14β-Hydroxy-10-deacetylbaccatin III, a New Taxane from Himalayan Yew (*Taxus wallichiana* Zucc.)

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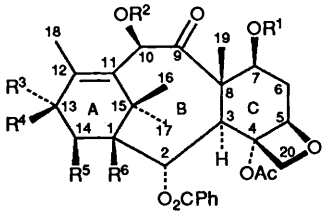
The needles of *T. wallichiana* Zucc. gave a new taxane, whose structure was established as 14β-hydroxy-10-deacetylbaccatin III on the basis of chemical reactions, spectroscopic data and X-ray analysis.

As part of a study on alternative sources of the anticancer compound taxol,[1] several collections of *Taxus wallichiana* Zucc. were investigated. Previous studies on a plant tentatively identified as *Taxus wallichiana* Zucc. had in fact shown the presence of this pseudo-alkaloidic diterpenoid in the needles and other plant parts.[2]† In the course of our studies, the novel taxane diterpenoid **1** was isolated. We present here the structure elucidation and a study on the reactivity of this compound, which is of potential importance for the preparation of more oxygenated analogues of taxol.[3]

Compound **1** showed spectral features similar to those of 10-deacetylbaccatin III **2**. The CI mass spectrum showed that **1** differed from **2** only by the introduction of an extra oxygen; the substitution of a methine for a methylene in the ^{13}C NMR spectrum revealed that the new introduced hydroxy group was secondary. Comparison of the ^{1}H NMR spectra of **1** and **2** (Table 1) showed differences that could be rationalized in terms of the introduction of a hydroxy group at C-14. Indeed, the ABX system of 13-H and $14_{a,b}$-H had been replaced by an AB-system, whereas the signals of $6_{a,b}$-H were still present (multiplicities for spin-system classification after D_2O exchange).



	R^1	R^2	R^3	R^4	R^5	R^6
1	H	H	OH	H	OH	OH
2	H	H	OH	H	H	OH
3	H	H	OH	H		
4	$CCl_3CH_2CO_2$	$CCl_3CH_2CO_2$	OH	H		
5	$CCl_3CH_2CO_2$	$CCl_3CH_2CO_2$	=O			

The splitting pattern of 13-H and 14-H ($J_{13,14}$ 5.5 Hz; in **2** ($J_{13,14\beta}$ 3.8 Hz, $J_{13,14\alpha}$ < 1 Hz) was stereochemically ambiguous, but the outcome of some chemical reactions tentatively suggested a *trans*-relationship between the 13-OH and 14-OH. Exclusively one acetonide **3** and one cyclic carbonate **4** were formed when **1** was treated with 2,2-dimethoxypropane and 2,2,2-trichloroethyl chloroformate respectively, showing that only one *syn*-relationship was present within the vicinal trihydroxy system. Since the cyclic carbonate **4** could be oxidized by MnO_2 to an enone **5**, the 13-OH was still free, and diol protection had thus taken place at C-1 and C-14. Molecular mechanics calculations have shown that the most stable conformation of baccatin III and its derivatives has ring A in a distorted-boat conformation, with the 13-OH oriented towards the concavity of the molecular skeleton,[4,5] and a conformation of this type was also found in a derivative of 10-deacetylbaccatin III studied by X-ray crystallography.[6] Assuming a distorted-boat conformation for ring A in **1**, inspection of models shows that, viewed along the line C(1)–C(14), the bond C(1)–O(1) bisects the angle between the 14α- and the 14β-bonds and thus formation of a cyclic ketal or a carbonate between 1-OH and 14-OH has no stereochemical implication. The lack of formation of a cyclic carbonate or acetonide between the secondary 13-OH and 14-OH suggests instead a *trans*-relationship between these groups, since *cis*-hydroxy groups 13-OH and 14-OH would be almost coplanar and thus ideally oriented for ring closure. However, the highly folded conformation of the taxane skeleton might also play a role, making the formation of a cyclic ring from the α-face of ring A sterically unfavourable on account of non-bonded interactions with ring C. Further evidence for the stereochemical assignment was thus sought, and a thorough spectroscopic investigation of **1** and its derivatives was undertaken.

