Acta Cryst. (1984). C**40**, 1745–1747

X-ray Structure of *O*-Cinnamoyltaxicin-I Triacetate, $C_{35}H_{42}O_{10}$, from the Yew, *Taxus baccata*

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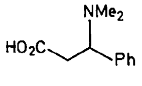
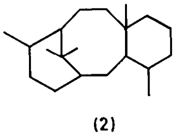
(*Received* 9 *March* 1984; *accepted* 13 *June* 1984)

Abstract. $M_r = 622{\cdot}72$, monoclinic, $P2_1$, $a = 9{\cdot}151$ (1), $b = 9{\cdot}321$ (1), $c = 19{\cdot}539$ (2) Å, $\beta = 91{\cdot}06$ (1)°, $U = 1666{\cdot}4$ Å^3, $Z = 2$, $D_x = 1{\cdot}24$ g cm^{-3}, $\lambda(\mathrm{Cu}\ K\alpha) = 1{\cdot}54178$ Å, $\mu = 7{\cdot}55$ cm^{-1}, $F(000) = 664$, room temperature. Final $R = 0{\cdot}0478$ for 2133 observed reflections. The stereochemistry and conformation of *O*-cinnamoyltaxicin-I triacetate have been established. Although the various rings are in their expected stable conformations the strain at the ring junctions was revealed by several unusually large bond lengths and angles [max. C—C 1·593 (7) Å]. A solid-state intermolecular hydrogen bond was successfully located.

Introduction. The mixture of alkaloids known as 'taxine' has long been recognized as being responsible for the poisonous properties of the yew *Taxus baccata*. The structures of these alkaloids, first isolated over a century ago, were investigated extensively by the research groups of Lythgoe (Lythgoe, 1968) and Nakanishi (Nakanishi, Gôtö, Ito, Natori & Nozoe, 1974) during the period 1958–1965, who showed that they were esters of 2-dimethylamino-2-phenylpropanoic acid (1) containing the unusual tricyclic diterpenoid ring system (2) (Miller, 1980). Thus, the main component of taxine, called taxine-I was shown to have the structure (3).



(1)



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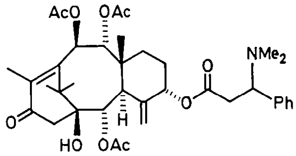
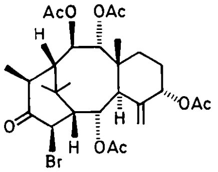
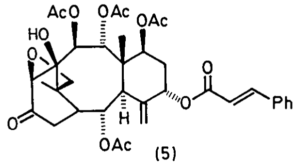


(3)

Although X-ray crystallographic data are available for the bromotaxinol (4) (Shiro & Koyama, 1971), a degradation product of taxine-I, and for taxagifine (5) (Chauvière, Guénard, Pascard, Picot, Potier & Prangé, 1982) from *T. baccata* and taxol (6) (Wani, Taylor, Wall, Coggon & McPhail, 1971) (*cf.* baccatin-V, Castellano & Hodder, 1973) from *T. brevifolia*, similar data for the historically important parent member, *i.e.* taxine-I (3) of this family of natural products have not hitherto been reported. In connection with synthetic investigations amongst the taxane diterpenes we required details of the precise stereochemistry and conformation of the tricyclic ring system, *viz.* (2), present in these compounds. Accordingly, we have examined the X-ray crystal structure of *O*-cinnamoyltaxicin-I triacetate (7) which is obtained after elimination of dimethylamine from 'taxine' followed by acetylation of the non-basic product and fractional crystallization.



(4)



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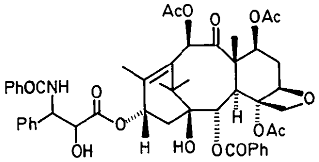

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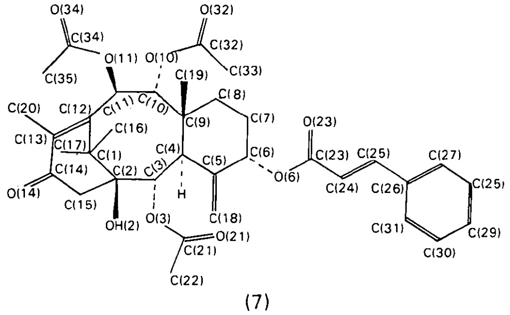

(7)

Experimental. (7) obtained from leaves of the yew *Taxus baccata*, according to the extraction procedure described earlier (Baxter, Lythgoe, Scales, Scrowston & Trippett, 1962). Small colourless crystals produced by recrystallization from ethanol, m.p. 509–511 K (lit. m.p. 510–512 K).

