Pergamon

0031-9422(94)00678-4

*Phytochemistry*, Vol. 38, No. 3, pp. 715–717, 1995

0031-9422/95 $9.50 + 0.00

# 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 500 007, India

(*Received in revised form* 14 *July* 1994)

**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.

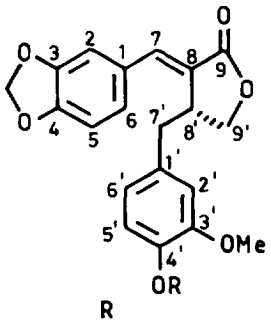
Besides lignans, the simple phenolic (−)-rhododendrol [1] and its 2-*O*-glucoside, (−)-rhododendrin [1, 9, 10], have been characterized. In both our samples of twigs and needles (−)-rhododendrol was found [1] to be a major constituent. As we did not use any acid during extraction of the plant and isolation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

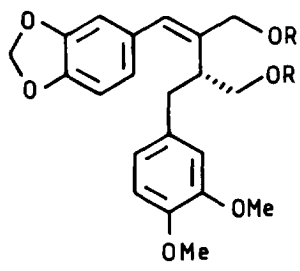
*Part 6 in the series, 'Studies on Phytochemicals'. For Part 5 see Das, B., Rao, S. P., Srinivas, K. V. N. S. and Yadav, J. S. (1995) *Phytochemistry* **38**, 671.

†IICT Communication No.: 3346.

‡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 $\nu_{max}^{KBr}$ $cm^{-1}$: 3445, 1725, 1630, 1595, 1480. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 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, $CDCl_3$): $\delta$ 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, $CDCl_3$): $\delta$ 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, $CDCl_3$): $\delta$ 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 $\lambda_{max}^{EtOH}$ nm: 258 (log ε 3.83). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3370, 1595, 1480, 920. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 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**.

*Acknowledgements*—The authors thank Dr A. V. Rama Rao, Director, for his constant encouragement and Dr R. S. Kapil, RRL, Jammu, India, for supply of the plant material. They also express their thanks to Professor S. Ghosal (B.H.U., India) for providing an authentic sample of suchilactone.

## REFERENCES

1. Das, B., Takhi, M., Srinivas, K. V. N. S. and Yadav, J. S. (1993) *Phytochemistry* **33**, 1489.
2. Kelsey, R. G. and Vance, N. C. (1992) *J. Nat. Prod.* **55**, 912.
3. Chatterjee, A., Das, B., Paseard, C. and Prangé, T. (1981) *Phytochemistry* **20**, 2047.
4. Ghosal, S., Kumarswamy, C., Chauhan, P. B. S. and Srivastava, R. S. (1973) *Phytochemistry* **12**, 2550.
5. Razakova, D. M. and Bessonova, I. A. (1981) *Khim. Prir. Soedin.* 516.
6. Burden, R. S., Combie, L. and Whiting, D. A. (1969) *J. Chem. Soc. (C)*, 693.
7. Chatterjee, A., Das, B., Chakrabarti, R., Bose, P., Banerji, J., Banerji, A. and Budzikiewicz, H. (1988) *Indian J. Chem.* **27B**, 740.
8. Banerji, J., Bose, P. and Das, B. (1989) *Indian J. Chem.* **28B**, 711.
9. Khan, M. S. Y., Kumar, I., Prasad, J. S., Nagarajan, G. R., Parthasarathy, M. R. and Krishnamurty, H. G. (1976) *Planta. Med.* **30**, 82.
10. Parmar, V. S., Vardhan, A., Taneja, P., Sinha, R., Patnaik, G. K., Tripathi, S. C., Boll, P. M. and Larsen, S. (1991) *J. Chem. Soc., Perkin Trans. I* 2687.
11. Kariyone, T. and Sawada, T. (1958) *Yakugaku Zasshi* **78**, 1016.
12. Baker,. W., Finch, A. C. M., Ollis, W. D. and Robinson, K. W. (1963) *J. Chem. Soc.* 1477.
13. Markham, K. R., Sheppard, C. and Geiger, H. (1987) *Phytochemistry* **26**, 3335.
14. Kariyone, T. and Sawada, T. (1958) *Yakugaku Zasshi* **78**, 1010.
15. Appendino, G., Barboni, L., Gariboldi, P., Bombardelli, E., Gabetta, B. and Viterbo, D. (1993) *J. Chem. Soc., Chem. Commun.* 1587.
16. Fuji, K., Tanaka, K., Li, B., Singu, T., Sun, H. and Taga, T. (1993) *J. Nat. Prod.* **56**, 1520.
17. Barboni, L., Gariboldi, P., Torregiani, E., Appendino, G., Gabetta, B. and Bombardelli, E. (1993) *Phytochemistry* **33**, 145.
18. Chauviere, G., Gúenard, D., Picot, F., Senith, V. and Potier, P. (1981) *C. R. Seances Acad. Sci. Ser.* 2 **293**, 501.
19. Vohora, S. B., Kumar, I., Shah, S. A. and Khan, M. S. Y. (1980) *Indian J. Med. Res.* **71**, 815.
20. Samaranayake, G., Magri, N. F., Jitrangsri, C. and Kingston, D. G. I. (1991) *J. Org. Chem.* **56**, 5114.
21. Wahl, A., Guéritte-Voegelin, F., Gúenard, D., Goff, M. T. le and Potier, P. (1992) *Tetrahedron* **48**, 6965.
22. Kato, Y. and Munakata, K. (1978) in *Chemistry of Lignans* (Rao, C. B. S., ed.), p. 116. Andhra University Press, Waltair, India.