All proton resonances in the NMR spectrum of **1** were unambiguously assigned by 2D 2QF-COSY experiments (Table 1),[7] and the carbon resonances by 2D C–H correlation experiments (Table 2). For the methyl and quaternary carbons, $^{2}J_{C-H}$ and $^{3}J_{C-H}$ correlations were examined (FLOCK

† From the same plant material, originally identified as *Cephalotaxus mannii* Hook, cephalomannine,[2] 19-hydroxybaccatin III, 10-deacetylcephalomannine, 10-deacetyltaxol (J. L. McLaughlin, R. W. Miller, R. G. Powell and C. R. Smith Jr, *J. Nat. Prod.*, 1981, **44**, 312) and lignanes (R. W. Miller, J. L. McLaughlin, R. G. Powell, R. D. Plattner, D. Weislender and C. R. Smith Jr., *J. Nat. Prod.*, 1982, **45**, 78) were also isolated. Biflavones were instead found in other collections of this plant (N. Parveen, H. M. Taufeeq and N. U. Khan, *J. Nat. Prod.*, 1985, **48**, 994; L. Qiu, M. Lian, Z. Ma and G. He, *Zhiwu Xuebao*, 1989, **31**, 54 (*CA*, 1989, **111**, 191505m).

Table 1 ^{1}H NMR data (300 MHz, $SiMe_4$, [$^2H_6$]DMSO, *J*-values in Hz)[a]

H	1	2	3	4	5
2	5.54 (d, 7.1)	5.40 (d, 6.9)	5.82 (d, 6.5)	5.92 (d, 7.1)	6.00 (d, 6.7)
3	3.75 (d, 7.1)	3.81 (d, 6.9)	3.80 (d, 6.5)	3.72 (d, 7.1)	3.85 (d, 6.7)
5	4.90 (br d, 9.1)	4.90 (br d, 8.9)	4.96 (br d, 9.8)	5.08 (br d, 9.3)	5.09 (br d, 9.3)
6α	2.28 (m)	2.28 (m)	2.30 (m)	2.54 (m)	2.57 (m)
6β	1.64 (m)	1.64 (m)	1.62 (m)	1.88 (m)	1.92 (m)
7	4.07 (m)	4.09 (m)	4.05 (m)	5.46 (dd, 11.0, 7.1)	5.47 (dd, 10.8, 7.3)
10	5.13 (d, 2.7)	5.13 (d, 2.4)	5.20 (d, 2.4)	6.16 (s)	6.23 (s)
13	4.41 (br t, 5.5)	4.62 (m)	4.57 (br t, 5.4)	4.98 (br t, 5.7)	—
14	3.79 (t, 5.5)	2.15 (dd, 9.0, < 1), 2.40 (dd, 9.0, 3.8)	4.20 (d, 5.4)	4.70 (d, 5.7)	4.96 (s)
16	0.92 (s)	0.93 (s)	0.98 (s)	1.11 (s)	1.12 (s)
17	0.97 (s)	0.94 (s)	1.02 (s)	1.09 (s)	1.19 (s)
18	1.91 (s)	1.90 (s)	1.94 (s)	2.05 (s)	2.16 (s)
19	1.53 (s)	1.51 (s)	1.48 (s)	1.72 (s)	1.74 (s)
20α	3.97 (d, 8.2)	4.02 (s)	3.85 (d, 8.0)	4.02 (d, 8.4)	4.07 (d, 8.7)
20β	3.99 (d, 8.2)		4.23 (d, 8.0)	4.17 (d, 8.4)	4.19 (d, 8.7)
1-OH	4.43 (s)	4.34 (s)	—	—	—
7-OH	5.01 (d, 7.1)	5.01 (d, 6.9)	5.08 (d, 7.1)	—	—
10-OH	4.82 (d, 2.7)	4.78 (d, 2.4)	4.94 (d, 2.4)	—	—
13-OH	5.53 (d, 5.5)	5.21 (d, 4.3)	3.91 (d, 5.4)	6.73 (d, 5.7)	—
14-OH	6.75 (d, 5.5)	—	—	—	—
Ac	2.24 (s)	2.20 (s)	2.22 (s)	2.30 (s)	2.26 (s)
Acetal	—	—	1.24 (s), 0.40 (s)	—	—
$CCl_3CH_2CO_2$	—	—	—	5.02 (d, 11.6), 4.97 (d, 11.6), 4.94 (d, 12.0), 4.78 (d, 12.0)	5.08 (d, 12.2), 4.97 (d, 12.2), 4.96 (d, 12.0), 4.82 (d, 12.0)

