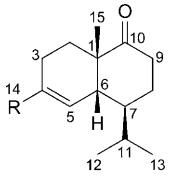
Two Novel 15(10 → 1)Abeomuurolane Sesquiterpenes from *Cosmos sulphureus*

by **Jyh-Horng Wu**[a]), **Yi-Fu Chang**[b]), **Yu-Tang Tung**[c]), **Minoru Tsuzuki**[d]), **Akira Izuka**[d]), **Sheng-Yang Wang***[a]), and **Yueh-Hsiung Kuo***[b])[e])[f])

[a]) Department of Forestry, National Chung-Hsing University, Taichung 402, Taiwan
[b]) Department of Chemistry, National Taiwan University, Taipei 106, Taiwan
(phone: +886-2-33661671; fax: +886-2-23636359; e-mail: yhkuo@ntu.edu.tw)
[c]) School of Forestry and Resource Conservation, National Taiwan University, Taipei 106, Taiwan
[d]) Nihon Pharmaceutical University, Saitama, Japan
[e]) Tsuzuki Institute for Traditional Medicine, College of Pharmacy, China Medical University, Taichung 404, Taiwan
[f]) Agricultural Biotechnology Research Center, Academia Sinica, Taipei 115, Taiwan

Two novel 15(10 → 1)abeomuurolane sesquiterpenes, cosmosoic acid (**1**) and cosmosaldehyde (**2**), were isolated from the whole plant of *Cosmos sulfurous*. Their structures were established by a combination of 1D- and 2D-NMR spectroscopic techniques. Additionally, a chemical correlation between **1** and **2** was also established.

Introduction. – *Cosmos sulphureus* is also known as Sulfur Cosmos and Yellow Cosmos. Its native habitat is Brazil and Mexico, and this plant is used traditionally to treat malaria in Brazil [1]. However, to date, the chemical studies on *C. sulphureus* have not yet been published. Thus, it was considered worthy investigating its chemical components. In this study, we isolated and identified two novel 15(10 → 1)abeomuurolane-type[1]) sesquiterpenes which are named cosmosoic acid[1]) (**1**) and cosmosaldehyde[1]) (**2**).



1[1]) R = COOH
2[1]) R = CHO

Results and Discussion. – Cosmosoic acid (**1**) was obtained as a colorless oil. The HR-EI-MS of compound **1** showed a molecular-ion peak at *m/z* 250.1566 (M^+), which corresponds to the molecular formula $C_{15}H_{22}O_3$, and indicated the presence of five degrees of unsaturation in the molecule. The IR spectrum revealed the presence of an α,β-unsaturated COOH and a saturated cyclohexanone moiety, characterized by absorptions at $\tilde{\nu}_{max}$ 3200–2500, 1715, 1701, 1635, and 939 cm^{-1}, and an UV maximum at

[1]) Trivial atom numbering according to IUPAC; for systematic names, see *Exper. Part.*

