.42 due to three tertiary methyl groups and two sets of isolated methylene signals at $\delta_H$ 2.33 (d, $J$=19.2 Hz) and 3.15 (d, $J$=19.2 Hz), and 3.96 (d, $J$=9.0 Hz) and 4.39 (d, $J$=9.0 Hz). The $^{13}$C NMR data ($\delta_C$ 178.8 and 181.2) and IR absorption (1750 $cm^{-1}$) indicated the presence of two γ-lactones. These data (Tables 1 and 2) were found to be similar to those of **5**. There were, however, large differences in resonance for C-1 and C-4: C-1 and C-4 in **1** were higher-field shifted by 16.5 ppm and lower-field shifted by 15.7 ppm than those of **5**, respectively, indicating that one γ-lactone ring was closed to the hydroxyl group on the C-4 position. This mode of lactone formation was supported not only by the C-4 chemical shift similar to that ($\delta_C$ 107.3) of merrilactone A (**3**)[10] but also by the routine analysis of HMBC as shown in Fig. 2. The relative stereochemistry of **1** was elucidated on the basis of the NOESY data as shown in Fig. 3. The C-15 methyl group was clarified to take a β-configuration since it showed the distinct NOE correlation with H-7 which had a cross peak to the α-oriented C-8 methyl group. Thus, the structure of merrilactone B was represented as **1**.

**Table 2.** $^{13}$C NMR data of compounds **1**, **2a**, **2c** and **5**

| C | **1**[a] | **2a**[a] | **2c**[b] | **5**[c] |
|---|---|---|---|---|
| 1 | 80.5 | 97.9 | 95.8 | 99.3 |
| 2 | 43.3 | 39.2 | 38.7 | 39.5 |
| 3 | 33.6 | 36.7 | 36.7 | 37.1 |
| 4 | 107.3 | 92.2 | 91.8 | 92.1 |
| 5 | 57.3 | 62.6 | 60.7 | 58.4 |
| 6 | 64.9 | 63.5 | 61.3 | 63.3 |
| 7 | 84.4 | 84.1 | 82.8 | 84.3 |
| 8 | 17.9 | 17.1 | 17.6 | 15.7 |
| 9 | 69.5 | 68.0 | 66.9 | 69.2 |
| 10 | 37.8 | 38.5 | 37.7 | 38.8 |
| 11 | 178.8 | 177.1 | 174.5 | 178.3 |
| 12 | 181.2 | 177.4 | 176.8 | 181.6 |
| 13 | 18.4 | 11.8 | 13.0 | 18.6 |
| 14 | 75.3 | | 107.1 | 76.0 |
| 15 | 22.5 | 21.4 | 21.8 | 21.2 |
| $COCH_3$ | | 21.3 | 21.3 | |
| $COCH_3$ | | 169.9 | 168.9 | |
| $OCH_3$ | | | 57.9 | |

[a] 150 MHz, $CD_3OD$.
[b] 150 MHz, $C_5D_5N$.
[c] 75 MHz, $CD_3OD$.

Merrilactone B (**1**) is presumably derived from anislactone B (**5**) by cross-esterification between the C-1 and C-4 hydroxyl groups. Thus intramolecular transesterification was attempted to obtain **1** from **5**. At first, **5** was subjected to acidic conditions at room temperature, but no reaction occurred. Next, heating a solution of **5** in methanol–water (1:1) in the presence of sodium hydroxide, followed by acidification, afforded a mixture of anislactone A (**4**) and two diastereomers of **1** (**9** and **10**) in 26, 12, and 14%, respectively (Scheme 1).

