Journal of Natural Products
Vol. 58, No. 10, pp. 1508-1514, October 1995

10-DEACETYLBACCATIN III ANALOGUES FROM *TAXUS BACCATA*[1]

BRUNO GABETTA, PAOLO DE BELLIS, ROBERTO PACE,

Indena S.p.A., Via Ripamonti 99, 20141 Milano, Italy

GIOVANNI APPENDINO,*

Dipartimento di Scienza e Tecnologia del Farmaco, Via Giuria 9, 10125 Torino, Italy

LUCIANO BARBONI, ELISABETTA TORREGIANI, PIERLUIGI GARIBOLDI,

Dipartimento di Scienze Chimiche, Via S. Agostino 1, 62032 Camerino (MC), Italy

and DAVIDE VITERBO

Dipartimento di Chimica Inorganica, Chimica Fisica e Chimica dei Materiali, Via Giuria 7, 10125 Torino, Italy

ABSTRACT.—The needles of the European yew, *Taxus baccata*, yielded two new analogues of 10-deacetylbaccatin III, identified as 13-*epi*-10-deacetylbaccatin III [**4**] and 2-debenzoyl-2-tigloyl-10-deacetylbaccatin III [**5**]. The crystal structure of baccatin III [**6**], corresponding to the terpenoid core of paclitaxel, was determined.

The antitumor drug paclitaxel (=Taxol®, **1**; known also in the literature as taxol) is a natural product obtained from the bark of the Pacific yew (*Taxus brevifolia* Nutt.) (2). This source is neither abundant nor rapidly renewable, and huge research efforts have been devoted to the search for sustainable alternatives (3). The most promising approach in terms of ecology and economy is at present the semi-synthesis of paclitaxel from 10-deacetylbaccatin III [**3**], a compound available in relatively high yield (up to 0.1% of fresh wt basis) from a renewable and plentiful source (foliage and clippings of several yew species) (3). Compound **3** is also the starting material for the synthesis of analogues of paclitaxel, one of which [docetaxel (Taxotere®) **2**] is in advanced clinical development (4). Considerable interest exists therefore in the isolation of modified derivatives of **3**, since new structural types of antitumor taxoids might be available after esterification of the 13-hydroxyl with a suitable side-chain synthon.

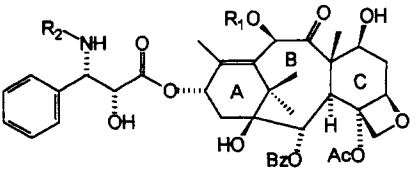
We report here the isolation of two novel analogues of **3** (compounds **4** and **5**) from the needles of the European yew (*T. baccata* L.). Baccatin III [**6**] (5), corresponding to the terpenoid core of paclitaxel, was also obtained from this source, and its solid-state conformation was investigated by X-ray analysis.

RESULTS AND DISCUSSION

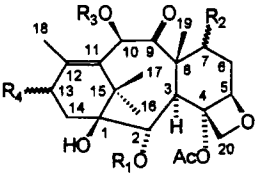
Compounds **4** and **5** are minor constituents of yew extracts, and their chromatographic behavior is very similar to that of **3**, a major constituent. Thus, the purification of **4** and **5** proved difficult (see Experimental), and only small amounts of these compounds were available for structure elucidation, which was based exclusively on spectroscopic data.

The nmr spectra of 10-deacetylbaccatin III [**3**] (6) and **4** (Tables 1 and 2) showed the same spin-systems and carbon multiplicities, suggesting that these compounds share the same constitution of the diterpenoid moiety and differ only in their acylation pattern

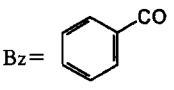
[1]Part XX in the series "The Chemistry and Occurrence of Taxane Derivatives." For Part 19, see Barboni *et al.* (1).

