$C_{19}H_{20}BrNO_6.0.5C_3H_8O$

# A C(10)-Oxygenated *ABC*-Ring Analogue† of Paclitaxel (Taxol™)

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## Abstract

The X-ray crystal structure of $C_{19}H_{20}BrNO_6.0.5C_3H_8O$, an *ABC*-ring analogue of the diterpene paclitaxel, establishes that the stereochemistry at C(10) is opposite to that seen in the natural product.

## Comment

We have previously observed (Banwell, Gable, Phyland & Peters, 1995) that certain cyclohexannulated [5.3.1]propellanes are readily converted into *ABC*-ring analogues, *e.g.* (1), of the potent antimitotic agent paclitaxel (taxol™) (Nicolaou, Dai & Guy, 1994). In seeking to exploit such chemistry for the purposes of developing a total synthesis of paclitaxel itself, we had occasion to attempt selective oxidation of the C(9)/C(10) enol ether moiety within (1) so as to generate the corresponding acyloin and thereby install a C(9) carbonyl and C(10) hydroxy group as required in paclitaxel. The desired conversion, which was readily accomplished by literature methods (Frimer, 1977), was completely stereoselective. However, NMR analysis of the product, (2), did not allow the stereochemistry at C(10) to be established in an unequivocal manner. In order to address this issue, compound (2) was subjected to single-crystal X-ray analysis. These data clearly show that the stereochemistry at C(10) is opposite to that seen in paclitaxel.



(1)    (2)
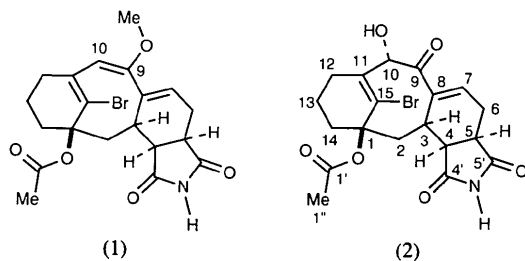
† 14-Bromo-1,2,3,3a,4,6,7,9,10,11,12,13,13a,13b-tetradecahydro-7-hydroxy-1,3,6-trioxo-8,12-methenocyclodeca[*e*]isoindol-12-yl acetate hemipropanol solvate.

Also present in the lattice is a propanol solvate molecule [O(01)–C(03)] which was refined with idealized H atoms and half occupancy across a centre of symmetry. The O(H) H atom was not located.
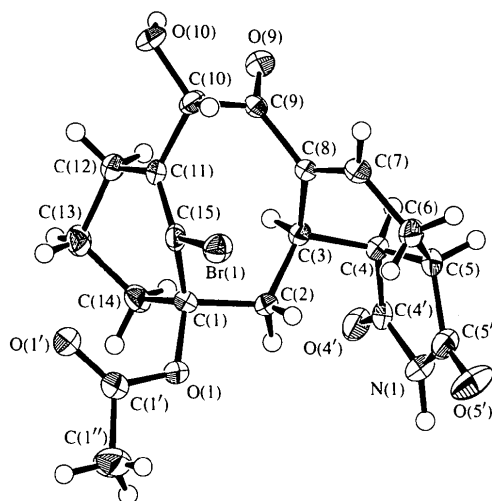


Fig. 1. View of the title compound showing the labelling of all non-H atoms. Thermal ellipsoids are shown at 50% probability levels. H atoms are drawn as circles of arbitrary radius.

## Experimental

Compound (2) was obtained in the following manner. A methanolic solution of (1) (Banwell, Gable, Phyland & Peters, 1995) and *m*-chloroperoxybenzoic acid was heated at reflux for 15 h. The cooled reaction mixture was subjected to standard work-up and the crude product thus obtained was treated with a mixture of 10% aqueous hydrochloric acid and tetrahydrofuran. After 15 h at 291 K the reaction mixture was worked-up and the resulting oil triturated with a small amount of ether. The solid so-formed was recrystallized from ethanol/313–333 K petroleum spirit mixtures then 2-propanol/313–333 K petroleum spirit mixtures to afford compound (2), m.p. 415–417 K.