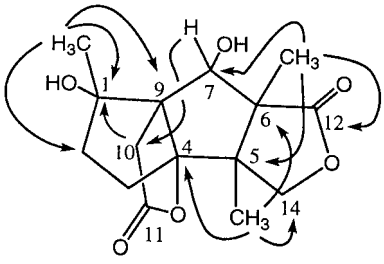



**Figure 2.** Representative HMBC correlations of **1**.

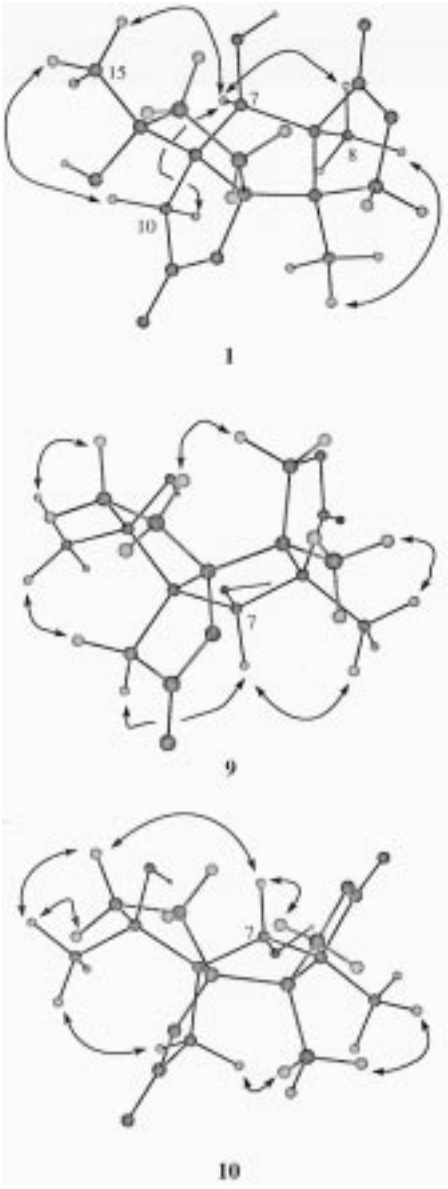
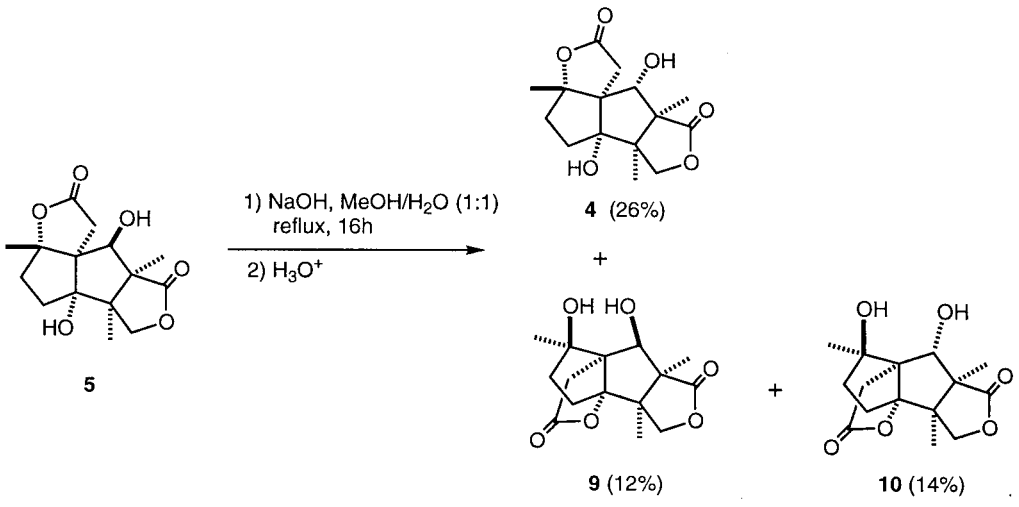



**Figure 3.** Selected NOESY of **1**, **9** and **10**.

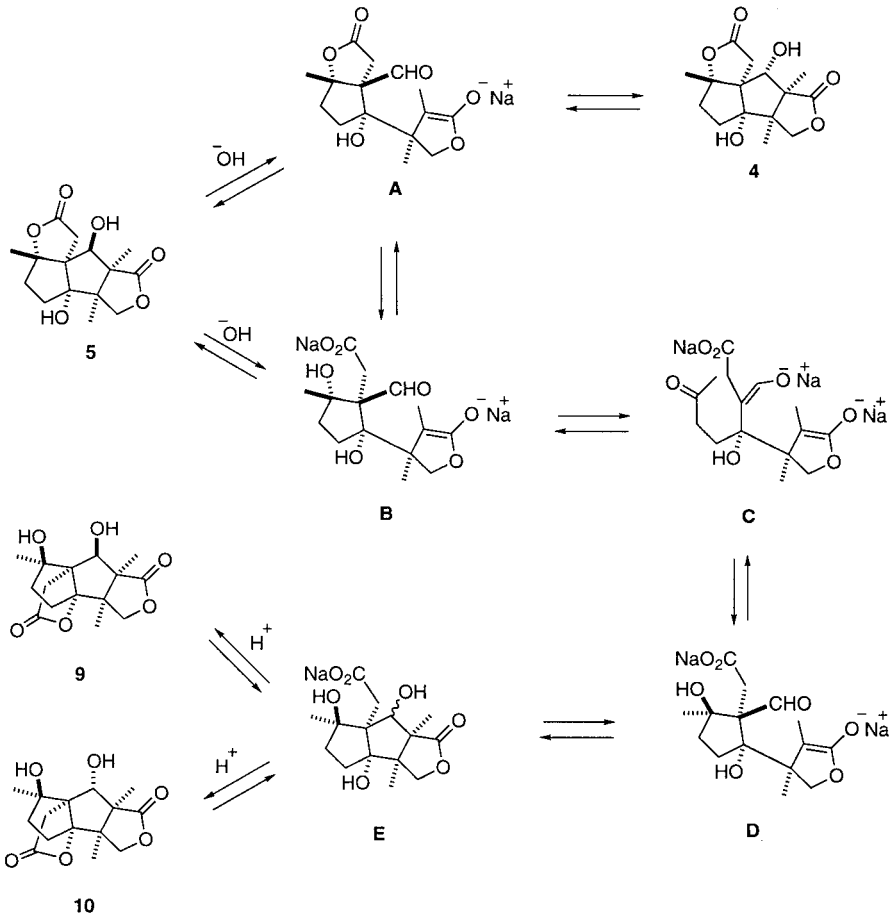
Contrary to our anticipation none of **1** was found in the products. The structural assignments for **9** and **10** were unambiguously done by extensive analysis of their 2D NMR data, indicating the plane structures of **9** and **10** being the same as **1**. Their NMR data, however, were not identical to one another. The 2D NOESY of **9** and **10** as shown in Fig. 3 clarified them to be epimers of **1** with respect to C-1 and C-7.