[a] The resonances of the benzoate protons were fairly constant in **1**–**5**; those observed in **2** are reported as representative: δ 8.08 (d, 7.8, 2′-H and 6′-H), 7.75 (t, 7.3, 4′-H), 7.61 (br t, *ca.* 7.5, 3′-H and 5′-H).

Table 2 ^{13}C NMR data (75.4 MHz, $SiMe_4$, [$^2H_6$]DMSO)

C	1[a]	2	3	4	5
1	75.24 (s)	76.87 (s)	87.80 (s)	87.64 (s)	86.04 (s)
2	74.00 (d)	74.78 (d)	69.65 (d)	68.45 (d)	67.03 (d)
3	46.00 (d)	46.47 (d)	47.68 (d)	46.14 (d)	45.09 (d)
4	79.95 (s)	80.03 (s)	80.17 (s)	78.77 (s)	77.96 (s)
5	83.65 (d)	83.70 (d)	83.76 (d)	82.12 (s)	82.03 (s)
6	36.58 (t)	36.52 (t)	36.74 (t)	32.38 (t)	32.28 (t)
7	70.94 (d)	70.88 (d)	70.90 (d)	75.71 (d)	75.44 (d)
8	57.26 (s)	56.99 (s)	57.66 (s)	55.65 (s)	56.24 (s)
9	210.04 (s)	210.25 (s)	209.81 (s)	200.27 (s)	198.58 (s)
10	74.36 (d)	74.32 (d)	74.38 (d)	78.59 (d)	78.93 (d)
11	135.27 (s)	134.42 (s)	134.83 (s)	128.61 (s)	147.85 (s)
12	139.53 (s)	141.48 (s)	139.77 (s)	146.98 (s)	140.43 (s)
13	74.64 (d)	66.01 (d)	72.47 (d)	70.07 (d)	190.13 (s)
14	72.23 (d)	39.18 (t)	83.45 (d)	83.92 (d)	76.43 (d)
15	42.25 (s)	42.40 (s)	42.19 (s)	40.34 (s)	40.79 (s)
16	26.55 (q)	26.70 (q)	26.81 (q)	25.46 (q)	31.82 (q)
17	21.37 (q)	20.11 (q)	20.77 (q)	21.18 (q)	18.63 (q)
18	14.89 (q)	14.75 (q)	15.03 (q)	14.90 (q)	13.60 (q)
19	9.67 (q)	9.66 (q)	9.29 (q)	10.39 (q)	10.26 (q)
20	75.37 (t)	75.40 (t)	75.69 (t)	74.65 (t)	74.66 (t)
Ac	22.31 (q), 169.81 (s)	22.25 (q), 169.48 (s)	22.36 (q), 169.45 (s)	21.85 (q), 170.31 (s)	21.36 (q), 171.26 (s)
$PhCO_2$	165.40 (s), 129.72 (s), 129.80 (d), 128.68 (d), 133.29 (s)	165.18 (s), 130.25 (s), 129.45 (d), 128.60 (d), 133.12 (s)	164.64 (s), 129.61 (s), 129.92 (d), 128.84 (d), 133.68 (s)	164.14 (s), 127.37 (s), 129.30 (d), 129.23 (d), 134.52 (s)	163.92 (s), 126.77 (s), 129.78 (d), 129.26 (d), 134.77 (s)
Acetal			108.27 (s), 28.12 (q), 27.81 (q)		
$CCl_3CH_2CO_2$				152.30 (s), 151.21 (s), 94.37 (s), 94.18 (s), 76.47 (t), 76.32 (t)	152.31 (s), 151.93 (s), 94.08 (s), 94.08 (s), 76.58 (t), 76.55 (t)
Carbonate				152.05 (s)	150.69 (s)