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Space group and preliminary unit-cell parameters determined photographically; Enraf–Nonius CAD-4 diffractometer; accurate lattice parameters by least-squares refinement of the positions of 25 reflections measured on the diffractometer with θ approximately 30°; Cu $K\alpha$ radiation, ω–$2/3\theta$ scans, scan angle 3°, $1 < \theta < 66°$. 3090 independent reflections measured, 2133 $[I \geq 3\sigma(I)]$ considered observed and used in subsequent refinement; index range h ±10, k 0/11, l 0/22; intensity of one standard reflection measured during data collection, total variation <10%; data corrected for Lorentz and polarization factors, but no absorption corrections applied; data reduction and subsequent crystallographic calculations performed largely with *CRYSTALS* (Carruthers, 1975). Atomic scattering factors from *International Tables for X-ray Crystallography* (1974).

Structure solved by direct methods with *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). Atomic parameters refined using full-matrix least squares initially isotropically and subsequently anisotropically, with minimization of $\sum w(F_o - F_c)^2$. H atoms located from difference synthesis or geometrically, and included in calculations but without refinement; the weighting scheme used was a Chebyshev series of the form: $w = 1{\cdot}0/A_0T_0(x)\ ....\ + A_nT_n(x)$ [where $x = F_o/F_o(\text{max.})$] with coefficients $A_0 = 162{\cdot}422$, $A_1 = 83{\cdot}159$, $A_2 = -83{\cdot}030$ and $A_3 = -61{\cdot}064$. Refinement converged with the largest parameter shifts $0{\cdot}1\sigma$; $R = 0{\cdot}0478$, $R_w = 0{\cdot}0577$. A final difference map showed no peaks or depressions $>0{\cdot}2$ e Å^{-3}.

Table 1. *Fractional atomic coordinates of the non-*H *atoms with e.s.d.'s in parentheses, and equivalent isotropic temperature factors calculated as* $U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}(Å^2)
C(1)	0·3920 (6)	0·4677	0·2016 (3)	0·061
C(2)	0·2923 (6)	0·4656 (9)	0·2640 (3)	0·053
C(3)	0·1385 (6)	0·5303 (9)	0·2471 (2)	0·046
C(4)	0·1317 (5)	0·698 (1)	0·2409 (3)	0·050
C(5)	0·0270 (6)	0·7802 (9)	0·2874 (3)	0·056
C(6)	0·0674 (6)	0·938 (1)	0·2926 (3)	0·063
C(7)	0·0626 (7)	1·006 (1)	0·2222 (3)	0·070
C(8)	0·1435 (7)	0·924 (1)	0·1686 (3)	0·062
C(9)	0·1041 (6)	0·759 (1)	0·1655 (3)	0·057
C(10)	0·2010 (6)	0·6862 (9)	0·1104 (3)	0·056
C(11)	0·3683 (6)	0·694 (1)	0·1201 (3)	0·059
C(12)	0·4215 (6)	0·6258 (9)	0·1855 (3)	0·060
C(13)	0·4820 (6)	0·710 (1)	0·2354 (3)	0·059
C(14)	0·4802 (6)	0·6541 (9)	0·3075 (3)	0·061
C(15)	0·3695 (6)	0·541 (1)	0·3247 (3)	0·060
C(16)	0·5429 (8)	0·398 (1)	0·2193 (4)	0·084
C(17)	0·3302 (8)	0·3727 (9)	0·1431 (3)	0·072
C(18)	−0·0973 (7)	0·740 (1)	0·3160 (4)	0·078
C(19)	−0·0531 (6)	0·734 (1)	0·1427 (3)	0·073
C(20)	0·5421 (7)	0·857 (1)	0·2270 (4)	0·080
C(21)	−0·0614 (7)	0·387 (1)	0·2860 (3)	0·065
C(22)	−0·1362 (7)	0·341 (1)	0·3492 (4)	0·087
C(23)	0·2512 (7)	1·0480 (9)	0·3655 (3)	0·057
C(24)	0·4014 (7)	1·031 (1)	0·3906 (3)	0·062
C(25)	0·4618 (6)	1·124 (1)	0·4342 (3)	0·063
C(26)	0·6113 (6)	1·113 (1)	0·4631 (3)	0·061
C(27)	0·6940 (7)	0·991 (1)	0·4599 (4)	0·080
C(28)	0·8332 (8)	0·985 (1)	0·4886 (4)	0·102
C(29)	0·8905 (8)	1·109 (1)	0·5203 (4)	0·090
C(30)	0·8108 (8)	1·229 (1)	0·5235 (3)	0·085
C(31)	0·6702 (7)	1·234 (1)	0·4959 (3)	0·072
C(32)	0·1143 (9)	0·680 (1)	−0·0057 (4)	0·084
C(33)	0·107 (1)	0·765 (1)	−0·0697 (3)	0·108
C(34)	0·5528 (9)	0·665 (1)	0·0374 (4)	0·088
C(35)	0·606 (1)	0·576 (1)	−0·0178 (4)	0·123
O(2)	0·2713 (5)	0·3170 (8)	0·2792 (2)	0·073
O(3)	0·0475 (4)	0·4808 (8)	0·3023 (2)	0·056
O(6)	0·2195 (4)	0·9464 (8)	0·3199 (2)	0·068
O(10)	0·1737 (4)	0·7571 (8)	0·0458 (2)	0·064
O(11)	0·4289 (5)	0·6187 (8)	0·0622 (2)	0·078
O(14)	0·5581 (4)	0·7048 (9)	0·3520 (2)	0·081
O(21)	−0·0933 (5)	0·3520 (9)	0·2295 (3)	0·091
O(23)	0·1637 (5)	1·1351 (8)	0·3839 (2)	0·074
O(32)	0·0741 (7)	0·557 (1)	0·0007 (3)	0·114
O(34)	0·6136 (7)	0·771 (1)	0·0593 (4)	0·136

