Bull. Chem. Soc. Jpn., ***68***, *3465—3467(1995)*

A Revised Structure of Chloranthalactone F and Chloranthalactone A Photodimer

Hiroaki Okamura, Tetsuo Iwagawa, and Munehiro Nakatani*

Department of Chemistry, Faculty of Science, Kagoshima University, 1-21-35 Korimoto, Kagoshima 890

(Received January 27, 1995)

Two known lindenane sesquiterpenoids, chloranthalactone F and chloranthalactone A photodimer, were identified to be the same by direct comparison of the samples and their spectra. Both of their structures were revised to a new structure, head-to-head, *anti* dimer of chloranthalactone A, from the spectroscopic and chemical studies. Chloranthalactone A photodimer has been reported as an artifact, but this compound was observed as a natural product in the leaves of *Chloranthus glaber.*

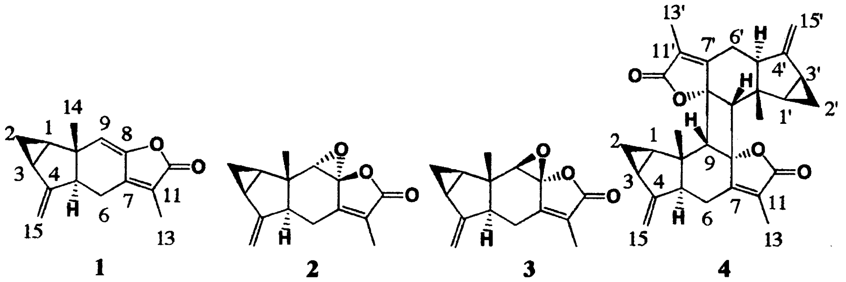
In our continuous study on the constituents of *Chloranthus glaber*,[1a)] we isolated three lindenane sesquiterpenoids, chloranthalactones A (**1**), B (**2**),[1b,1c)] and a compound that showed identical ^{1}H and ^{13}C NMR spectral data with those of chloranthalactone F (**3**) obtained from the same plant.[2a)] However, almost the same NMR spectra as that of **3** had been also reported for chloranthalactone A photodimer (**4**) obtained as an artifact from *C. japonicus* (Fig. 1).[2b)] Identification of these compounds was established by direct comparison of the samples and their spectra.[3)] Thus, it was clarified that *two different structures, 3 and 4, were given for the same compound.* From the spectroscopic and chemical investigation of this compound, the structures **3** and **4** were revised to a new structure **5**.

Table 1. ^{1}H and ^{13}C NMR Data in CDCl$_3$

	^{1}H	^{13}C
1 (1′)	1.45 (dt, J=3.7, 7.6 Hz)	24.1 d
2 (2′)	0.92—0.81 (m)	16.3 t
3 (3′)	2.12—2.06 (m)	23.9 d
4 (4′)		152.1 s
5 (5′)	3.77 (ddd, J=2.2, 6.6, 12.1 Hz)	53.3 d
6a (6a′)	2.81 (ddd, J=2.2, 6.6, 18.3 Hz)	24.1 t
6b (6b′)	2.31 (br dd, J=12.1, 18.3 Hz)	
7 (7′)		160.5 s
8 (8′)		91.0 s
9 (9′)	3.06 (s)	48.1 d
10 (10′)		41.1 s
11 (11′)		124.8 s
12 (12′)		172.3 s
13 (13′)	1.77 (d, J=1.1 Hz)	8.8 q
14 (14′)	0.53 (s)	19.9 q
15 (15′)	5.09 (brs), 4.80 (brs)	106.8 t

Results and Discussion

The compound was obtained as colorless needles, mp 238—239 °C, from the acetone extract of fresh leaves of *C. glaber*. Though the ^{1}H, ^{13}C NMR (Table 1), and IR spectra of this compound were completely identical with those of chloranthalactone F (**3**), there was a disagreement in the mass spectrum. In the structure **3**, the highest ion peak at m/z 228.1138 was assigned as $[\mathrm{M-O}]^+$ ion, but in our sample, a small signal (6% relative intensity) was found at m/z 456 in addition to the base peak at m/z 228. Except for the signal at m/z 456, both mass spectra were superimposable on each other. Furthermore, the high resolution mass spectrum of our sample showed a signal at m/z 456.2335, indicating $C_{30}H_{32}O_4$ as a molecular formula (Calcd for



1 **2** **3** **4**

Fig. 1. Structures of lindenane sesquiterpenes.