[a] ^{1}H–^{13}C long-range correlations of quaternary carbons in the FLOCK experiment: δ 75.24 (C-1), 2-H, 1-OH, 3-H, 16-H, 17-H; δ 79.95 (C-4), 3-H, 5-H, 20-H; δ 57.26 (C-8), 2-H, 3-H, 6α-H, 19-H; δ 135.27 (C-11), 10-H, 10-OH, 16-H, 17-H; δ 139.53 (C-12), 10-H, 13-H, 18-H; δ 42.25 (C-15), 10-H, 14-H, 16-H and 17-H.

experiments)[8] (Table 2). The stereochemistry at C-14 could then be assigned in a straightforward way by the analysis of the 2D-ROE spectrum (Table 3):[9] the cross-peaks pattern of 14-H and 14-OH; (14-H–13-OH; 14-H–CH_3CO; 14-H–3-H; 14-OH–10-OH; 14-OH–13-H) clearly indicated a β-configuration for 14-OH. The 2D-ROESY spectrum also established

Table 3 Cross-peaks detected in the 2D-ROESY spectrum of **1**

H	Cross correlation[a]
2	1-OH (m), 19-H (m), 17-H (m)
3	7-H (s), 14-H (w), 18-H (w)
5	6α-H (s)
6α	5-H (s), 6β-H (s)
6β	6α-H (s), 19-H (w)
7	3-H (s), 10-H (m)
10	7-H (m), 10-OH (m), 18-H (m)
13	16-H (m), 13-OH (m), 14-H (m)
14	3-H (w), acetate (m), 14-OH (s), 13-OH (m), 2′,6′-H (m)
16	10-OH (w)
17	2-H (m), 10-OH (m)
18	3-H (w), 10-H (m), 13-OH (m)
19	2-H (m), 6b-H (w), 20β-H (w)
20α	2′,6′-H (w)
20β	19-H (w)
1-OH	2-H (m), 14-OH (s)
10-OH	10-H (m), 16-H (w), 17-H (m)
13-OH	13-H (m), 18-H (m), acetate (w)
14-OH	13-H (m), 14-H (s), 1-OH (s)
Acetate	14-H (m), 13-OH (w), 2′,6′-H (w)
2′,6′	3′,5′-H (s), 14-H (m), 20α-H (w), acetate (w)

[a] s = strong, m = medium, w = weak.