Discussion. The final atomic coordinates with their e.s.d.'s are given in Table 1[*] for the non-H atoms. The atomic-numbering scheme used is shown in (7); the H atoms are numbered according to the atoms to which they are attached. Bond lengths, bond angles and some selected torsion angles about those bonds that make up the cyclic portions of the molecule are listed in Table 2.

The resulting molecular structure of the title compound is shown in Fig. 1 which indicates that the molecule has the structure and stereochemistry of formula (7). The central eight-membered ring adopts the most stable boat–chair conformation as revealed by the torsion angles (Table 2) which are close to the ideal undistorted values. This ring is *trans*-fused to the six-membered ring with one common bond [C(4)–C(9)]. The conformation of this ring is an almost perfect chair (Table 2). Although the torsion angles suggest that these two rings and their junction are comparatively strain-free, this is not borne out by the bond lengths and angles in this region. Two bonds [C(4)–C(9) 1·593 (7) and C(8)–C(9) 1·582 (9) Å] are significantly long and the C(3)–C(4)–C(5) bond angle of 118·2 (5)° deviates significantly from the idealized sp^3 value. In contrast, the other six-membered ring (with two bonds in common with the central eight-membered ring) is much more distorted. Its conformation is best described as a boat severely flattened at one end. Thus four atoms [C(2), C(12), C(13) and C(15)] are approximately coplanar with C(14) only 0·21 (1) Å and C(1) fully 0·72 (1) Å above this mean plane. The double bond in this ring is distorted from planarity [torsion angle C(1)–C(12)–C(13)–C(14) −15·5 (6)°] as is the potential conjugation to the carbonyl group [torsion angle C(12)–C(13)–C(14)–C(15) −21·7 (6)°]. This strain is confirmed by the long length of the double bond [C(12)–C(13) 1·361 (8) Å].

The arrangement of the molecules within the crystallographic unit cell is shown in Fig. 2 projected down the short x axis. This illustrates the intermolecular hydrogen bond found to link the molecules within the crystal

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[*] Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39582 (23 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

structure. The bond is between the alcohol [OH(2)] and the carbonyl oxygen of the cinnamate ester [O(23)] in a neighbouring unit cell (*x*, *y* − 1, *z*). The hydrogen-bond distance is 2·846 (6) Å. The associated H atom was located in a difference map with an O–H distance of 0·905 Å and a bond angle at H of 125°.