It turns out that two hydroxyl groups on the C-1 and C-7 positions take β-configurations in **9**, whereas they take a β- and an α-configuration in **10**, respectively. This reaction probably involves a series of retro-aldol reactions and subsequent aldol-type ring construction as shown in Scheme 2. When **5** was treated with base, the β-hydroxyl ester moiety initiated a retro-aldol mediated C6–C7 bond cleavage to give **A**, which underwent an intramolecular aldol condensation to yield anislactone A (**4**). Additional formation of β-hydroxyaldehyde **B** under basic conditions caused another retro-aldol mediated C1–C9 bond cleavage to give **C**, which in turn brought about consecutive ring closures (**D**, **E**) by an aldol condensation, thereby giving rise to **9** and **10** after acid work-up. Taking this mechanism into consideration, the conversion to **9** and/or **10** from **5** is favorable when the C-1 hydroxyl group takes β-configuration, whereas the C-1α hydroxyl group leads to anislactones **4** and/or **5** rather than **1** due to ring strain of γ-lactone. Thus it is concluded that merrilactone B (**1**) is not an artifact, but a natural product.

Merrilactone C (**2**) was obtained as an inseparable mixture with a ratio of 5:1. The NMR data (Tables 1 and 2) of main component **2a** showed the presence of an acetyl group at $\delta_H$ 2.06, and $\delta_C$ 169.9 and 21.3. Its $^1H$ and $^{13}C$ NMR spectra resembled those of 7-*O*-acetylanislactone B (**6**),[3] but **2a** missed typical AB type proton and carbon signals due to $CH_2$-14 existing in **6**. A broad singlet signal at $\delta_H$ 6.05 was newly appeared in **2a** in place of these characteristic $H_2$-14 signals, indicating the presence of an acetal group on the C-14 position. However, the signal for C-14 could not be found in the $^{13}C$ NMR spectrum because a rapid exchange between two lactols **2a** and **2b** presumably weakened the intensity of the C-14 signal. The above spectral data implied




**Scheme 1.**




**Scheme 2.** Possible mechanism for transformation of anislactone B (**5**) to **4**, **9** and **10** upon treatment with base via sequential retro-aldol and aldol-type reactions.

that **2** had a lactol ring instead of the γ-lactone presented on the C-5 and C-6 positions in **6**. In fact, **2** was treated with trimethylsilyldiazomethane[16] in methanol to give a sole methylated product **2c**, the molecular formula of which was determined as $C_{18}H_{24}O_8$ by HR-FAB-MS. The $^1$H NMR spectrum (Table 1) of **2c** showed an additional signal at $\delta_H$ 3.49 due to a methoxyl group, which correlated with $\delta_C$ 107.1 (C-14) in HMBC spectrum, indicating that the hydroxyl group of the acetal moiety was methylated to give 14-*O*-methyl derivative of **2**. Fortunately, **2c** gave single crystals suitable for X-ray analysis. The ORTEP drawing of **2c** as shown in Fig. 4 reflects that the methoxyl group attaches in the down direction on the C-14 position and **2c** makes up the same convex-shaped structure as **6**.

