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LIGNANS, BIFLAVONES AND TAXOIDS FROM HIMALAYAN *TAXUS BACCATA**†

B. DAS,‡ S. PADMA RAO, K. V. N. S. SRINIVAS and J. S. YADAV

Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad 500007, India

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Key Word Index—*Taxus baccata*; Taxaceae; twigs; phenolics; biflavones; lignans; taxoids; 4′-*O*-demethylsuchilactone.

Abstract—Chemical investigation of the twigs (separated from the needles) of the Himalayan yew, *Taxus baccata*, has culminated in the isolation of a new lignan, 4′-*O*-demethylsuchilactone, along with eight phenolic compounds, (−)-rhododendrol, (−)-rhododendrin, sciadopytisin, ginkgetin, kayaflavone, (−)-secoisolariciresinol, suchilactone and a lignan diol, not previously encountered in nature. Three taxoids, brevifoliol, 13-decinnamoyltaxchinin B and 10-deacetylbaccatin III were also isolated. This is the first report on the phytoconstituents isolated only from the twigs of the Himalayan yew.

INTRODUCTION

As a part of our investigation on the isolation of taxol and related bioactive taxoids from the Himalayan yew, *Taxus baccata*, we have examined different parts of the plant. Recently, we have published [1] the chemical composition of its needles. We were interested in investigating separately the twigs of the plant which were carefully separated from the needles as a previous investigation [2] on the needles and on the twigs of other yew trees has been reported with different results. Our investigation has led to the isolation of a new lignan, 4′-*O*-demethylsuchilactone (**1**), together with several phenolics and taxoids. Herein, we report the phytoconstituents isolated from twigs of the Himalayan yew.

RESULTS AND DISCUSSION

The dichloromethane–methanol (1:1) extract of the twigs of *T. baccata* contained a mixture of phenolics and taxoids, along with some sterols and fatty compounds. The phenolic compounds were the major constituents of the extract. The new lignan, 4′-*O*-demethylsuchilactone (**1**) was isolated as yellow oil. Its ^{1}H and ^{13}C NMR spectra and the mass fragmentation pattern (see Experimental) clearly established its structure as 4′-*O*-demethylsuchilactone (**1**) [3, 4]. On treatment with diazomethane, the new lignan afforded suchilactone (**2**) [4], thus confirming the structure **1** proposed for it.

Three other lignans, suchilactone (**2**), the diol **3** and (−)-secaisolariciresinol [1] were also isolated. Suchilactone (**2**) [α-(*trans*-3,4-methylenedioxybenzylidene-β-*R*-(3,4-dimethoxybenzyl)-γ-butyrolactone] has been isolated for the first time from a species of the Taxaceae. Previously, it was reported from two other species, *Polygala chinensis* [4] and *Haplophyllum popovii* [5] and as the pyrolytic product of the lignan helianthoidin [6]. However, its detailed NMR spectral data were not mentioned and its nomenclature was wrongly given [4] as 2-piperonylidene-3-veratryl-3*S*-γ-butyrolactone. We have studied the 400 MHz ^{1}H and 100 MHz ^{13}C NMR spectra of **2** (Experimental).

The lignan diol, **3**, has not previously been isolated from a natural source, but it was prepared from suchilactone (**2**) [4]. We have determined the structure of the naturally occurring **3** from spectral evidence. On acetylation with acetic anhydride and pyridine, it yielded a diacetate. The physical and spectral properties of the latter suggested that it was similar to prasanthaline (**4**) previously isolated [7, 8] from *Jatropha gossypifolia*. The lignan, **3**, was identical to the lithium aluminium hydride reduction product of suchilactone (**2**) in all respects.

Besides lignans, the simple phenolic (−)-rhododendrol [1] and its 2-*O*-glucoside, (−)-rhododendrin [1, 9, 10], have been characterized. In both our samples of twigs and needles (−)-rhododendrol was found [1] to be a major constituent. As we did not use any acid during extraction of the plant and isolation of the constituents we feel that the compound is a true natural product.

Sciadopytisin [11, 12], ginkgetin [12, 13] and kayaflavone [12, 14] are the biflavonoid constituents of the twigs. The latter has not previously been reported from *T. baccata* by other workers.