Table 4 Atomic coordinates (× 10^4) for compound **1**

	x	*y*	*z*
O(1)	6 606	7 662	10 603
O(2)	5 414(1)	6 438(1)	9 016(1)
O(3)	3 011(2)	7 412(2)	10 546(2)
O(4)	7 104(2)	4 011(1)	7 128(1)
O(5)	8 481(2)	1 802(2)	7 399(2)
O(6)	3 818(2)	2 960(2)	7 948(2)
O(7)	4 823(2)	392(2)	11 911(2)
O(8)	4 074(2)	3 104(2)	13 793(2)
O(9)	6 694(2)	2 728(2)	14 248(2)
O(10)	10 703(2)	3 902(2)	7 998(2)
O(11)	9 323(2)	7 077(2)	8 711(2)
C(1)	7 065(2)	6 102(2)	10 501(2)
C(2)	5 692(2)	5 533(2)	10 229(2)
C(3)	5 916(2)	3 878(2)	9 844(2)
C(4)	5 738(2)	3 646(2)	8 340(2)
C(5)	5 278(2)	2 175(2)	8 112(2)
C(6)	5 022(3)	996(2)	9 345(2)
C(7)	5 465(2)	1 313(2)	10 657(2)
C(8)	4 896(2)	2 940(2)	11 140(2)
C(9)	5 175(2)	2 985(2)	12 633(2)
C(10)	6 841(2)	2 739(2)	12 724(2)
C(11)	7 846(2)	3 833(2)	11 776(2)
C(12)	9 138(2)	3 391(2)	10 594(2)
C(13)	9 865(2)	4 533(2)	9 419(2)
C(14)	8 631(2)	5 768(2)	9 154(2)
C(15)	7 275(2)	5 486(2)	11 998(2)
C(16)	8 526(3)	6 230(3)	12 285(3)
C(17)	5 763(3)	5 921(2)	13 322(2)
C(18)	9 901(3)	1 821(2)	10 272(3)
C(19)	3 113(2)	3 359(2)	11 483(2)
C(20)	4 269(2)	4 369(2)	7 996(2)
C(1′)	4 028(2)	7 350(2)	9 334(2)
C(2′)	3 882(2)	8 229(2)	8 005(2)
C(3′)	5 180(2)	8 400(2)	6 737(2)
C(4′)	4 965(3)	9 286(3)	5 552(3)
C(5′)	3 490(3)	9 970(3)	5 632(3)
C(6′)	2 200(3)	9 784(3)	6 885(3)
C(7′)	2 384(2)	8 909(2)	8 082(2)
C(8′)	8 400(2)	2 955(2)	6 726(2)
C(9′)	9 639(3)	3 418(3)	5 358(3)
O(12)	9 116(3)	8 081(4)	6 012(3)
C(10′)	10 186(3)	8 158(3)	4 854(3)
C(11′)	11 682(4)	7 119(5)	4 500(6)
C(12′)	10 081(7)	9 344(5)	3 725(5)

the conformation of the molecule (distorted-boat for ring A, boat–chair for ring B and half-chair for ring C). The proton and carbon resonances of **3–5** were assigned by comparison with the spectra of **1**, but selective decoupling experiments had to be used for the oxygenated carbons, since simple comparison was not possible. The ^{1}H and ^{13}C NMR spectra of 10-deacetylbaccatin III **2** were assigned in a similar way, correcting some errors in the literature (assignments of C-5, C-7, C-10, C-11, C-12, C-13, C-16 and C-18).[10] These revised assignments are in accord with a recently reported 2D-NMR investigation on taxol and some derivatives.[11]

Only acyl derivatives of **2** have been studied so far by X-ray analysis,[6] and no information on the intramolecular hydrogen-bonding pattern in the natural product could be established. Inspection of models showed that the heavy concentration of oxygenated functions makes it possible for each hydroxy group to form an intramolecular hydrogen bond with a suitably located carbonyl acceptor (9-CO for OH-7 and OH-10, Ph*CO* for OH-1 and Me*CO* for OH-13). The formation of intramolecular bondings has dramatic effects on the reactivity of **2**, and this has been invoked to explain the low reactivity of OH-13 in esterification reactions[4] and the easy isomerization of OH-7.[12] Since the hemisynthesis of taxol involves the painstaking manipulation of the secondary OH groups of **2**,[3,4] a better knowledge of their hydrogen-bonding status is important. Although we were unable to get crystals of **2** suitable for an X-ray analysis, **1** formed an acetone solvate that could be analysed (Fig. 1, Table 4). In spite of the presence of an additional hydroxy group, no intramolecular hydrogen-bonding was present, and only intramolecular hydrogen bonds were detected: OH-14 is bound to Me_2CO [distance O(11)–H···O(12) = 2.704 Å] and those at C-7 and C-13 act as donors toward the OH-1 and the oxetane oxygen of another molecule [distance O(7)–H···O(1) (at $x,y-1,z$) = 2.845 Å; distance O(10)–H···O(6) (at $x,y-1,z$) = 2.800 Å]. Most importantly, the acetyl group adopts a conformation with the carbonyl oxygen oriented towards ring C [C(4)–O(4)–C(8′)–O(5) = −5.6°] and not towards OH-13, for which no intramolecular bonding is possible. This geometry is not the result of packing forces alone, since in the ^{1}H NMR spectrum of **1** a ROE-effect was observed between 14-H and $MeCO_2$ (Table 3), as expected from the conformation found in the solid state [distance H(14)–H(9′) = 2.72 Å]. The low-reactivity of the OH-13 in **1** and **2** is thus ascribed exclusively to steric factors.

