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著者	NAKATANI Munehiro, ISHIBA Keiichi, FUJIMOTO Koichi, HASE Tsunao
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COUMARINS AND TRITERPENES FROM *SKIMMIA JAPONICA* THUNB.

By
Munehiro NAKATANI, Keiichi ISHIBA, Koichi FUJIMOTO
and Tsunao HASE

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Abstract

The isolation and characterization of coumarins and triterpenes from *Skimmia japonica* are reported.

Introduction

Skimmia japonica Thunb. (Rutaceae) is one species of the genus endemic to forest shades of the west of the Kanto district. The genus is a treasure of chromones and coumarins and many compounds have been reported. Recently, J. Reisch et al. reported the isolation of ten furanocoumarins containing two new compounds from *S. japonica* [1]. On the other hand, M. Ochi et al. iolated two insect growth inhibitory triterpenes from it [2].

During our study on Rutaceae plants, we isolated and characterized five known coumarins, imperatorin (**1**) [1], phellopterin (**2**) [3], xanthotoxol (**3**) [4], osthol (**4**) [4] and isoimperatorin (**7**) [1, 5], along with two triterpenes, taraxerone (**5**) [6] and taraxerol (**6**) [5], in which compounds **2**, **3**, **4** and **6** were first observed in this species.

Results and Discussion

From the methanol extract of the fresh leaves of *S. japonica,* four coumarins and two taraxerane triterpenes were isolated. On the other hand, one another coumarin was obtained from the root bark. These compounds were characterized mainly by spectroscopic methods and some chemical transformations.

Compounds **1–4** and **7** were found to be coumarins from their UV absorptions (Table 1) [7]. The downfield ^{1}H NMR spectral patterns of the compounds **1–3** and **7** were typical of linear furanocoumarins [8], in which the compounds **1**, **2** and **7** showed the presence of a 3,3-dimethylallyloxy chain attached to C-5 or C-8. The distinction between the C-5 and C-8 substituted linear furanocoumarins **1–3** and **7** was made on the basis of the chemical shift of

* Department of Chemistry, Faculty of Science, Kagoshima University, Kagoshima 890, Japan.