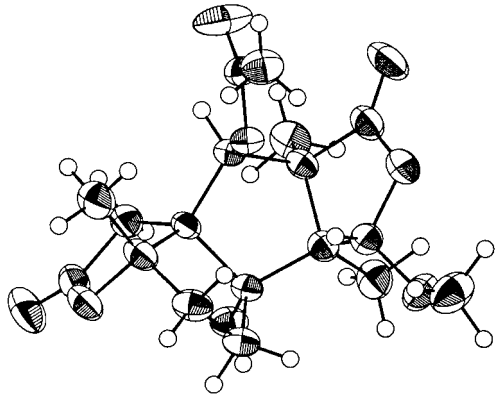
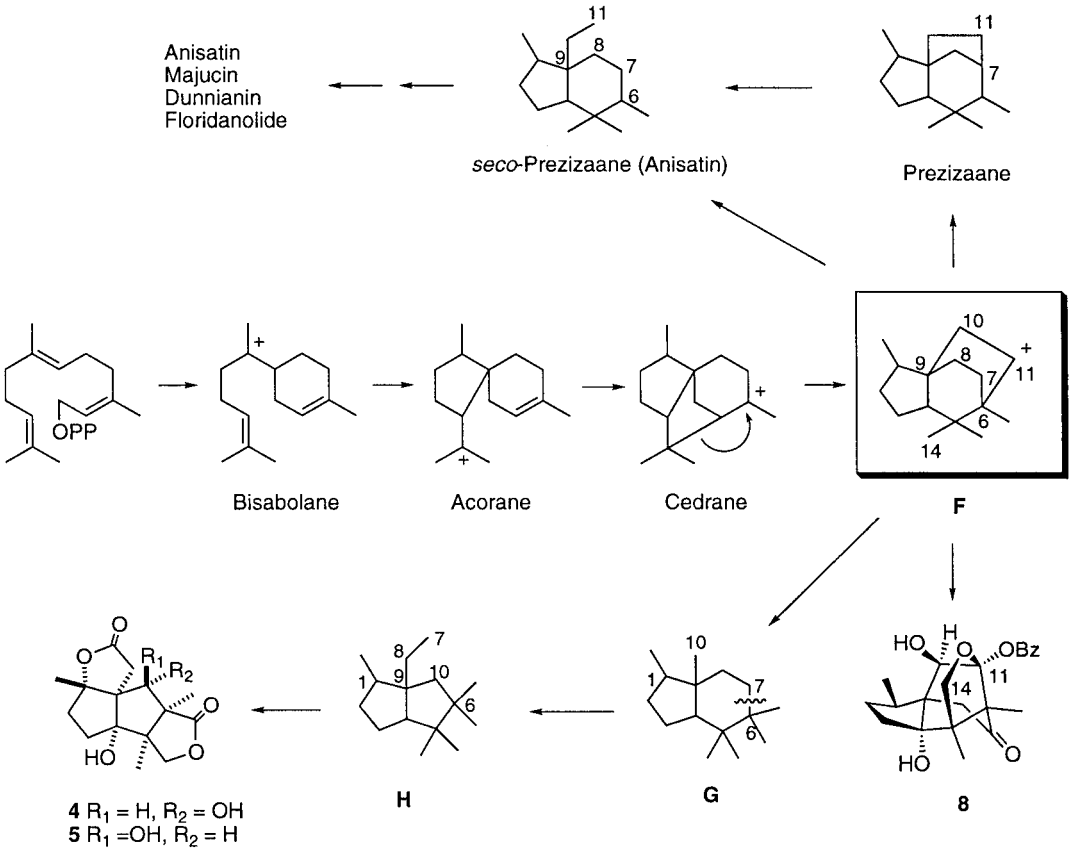


**Figure 4.** The ORTEP drawing of **2c**.

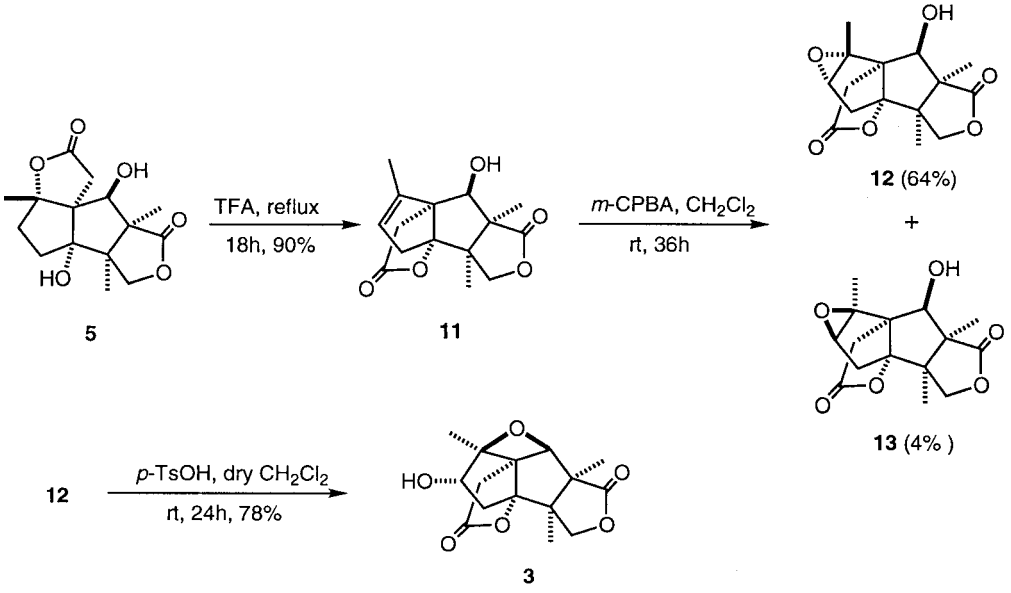
Thus the structure of **2c** was determined to be 7-*O*-acetyl-14-methoxyanislactone B. As a result, merrilactone C (**2**) turns out to be 7-*O*-acetyl-14-hydroxyanislactone B as an epimeric mixture on the C-14 position.