Very few taxanes functionalized at C-14 have been described,[13–15] and the availability of hydroxylated derivatives of 10-deacetylbaccatin III **2** has great pharmacological potential, allowing the synthesis of more oxygenated and hydrophilic derivatives of taxol. These should provide insights into the structure-activity relationship within the diterpenoid moiety of antitumour taxoids, an important topic of which very little is known.

Experimental

M.p.s were determined on a Büchi SMP 20 apparatus and are uncorrected; 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. CI-Mass spectra were taken on a VG EQ 70/70 apparatus. ^{1}H and ^{13}C NMR spectra were taken on a Varian VXR 300 spectrometer (300 and 75.4 MHz respectively), with $SiMe_4$ as reference. Silica gel 60 (70–230 mesh, Merck) was used for column chromatography. All solvents used for chromatography were bought as technical grade, and distilled before use. Dry acetone was distilled from $CuSO_4$, dry CH_2Cl_2 and pyridine were distilled from CaH_2.

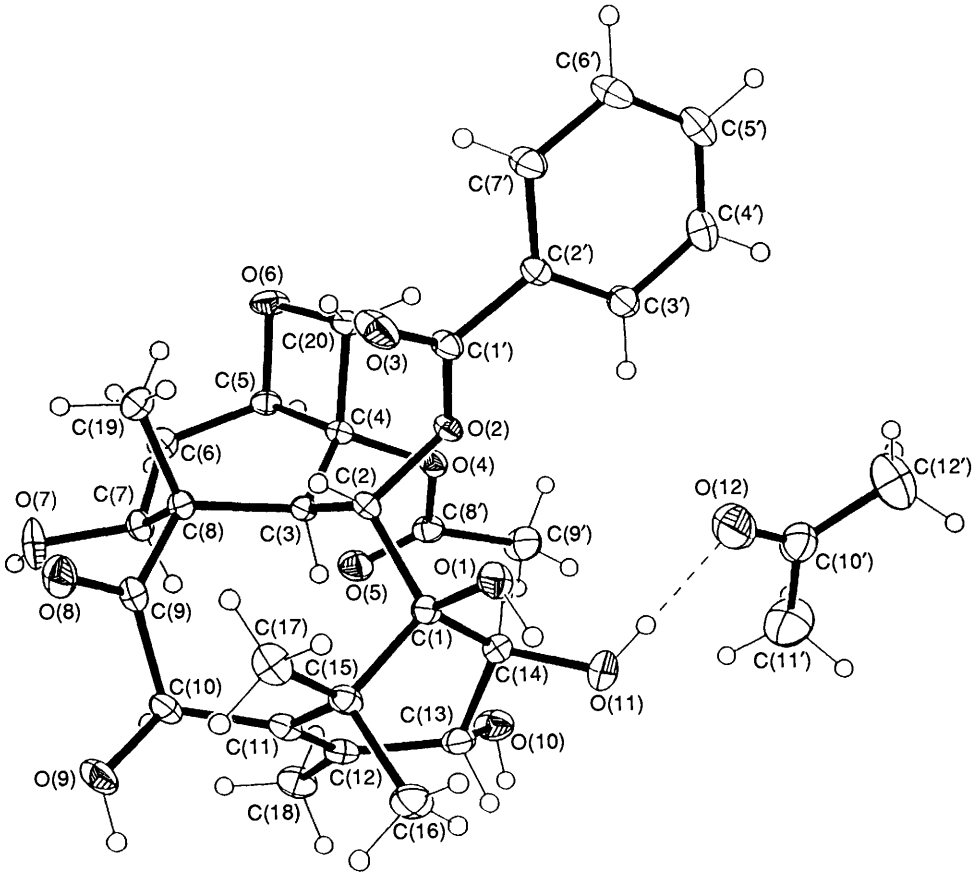


Fig. 1 ORTEP-II drawing of **1** with thermal ellipsoids at the 25% probability level

T. wallichiana Zucc. was collected in Western Himalaya, and was identified by Dr. U. Boni (Indena S.p.A., Milano). A voucher specimen is kept at Inverni della Beffa, Laboratori Ricerca e Sviluppo, Milano.

Isolation of 14β-*Hydroxy*-10-*deacetylbaccatin III* **1**.—Dried powdered leaves of *T. wallichiana* Zucc. (1 kg) were extracted with methanol (6 × 1 dm^3). The combined extracts were concentrated to a volume of *ca.* 1 dm^3; after standing overnight at room temp., the solution was filtered and the filtrate exhaustively extracted with CH_2Cl_2 (6 × 500 cm^3). The combined extracts were evaporated and the residue was chromatographed on a silica gel column (*ca.