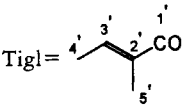


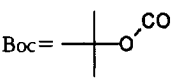
	R_1	R_2
1	Ac	Bz
2	H	Boc



	R_1	R_2	R_3	R_4
3	Bz	β-OH	H	α-OH
4	Bz	β-OH	H	β-OH
5	Tigl	β-OH	H	α-OH
6	Bz	β-OH	Ac	α-OH
7	Bz	α-OH	H	α-OH
8	Bz	α-OH	Ac	α-OH







and/or stereochemistry. An alternative connectivity of the acyloin system, with a C-9 hydroxyl and a C-10 oxo group, was excluded by the chemical shift of the ketone carbonyl (δ 210.1) which ruled out conjugation (7). Indeed, the uv spectra of **3** and **4** were identical, and displayed only the maxima of a benzoate chromophore. Inspection of the long-range (^3J) ^{1}H-^{13}C couplings (FLOCK spectrum) showed a correlation between the benzoate carbonyl (δ 165.5) and H-2 (δ 5.36), whereas the downfield shift of C-4 (δ 81.7)

TABLE 1. ^{1}H-Nmr Data for Compounds **4** and **5**.[a]

Proton	Compound	
	4[b]	**5**[c]
2	5.36 d (6.9)	5.18 d (7.0)
3	3.52 d (6.9)	3.67 d (7.0)
5	4.92 br d (8.5)	4.87 br d (7.6)
6α	2.30 m	2.24 m
6β	1.62 m	1.60 m
7	4.02 m	4.03 m
10	5.11 d (2.4)	5.06 d (2.4)
13	3.71 m	4.55 br t (8.0)
14α	2.56 dd (14.0, 9.8)	2.06 dd (14.5, 9.4)
14β	1.73 br d (14.0)	2.03 dd (14.5, 7.3)
16	0.95 s	0.85 s
17	1.12 s	0.90 s
18	1.85 br s	1.78 br s
19	1.51 s	1.45 s
20α	4.02 s	3.95 d (8.1)
20β	4.02 s	4.12 d (8.1)
Ac	2.25 s	2.10 s

[a]300 MHz; DMSO-d_6, TMS as reference, J in Hz. The assignments were confirmed by a ROESY experiment. Significant correlations for the diastereotopic methylene protons were: H-6α/H-5, H-6β/H-19, H-14β/H-17, H-14α/H-3, H-20α/H-5, H-20α/Ac.

[b]Benzoate resonances: δ 8.00 (2H, d, J=7.6 Hz, H-ortho), 7.54 (2H, t, J=7.6 Hz, H-meta), 7.64 (1H, t, J=7.6 Hz, H-para).

[c]Tiglate resonances: δ 6.80 (1H, qq, J=7.5 and 1.3 Hz, H-3′), 1.75 (3H, d, J=7.5 Hz, H-4′), 1.84 (3H, d, J=1.3 Hz, H-5′).

located the acetoxyl at this carbon (8). Thus, the acylation pattern of **3** and **4** is the same and these compounds are diastereomers. An alternative structure of the 11(15→1)*abeo*-taxane type was ruled out by the observed ^{13}C-nmr data [singlet for C-15 at δ 42.1 (9)] and by the detection of a long-range (^{3}J) correlation (FLOCK) between C-11 and H-16/H-17. The most obvious site of isomerization in baccatin III derivatives is C-7. However, epimerization at this center in **4** was ruled out by the upfield chemical shift of C-19 (δ 9.82), which showed the presence of a γ-gauche interaction, and therefore a cis relationship, with the 7-hydroxyl (10), and was further confirmed by comparison with an authentic sample of 10-deacetylbaccatin V [**7**] (11).