Anislactone-type sesquiterpenes are composed of a new type of carbon skeleton and their occurrence is limited only to *I. anisatum*[1,2] and *I. merrillianum*.[3] As these rare natural products feature the presence of a γ-lactone ring closed between C-5 and C-6, they are most likely to be biogenetically derived from the majucin-type sesquiterpenes[8] having a γ-lactone on the same positions. Kouno proposed that anislactones came from the majucin-type compound by the ring contraction between C-7 and C-8, followed by the bond formation of C-6 and C-8.[2] This biogenetic hypothesis, however, is not able to reasonably explain the inversion of the C-9 configuration and the origin of the C-8 methyl group in the anislactones. As shown in Scheme 3, it is generally accepted that a tricyclic carbon skeleton **F** turns into *seco*-prezizaanes such as anisatin, majucin, dunnanin and floridanolide[17] after breaking the C6–C11 bond of **F** or the C7–C11 bond of the prezizaane, which is also derived form **F**.[18] Co-occurrence of tashironin (**8**) and its debenzoate **7**[14] suggests that a precursor **F** plays




**Scheme 3.** Plausible biosynthetic route of anislactone-type sesquiterpenes via a common intermediate **F**.

an important role in biosynthesis of *seco*-prezizaane-type sesquiterpenes. Herein we propose an alternative biosynthetic pathway leading to anislactones from **F** as shown in Scheme 3. The bond cleavage between C-10 and C-11 in **F** gives rise to a bicyclic carbon skeleton **G**, which repeats the breaking of the C6–C7 bond and then the five-member ring construction between C-6 and C-10, resulting in the formation of anislactone-type carbon skeleton **H**. This biogenetic hypothesis seems to have no contradiction in explaining the inversion of the C-9 configuration and the origin of the C-8 methyl group. It is noted that illicinolides A and B[19,20] isolated from *I. tashiroi* are natural products derived from the bond cleavage between C-10 and C-11 of **F**.




**Scheme 4.**

### 2.2. Chemical conversion of anislactone B (5) to merrilactone A (3)

In a previous paper,[10] we reported the unique oxetane ring-bearing structure and potent neurite outgrowth promoting activity of merrilactone A (**3**) which was also isolated from the same source. An available amount of **3**, however, was very limited to further biological studies. This prompted us to attempt an effective synthesis of **3**. We envisioned a way to use anislactone B (**5**), a large amount of which can be easily obtained from *I. merrillianum*. Our synthetic plan of **3** starting from **5** involved three-step procedures such as dehydration, epoxidation and ring expansion (Scheme 4). At first, a solution of **5** in trifluoroacetic acid was refluxed to bring about the lactone transformation to the C-4 hydroxyl group and the dehydration of the C-1 hydroxyl group, giving rise to **11** in 90% yield. Then, epoxidation of **11** with *m*-chloroperoxybenzoic acid afforded a separable mixture of the desired α-epoxide **12** and β-epoxide **13** in 64 and 4% yield, respectively. High stereoselectivity of epoxidation could be rationalized due to a favorable attack of the peroxyacid from less hindered convex face of **11**. Finally, **12** was treated with *p*-toluenesulfonic acid to give **3** in 78% yield, which was identical in all respects with natural merrilactone A.

In conclusion, we have established a practical preparation of merrilactone A from anislactone B, and thereby have been able to prove the absolute stereochemistry of anislactones A (**4**) and B (**5**) to be the same as that of merrilactone A which has been already established by us.[10]

## 3. Experimental

### 3.1. General

Optical rotations were measured on a Jasco DIP-1000 digital polarimeter. IR spectra were measured on a Jasco FT-IR 5300 infrared spectrophotometer. NMR spectra were recorded on a Varian Unity 600 or 300 instrument. Chemical shifts were given as $\delta$ (ppm) with TMS as internal standard. The MS were recorded on a JEOL AX-500 instrument. Column chromatography was carried out on Kiselgel 60 (70–230 mesh and 230–400 mesh) and Sephadex LH-20.

