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Terpenoids from *Ligularia virgaurea* collected in China: the first example of two bakkane derivatives with an anhydride-type ring C and nineteen new chemical constituents

Yoshinori Saito [a], Saori Iga [b], Katsuyuki Nakashima [b], Yasuko Okamoto [b], Xun Gong [c,*,‡], Chiaki Kuroda [d,*,†], Motoo Tori [b,*,§]

[a] Graduate School of Biomedical Sciences, Nagasaki University, Bunkyo-machi, Nagasaki 852-8521, Japan
[b] Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-cho, Tokushima 770-8514, Japan
[c] Kunming Institute of Botany, Chinese Academy of Science, Kunming 650201, China
[d] Department of Chemistry and Research Center of Smart Molecules, Rikkyo University, Nishi-Ikebukuro, Toshima-ku, Tokyo 171-8501, Japan

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ABSTRACT

Further chemical investigation of two *Ligularia virgaurea* samples collected in China resulted in the isolation of 21 new compounds, two of which were bakkane-type sesquiterpenoids bearing an anhydride-type ring C, which was a previously unknown partial structure. These samples belonged to the V-type (the major component was virgaurenone) among the five chemotypes found in this species.

1. Introduction

Ligularia (Asteraceae) is a highly diversified genus in the Hengduan Mountain region of China, and we have expressed the presence of intra-specific diversity in many species in terms of both the chemical composition and DNA sequence of an evolutionarily neutral region.[1] *Ligularia virgaurea* (Maxim.) Mattf. is an abundant species in the western area of the Sichuan province. We previously reported that the species collected in the Sichuan, Qinghai, and Gansu provinces were grouped into the following five chemotypes on the basis of their terpenoid constituents: L-type (the major component was ligularol), V-type (virgaurenone A), C-type (cacalol), H-type (6-hydroxyeuryopsin), and N-type (neoadenostylone).[2–4] The species were grouped into three clades on the basis of their DNA sequences, which were in good agreement with the chemotypes (clade A=L-type, clade B=V- and H-types, clade C=C- and N-types). In addition to furanoeremophilanes, the major components, we previously isolated a variety of new compounds such as seco-eremophilanes, bakkanes, and compounds having further rearranged carbon skeletons from 38 samples of *L. virgaurea*.[3] Various sesquiterpene dimers were also isolated.[3–7] Since then, four new compounds, including rearranged norsesquiterpenes, were characterized from another sample.[8] We have analyzed two more samples (one from northern Sichuan province and the other from southern Gansu province)[3] and 26 compounds were isolated, 21 of which were new. Two of these compounds have a unique structure, a bakkane bearing an anhydride partial structure. In this study, we describe the details of their structure elucidation.

2. Results and discussion

Compound **1** exhibited a quasi-molecular ion peak at *m*/*z* 361, and its molecular formula was determined to be $C_{20}H_{24}O_6$ by

* Corresponding authors. Tel.: +86 871 5223625 (X.G.); tel./fax: +81 3 3985 2396 (C.K.); tel.: +81 88 602 8464; fax: +81 88 655 3051 (M.T.); e-mail addresses: gongxun@mail.kib.ac.cn (X. Gong), kuroda5000144@rikkyo.ac.jp (C. Kuroda), tori@ph.bunri-u.ac.jp (M. Tori).
† For general information.
‡ For taxonomy.
§ For structure determination.

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HRCIMS and ^{13}C NMR data. An angelate moiety was apparent from chemical shift values of δ 5.61 (1H, qq, J=7.3, 1.5 Hz), 1.87 (3H, dq, J=7.3 and 1.5 Hz), and 1.69 (3H, quintet, J=1.5 Hz) (Table 1) as well as an IR absorption band at 1722 cm^{-1}. The IR absorption at 1850 cm^{-1} indicated the presence of any of an epoxy-lactone, an enol-lactone, or an anhydride. The observed value was at a slightly higher wavenumber than that at which an epoxy- and an enol-lactone have ever been encountered.[2,3,8] The ^{13}C NMR spectrum indicated the presence of five methyl, two methylene, five methine, and eight quaternary carbon atoms including eight sp^2 carbon atoms (four carbonyl and four olefinic carbons). The degree of unsaturation was 9, and therefore, this compound should be tricyclic. The 2D correlations are shown in Fig. 2. The HMBC correlations between H_3-15 and C-3 and 4, between H_3-14 and C-4, 5, 6, and 10, between H-3 and C-2, and between H-9 and C-1 suggested a six-membered carbocycle for ring A. Because H-6 showed a correlation with C-7 (quaternary carbon), H-9 with C-8 (carbonyl), and H-11 with C-7, this compound was deduced to be a bakkane derivative. Both carbons C-8 and 12 were carbonyl groups; therefore, ring C must be an anhydride, as shown in Fig 2. The angeloyloxy group was substituted at C-6 as indicated by the correlation between H-6 and C-1′. The stereochemistry was determined by the NOESY correlations shown in Fig. 2. Because the NOE between H_3-

Table 1
^1H and ^{13}C NMR data of virgaureno-anhydrides A (**1**) and B (**2**)