The main difference between the ^{1}H-nmr spectra of **3** and **4** was the chemical shift of H-13. This proton resonated at higher field in **4** (Δδ −0.91), suggesting that **3** and **4** are C-13 epimers. Indeed, H-13 in **4** showed rOe correlations with H-3 and H-14α, indicative of a location in the concave α-face of the molecule. Conversely, no rOe effect could be detected with the 17-methyl, whose downfield shift in **4** (Δδ +0.19) is presumably due to the magnetic anisotropy of the β-hydroxyl at C-13. Comparison of the ^{13}C-nmr spectra of **3** and **4** showed changes in the chemical shifts of C-1, C-13, C-17, C-18 (downfield in **4**), and C-2 (upfield in **4**). The downfield shift of the 18-methyl

TABLE 2. ^{13}C-Nmr Data for Compounds **4** and **5**.[a]

Carbon	Compound	
	4[b]	**5**[c]
1	81.7 s	77.2 s
2	71.1 d	74.6 d
3	46.8 d	47.0 d
4	81.0 s	80.4 s
5	83.9 d	84.2 d
6	37.1 t	37.0 t
7	71.3 d	71.4 d
8	57.8 s	57.4 s
9	210.1 s	210.8 s
10	75.4 d	74.8 d
11	138.6 s	134.9 s
12	139.4 s	141.9 s
13	68.2 d	66.5 d
14	38.2 t	39.2 t
15	42.1 s	42.8 s
16	19.2 q	20.6 q
17	32.0 q	27.2 q
18	18.2 q	15.2 q
19	9.8 q	10.1 q
20	75.7 t	75.9 t
Ac	170.3 s	169.9 s
	22.3 q	22.6 q

[a]75.4 MHz, DMSO-d_6; TMS as reference. Assignments were made by inspection of the C-H correlation and FLOCK nmr spectra.

[b]Benzoate resonances: δ 165.5 (s, CO), 130.6 (s, ipso), 129.9 (d, ortho), 129.1 (d, meta), 133.7 (d, para).

[c]Tiglate resonances: δ 167.1 (s, C-1′), 129.0 (s, C-2′), 137.9 (d, C-3′), 14.7 (q, C-4′), 12.3 (q, C-5′).

($\Delta\delta$ +3.5) signal is probably due to the removal of a shielding γ-gauche interaction with the 13α-hydroxyl group. The remaining changes might be the result of the anisotropy of the C-13 β-hydroxyl (C-17, $\Delta\delta$ +5.3) and the formation of an intramolecular hydrogen bond between the hydroxyls at C-13 and C-1 (C-13 and C-1, $\Delta\delta$ +2.2 and +4.8, respectively). This might interfere with hydrogen-bond formation between the C-1 hydroxyl and the benzoate carbonyl at C-2, thus explaining the effect also on the chemical shift of C-2 ($\Delta\delta$ −3.7).

The nmr spectra of **5** showed all the signals of the diterpenoid moiety of **3**, but the resonances of the benzoyl moiety were replaced by those of a tigloyl (*E*-2-methyl-2-butenoyl) group (12). Inspection of the long range ^{1}H-^{13}C couplings [FLOCK spectrum, correlation H-2 (δ 5.18)/δ 167.1 (C-1′)] located the unsaturated ester group at C-2, whereas chemical shift considerations showed that the acetyl group was at C-4 (see above). Thus, **5** is 2-debenzoyl-2-tigloyl-10-deacetylbaccatin III. Apart from the presence of different ester groups, the ^{13}C-nmr spectra of **3** and **5** were almost identical. Significant differences were found instead between the ^{1}H-nmr spectra, because H-2 and all the protons oriented toward the α-face of the molecule were moved upfield in **5** as a result of the different anisotropic effects of the benzoyl and tigloyl groups.

The structures of **4** and **5** are unusual in several aspects. Indeed, **4** is a taxane with a 13β-oxygen function, a feature very rare, but not unprecedented in taxoids (13), whereas **5** is the only baccatin III derivative lacking a benzoyl residue. Compound **5** is also the first taxoid bearing an *O*-tigloyl group, although an *N*-tigloyl group occurs in the amino acid side-chain of cephalomannine (=taxol B)-type taxoids (14).