### 3.2. Isolation and structure elucidation

**3.2.1. Plant material.** The ripe fruits of *I. merrillianum* were collected in Yunnan, China in September 1998 and a voucher specimen (94041) is available in Beijing University of Chinese Medicine.

**3.2.2. Extraction and isolation.** The dried pericarps of *I. merrillianum* (3.7 kg) were powdered and extracted with methanol at room temperature to give 1 kg of pale yellow extract. The extract (430 g) was chromatographied on silica gel (70–230 mesh) eluted successively with $CH_2Cl_2$, $CH_2Cl_2$/EtOAc (9:1, 1:1), EtOAc, EtOAc/MeOH (7:3) and MeOH to yield seven fractions (A–G).

Fraction C was divided by column chromatography on silica gel eluting with hexane/EtOAc (1:1) to fractions 1–11. Fraction 9 was further subjected to column chromatography on silica gel using $CH_2Cl_2$/MeOH (15:1) as eluent to afford fractions 12–17. Fraction 16 was purified first by reverse phase column and then by preparative TLC on silica gel to give merrilactone B (**1**) (5 mg). Fraction 10 was chromatographied on Sephadex LH-20 to yield fractions 18–22, fraction 20 of which was purified by HPLC (SP-120-5-ODS-BP, ∅10×250 mm; MeOH/$H_2O$=3:7, 2 mL/min; UV: 220 nm) to give a mixture of merrilactone C (**2**) (9 mg).

**3.2.3. Merrilactone B (1).** Colorless amorphous solid; $[\alpha]^{21}_D$=+8.6° (*c* 0.74, $CH_3OH$); IR $\nu_{max}$ (film): 3456, 1750 $cm^{-1}$; HR-FAB-MS *m/z* 297.1335 $[M+H]^+$ (calcd for $C_{15}H_{21}O_6$: 297.1338); $^1H$ and $^{13}C$ NMR: see Tables 1 and 2.

**3.2.4. Merrilactone C (2).** An equilibrium mixture of **2a** and **2b** (5:1); IR $\nu_{max}$ (film): 3349, 1750 $cm^{-1}$; $^1H$ and $^{13}C$ NMR for **2a**: see Tables 1 and 2.

**3.2.5. 14-*O*-Methylmerrilactone C (2c).** To a solution of **2** (2.4 mg) in 0.1 mL of methanol was added 30 μL of trimethylsilyldiazomethane, and then the mixture was kept at room temperature for 4 h. The reaction mixture was subjected to preparative TLC ($CHCl_3$/MeOH=15:1) to give a methylated derivative **2c** (1.5 mg). Colorless prisms; mp. >300°C; $[\alpha]^{24}_D$=+15.3° (*c* 0.40, $CH_3OH$); IR $\nu_{max}$ (film): 3349, 1750 $cm^{-1}$; HR-FAB-MS *m/z* 391.1388 (calcd for $C_{18}H_{24}O_8Na$: 391.1368); EI-MS *m/z* (rel. int.): 368 (2), 350 (4), 220 (100), 143 (57); $^1H$ and $^{13}C$ NMR: see Tables 1 and 2.

**3.2.6. X-ray crystallographic analysis of 2c.** Crystal data: orthorhombic, space group $P2_1P2_1P2_1$ (*Z*=4), *a*=9.967 (0) Å, *b*=12.491 (0) Å, *c*=14.691 (0) Å, radiation=Mo Kα, final *R*=0.035; Data collection: DIP Image plate; Program used to solve structure: maXus SIR 92; Data reduction: maXus; Molecular graphics: maXus; Software used to prepare material for publication: maXus.[21]

### 3.3. Chemical transformation

**3.3.1. Treatment of 5 with sodium hydroxide.** A solution of **5** (10 mg) in 1 mL of methanol and 1 mL of water containing sodium hydroxide (4.8 mg) was refluxed for 16 h. The reaction mixture was adjusted to pH 7 by 2N HCl, and then extracted with EtOAc. The extract was dried over $MgSO_4$, filtered and condensed in vacuo to give the residue, which was subjected to reverse phase HPLC (Cosmosil 5C18-AR-II, ∅10×250 mm; MeOH/$H_2O$=1:3, 2 mL/min; UV: 220 nm) to give anislactone A (**4**) (2.6 mg, 26%), **9** (1.2 mg, 12%) and **10** (1.4 mg, 14%).