$C_{30}H_{32}O_4$: M, 456.2300). It is to be noted that no signal at *m*/*z* 228 has been reported for chloranthalactone B (**2**), the stereoisomer of **3**.

Almost the same spectral data with **3** and our sample were reported for chloranthalactone A photodimer (**4**) which was obtained as a photodimerized artifact of chloranthalactone A (**1**). We also confirmed photoirradiation of **1** afforded a dimerized product, and identification with **3**, **4**, and our sample was established by direct comparison of the samples and their spectra. However, there was an inconsistency in the CD spectrum. In the structure **4**, a positive Cotton effect at 275 nm had been reported, but we observed a positively split Cotton effect (240 nm $\Delta\varepsilon_1=+64$ and 217 nm, $\Delta\varepsilon_2=-115$) for both our sample and the authentic sample of **4** (Fig. 2).

The above-mentioned ^{1}H, ^{13}C, and mass spectra indicated that this compound was a symmetrical dimer of chloranthalactone A (**1**) linked at the C-8 and C-9 positions. Furthermore, since this compound was synthesized from photoirradiation of **1**, the expected product should be the [2πs+2πs] adduct. As the symmetrical [2πs+2πs] adduct of **1**, the following four stereoisomers were allowed (Fig. 3): 1) head-to-head (hereafter referred to as HH), *anti*, and *si* face (of C-8 of **1**) to *si* face adduct (**5**); 2) HH, *anti*, and *re* face to *re* face adduct (**6**); 3) head-to-tail (hereafter referred to as HT), *syn*, and *re* face to *re* face adduct (**7**); and 4) HT, *syn*, and *si* face to *si* face adduct (**8**).

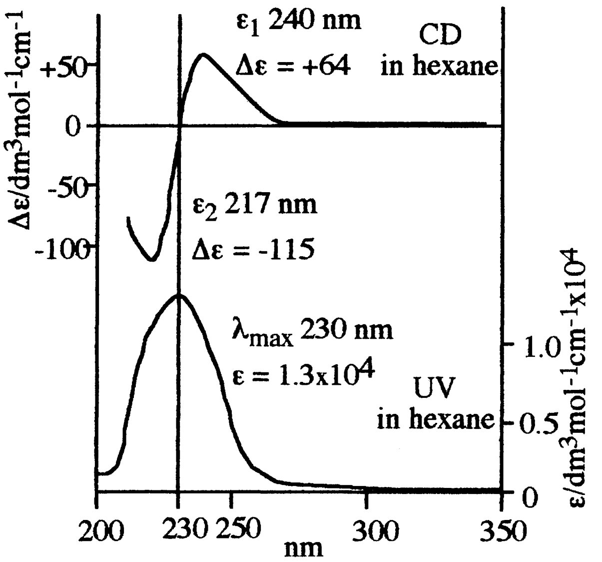


Fig. 2. CD and UV spectra of **5**.

By irradiation of H-9 (or H-9′) at δ=3.06, the NOEs were observed for the signals corresponding to H-1 (or H-1′), H-5 (or H-5′), and H-14 (or H-14′) at δ=1.45, 3.77, and 0.53, respectively.[4] Among the structures listed in Fig. 3, only HH isomers (**5** and **6**) could explain the observed NOEs. Finally, the structure of this compound was decided from the CD spectrum. The observed positively split Cotton effect was assigned to positively twisted chromophores, i.e., two unsaturated lactone groups. The expected CD signals for the structures **5** and **6** were positive and negative, respectively. Hence the structure of this compound was identified as **5**.