Many natural taxoids have been analyzed by X-ray diffraction methods, and data are available for all the major structural types. Furthermore, several derivatives of natural taxoids and many synthetic compounds related to the taxoids have also been subjected to X-ray analysis. Nevertheless, X-ray data on paclitaxel or its diterpenoid core (baccatin III, **6**) have never been reported, although data on a semisynthetic analogue (docetaxel, **2**) are available (15). Furthermore, a diester (16) and the C-7 epimer of baccatin III (baccatin V, **8**) (17) have also been investigated by X-ray diffraction. We have been unable to obtain crystals of paclitaxel amenable to X-ray analysis, but suitable crystals of baccatin III [**6**] could be obtained from Me_2CO/H_2O. The crystals include two water molecules, not shown in Figure 1 for sake of clarity, and Table 3 lists the atomic coordinates. The solid-state conformation of **6** is very close to that of its 7-epimer [**8**] (17) and to that of the diterpenoid core of docetaxel (15), showing that epimerization at C-7, deacetylation at C-10, and esterification of the 13-hydroxyl have little effect on the conformation of the tetracyclic system. The solid-state conformation of **6** is also very close to that of the 14β-hydroxy derivative of **3** (6), and these similarities suggest that baccatin III derivatives are a conformationally homogenous group of taxanes. The chair-boat conformation of the cyclooctane ring of **6** is stabilized by an intramolecular hydrogen bond between the 7-hydroxyl and the 9-oxo group. Several intermolecular hydrogen bonds involving the diterpenoid oxygens and the water molecules also contribute to the crystal packing.

Some bond lengths in the cyclooctane ring of **6** are unusually long. The largest deviation is found in the C-3–C-8 bond (1.599 Å), but also the C-1–C-2, C-2–C-3- and C-9–C-10 bonds (>1.578 Å) are significantly longer than normal. Similar deviations have also been observed in other taxanes (18,19). In baccatin V [**8**], where the 7-hydroxyl is α and hydrogen bonded to the 4-acetyl group, the linear strain affects mainly the bonds C-4–C-5 (1.587 Å), C-7–C-8 (1.586 Å), and, to a lesser extent, C-2–C-3 (1.576 Å) (17). Interestingly, in docetaxel [**2**], the linear strain is reduced, and only the bonds C-7–C-8 and C-1–C-2 are slightly longer than 1.570 Å (15). These differences indicate that

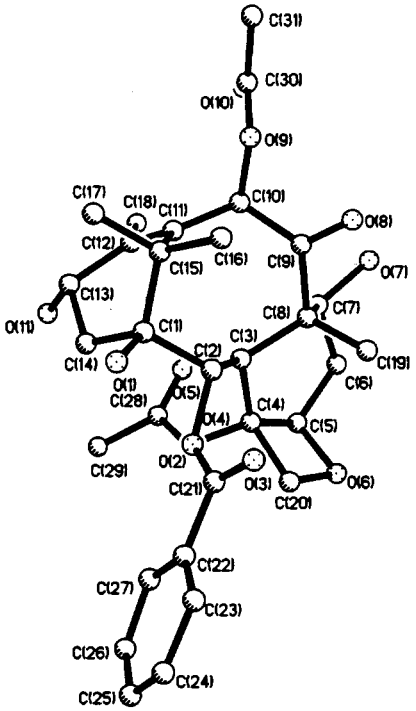


FIGURE 1. Crystal structure of baccatin III [**6**].

linear strain in baccatin III derivatives is affected by acylation and by the substitution pattern of the diterpenoid core. These subtleties are difficult to explain, but might play a role in the bizarre chemical reactivity sometimes observed in taxanes (20).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Optical rotations were measured on a Perkin-Elmer 141 automatic polarimeter. Uv spectra were taken on a Beckman DB-GT spectrophotometer. Ir spectra were recorded on a Perkin-Elmer model 237 spectrophotometer. Cims were taken on a Finnigan-MAT 4610 quadrupole instrument. ^{1}H- and ^{13}C-nmr spectra were taken on a Varian VXR 300 spectrometer (300 and 75.4 MHz, respectively), with TMS as internal standard. Si gel 60 (70–230 mesh, Merck) was used for cc. Hplc analysis was performed on a Waters 600E liquid chromatograph, connected to a Waters WISP 712 autosampler and to a Waters 490E uv detector. Data were registered with Millenium™ software (Waters). Prep. hplc was carried out on a Waters Delta Prep 4000 connected to a Waters 490E prep. uv detector. Semi-prep. hplc was carried out on a Waters 590 pump connected to a Waters 484 uv detector.