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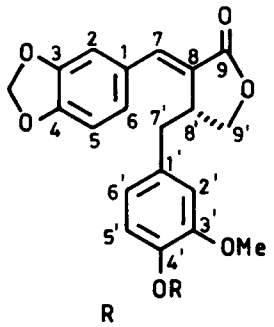
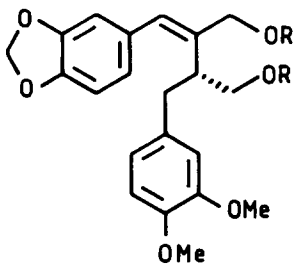
‡Author to whom correspondence should be addressed.



R
1 H
2 Me



R
3 H
4 Ac

The taxoids present in the twigs are mainly of the rearranged 11 (15 → 1) *abeo*-taxane skeleton [15, 16] as evident from their spectral data. Two pure compounds, brevifoliol [15, 17] and 13-decinnamoyl-taxchinin B [15–17] possessing such rearranged skeleton have been isolated along with a minor taxoid, 10-deacetylbaccatin III [18], having the taxane structure.

The compounds isolated from the twigs are biologically important. (−)-Rhododendrin exhibits hepatoprotective activity [10] and the biflavonoids possess antipyretic and analgesic properties [19]. The diterpenoid constituents of the twigs were mainly of the 11 (15 → 1) *abeo*-taxane skeleton and the taxoids of this type of rearranged structure have been reported to show tubulin-binding activity [20, 21], but no *in vitro* cytotoxicity [20]. The lignans containing the 2,3-diarylbutyrolactone skeleton have been shown [22] to possess a synergetic action for insecticides. Thus, the twigs of the Himalayan yew may be considered as a potential source of different types of bioactive natural products.

EXPERIMENTAL

General. Mps uncorr. CC: silica gel (BDH, 100–200 mesh). TLC: silica gel G. TLC spots were visualized by exposure to I_2 vapour and after spraying with 10% methanolic H_2SO_4.

Plant material. Twigs of *T. baccata* L. were collected from the Himalayan region in October, 1991. These were carefully separated from needles and all buds removed. A voucher specimen (Tb-T) is deposited in our laboratory.

Extraction and isolation of constituents. Twigs were dried (2 kg) and powdered. The material was extracted with CH_2Cl_2–MeOH (1:1, 3 × 21) at room temp., filtered and the solvent removed under red. pres. to yield a residue (72 g). This was chromatographed on silica gel. By elution with gradient of hexane, C_6H_6 and EtOAc, sciadopytisin (22 mg) [11, 12], kayaflavone (17 mg) [12, 14], ginkgetin (6 mg) [12, 13], 13-decinnamoyltaxchinin B (15 mg) [15–17], suchilactone (**2**, 18 mg) [4, 6], 4′-*O*-demethylsuchilactone (**1**, 7 mg), (−)-secoisolariciresinol (12 mg) [1], (−)-rhododendrin (48 mg) [1], 10-deacetylbaccatin III (7 mg) [18], brevifoliol (14 mg) [15, 17], lignan diol **3** (11 mg) and (−)-rhododendrol (42 mg) [1] were obtained in ascending order of polarity. Known compounds were characterized by comparison of their physical and spectral properties with those of authentic samples reported in the literature.

4′-*O*-*Demethylsuchilactone* (**1**). Yellow oil. $[\alpha]_D^{25}$ − 38.3° ($CHCl_3$; *c* 0.2371). IR ν_{max}^{KBr} cm^{-1}: 3445, 1725, 1630, 1595, 1480. ^1H NMR (200 MHz, $CDCl_3$): δ 7.47 (1H, *d*, *J* = 1.6 Hz, H-7), 7.01–6.62 (6H, *m*, Ar-H), 5.98 (2H, *s*, OCH_2O), 4.30–4.22 (2H, *m*, H_2-9′), 3.82 (3H, *s*, OMe), 3.78 (1H, *m*, H-8′), 3.03 (1H, *dd*, *J* = 14.6 and 4.4 Hz, H-7′a), 2.62 (1H, *dd*, *J* = 14.6 and 10.1 Hz, H-7′b). ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.3 (C-1), 108.6 (C-2), 148.9 (C-3), 149.0 (C-4), 112.0 (C-5), 125.9 (C-6), 137.0 (C-7), 126.1 (C-8), 172.4 (C-9), 127.9 (C-1′), 108.3 (C-2′), 146.5 (C-3′), 143.2 (C-4′), 111.3 (C-5′), 120.7 (C-6′), 37.4 (C-7′), 39.8 (C-8′), 69.6 (C-9′), 101.6 (OCH_2O), 55.7 (OMe). MS *m/z* (rel. int.): 354 $[M]^+$ (4), 217 (3), 137 (100).