**3.3.2. Compound 9.** Colorless amorphous solid; $[\alpha]^{20}_D$=−11.5° (*c* 0.25, $CH_3OH$); IR $\nu_{max}$ (film): 3503, 3302, 1755 $cm^{-1}$; HR-EI-MS *m/z* 296.1232 (calcd for $C_{15}H_{20}O_6$: 296.1260); EI-MS *m/z* (rel. int.): 296 ($M^+$), 278 (29), 260 (17), 137 (18), 113 (100); $^1H$ NMR ($CDCl_3$, 600 MHz): $\delta$ 1.14 (s, 3H, $H_3$-13), 1.29 (s, 3H, $H_3$-8), 1.48 (s, 3H, $H_3$-15), 1.85 (m, 2H, H-2), 1.94 (ddd, *J*=13.5, 6.3, 1.9 Hz, 1H, H-3), 2.28 (ddd, *J*=13.5, 11.5, 7.4 Hz, 1H, H-3), 2.69 (d, *J*=19.5 Hz, 1H, H-10), 2.85 (d, *J*=19.5 Hz, 1H, H-10), 3.91 (d, *J*=9.6 Hz, 1H, H-14), 4.07 (d, *J*=6.0 Hz, 1H, HO-7),

4.12 (d, $J$=6.0 Hz, 1H, H-7), 4.85 (d, $J$=9.6 Hz, 1H, H-14); $^{13}$C NMR ($CDCl_3$, 150 MHz): $\delta$ 17.4 (C-13), 18.6 (C-8), 24.4 (C-15), 32.6 (C-3), 40.4 (C-2), 42.8 (C-10), 52.9 (C-5), 59.9 (C-6), 63.6 (C-9), 73.4 (C-14), 83.5 (C-1), 90.1 (C-7), 106.9 (C-4), 174.9 (C-11), 178.9 (C-12).

**3.3.3. Compound 10.** Colorless amorphous solid; $[\alpha]^{22}_D$=+3.4° ($c$ 0.28, $CH_3OH$); IR $\nu_{max}$ (film): 3468, 1749 cm$^{-1}$; HR-EI-MS $m/z$ 296.1277 (calcd for $C_{15}H_{20}O_6$: 296.1260); EI-MS $m/z$ (rel. int.): 296 ($M^+$), 278 (6), 137 (17), 113 (100); $^1$H NMR ($CDCl_3$, 600 MHz): $\delta$ 1.09 (s, 3H, $H_3$-8), 1.20 (s, 3H, $H_3$-13), 1.39 (s, 3H, $H_3$-15), 1.83 (m, 2H, H-3) 1.93 (ddd, $J$=13.7, 5.5, 1.4 Hz, 1H, H-2), 2.08 (ddd, $J$=13.7, 11.5, 8.5 Hz, 1H, H-2), 2.41 (d, $J$=20.0 Hz, 1H, H-10), 3.45 (d, $J$=20.0 Hz, 1H, H-10), 3.81 (d, $J$=9.1 Hz, 1H, H-14), 4.87 (d, $J$=9.1 Hz, 1H, H-14), 4.96 (s, 1H, H-7); $^{13}$C NMR ($CDCl_3$, 150 MHz): $\delta$ 10.3 (C-8), 17.1 (C-13), 24.0 (C-15), 30.3 (C-3), 33.4 (C-10), 41.6 (C-2), 53.5 (C-5), 60.7 (C-6), 68.1 (C-9), 70.2 (C-7), 72.8 (C-14), 79.9 (C-1), 104.8 (C-4), 175.8 (C-11), 180.3 (C-12).

### 3.4. Synthesis of merrilactone A from anislactone B

**3.4.1. Dehydration of anislactone B (5).** A solution of **5** (66 mg, 0.22 mmol) in 2 mL of trifluoroacetic acid was refluxed for 18 h. After being cooled to room temperature, the reaction solution was carefully diluted with 40 mL of saturated $NaHCO_3$ solution, and then extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$ and condensed in vacuo to give the crude product, which was purified by column chromatography on silica gel eluting with $CHCl_3$/MeOH (15:1) to yield **11** (62 mg, 90%): colorless crystals (from MeOH); mp 185–187°C; IR $\nu_{max}$ (film): 3400, 3067, 1780, 1761 cm$^{-1}$; HR-EI-MS $m/z$ 278.1168 (calcd for $C_{15}H_{18}O_5$: 278.1154); EI-MS $m/z$ (rel. int.): 278 ($M^+$, 33), 260 (9), 176 (6), 165 (53), 113 (100); $^1$H NMR ($CDCl_3$, 600 MHz): $\delta$ 1.15 (s, 3H), 1.18 (d, $J$=0.8 Hz, 3H), 1.79 (ddd, $J$=2.4, 2.2, 1.6 Hz, 3H), 2.36 (ddq, $J$=18.4, 2.4, 2.4 Hz, 1H), 2.56 (ddq, $J$=18.4, 2.2, 2.2 Hz, 1H), 2.76 (d, $J$=19.5 Hz, 1H), 2.86 (d, $J$=19.5 Hz, 1H), 3.97 (d, $J$=8.5 Hz, 1H), 4.08 (s, 1H), 4.16 (dd, $J$=8.5, 0.8 Hz, 1H), 5.33 (ddq, $J$=2.4, 2.2, 1.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 150 MHz): $\delta$ 15.1, 16.1, 16.9, 40.6, 41.9, 57.0, 64.0, 71.6, 74.4, 87.1, 106.5, 125.1, 143.8, 177.9, 180.3.