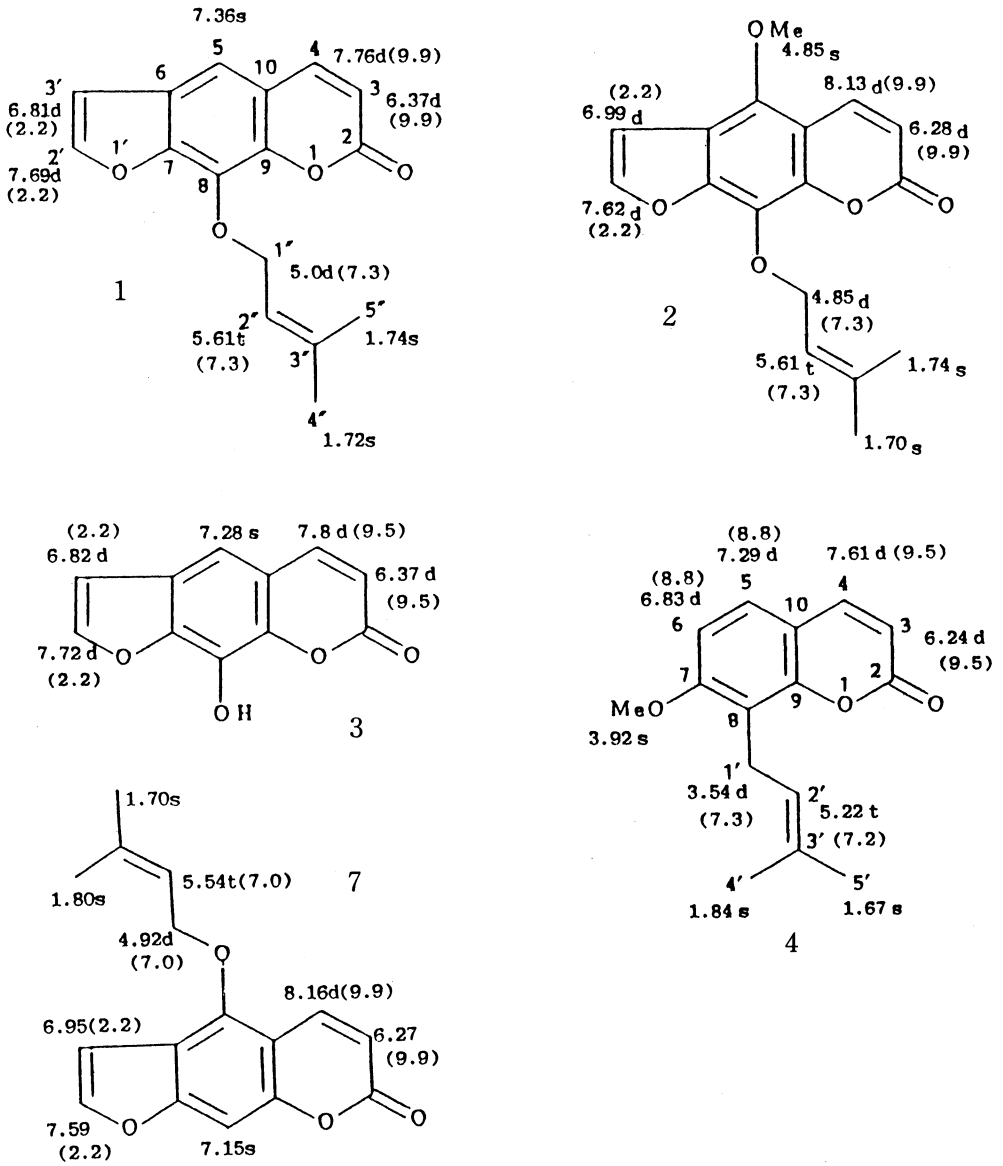


Fig. 1 Structures and ^{1}H NMR chemical shifts of coumarins **1**–**4** and **7** ($CDCl_3$, δ values, Hz in parenthesis).

H-4 which appeared downfield at δ 8.13 and 8.16 in the compounds **2** and **7**, respectively, indicating that they were substituted at C-5 [3]. The H-4 protons in the compounds **1** and **3** resonated at δ 7.76 and 7.80 confirming that they were substituted at C-8 [9]. The compound **2** exhibited no signal for an aromatic proton in the ^{1}H NMR spectrum. The substitution of OMe group in **2** was clarified to be at C-5 by ^{1}H NOE experiments. Irradiation of the OMe protons at δ 4.85 induced 13 and 8% peak enhancements on the 4-H and 3′-H signals, respectively. The ^{13}C NMR chemical shifts of these compounds are presented in Table 2. The compounds have been characterized as imperatorin (**1**), phellopterin (**2**), xanthotoxol (**3**) and isoimperatorin (**7**).

Table 1. UV spectra of coumarins from *S. japonica*

Compound	λ_{max} ($CHCl_3$) nm			Compound	λ_{max} ($CHCl_3$) nm			
1	253	265	301	4	240	245	265	315
2	252	269	314	7	243	249	263	299*
3	252	268	309				* in EtOH	

Table 2. ^{13}C NMR chemical shifts of benzopyrone and furobenzopyrone nucleus (δ values, $CDCl_3$)

Compound	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C10	C-2′	C-3′
1	160.5	114.7	143.9	113.1	125.4	148.6	131.7	144.3	116.5	146.6	106.7
2	160.7	112.8	134.3	144.4	116.5	148.0	125.8	139.7	107.5	145.1	105.0
3	160.0	114.6	145.3	110.9	125.2	145.2	130.8	140.6	116.2	147.2	107.1
4	160.5	113.3	144.0	125.2	113.3	147.3	126.5	149.3	107.7		
7	161.2	112.6	139.7	149.0	114.3	158.1	94.3	153.0	107.8	145.0	105.0

Table 3. ^{13}C NMR chemical shifts of side-chain carbons (δ values, $CDCl_3$)

Compound	C-1″	C-2″	C-3″	C-4″	C-5″	OMe
1	70.2	119.8	139.7	25.8	18.1	
2	70.4	119.9	139.3	25.8	18.1	
4	22.2	120.7	138.3	26.1	18.1	56.4
7	69.9	119.2	139.9	25.9	18.2	

The downfield ^1H NMR spectral pattern containing two sets of doublets of the compound **4** suggested that it was a 7,8-disubstituted coumarin. As all the coumarins observed in the genus *Skimmia* possess an O-function at C-7, other substituent of 3,3-dimethylallyl group must be at C-8. This was also supported well by the chemical shift of δ 113.3 (C-6), 147.3 (C-7) and 126.5 (C-8) in the ^{13}C NMR spectrum. Thus, this compound was identified as osthol (**4**).

Compound **5**, $C_{30}H_{48}O$, mp 250–251°, exhibited the following data; $[\alpha]_D+7°$ ($CHCl_3$); IR: 1705 cm^{-1} (>CO). The ^{13}C NMR spectrum revealed 30 signals (–Ç–Me×8, $-CH_2-$×10, ≥CH×3, –Ç–×6, >C=CH–×1 and >C=O×1). Unequivocal information for the structure was obtained from its EI mass spectrum (Scheme 1). There were two characteristic peaks at m/z 300 and 204 denoting the retro-Diels-Alder cleavage fragments found in the spectra of taraxene derivatives possessing one oxo group in rings A/B [10]. These spectral data suggested **5** to be taraxerone.