* 300 g). Fractions eluted with CH_2Cl_2–EtOAc (85:15) were crystallized from methanol (*ca.* 5 cm^3) to give compound **1** (400 mg, 0.040%) as a white powder. Crystals suitable for the X-ray analysis were obtained by slow evaporation (room temp.) of a saturated acetone solution. M.p. 215–217 °C; $[\alpha]_D^{25}$ −43.2 (MeOH, *c* 0.2); λ_{max}(EtOH)/nm 225 and 263; ν_{max}(KBr disc)/cm^{-1} 3420, 1730, 1600, 1270, 1240, 1090, 1020 and 990; *m/z* (CI, NH_3) 561 [(M + H)$^+$ ($C_{29}H_{36}O_{11}$ + H)$^+$, 100%]; *m/z* (EI, 70 eV) 560 (M^+, 5%), 542 [(M − H_2O)$^+$, 23], 420 [(M − H_2O − $PhCO_2H$)$^+$, 91], 360 [(M − H_2O − HOAc − $PhCO_2H$)$^+$, 34], 105 (100) (Found: C, 62.1; H, 6.5. $C_{29}H_{36}O_{11}$ requires C, 62.13; H, 6.47%).

Reaction of **1** *with* 2,2-*Dimethoxypropane*.—A sample of **1** (200 mg) was suspended in dry acetone (17 cm^3), and excess 2,2-dimethoxypropane (7 cm^3) and pyridinium toluene-*p*-sulfonate (150 mg) were added. A limpid solution was obtained which was stirred at room temp. for 72 h [TLC control, hexane–EtOAc (1:9) as eluent, R_f **1** = 0.22, R_f **3** = 0.42] and then evaporated. The residue was dissolved in CH_2Cl_2, washed with water and dried ($MgSO_4$). The semi-solid residue was filtered on a short pad of silica gel; evaporation of the filtrate gave a powder, which was washed with ether to give the 1,14-isopropylidene derivative **3** (164 mg, 76%) as a white powder. M.p. 166–170 °C; λ_{max}(EtOH)/nm 220 and 260; ν_{max}(KBr disc)/cm^{-1} 3460, 1730, 1250, 1210, 1090, 1065 and 1050; *m/z* (CI, NH_3) 601 [(M + H)$^+$ ($C_{32}H_{40}O_{11}$ + H)$^+$, 100%].