*Crystal data*

| | |
|---|---|
| $C_{19}H_{20}BrNO_6.0.5C_3H_8O$ | Cu $K\alpha$ radiation |
| $M_r = 468.32$ | $\lambda = 1.5418$ Å |
| Triclinic | Cell parameters from 25 |
| $P\bar{1}$ | reflections |
| $a = 7.623\,(2)$ Å | $\theta = 48.5–50.0°$ |
| $b = 9.046\,(2)$ Å | $\mu = 3.107$ mm$^{-1}$ |
| $c = 15.768\,(3)$ Å | $T = 213\,(1)$ K |
| $\alpha = 80.06\,(2)°$ | Plate |
| $\beta = 86.19\,(2)°$ | $0.240 \times 0.160 \times 0.080$ mm |
| $\gamma = 72.03\,(1)°$ | Colourless |
| $V = 1018.7\,(3)$ Å$^3$ | |
| $Z = 2$ | |
| $D_x = 1.527$ Mg m$^{-3}$ | |

*Data collection*

| | |
|---|---|
| AFC-6R diffractometer | $R_{int} = 0.051$ |
| $\omega/2\theta$ scans | $\theta_{max} = 60.07°$ |

Absorption correction:
empirical, using azimuthal
($\psi$) scan data (North,
Phillips & Mathews,
1968)
$T_{min}$ = 0.820, $T_{max}$ =
1.000
3247 measured reflections
3022 independent reflections
2704 observed reflections
[$I > 3\sigma(I)$]

$h = -8 \rightarrow 8$
$k = -10 \rightarrow 0$
$l = -17 \rightarrow 17$
3 standard reflections
monitored every 150
reflections
intensity decay: none

*Refinement*

Refinement on $F$
$R$ = 0.0366
$wR$ = 0.0461
$S$ = 2.904
2704 reflections
277 parameters
H-atom parameters not
refined
$w = 4F_o^2/[\sigma^2(F_o^2) + (0.010F_o^2)^2]$

$(\Delta/\sigma)_{max}$ = 0.0390
$\Delta\rho_{max}$ = 0.98 e Å$^{-3}$
$\Delta\rho_{min}$ = -0.44 e Å$^{-3}$
Extinction correction: none
Atomic scattering factors
from *International Tables
for Crystallography* (1992,
Vol C, Tables 4.2.6.8 and
6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å$^2$)*

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

| | $x$ | $y$ | $z$ | $U_{eq}$ |
|---|---|---|---|---|
| Br(1) | 0.22324 (6) | 0.21947 (5) | 0.30007 (3) | 0.0297 (1) |
| O(1) | 0.6155 (4) | 0.2322 (3) | 0.3333 (2) | 0.0288 (8) |
| O(1′) | 0.6767 (4) | -0.0246 (3) | 0.3250 (2) | 0.0370 (9) |
| O(4′) | 0.6166 (4) | 0.7896 (3) | 0.1453 (2) | 0.0350 (9) |
| O(5′) | 0.1930 (5) | 0.8351 (4) | 0.3641 (2) | 0.050 (1) |
| O(9) | 0.2211 (4) | 0.4782 (4) | -0.0119 (2) | 0.0338 (9) |
| O(10) | 0.2080 (4) | 0.1735 (3) | 0.0237 (2) | 0.0326 (9) |
| N(1) | 0.4264 (5) | 0.8301 (4) | 0.2633 (2) | 0.031 (1) |
| C(1) | 0.5637 (5) | 0.2817 (5) | 0.2425 (3) | 0.023 (1) |
| C(1′) | 0.6738 (6) | 0.0786 (5) | 0.3646 (3) | 0.032 (1) |
| C(1″) | 0.7364 (9) | 0.0507 (6) | 0.4557 (3) | 0.060 (2) |
| C(2) | 0.4737 (5) | 0.4618 (5) | 0.2386 (3) | 0.024 (1) |
| C(3) | 0.3787 (5) | 0.5558 (5) | 0.1530 (2) | 0.022 (1) |
| C(4′) | 0.4734 (6) | 0.7883 (5) | 0.1833 (3) | 0.026 (1) |
| C(4) | 0.3199 (5) | 0.7359 (5) | 0.1543 (3) | 0.023 (1) |
| C(5′) | 0.2530 (6) | 0.8200 (5) | 0.2930 (3) | 0.032 (1) |
| C(5) | 0.1605 (6) | 0.7906 (5) | 0.2183 (3) | 0.027 (1) |
| C(6) | 0.0378 (6) | 0.6828 (5) | 0.2430 (3) | 0.029 (1) |
| C(7) | 0.0469 (5) | 0.5804 (5) | 0.1761 (3) | 0.028 (1) |
| C(8) | 0.2025 (5) | 0.5206 (5) | 0.1340 (3) | 0.023 (1) |
| C(9) | 0.2065 (5) | 0.4260 (5) | 0.0637 (3) | 0.023 (1) |
| C(10) | 0.2181 (5) | 0.2518 (5) | 0.0921 (3) | 0.026 (1) |
| C(11) | 0.4034 (5) | 0.2008 (4) | 0.1360 (3) | 0.021 (1) |
| C(12) | 0.5702 (6) | 0.1754 (5) | 0.0765 (3) | 0.027 (1) |
| C(13) | 0.7475 (5) | 0.1251 (5) | 0.1267 (3) | 0.029 (1) |
| C(14) | 0.7391 (5) | 0.2457 (5) | 0.1847 (3) | 0.028 (1) |
| C(15) | 0.4189 (5) | 0.2178 (5) | 0.2170 (3) | 0.023 (1) |
| O(01)† | 1.336 (2) | 0.438 (2) | 0.556 (1) | 0.198 (9) |
| C(01)† | 1.182 (4) | 0.429 (3) | 0.515 (1) | 0.116 (9) |
| C(02)† | 1.0 | 1/2 | 1/2 | 0.183 (9) |
| C(03)† | 0.835 (4) | 0.472 (3) | 0.454 (2) | 0.14 (1) |