Positions	**1**[a]		**2**[a]	
	^1H (mult, J in Hz)	^{13}C	^1H (mult, J in Hz)	^{13}C
1	5.63 (d, 2.4)	123.8	5.68 (br s)	124.0
2	—	196.2	—	196.6
3	1.97 (dd, 17.6, 4.4)	41.4	2.00 (dd, 17.9, 3.4)	41.7
	1.83 (dd, 17.6, 13.7)	—	1.77 (dd, 17.9, 13.4)	—
4	1.47 (dqd, 13.7, 6.6, 4.4)	40.0	1.50–1.57 (m)	39.0
5	—	49.1	—	48.4
6	5.06 (s)	79.4	5.01 (s)	81.6
7	—	57.5	—	55.7
8	—	172.5	—	177.3
9	3.24 (dd, 18.8, 2.4)	38.2	2.07 (dd, 18.8, 1.5)	36.6
	1.42 (d, 18.8)	—	2.02 (dd, 18.8, 2.2)	—
10	—	167.0	—	167.2
11	1.81 (q, 7.1)	45.3	2.58 (q, 7.6)	61.2
12	—	170.2	—	81.5
13	1.10 (d, 7.1)	8.3	0.61 (d, 7.6)	14.0
14	1.06 (s)	11.5	0.33 (s)	12.9
15	0.43 (d, 6.6)	15.4	0.41 (d, 6.8)	15.6
1′	—	166.2	—	168.0
2′	—	126.0	1.41 (s)	20.3
3′	5.61 (qq, 7.3, 1.5)	142.9	—	—
	—	15.9	—	—
4′	1.87 (dq, 7.3, 1.5)	20.1	—	—
5′	1.69 (quint, 1.5)	—	—	—

[a] In C_6D_6.

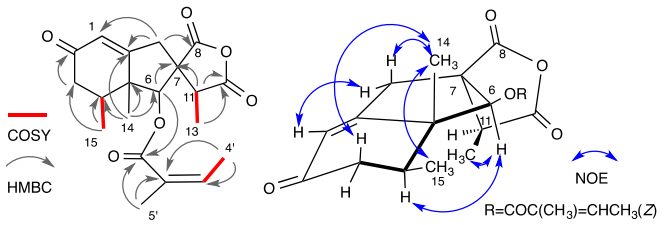

Fig. 2. Selected 2D correlations detected for compound **1**.

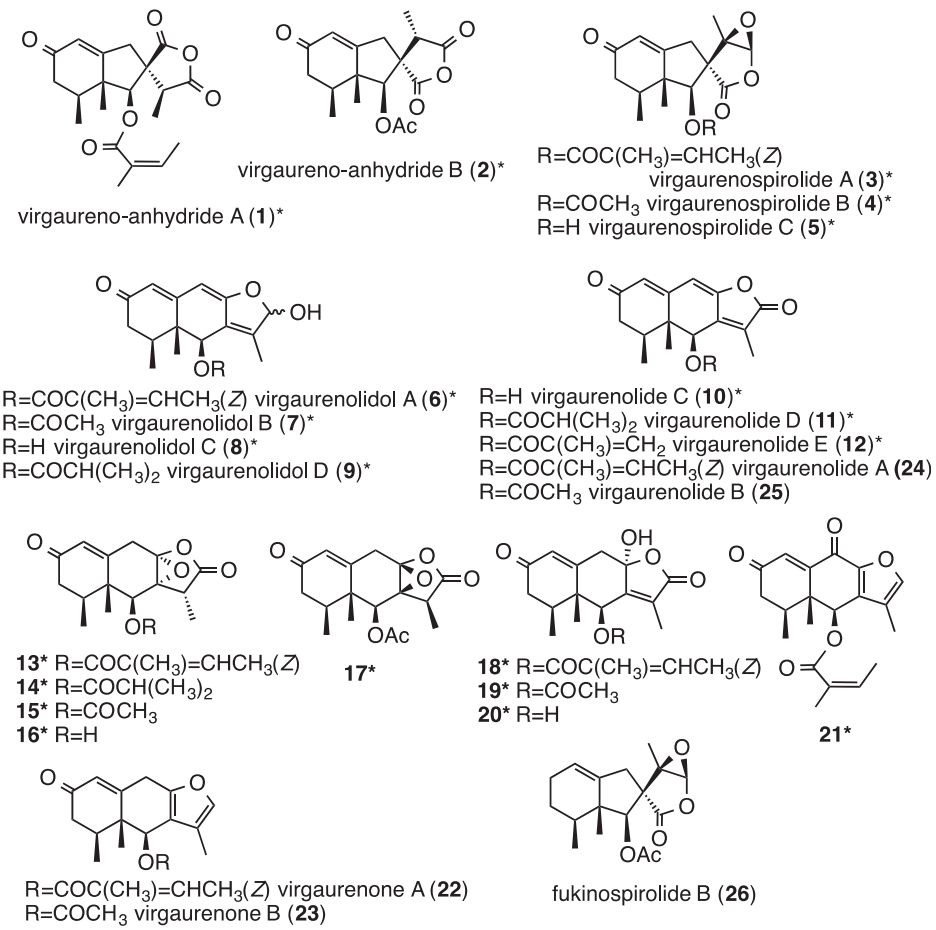

Fig. 1. Compounds isolated in this study (asterisks indicate new compounds).