Table 2. *Bond lengths* (Å), *bond angles and selected torsion angles* (°) *with e.s.d.'s in parentheses*

C(1)–C(2)	1·537 (8)	C(13)–C(14)	1·501 (8)
C(1)–C(12)	1·532 (9)	C(13)–C(20)	1·491 (10)
C(1)–C(16)	1·558 (9)	C(14)–C(15)	1·501 (9)
C(1)–C(17)	1·545 (9)	C(14)–O(14)	1·210 (6)
C(2)–C(3)	1·561 (7)	C(21)–C(22)	1·487 (9)
C(2)–C(15)	1·540 (8)	C(21)–O(3)	1·361 (7)
C(2)–O(2)	1·430 (7)	C(21)–O(21)	1·182 (7)
C(3)–C(4)	1·573 (8)	C(23)–C(24)	1·460 (8)
C(3)–O(3)	1·450 (6)	C(23)–O(6)	1·328 (7)
C(4)–C(5)	1·535 (8)	C(23)–O(23)	1·200 (7)
C(4)–C(9)	1·593 (7)	C(24)–C(25)	1·326 (8)
C(5)–C(6)	1·519 (9)	C(25)–C(26)	1·474 (8)
C(5)–C(18)	1·330 (9)	C(26)–C(27)	1·368 (10)
C(6)–C(7)	1·515 (9)	C(26)–C(31)	1·402 (9)
C(6)–O(6)	1·484 (7)	C(27)–C(28)	1·383 (10)
C(7)–C(8)	1·505 (9)	C(28)–C(29)	1·403 (12)
C(8)–C(9)	1·582 (9)	C(29)–C(30)	1·337 (12)
C(9)–C(10)	1·562 (8)	C(30)–C(31)	1·387 (9)
C(9)–C(19)	1·515 (8)	C(32)–C(33)	1·481 (11)
C(10)–C(11)	1·541 (8)	C(32)–O(10)	1·346 (8)
C(10)–O(10)	1·443 (6)	C(32)–O(32)	1·205 (10)
C(11)–C(12)	1·500 (8)	C(34)–C(35)	1·455 (11)
C(11)–O(11)	1·448 (7)	C(34)–O(11)	1·316 (9)
C(12)–C(13)	1·361 (8)	C(34)–O(34)	1·205 (10)

C(2)–C(1)–C(12)	106·5 (4)	C(12)–C(11)–O(11)	109·8 (5)
C(2)–C(1)–C(16)	110·8 (5)	C(1)–C(12)–C(11)	121·7 (5)
C(2)–C(1)–C(17)	111·5 (5)	C(1)–C(12)–C(13)	118·6 (6)
C(12)–C(1)–C(16)	106·6 (5)	C(11)–C(12)–C(13)	119·3 (6)
C(12)–C(1)–C(17)	117·6 (5)	C(12)–C(13)–C(14)	117·4 (6)
C(16)–C(1)–C(17)	103·7 (5)	C(12)–C(13)–C(20)	126·7 (6)
C(1)–C(2)–C(3)	111·9 (4)	C(14)–C(13)–C(20)	115·7 (6)
C(1)–C(2)–C(15)	109·5 (5)	C(13)–C(14)–C(15)	118·1 (5)
C(1)–C(2)–O(2)	105·1 (4)	C(13)–C(14)–O(14)	121·5 (6)
C(3)–C(2)–C(15)	112·6 (5)	C(15)–C(14)–O(14)	120·2 (6)
C(31)–C(2)–O(2)	107·1 (5)	C(2)–C(15)–C(14)	116·8 (5)
C(15)–C(2)–O(2)	118·3 (5)	C(22)–C(21)–O(3)	109·7 (6)
C(2)–C(3)–C(4)	115·8 (5)	C(22)–C(21)–O(21)	126·0 (7)
C(2)–C(3)–O(3)	104·4 (4)	O(3)–C(21)–O(21)	124·2 (6)
C(4)–C(3)–O(3)	110·6 (4)	C(24)–C(23)–O(6)	110·0 (5)
C(3)–C(4)–C(5)	118·2 (5)	C(24)–C(23)–O(23)	127·0 (6)
C(3)–C(4)–C(9)	115·5 (5)	O(6)–C(23)–O(23)	123·0 (5)
C(5)–C(4)–C(9)	106·4 (4)	C(23)–C(24)–C(25)	121·7 (6)
C(4)–C(5)–C(6)	111·5 (5)	C(24)–C(25)–C(26)	125·1 (6)
C(4)–C(5)–C(18)	131·1 (6)	C(25)–C(26)–C(27)	123·3 (6)
C(6)–C(5)–C(18)	116·9 (6)	C(25)–C(26)–C(31)	117·8 (6)
C(5)–C(6)–C(7)	110·1 (5)	C(27)–C(26)–C(31)	118·9 (6)
C(5)–C(6)–O(6)	107·5 (5)	C(26)–C(27)–O(28)	121·2 (7)
C(7)–C(6)–O(6)	108·4 (5)	C(27)–C(28)–C(29)	118·8 (8)
C(6)–C(7)–C(8)	114·2 (5)	C(28)–C(29)–C(30)	120·4 (6)
C(7)–C(8)–C(9)	114·1 (5)	C(29)–C(30)–C(31)	121·0 (7)
C(4)–C(9)–C(8)	106·1 (5)	C(26)–C(31)–C(30)	119·6 (7)
C(4)–C(9)–C(10)	113·7 (4)	C(33)–C(32)–O(10)	110·8 (7)
C(4)–C(9)–C(19)	110·6 (5)	C(33)–C(32)–O(32)	125·8 (8)
C(8)–C(9)–C(10)	108·4 (5)	O(10)–C(32)–O(32)	123·3 (7)
C(8)–C(9)–C(19)	111·8 (5)	C(35)–C(34)–O(11)	113·0 (9)
C(10)–C(9)–C(19)	106·3 (5)	C(35)–C(34)–O(34)	124·8 (9)
C(9)–C(10)–C(11)	118·1 (5)	O(11)–C(34)–O(34)	122·2 (8)
C(9)–C(10)–O(10)	108·2 (4)	C(3)–O(3)–C(21)	117·3 (4)
C(11)–C(10)–O(10)	104·0 (4)	C(6)–O(6)–C(23)	118·1 (4)
C(10)–C(11)–C(12)	113·0 (5)	C(10)–O(10)–C(32)	118·0 (5)
C(10)–C(11)–O(11)	106·0 (4)	C(11)–O(11)–C(34)	118·3 (6)