PLANT MATERIAL.—*T. baccata* L. (Taxaceae) came from Indena cultivations, and was identified by Dr. U. Boni, Indena S.p.A., Milan). A voucher specimen (#BE 2121) is kept at the Indena laboratories, Milan, Italy.

EXTRACTION AND ISOLATION.—Ground needles of *T. baccata* (100 kg) were extracted with 80% MeOH. The extract was concentrated and shaken with CH_2Cl_2. Cc of the organic phase (eluent: CH_2Cl_2 containing increasing amounts of MeOH) provided 0.7 g of baccatin III [**6**] and about 40 g of raw 10-deacetylbaccatin III [**3**]. The latter was crystallized three times from MeOH, and the mother liquors were pooled and concentrated. An additional crop of **3** was obtained, and after filtration and evaporation, a mixture of compounds containing **4** and **5** (4 g) was obtained. This mixture was dissolved in MeOH (40 ml) and the solution was subjected to prep. hplc (20 portions, 2 ml each) on a Waters Prep-pak Bondapak C_{18} column (15 μm, 47 mm i.d.×30 cm). H_2O-MeCN (75:25) was used as eluent, at a flow rate of 80 ml/min and with detection at 227 nm. Fractions containing **4** and **5** were pooled, concentrated under reduced pressure, extracted with EtOAc, and evaporated to give 80 and 40 mg of crude products, respectively. These were dissolved in 2 ml MeOH and rechromatographed (1-ml portions) under the same conditions to give

TABLE 3. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients[a] ($Å^2 \times 10^3$) for Baccatin III [**6**].

	x	*y*	*z*	U(eq)
O-1	−2862 (9)	−3589 (8)	3965 (2)	44 (3)
O-2	−1048 (8)	−2081 (8)	4353 (2)	34 (3)
O-3	−3349 (9)	−887 (10)	4408 (2)	48 (3)
O-4	2171 (9)	−2156 (8)	4377 (2)	35 (3)
O-5	4049 (9)	−2264 (9)	3996 (2)	46 (3)
O-6	2133 (11)	1171 (10)	4520 (2)	57 (3)
O-7	2576 (11)	1972 (9)	3446 (2)	53 (3)
O-8	−790 (12)	1313 (10)	3282 (2)	61 (4)
O-9	−582 (10)	−814 (10)	2884 (2)	57 (3)
O-10	1567 (15)	−860 (22)	2587 (2)	154 (9)
O-11	2247 (10)	−5257 (9)	3717 (2)	49 (3)
C-1	−1428 (13)	−3077 (12)	3818 (3)	29 (4)
C-2	−979 (14)	−1665 (13)	4012 (2)	35 (4)
C-3	709 (12)	−995 (11)	3952 (2)	25 (4)
C-4	1661 (13)	−789 (13)	4262 (2)	32 (4)
C-5	3012 (14)	336 (13)	4275 (3)	40 (4)
C-6	3361 (15)	1234 (14)	3973 (3)	52 (5)
C-7	2426 (15)	816 (13)	3669 (3)	41 (4)
C-8	669 (15)	437 (12)	3739 (3)	37 (4)
C-9	−54 (15)	316 (14)	3397 (3)	39 (4)
C-10	361 (14)	−1005 (14)	3173 (2)	40 (4)
C-11	16 (14)	−2448 (13)	3327 (2)	31 (4)
C-12	1138 (14)	−3400 (14)	3367 (3)	37 (4)
C-13	827 (14)	−4692 (13)	3585 (3)	37 (4)
C-14	−218 (15)	−4293 (13)	3866 (3)	42 (4)
C-15	−1681 (14)	−2726 (13)	3455 (2)	34 (4)
C-16	−2923 (14)	−1512 (14)	3407 (3)	49 (3)
C-17	−2407 (16)	−4046 (14)	3285 (3)	52 (3)
C-18	2834 (13)	−3261 (13)	3249 (3)	41 (3)
C-19	−207 (15)	1668 (13)	3909 (3)	45 (4)
C-20	968 (15)	47 (15)	4548 (3)	49 (5)
C-21	−2350 (15)	−1662 (13)	4517 (3)	35 (3)
C-22	−2391	−2234	4848	41
C-23	−3793	−2086	5022	49
C-24	−3911	−2656	5333	59
C-25	−2627	−3375	5469	53
C-26	−1225	−3523	5295	64
C-27	−1107	−2953	4985	51
C-28	3455 (15)	−2785 (13)	4231 (3)	38 (3)
C-29	3879 (16)	−4162 (14)	4387 (3)	57 (4)
C-30	167 (20)	−865 (16)	2607 (3)	60 (4)
C-31	−874 (20)	−866 (18)	2325 (3)	86 (5)
O-1W	3871 (21)	972 (19)	2905 (3)	166 (6)
O-2W	6906 (18)	1835 (16)	2790 (4)	155 (6)