Compound **6**, $C_{30}H_{50}O$, mp 285–288.5°, was a triterpenol from an OH absorption at 3480 cm^{-1} and afforded a monoacetate **9**, mp 294–296°. The EI mass spectrum showed a similar retro-Diels-Alder cleavage to the compound **5** at m/z 302 and 204. The ^1H and ^{13}C NMR spectra of **6** and the acetate **9** indicated that **6** was taraxerol [10] and the oxidation of **6** with pyridinium chlorochromate afforded the compound **5**.

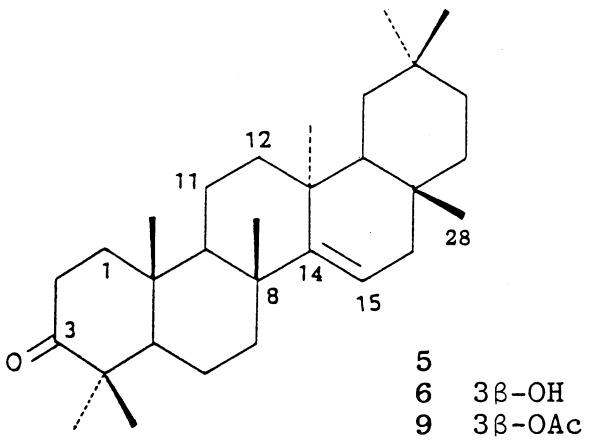


Table 4. ^{13}C NMR chemical shifts of compounds **5** and **6** (δ values, $CDCl_3$)

Carbon No	5	6	Carbon No	5	6
C-1	38.3	38.0	C-16	36.7	36.7
C-2	34.1	27.3	C-17	37.8	37.6
C-3	217.5	79.2	C-18	48.8	48.8
C-4	47.6	39.1	C-19	40.6	41.3
C-5	55.8	55.8	C-20	28.8	28.8
C-6	19.9	18.8	C-21	33.6	33.7
C-7	35.1	35.1	C-22	33.1	33.1
C-8	39.9	38.9	C-23	26.1	28.0
C-9	48.7	47.3	C-24	21.5	15.4
C-10	37.6	37.8	C-25	14.8	15.4
C-11	17.4	17.5	C-26	29.9	29.9
C-12	35.8	35.8	C-27	25.6	26.0
C-13	37.7	37.7	C-28	29.9	29.8
C-14	157.6	158.1	C-29	33.3	33.4
C-15	117.3	116.9	C-30	21.3	21.3

Experimental

Mps: uncorr. All the compounds were identified by IR, UV, MS and NMR spectra. IR and UV spectra were recorded on Shimadzu IR-408 and UV-210A spectrophotometers, respectively. ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ at 400 and 100 MHz using a JEOL FX-400 spectrometer. Mass spectra were recorded on a JEOL D-300 spectrometer. Optical rotation was measured using a JASCO J-20A spectropolarimeter.

Plant material. Collected at Mt. Takakuma, Kagoshima prefecture, and identified by Mr. Umada (Kagoshima University).

Extraction and isolation. i) The fresh leaves (1.2 Kg) was extracted with methanol. The methanol extract was fractionated successively with *n*-hexane, ether and ethyl acetate. The hexane extract was chromatographed on silica gel to give two triterpenes, **5** and **6**, and

a mixture of a coumarin **4** and three furanocoumarins, **1–3**, which were isolated by HPLC using a solvent system of MeOH (0.03–0.5%)/CH_2Cl_2. Yields; **1**: 2 mg, **2**: 2 mg, **3**: 0.8 mg, **4**: 1 mg, **5**: 68 mg and **6**: 145 mg. ii) The fresh root bark (550 g) was extracted with MeOH. The ether-soluble part of the MeOH extract was chromatographed on SiO_2 to give furanochmarin **7**; 35 mg and **8**; 12 mg, which were purified by prep TLC using ether/hexane solvent system.