Chloranthalactone A photodimer (**4**) was originally reported to be present as an photodimerized artifact in the extract of the root of *C. japonicus*, since it could not be isolated from the extract treated under dark conditions.[2a] However, we confirmed by TLC and HPLC analyses that the crude extract of the leaves of *C. glaber* treated under dark conditions contained this compound. Therefore, it was present in the leaves of *C. glaber* as a natural product. This difference can be ascribed to the difference in the growing conditions between the leaves and the root.

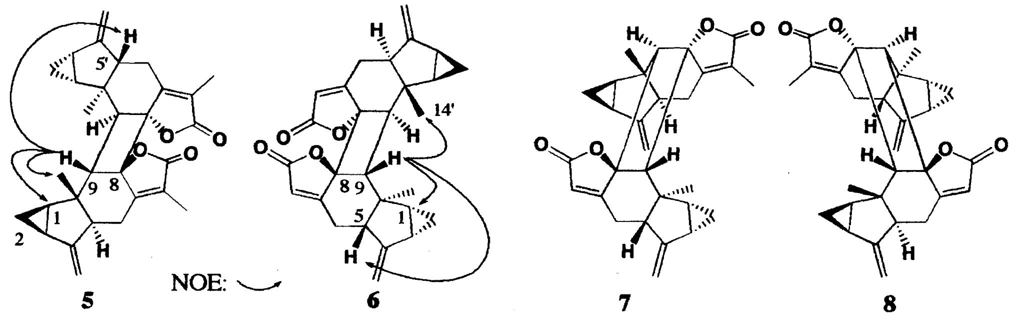
To avoid further confusion, we wish to propose to use chloranthalactone A photodimer as the name of this compound, which is the name originally given to this compound.

Experimental

Melting points were measured by a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL-GX400 instrument in $CDCl_3$. IR and UV spectra were measured on JASCO FT/IR-5300 and Shimadzu UV210A spectrometers. EI-Mass spectra were recorded on a JEOL-D 300 instrument.

Plant Material: *C. glaber* Makino was purchased from a garden shop in November 1992 at Kagoshima, Japan.

Isolation: Finely cut fresh leaves (3.3 kg) were ex-



5
HH, *anti*, *si* face-*si* face

6
HH, *anti*, *re* face-*re* face

7
HT, *syn*, *re* face-*re* face

8
HT, *syn*, *si* face-*si* face

Fig. 3. Structures of symmetrical [2πs+2πs] dimers of **1**.

tracted with acetone (10 dm^3) for two weeks at room temperature, and the extract was concentrated under reduced pressure at less than 50 °C. The resulting aqueous suspension (ca. 300 cm^3) was diluted with water (300 cm^3) and extracted with ether (500 ml × 3). The ether solution was dried with $MgSO_4$ and concentrated. The residue was chromatographed on SiO_2 with a gradient solvent system of MeOH–CH_2Cl_2. A mixture (10.45 g) from the CH_2Cl_2 and 1% MeOH–CH_2Cl_2 eluants was further chromatographed on a column using hexane–ether eluants. A crystalline compound (6.64 g) from the fraction eluted with 20% ether–hexane was recrystallized from hexane to give chloranthalactone A (**1**, 4.09 g), and from column chromatography of the mother liquor, chloranthalactone B (**2**, 13 mg) was obtained. The fraction of 30% ether–hexane eluants also afforded a crystalline compound (110 mg), which was recrystallized from pet. ether (bp 45—60 °C) followed by recrystallization from MeOH to give chloranthalactone A photodimer (**5**, 40 mg).

Photodimerization of Chloranthalactone A: A solution of chloranthalactone A (**1**, 114 mg) in hexane (5 ml) was put into a quartz tube and irradiated for 24 h by using a high pressure Hg lamp at room temperature. The reaction mixture was concentrated and chromatographed (hexane : ether=6 : 4) to give chloranthalactone A photodimer (**5**, 70.0 mg, 61%) in crystalline form.