[a]Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

4 (30 mg) and **5** (5 mg), with a chromatographic purity of 80% and 95%, respectively [analytical hplc, Supelco RP-18 (5 μm, 4.6 mm i.d.×25 cm) column, H_2O-MeCN (75:25) as eluent]. Compound **4** was further purified by semi-prep. hplc (Waters Delta pack C_{18} column (8 mm i.d.×30 cm), H_2O-MeCN (1:3) as eluent; 5.2 mg of product were obtained.

13-epi-10-Deacetylbaccatin III [**4**].—Amorphous, $[\alpha]^{25}D$ −10.7° (*c*=1.0, MeOH); uv (EtOH) λ max 225, 260 nm; ir (liquid film) ν max 3465, 1710, 1240, 1100, 710 cm^{-1}; cims (NH_3) $[(M+NH_4)]^+$ 562 $[C_{29}H_{36}O_{10}+NH_4]^+$ (66), 527 $[(M+H-H_2O)]^+$ (100). ^1H- and ^{13}C-nmr data, see Tables 1 and 2.

2-Debenzoyl-2-tigloyl-10-deacetylbaccatin III [**5**].—Amorphous, $[\alpha]^{25}D$ −30.4° (*c*=0.5, EtOH); uv

(EtOH) λ max 218 nm; ir (liquid film) ν max 3600, 1710, 1250, 1120, 760 cm^{-1}; cims (NH_3) [(M+NH_4]$^+$ 540 [$C_{27}H_{38}O_{10}$+NH_4]$^+$ (100).

X-RAY ANALYSIS.—Diffraction data were collected with a Siemens P4 diffractometer equipped with a graphite monochromator. The intensities were measured by ω-scans with variable speed; the cell parameters were obtained and refined from 50 reflections. The intensities were corrected for background and Lorentz-polarization effects, but no corrrection was applied for absorption. The structure was solved by direct methods using the SIR92 program (21). All subsequent calculations were carried out by the SHELXTL IRIS system (22). The structure was refined by full-matrix least-squares techniques. Not all non-hydrogen atoms could be assigned anisotropic thermal parameters because of the limited number of observed reflections, due to the poor quality of the crystals. The carbon atoms of the methyls and the acyl residues and the water oxygens were given isotropic temperature factors.

Crystal data[2].—$C_{31}H_{38}O_{11}\cdot 2H_2O$, mw=622, orthorhombic, space group $P22_12_1$, a=8.460(4), b=9.301(4), c=41.451(19) Å; Z=4, Dc=1.260 (mg m^{-3}); Mo-Kα radiation, λ=0.71069 Å; μ=0.090 mm^{-1}; R=0.0828 for 1575 observed reflections having $F>4.0\sigma(F)$.

ACKNOWLEDGMENTS

We are grateful to Dr. Federico Peterlongo, Indena Research Laboratories, for the measurement of the mass spectra.