218 nm. The ^{1}H-NMR spectrum of **1** (*Table*) showed one Me group at δ(H) 1.29 (*s*, Me(15)), attached to a tertiary C-atom, and two Me *d* at δ(H) 0.90 (2*d*, $J = 6.7$ Hz, Me(12), Me(13)), characteristic of an i-Pr group. A *d* at δ(H) 6.98 (*d*, $J = 5.2$ Hz, H–C(5)) suggested the presence of a trisubstituted C=C bond, conjugated with a COOH functionality [2]. Analysis of the ^{13}C-NMR spectrum (*Table*) with the aid of DEPT and HSQC experiments, revealed a C=O group at δ(C) 212.2 (*s*, C(10)), a C=C bond at δ(C) 132.9 (*s*, C(4)) and 151.4 (*d*, C(5)), a conjugated COOH group at δ(C) 171.0 (*s*, C(14)), an i-Pr group at δ(C) 32.8 (*d*, C(11)), 21.9 (*q*, C(12)), and 19.8 (*q*, C(13)), a quaternary C-atom at δ(C) 59.4 (*s*, C(1)), a Me group at δ(C) 25.0 (*q*, C(15)), four CH_2 groups at δ(C) 39.4 (*t*, C(2)), 34.9 (*t*, C(9)), 27.0 (*t*, C(8)), and 22.6 (*t*, C(3)), and two CH groups at δ(C) 55.8 (*d*, C(7)) and 52.8 (*d*, C(6)). Since three (COOH, C=O, and C=C) out of five degrees of unsaturation deduced from the molecular formula $C_{15}H_{22}O_3$ were accounted for, compound **1** was inferred to be a bicyclic sesquiterpenoid. The constitutional formula of compound **1** was established from HMBC data, and the key starting points for the interpretation of the ^{13}C,^{1}H correlations were those of the three Me, the C=O, and the COOH groups, as depicted in the *Figure*. Two- or three-bond couplings from C(14) to H–C(3) and H–C(5), from C(5) to H–C(3), H–C(6), and H–C(7), from C(10) to H–C(2), H–C(6), H–C(9), and Me(15), from C(15) to H–C(6), and from C(11) to H–C(8) and H–C(6) allowed to establish the structure of cosmosoic acid as **1**. The C-atom skeleton of **1** is different from cadinane (Me groups at C(4) and C(10)) [3], gorgonane (Me groups at C(4) and

Table. *^{1}H-* (500 MHz, $CDCl_3$) *and ^{13}C-NMR* (125 MHz, $CDCl_3$) *Data of Compounds* **1** *and* **2**. δ in ppm, J in Hz.

	1		**2**	
	δ(H)	δ(C)[a])	δ(H)	δ(C)[a])
C(1)		59.4 (*s*)		59.8 (*s*)
CH_2(2)	2.43–2.49 (*m*, H_α), 2.76–2.82 (*m*, H_β)	39.4 (*t*)	2.38–2.46 (*m*, H_α), 2.73–2.79 (*m*, H_β)	39.2 (*t*)
CH_2(3)	2.76–2.82 (*m*, H_α), 2.54–2.60 (*m*, H_β)	22.6 (*t*)	2.68–2.74 (*m*, H_α), 2.38–2.46 (*m*, H_β)	20.1 (*t*)
C(4)		132.9 (*s*)		143.3 (*s*)
CH(5)	6.98 (*d*, $J = 5.2$)	151.4 (*d*)	6.62 (*d*, $J = 5.6$)	158.1 (*d*)
CH(6)	2.39 (*dd*, $J = 8.0$, 5.2)	52.8 (*d*)	2.52 (*dd*, $J = 8.8$, 5.6)	53.3 (*d*)
CH(7)	1.74–1.82 (*m*)	55.8 (*d*)	1.76–1.89 (*m*)	55.5 (*d*)
CH_2(8)	1.79–1.85 (*m*, H_α), 1.34–1.42 (*m*, H_β)	27.0 (*t*)	1.76–1.89 (*m*, H_α), 1.36–1.45 (*m*, H_β)	27.2 (*t*)
CH_2(9)	1.34–1.42 (*m*, H_α), 2.08–2.14 (*m*, H_β)	34.9 (*t*)	1.36–1.45 (*m*, H_α), 2.16–2.22 (*m*, H_β)	35.4 (*t*)
C(10)		212.2 (*s*)		211.2 (*s*)
CH(11)	1.58 (*sept.*, $J = 6.7$)	32.8 (*d*)	1.60 (*sept.*, $J = 6.4$)	32.7 (*d*)
Me(12)	0.90 (*d*, $J = 6.7$)	21.9 (*q*)	0.93 (*d*, $J = 6.4$)	22.4 (*q*)
Me(13)	0.90 (*d*, $J = 6.7$)	19.8 (*q*)	0.93 (*d*, $J = 6.4$)	19.9 (*q*)
C(14)		171.0 (*s*)	9.33 (*s*)	191.9 (*d*)
Me(15)	1.29 (*s*)	25.0 (*q*)	1.32 (*s*)	25.4 (*q*)

[a]) Multiplicities inferred from the DEPT and HMQC experiments.