C(12)–C(1)–C(2)–C(3)	66·2 (5)	C(5)–C(6)–C(7)–C(8)	−49·2 (5)
C(1)–C(2)–C(3)–C(4)	−75·2 (5)	C(6)–C(7)–C(8)–C(9)	49·5 (5)
C(2)–C(3)–C(4)–C(9)	109·5 (5)	C(7)–C(8)–C(9)–C(4)	−54·8 (5)
C(3)–C(4)–C(9)–C(10)	−46·1 (5)	C(8)–C(9)–C(4)–C(5)	61·5 (5)
C(4)–C(9)–C(10)–C(11)	−58·1 (5)	C(2)–C(1)–C(12)–C(13)	57·0 (6)
C(9)–C(10)–C(11)–C(12)	59·8 (5)	C(1)–C(12)–C(13)–C(14)	−15·5 (6)
C(10)–C(11)–C(12)–C(1)	59·0 (6)	C(12)–C(13)–C(14)–C(15)	−21·7 (6)
C(11)–C(12)–C(1)–C(2)	−115·0 (6)	C(13)–C(14)–C(15)–C(2)	14·6 (6)
C(9)–C(4)–C(5)–C(6)	−66·9 (6)	C(14)–C(15)–C(2)–C(1)	26·9 (5)
C(4)–C(5)–C(6)–C(7)	59·3 (6)	C(15)–C(2)–C(1)–C(12)	−59·4 (5)

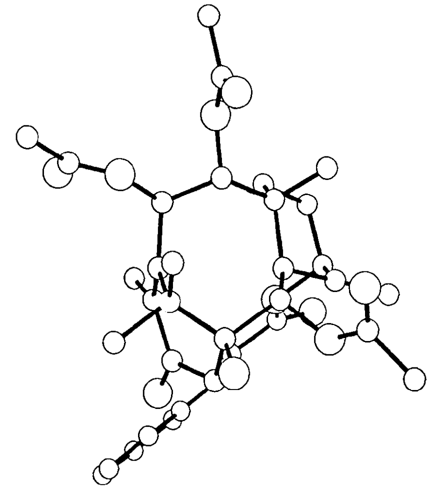

Fig. 1. Molecular structure of *O*-cinnamoyltaxicin-I triacetate.

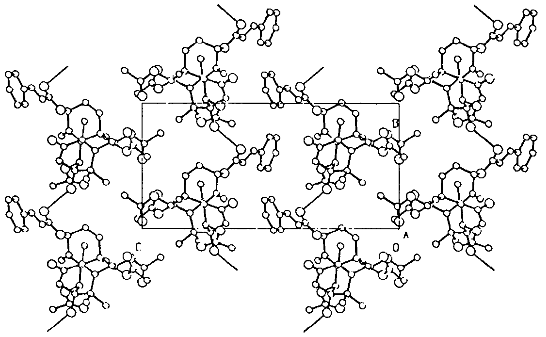

Fig. 2. The molecular packing viewed along the *x* axis showing the hydrogen bond (thin line).

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