LITERATURE CITED

1. L. Barboni, P. Gariboldi, E. Torregiani, G. Appendino, M. Varese, B. Grabetta, and E. Bombardelli, *J. Nat. Prod.*, **58**, 934 (1995).
2. M. Suffness, *Ann. Rep. Med. Chem.*, **28**, 305 (1993).
3. G.M. Cragg, S.A. Schepartz, M. Suffness, and M.R. Grever, *J. Nat. Prod.*, **56**, 1657 (1993).
4. D. Guénard, F. Guéritte-Voegelein, and P. Potier, *Acc. Chem. Res.*, **26**, 160 (1993).
5. D.P. Della Casa de Marcano and T.G. Halsall, *Chem. Commun.*, 365 (1975).
6. G. Appendino, P. Gariboldi, B. Gabetta, R. Pace, E. Bombardelli, and D. Viterbo, *J. Chem. Soc., Perkin Trans. I*, 2925 (1992).
7. G. Appendino, I. Fenoglio, G. Cravotto, M. Varese, P. Gariboldi, and B. Gabetta, *Gazz. Chim. Ital.*, **124**, 253 (1994).
8. G. Appendino, G. Cravotto, R. Enriù, P. Gariboldi, L. Barboni, E. Torregiani, B. Gabetta, G. Zini, and E. Bombardelli, *J. Nat. Prod.*, **57**, 607 (1994).
9. G. Appendino, L. Barboni, P. Gariboldi, E. Bombardelli, B. Gabetta, and D. Viterbo, *J. Chem. Soc., Chem. Commun.*, 1587 (1993).
10. G.N. Chmurny, B.D. Hilton, S. Brobst, S.A. Look, K.M. Witherup, and J.A. Beutler, *J. Nat. Prod.*, **55**, 414 (1992).
11. R.W. Miller, R.G. Powell, C.R. Smith Jr., E. Arnold, and J. Clardy, *J. Org. Chem.*, **46**, 1469 (1981).
12. M. Buděšínský and D. Šaman, *Collect. Czech. Chem. Commun.*, **52**, 453 (1987).
13. L. Barboni, P. Gariboldi, E. Torregiani, G. Appendino, G. Cravotto, E. Bombardelli, B. Gabetta, and D. Viterbo, *J. Chem. Soc., Perkin Trans. I*, 3233 (1994).
14. R.G. Powell, R.W. Miller, and C.R. Smith Jr., *J. Chem. Soc., Chem. Commun.*, 102 (1979).
15. F. Guéritte-Voegelein, D. Guénard, L. Mangatal, P. Potier, J. Guilhem, M. Cesario, and C. Pascard, *Acta Cryst.*, **C46**, 781 (1990).
16. M.C. Wani, H.L. Taylor, M.E. Wall, P. Coggon, and A.T. McPhail, *J. Am. Chem. Soc.*, **93**, 2325 (1971).
17. E.E. Castellano and O.J.R. Hodder, *Acta Cryst.*, **B29**, 2566 (1973).
18. T.-I. Ho, Y.-C. Lin, G.-H. Lee, S.-M. Peng, M.-K. Yeh, and F.-C. Chen, *Acta Cryst.*, **C43**, 1380 (1987).
19. M.J. Begley, E.A. Frecknall, and G. Pattenden, *Acta Cryst.*, **C40**, 1745 (1984).
20. G. Appendino, J. Jakupovic, G. Cravotto, and M. Varese, *Tetrahedron Lett.*, **35**, 6547 (1994).
21. A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M.C. Burla, G. Polidori, and M. Camalli, *J. Appl. Crystallogr.*, **27**, 435 (1994).
22. SHELXTL IRIS, Siemens Analytical X-Ray Instruments Inc., Madison, WI, 1990.

Received 10 February 1995

[2]Hydrogen coordinates, thermal parameters, bond distances and angles, and observed and calculated structure factors have been deposited with the Cambridge Crystallographic Data Centre and can be obtained upon request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK.