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(+)-ARCTIGENIN, A LIGNAN FROM *WIKSTROEMIA INDICA*

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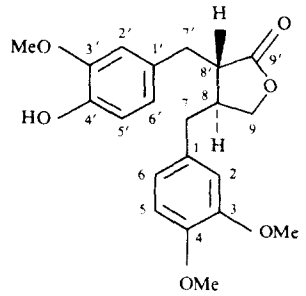
Key Word Index—*Wikstroemia indica*; Thymelaeaceae; (+)-arctigenin; lignan; enantiomer.

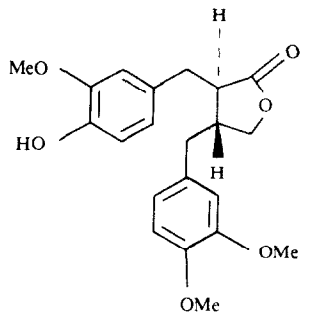
Abstract—A new lignan, (+)-arctigenin has been isolated from the roots of *Wikstroemia indica* (Nan-Ling-Jao-Hua) and identified as 8(*R*) 8′(*S*)-4′-hydroxy-3, 4,3′-trimethoxylignan-olid (9, 9′) on the basis of spectral evidence as well as a direct comparison with its enantiomer, (−)-arctigenin.

The whole plant of *Wikstroemia indica*; C. A. Mey (Nan-Ling-Jao-Hua) afforded four antitumor agents: tricin, kaempferol-3-*O*-β-D-glucopyranoside, (+)-nortrachelogenin and daphnoretin [1]. An examination of the extract of roots of this plant§ has led to the isolation of a new lignan, provisionally named (+)-arctigenin (**1**), in addition to the foregoing four compounds. The isolation of **1** involved an initial extraction of the ground air-dried roots of *W. indica* with *n*-hexane followed by methanol. The methanolic extract was concentrated and partitioned between chloroform and water. The chloroform extract underwent CC on Si gel (Merck Si gel 60, 230–400 mesh, 3 × 15 cm). Purification of the eluates [*ca* 200 ml, $CHCl_3$–MeOH (20 : 1)] by prep. TLC [Analtech Si gel GF-254, 1000 μm, $CHCl_3$–MeOH (10:1)] led to the isolation of **1** in 0.0005% yield as a yellow gum.

Compound **1**, $[\alpha]_D^{23}$ +28.05° (EtOH; *c* 1.23) $C_{21}H_{24}O_6$, showed a M^+ at *m/z* 372.1571 (base peak) in the mass spectrum. The ^1H NMR spectrum (250.132 MHz, $CDCl_3$, TMS) of **1** revealed the presence of three methoxyl groups at δ 3.81 (6H, *s*) and 3.85 (3H, *s*), and six aromatic protons at δ 6.47, 6.65 (1H each, *d* and $J = 2.2$ Hz each, H-2 or H-2′), 6.55, 6.62 (1 H each, *dd* and $J = 2.2$ and 9.4 Hz each, H-6 or H-6′), 6.75 and 6.83 (1H each, *d* and $J = 9.4$ Hz each, H-5 or H-5′). The mass spectrum of **1** displayed characteristic fragment ions [*m/z* 137 (86%), 151 (64%), and 235 (5%, $[M - 137]^+$)] indicative of the presence of a 4-hydroxy-3-methoxybenzyl and a 3,4-dimethoxybenzyl group [1]. The co-occurrence of (−)-nortrachelogenin and (−)-arctigenin from *Trachelospermum asiaticum* var. *intermedium* [2, 3], coupled with the isolation of (+)-nortrachelogenin, an 8(*R*), 8′(*R*)-4, 4′, 8′-trihydroxy-3, 3′-dimethoxylignan-olid (9, 9′), from *W. indica* [1] suggested a trimethoxylignan-olide (9, 9′) for compound **1**. The presence of this lignan-olide (9, 9′) skeleton [3] in **1** was further supported by its NMR signals at δ 3.88, 4.14 (1H each, *m*, H-9), 2.92 (2H, AB part of ABX, H-8 and H-8′), 2.40–2.70 (4H, *m*, H-7 and H-7′). The above evidence led to the consideration of **1** for the structure of arctigenin. A direct comparison of the TLC‖ [Merck Si gel 60, GF-254 in three solvent systems: $CHCl_3$–Me_2CO (15 : 1), C_6H_6–MEOH (5 : 1)



1 [8(R), 8′(S)]



2 [8(S), 8′(R)]

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§Collected and identified by H. C. Huang. A voucher specimen is available for inspection at the Herbarium of the School of Pharmacy, Kaohsiung Medical College, Kaohsiung, Taiwan.

‖Identical TLC behaviour was also observed for the diazomethanemethylated products of **1** and (−)-arctigenin.

Table 1. ^{13}C NMR of 1*

Carbon no.	δ(multiplicity)	Carbon no.	δ(multiplicity)
C-1	130.79 (*s*)	C-1′	129.56 (*s*)
C-2	114.55 (*d*)	C-2′	112.28 (*d*)
C-3	148.14 (*s*)	C-3′	149.31 (*s*)
C-4	147.10 (*s*)	C-4′	144.89 (*s*)
C-5	111.82 (*d*)	C-5′	112.02 (*d*)
C-6	120.78 (*d*)	C-6′	122.15 (*d*)
C-7 or 7′	34.63 (*t*)	C-7′ or 7	38.20 (*t*)
C-8 or 8′	41.06 (*d*)	C-8′ or 8	46.72 (*d*)
C-9	71.41 (*t*)	C-9′	179.00 (*s*)
3, 4, 3′-OMe	55.94 (*q*)		

*Carried out at 15.03 MHz in $CDCl_3$ (TMS). The ^{13}C NMR analysis of the related lignans, such as pluviatolide, its acetate and hinokinin, have been reported previously [5].

and *n*-hexane–Me_2CO (1 : 1)] and the IR, ^1H NMR and mass spectral data of **1** with (−)-arctigenin [8(*S*), 8′(*R*)-4′-hydroxy-3, 4, 3′-trimethoxylignan-olid (9, 9′)] (**2**) [2, 3] established the identity of both compounds. However, the opposite sign of both specific rotation and Cotton effects in circular dichroism of **1** compared to those of (−)-arctigenin (**2**), in which **1** showed $[\theta]_{230}^{27°}$ + 24 180 and **2** had $[\theta]_{230}^{27°}$ − 23 250, led to the assignment of the structure of **1** as the enantiomer of **2**, i.e. (+)-arctigenin, beyond doubt. The ^{13}C NMR spectral assignment, which was also in accord with the structure of **1**, is listed in Table 1.

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