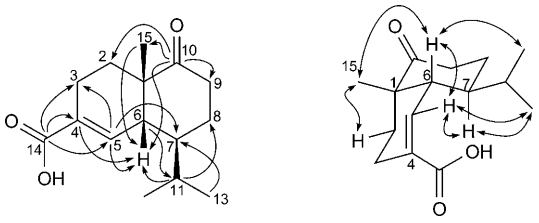


Figure. *Key HMBCs* (C → H) *and NOESY* (H ↔ H) *correlations of compound* **1**

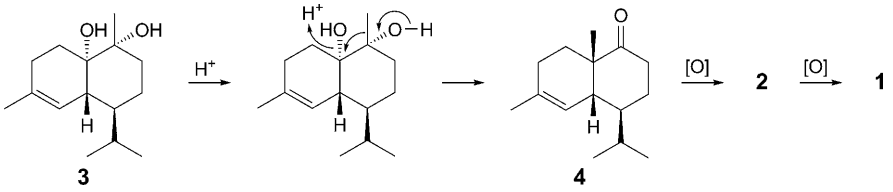
C(10)) [4], and nardosinane (Me groups at C(4) and C(5)) [5]. Compound **1** was named cosmosane, according to its isolation from the genus *Cosmos*.

The relative configuration of **1** was determined mainly by NOESY experiments (*Fig.*). H–C(6) resonated as a double *d* at δ(H) 2.39 and showed a diaxial coupling with H–C(7) ($J = 8.0$ Hz). Accordingly, the *trans* diaxial coupling H–C(6)/H–C(7) permitted us to establish a β-configuration for H–C(6) and an α-configuration for H–C(7). In addition, H–C(6) also showed a NOESY cross-peak with the Me(15) H-atoms (δ(H) 1.29). This NOESY correlation suggested that H–C(6) and Me(15) have the same orientation, *i.e.*, β-configuration, as shown in the *Figure*. Furthermore, the *d* of H–C(5) ($J = 5.2$ Hz) unambiguously confirmed the muurolene skeleton of **1** [3].

Cosmosaldehyde (**2**) was also obtained as a colorless oil. Its HR-EI-MS showed a molecular-ion peak at *m*/*z* 234.1624 (M^+), which corresponds to the molecular formula $C_{15}H_{22}O_2$. The IR spectrum of **2** indicated the presence of an α,β-unsaturated CHO group (2720 and 1689 cm^{-1}) and of a cyclohexanone unit (1714 cm^{-1}). The ^{1}H-NMR data of **2** were similar to those of **1**, except for the presence of a CHO group (δ(H) 9.33) instead of a COOH group (*Table*). This CHO group was positioned at C(14) because the C=O C-atom showed HMBCs with CH_2(3) and H–C(5) as well as a UV absorption at λ_{max} 232 nm. In addition, the deshielding of H–C(5) (δ(H) 6.62 (*d*, $J =$ 5.6 Hz)) and C(5) (δ(C) 158.1) is consistent with a β-position in a conjugated enal. The structure of compound **2** was further elucidated by 1D- and 2D-NMR techniques, and the results suggested that cosmosaldehyde possesses structure **2**. Furthermore, compound **2** was oxidized by *Jones* reagent to give a product which was identified as cosmosoic acid (**1**). Therefore, the structure of compound **2** was assigned unambiguously as shown.