Reaction of **1** *with* 2,2,2-*Trichloroethyl Chloroformate*.—Under a nitrogen atmosphere, a solution of **1** (910 mg, 1.63 mmol) in dry pyridine (18 cm^3) was heated at 80 °C (oil bath temperature), and 2,2,2-trichloroethyl chloroformate (1.4 cm^3, 2.15 g, 9.71 mmol, 6 molar equiv.) was then added dropwise. After 5 min the flask was removed from the oil bath, and the reaction quenched by the careful addition of a few drops methanol and ice. The reaction mixture was extracted with $CHCl_3$, and the organic phase was washed with dil. HCl and brine. After drying ($MgSO_4$) and removal of the solvent, a semi-solid residue was obtained, which was dissolved in $CHCl_3$ and filtered through a short pad of silica gel. The residue was washed with ether, giving the bis(trichloroethoxycarbonyl) derivative **4** (952 mg) as a white powder. From the mother liquors, a further 207 mg were obtained after column chromatography (hexane–EtOAc 1:1 as eluent). The overall yield was 1.159 g (75%). M.p. 272 °C (dec.); λ_{max}(EtOH)/nm 222, 264; ν_{max}(KBr disc)/cm^{-1} 3560, 1810, 1760, 1730, 1280, 1235, 1080, 1060 and 700; *m/z* (CI, NH_3) 937 [(M + H)$^+$ ($C_{36}H_{36}Cl_6O_{16}$ + H)$^+$, most intense peak of the isotopic cluster].

Oxidation of the Cyclic Carbonate **4** *with Activated* MnO_2.—A sample of **4** (50 mg) was dissolved in EtOAc (4 cm^3), and an excess activated MnO_2 (1.2 g) was added. After stirring at room temp. for 5 h, the reaction was filtered over Celite. Removal of

the solvent gave the 13-oxo derivative **5** (41 mg, 82%) as a colourless powder. M.p. 138–142 °C; λ_{max}(EtOH)/nm 226 and 262; ν_{max}(KBr disc)/cm^{-1} 3420, 1820, 1760, 1720, 1230, 1080, 1060, 810 and 700; *m/z* (CI, NH_3) 935 [$(M + H)^+$ ($C_{36}H_{34}Cl_6O_{16} + H)^+$, 100% (most intense peak of the isotopic cluster)].

X-Ray Analysis.—Diffraction data were collected with Siemens R3m/V diffractometer equipped with a graphite monochromator. The intensities were measured by ω-scan with variable speed; the cell parameters were obtained and refined from 30 reflections. The intensities were corrected for background and Lorentz-polarization effects, and for absorption using the empirical ψ-scan technique.[16] All subsequent calculations were carried out by the SHELXTL PC™ system.[17] The structure was solved by direct methods and refined by full-matrix least-squares techniques with anisotropic temperature factors for non-hydrogen atoms. Hydrogen atoms were generated in idealized positions, and refined riding on previous normal atom. Hydrogen atom coordinates, bond lengths, angles, torsion angles and thermal parameters have been deposited at the Cambridge Crystallographic Data centre.*

Crystal data. $C_{32}H_{42}O_{12}$, $M = 618.7$, prismatic, space group $P\bar{1}$ (No. 1), $a = 9.113(5)$, $b = 9.161(5)$, $c = 9.491(5)$ Å; $\alpha = 84.93(4)$, $\beta = 68.99(4)$, $\gamma = 79.74(5)°$; $Z = 1$, $D_c = 1.412$ Mg m^{-3}; Mo-Kα radiation, $\lambda = 0.710\,73$ Å, $\mu = 0.101$ mm^{-1}; $R = 0.0362$ for 4172 observed intensities ($2° < 2\theta < 60°$) having $F > 4.0\sigma F$.

* For details, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1992, issue 1.

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