**3.4.2. Epoxidation of 11.** To a solution of **11** (55 mg, 0.2 mmol) in 5 mL of $CH_2Cl_2$ was added *m*-chroloperoxybenzoic acid (70 mg), and the reaction mixture was stood on at room temperature for 36 h. After 5 mL of saturated $NaS_2O_3$ solution and 5 mL of saturated $NaHCO_3$ solution were added, the reaction mixture was extracted with 10 mL of $CH_2Cl_2$ twice. The combined organic layers were dried over $MgSO_4$ and condensed in vacuo to give the residue, which was purified by column chromatography on silica gel eluting with $CHCl_3$/MeOH (15:1) to afford **12** (29 mg, 64%), **13** (2 mg, 4%) and recovery **11** (10 mg).

**3.4.3. Compound 12.** Colorless needles (MeOH); mp 216°C (decomp.); IR $\nu_{max}$ (film): 3460, 1782, 1760 cm$^{-1}$; HR-EI-MS $m/z$ 294.1080 (calcd for $C_{15}H_{18}O_6$: 294.1103); EI-MS $m/z$ (rel. int): 294 ($M^+$, 11), 276 (6), 176 (9), 126 (11), 113 (100); $^1$H NMR ($CD_3OD$, 300 MHz): $\delta$ 1.10 (s, 3H), 1.16 (s, 3H), 1.54 (s, 3H), 2.07 (d, $J$=16.5 Hz, 1H), 2.25 (dd, $J$=16.5, 1.9 Hz, 1H), 2.57 (d, $J$=18.9 Hz, 1H), 3.01 (d, $J$=18.9 Hz, 1H), 3.65 (d, $J$=1.9 Hz, 1H), 3.93 (d, $J$=8.2 Hz, 1H), 4.12 (s, 1H), 4.47 (d, $J$=8.2 Hz, 1H); $^{13}$C NMR ($CD_3OD$, 75 MHz): $\delta$ 16.1, 16.6, 17.9, 37.3, 38.6, 57.3, 64.8, 67.4, 69.4, 71.7, 75.8, 83.9, 108.3, 177.4, 180.2.

**3.4.4. Compound 13.** Colorless amorphous solid; IR $\nu_{max}$ (film): 3518, 1761, 1253 cm$^{-1}$; HR-EI-MS $m/z$ 294.1070 (calcd for $C_{15}H_{18}O_6$: 294.1103); EI-MS $m/z$ (rel. int): 294 ($M^+$, 16), 276 (5), 206 (19), 125 (21), 113 (100); $^1$H NMR ($CD_3OD$, 300 MHz): $\delta$ 1.10 (s, 3H), 1.13 (s, 3H), 1.54 (s, 3H), 2.03 (dd, $J$=16.2, 2.2 Hz, 1H), 2.39 (d, $J$=16.2 Hz, 1H), 2.83 (d, $J$=18.9 Hz, 1H), 3.29 (d, $J$=18.9 Hz, 1H), 3.40 (d, $J$=2.2 Hz, 1H), 3.74 (d, $J$=8.8 Hz, 1H), 4.13 (s, 1H), 5.21 (d, $J$=8.8 Hz, 1H); $^{13}$C NMR ($CD_3OD$, 75 MHz): $\delta$ 16.0, 17.0, 17.8, 37.4, 41.6, 56.4, 64.2, 65.5, 67.9, 73.3, 87.9, 107.4, 176.6, 180.2.

**3.4.5. Merrilactone A (3).** A solution of **12** (10.8 mg, 0.0367 mmol) in 2 mL of $CH_2Cl_2$ was stirred in the presence of *p*-toluenesulfonic acid (6.8 mg) at room temperature for 24 h. After being filtered, solvent was evaporated in vacuo and the resulting crude product was purified by column chromatography on silica gel eluting with EtOAc to afford **3** (8.4 mg, 78%). Its optical rotation constant, IR spectrum, $^1$H and $^{13}$C NMR data were identical with those of merrilactone A (**3**).

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