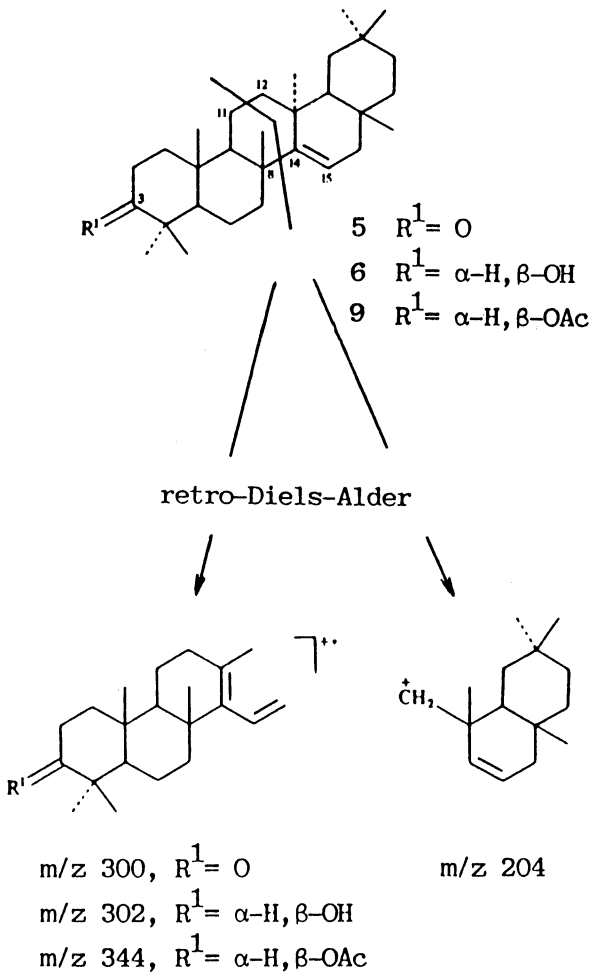
Imperatorin (*1*). $[M]^+$ m/z 270.0885 (calc. for $C_{16}H_{14}O_4$, 270.0875). Ms m/z: 270 $[M]^+$, 255, 202, 201, 173, 145.

Phellopterin (*2*). $[M]^+$ m/z 300.1012 (calc. for $C_{17}H_{16}O_5$, 300.0998).

Xanthotoxol (*3*). $[M]^+$ m/z 202.0239 (calc. for $C_{11}H_8O_4$, 202.0249). MS m/z: 202 $[M]^+$, 201, 173, 145.

Osthol (*4*). $[M]^+$ m/z 244.1095 (calc. for $C_{15}H_{16}O_3$, 244.1099). MS m/z: 244 $[M]^+$, 229, 214, 213, 175.

Taraxerone (*5*). Mp 250–251° (from ether/hexane). $[\alpha]_D+7°$ ($CHCl_3$). IR (Nujol):



Scheme 1. Mass fragmentations of compounds **5**, **6** and **9**.

1705 cm^{-1}. ^1H NMR ($CDCl_3$): δ 5.56 (1H, dd, J=8.1 and 3.3 Hz), 1.14, 1.09, 1.08, 1.07, 0.96, 0.92, 0.91 and 0.83 (each 3H, s). $[M]^+$ m/z 424.3701 (calc. for $C_{30}H_{48}O$, 424.3705).

Taraxerol (***6***). Mp 285–288.5° (from ether/hexane). IR (Nujol): 3480 cm^{-1}. ^1H NMR ($CDCl_3$): δ 5.54 (1H, d, J=8.1 and 3.3 Hz), 3.20 (1H, dd, J=11.0 and 4.4 Hz), 1.55, 1.09, 0.98, 0.95, 0.92, 0.91, 0.82 and 0.80 (each 3H, s). $[M]^+$ m/z 426.3855 (calc. for $C_{30}H_{50}O$, 426.3862).

Isoimperatorin (***7***). Mp 110° (from ether/EtOH). IR (Nujol): 1730, 1620 cm^{-1}. $[M]^+$ m/z 270.0890 (calc. for $C_{16}H_{14}O_4$, 270.0875).

Compound (*8*). Mp 49–49.5°. $[\alpha]_D -94°$ (MeOH). UV ($CHCl_3$): 242 nm. IR (Nujol): 1750, 1710 cm^{-1}.

Acetyltaraxerol (***9***). Taraxerol (**6**) was acetylated with Ac_2O in pyridine to give a monoacetate (**9**): mp 294–296°. ^1H NMR ($CDCl_3$): δ 5.54 (1H, dd, J=8.1 and 3.3 Hz), 4.48 (1H, dd, J=10.6 and 5.1 Hz), 2.05 (3H, s, OAc), 1.10, 2×0.96, 0.92, 0.91, 0.89, 0.87. 0.83 (each 3H, s).

Oxidation of taraxerol (***6***). Compound **6** was oxidized with pyridinium chlorochromate in $CHCl_3$ at room temperature. The product was identified to be taraxerone (**5**).

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