The biotransformation of the two novel sesquiterpenes **1** and **2** presumably starts from (1α,10α)-cadin-4-ene-1,10-diol (**3**) *via* the pathway sketched in the *Scheme*. Under acidic conditions, compound **3** should be converted to 15(10 → 1)abeomuurol-

Scheme. *Possible Biosynthetic Pathway to* **1** *and* **2**



4-en-10-one (**4**), and then this compound is oxidized to yield compound **2** and then compound **1** by further oxidation.

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Experimental Part

General. Column chromatography (CC): silica gel *60* (SiO_2; 70–230 mesh; *Merck*). HPLC: *LDC-Analytical-III*; *Phenomenex-00G-4274-N0-Luna-Si* (5 μm, 10 × 250 mm) semiprep. column. Optical rotations: *Jasco-DIP-1000* digital polarimeter. IR Spectra: *Nicolet-MAGNA-IR-550* spectrophotometer, series *II*; KBr pellets; $\tilde{\nu}$ in cm^{-1}. UV Spectra: *Helios-Beta*-UV/VIS spectrometer; λ_{max} (log ε) in nm. 1D- and 2D-NMR Spectra: *Bruker-DMX-500SB* spectrometer; in $CDCl_3$ at 500 (^1H) and 125 MHz (^{13}C); δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: *Finnigan-TSQ-46C* and *Jeol-SX-102A* mass spectrometers; in *m*/*z* (rel.%).

Plant Material. The whole plant of *C. sulphureus* was collected from Pin-Ton County (Taiwan). The plant material was identified by Prof. *Shang-Tzen Chang* of the School of Forestry and Resource Conservation, National Taiwan University, and a voucher specimen was deposited with the Herbarium of the School of Forestry and Resource Conservation, National Taiwan University, Taipei, Taiwan.

Extraction and Isolation. The air-dried whole plant (4.7 kg) of *C. sulphureus* was extracted with MeOH (3 × 20 l) at r.t. for 2 weeks totally. The extract was filtered under vacuum and concentrated to a residue (320 g). The residue was suspended in H_2O and extracted successively with AcOEt and BuOH to yield AcOEt- (141 g), BuOH- (19 g), and H_2O-soluble (56 g) fractions. The AcOEt-soluble fraction was repeatedly subjected to CC (SiO_2, hexane/AcOEt 0–100% and AcOEt/MeOH 0–30%) to yield several subfractions. A subfraction obtained with hexane/AcOEt 1:1 was subjected to normal-phase HPLC: **1** and **2**.

Cosmosoic Acid (= rel-*(4a*R,*8*R,*8a*S*)-3,4,4a,5,6,7,8,8a-Octahydro-4a-methyl-8-(1-methylethyl)-5-oxonaphthalene-2-carboxylic Acid*; **1**): Colorless oil. $[\alpha]_D^{20} = +30.6$ ($c = 0.04$, MeOH). UV (MeOH): 218 (4.21). IR: 3200–2500, 1715, 1701, 1635, 1281, 939. ^1H- and ^{13}C-NMR ($CDCl_3$): *Table*. EI-MS: 250 (40, M^+), 207 (100), 189 (63), 167 (81). HR-EI-MS: 250.1566 (M^+, $C_{15}H_{22}O_3^+$; calc. 250.1569).

Cosmosaldehyde (= rel-*(4a*R,*8*R,*8a*S*)-3,4,4a,5,6,7,8,8a-Octahydro-4a-methyl-5-oxo-8-(1-methylethyl)naphthalene-2-carboxaldehyde*; **2**): Colorless oil. $[\alpha]_D^{15} = +31.7$ ($c = 0.03$, MeOH). UV (MeOH): 232 (4.04). IR: 2720, 1714, 1689, 1642, 1253, 1175, 946. ^1H- and ^{13}C-NMR ($CDCl_3$): *Table*. EI-MS: 234 (19, M^+), 191 (100), 163 (41), 151 (52). HR-EI-MS: 234.1624 (M^+, $C_{15}H_{22}O_2^+$; calc. 234.1620).

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