Suchilactone (**2**). Mp 131–132° (C_6H_6). $[\alpha]_D^{25}$ − 85.5° ($CHCl_3$; *c* 0.3494). ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (1H, *d*, *J* = 1.6 Hz, H-7), 7.03 (1H, *dd*, *J* = 8.0 and 1.5 Hz, H-6), 7.02 (1H, *d*, *J* = 1.5 Hz, H-2), 6.84 (1H, *d*, *J* = 8.0 Hz, H-5), 6.78 (1H, *d*, *J* = 8.0 Hz, H-5′), 6.68 (1H, *dd*, *J* = 8.0 and 1.5 Hz, H-6′), 6.64 (1H, *d*, *J* = 1.5 Hz, H-2′), 6.01 (2H, *s*, OCH_2O), 4.32–4.21 (2H, *m*, H-9′), 3.84 and 3.82 (3H each, *s*, 2OMe), 3.76 (1H, *m*, H-8′), 3.00 (1H, *dd*, *J* = 14.8 and 4.6 Hz, H-7′a), 2.60 (1H, *dd*, *J* = 14.8 and 10.2 Hz, H-7′b). ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.3 (C-1), 108.7 (C-2), 149.0 (C-3), 149.1 (C-4), 112.0 (C-5), 125.9 (C-6), 137.1 (C-7), 126.3 (C-8), 172.5 (C-9), 128.1 (C-1′), 108.4 (C-2′), 147.9 (C-3′), 148.3 (C-4′), 111.3 (C-5′), 122.0 (C-6′), 37.6 (C-7′), 40.0 (C-8′), 69.7 (C-9′), 100.7 (OCH_2O), 56.0 and 55.8 (2 OMe). MS *m/z* (rel. int.): 368 $[M]^+$ (6), 217 (3), 151 (100). The compound was directly compared with an authentic sample of suchilactone [4].

Lignan diol **3**. Mp 120–121° (C_6H_6). $[\alpha]_D^{25}$ − 35.7° ($CHCl_3$; *c* 0.4239). UV λ_{max}^{EtOH} nm: 258 (log ε 3.83). IR ν_{max}^{KBr} cm^{-1}: 3370, 1595, 1480, 920. ^1H NMR (200 MHz, $CDCl_3$): δ 6.81–6.47 (7H, *m*, Ar-H and H-7), 5.92 (2H, *s*, OCH_2O), 4.39 (1H, *d*, *J* = 11.8 Hz, H-9a), 4.09 (1H, *d*, *J* = 11.8 Hz, H-9b), 3.84 and 3.75 (3H, *s*, 2 OMe), 3.74–3.65 (2H, *m*, H_2-9′), 3.34 (1H, *m*, H-8′), 2.72–2.61 (2H, *m*, H_2-7′). MS *m/z* (rel. int.): 3.72 $[M]^+$ (8), 354 $[M - H_2O]^+$ (5), 221 (2), 203 (38), 151 (100).

Methylation of 4'-O-demethylsuchilactone (**1**). 4'-*O*-Demethylsuchilactone (**1**, 3 mg) dissolved in Et_2O (0.5 ml) was treated with CH_2N_2 in Et_2O (1 ml) to yield a compound, 3 mg, mp 130–131° (C_6H_6), $[\alpha]_D^{25}$ − 83.8° ($CHCl_3$; *c* 0.1132) which was identified as suchilactone (**2**) from its physical and spectral properties.

Acetylation of compound **3**. A mixt. of **3** (5 mg), Ac_2O (0.2 ml) and a few drops of pyridine was stood at room temp. overnight. Usual work-up afforded a product as a viscous mass, 5 mg, $[\alpha]_D^{25}$ − 33.4° ($CHCl_3$; *c* 0.3476), identical in all respects to prasanthaline (**4**) [7, 8], previously isolated from *Jatropha gossypifolia*.

$LiAlH_4$ *reduction of suchilactone* (**2**). Suchilactone (**2**, 15 mg) was reduced with $LiAlH_4$ (30 mg) in dry THF (20 ml) for 6 hr yielding a gummy mass which was purified by CC over silica gel to produce a solid, 11 mg, mp 119–120° (C_6H_6), identical to the naturally occurring lignan diol, **3**.

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