Chloranthalactone A: ^{1}H NMR δ=6.25 (s, 1H), 5.06 (br s, 1H), 4.79 (br s, 1H), 2.97 (ddt, J=3.7, 13.6, 2.2 Hz, 1H), 2.70 (dd, J=3.7, 16.9 Hz, 1H), 2.27 (ddq, J=13.6, 16.9, 1.8 Hz, 1H), 2.00—1.95 (m, 1H), 1.90 (d, J=1.8 Hz, 3H), 1.66 (dt, J=3.7, 7.3 Hz, 1H), 0.94—0.88 (m, 2H), 0.79 (s, 3H); ^{13}C NMR δ=169.0 (s), 150.1 (s), 149.6 (s), 148.0 (s), 122.4 (s), 119.8 (d), 106.5 (t), 62.0 (d), 40.1 (s), 26.4 (d), 22.4 (d), 22.1 (q), 21.4 (t), 17.0 (t), 8.6 (q).

Chloranthalactone B: ^{1}H NMR δ=5.04 (br s, 1H), 4.70 (br s, 1H), 4.18 (s, 1H), 3.39 (ddd, J=2.6, 5.2, 13.2 Hz, 1H), 2.56 (dddd, J=1.5, 1.8, 5.2, 17.2 Hz, 1H), 2.13 (dddd, J=1.5, 1.8, 13.2, 17.2 Hz, 1H), 2.05—1.95 (m, 1H), 1.90 (dd, J=1.5, 1.8 Hz, 1H), 1.72 (dd, J=3.3, 7.7 Hz, 1H), 0.94—0.83 (m, 2H), 0.65 (s, 3H); ^{13}C NMR δ=170.4 (s), 152.3 (s), 149.9 (s), 129.1 (s), 106.8 (t), 87.9 (s), 64.4 (d), 50.6 (d), 41.1 (s), 23.9 (d), 22.9 (d), 21.3 (q), 16.9 (t), 16.8 (t), 8.9 (q).

Chloranthalactone A Photodimer: Mp 238—239 °C; $[\alpha]_D^{23}$ +20° ($CHCl_3$, c 0.46); IR ($CHCl_3$) 1750, 1702, 1660, and 882 cm^{-1}; UV and CD see Fig. 2; ^{1}H and ^{13}C NMR see Table 1; MS m/z 456 (6%, M$^+$), 228 (100%); HRMS Found: m/z 456.2335. Calcd for $C_{30}H_{32}O_4$: M, 456.2300.

We are grateful to Professor Genjiro Kusano, Osaka University of Pharmaceutical Science, and to Professor Yoshio Takeda, The University of Tokushima, for helpful advice and providing the authentic sample and spectra charts. We also thank Professor Tsutomu Sakakibara, Kagoshima University, for providing photoreaction apparatus.

References

1) a) H. Okamura, N. Nakashima, T. Iwagawa, N. Nakayama, and M. Nakatani, *Chem. Lett.*, **1994**, 1541; b) M. Uchida, G. Kusano, Y. Kondo, and S. Nozoe, *Heterocycles*, **9**, 139 (1978); c) M. Uchida, Y. Koike, G. Kusano, Y. Kondo, S. Nozoe, C. Kabuto, and T. Takemoto, *Chem. Pharm. Bull.*, **28**, 192 (1980).

2) a) Y. Takeda, H. Yamashita, T. Matsumoto, and H. Terao, *Phytochemistry*, **33**, 713 (1993); b) G. Kusano, M. Abe, Y. Koike, M. Uchida, S. Nozoe, and Z. Taira, *Yakugaku Zasshi*, **111**, 756 (1991).

3) IR and EI-mass spectra of chloranthalactone F (**3**) and a sample of chloranthalactone A photodimer (**4**) were provided by Professor Yoshio Takeda, University of Tokushima, and Professor Genjiro Kusano, Osaka University of Pharmaceutical Science, respectively.

4) The same NOE was observed for chloranthalactone F (**3**),[2b] but the assignment was different.