† These atoms belong to the propanol solvate molecule (0.5 occupancy).

Table 2. *Selected geometric parameters (Å, °)*

| Br(1)—C(15) | 1.917 (4) | C(3)—C(4) | 1.554 (5) |
|---|---|---|---|
| O(1)—C(1) | 1.466 (5) | C(3)—C(8) | 1.531 (5) |
| O(1)—C(1′) | 1.336 (5) | C(4′)—C(4) | 1.514 (6) |
| O(1′)—C(1′) | 1.204 (5) | C(4)—C(5) | 1.542 (5) |
| O(4′)—C(4′) | 1.212 (5) | C(5′)—C(5) | 1.513 (6) |
| O(5′)—C(5′) | 1.196 (5) | C(5)—C(6) | 1.536 (6) |
| O(9)—C(9) | 1.215 (5) | C(6)—C(7) | 1.504 (6) |
| O(10)—C(10) | 1.405 (4) | C(7)—C(8) | 1.328 (6) |
| N(1)—C(4′) | 1.373 (5) | C(8)—C(9) | 1.508 (5) |
| N(1)—C(5′) | 1.397 (6) | C(9)—C(10) | 1.539 (6) |
| C(1)—C(2) | 1.552 (5) | C(10)—C(11) | 1.518 (5) |
| C(1)—C(14) | 1.548 (5) | C(11)—C(12) | 1.512 (5) |
| C(1)—C(15) | 1.499 (5) | C(11)—C(15) | 1.331 (5) |
| C(1′)—C(1″) | 1.498 (6) | C(12)—C(13) | 1.517 (6) |
| C(2)—C(3) | 1.556 (5) | C(13)—C(14) | 1.525 (6) |
| | | | |
| C(1)—O(1)—C(1′) | 118.9 (3) | C(4)—C(5)—C(5′) | 104.2 (3) |
| C(4′)—N(1)—C(5′) | 113.8 (4) | C(4)—C(5)—C(6) | 115.9 (3) |
| O(1)—C(1)—C(2) | 101.5 (3) | C(5′)—C(5)—C(6) | 115.1 (4) |
| O(1)—C(1)—C(14) | 109.6 (3) | C(5)—C(6)—C(7) | 111.8 (3) |
| O(1)—C(1)—C(15) | 114.1 (3) | C(6)—C(7)—C(8) | 121.7 (4) |
| C(2)—C(1)—C(14) | 111.1 (3) | C(3)—C(8)—C(7) | 120.0 (4) |
| C(2)—C(1)—C(15) | 106.9 (3) | C(3)—C(8)—C(9) | 119.0 (3) |
| C(14)—C(1)—C(15) | 112.9 (3) | C(7)—C(8)—C(9) | 120.9 (4) |
| O(1)—C(1′)—O(1′) | 124.6 (4) | O(9)—C(9)—C(8) | 122.0 (4) |
| O(1)—C(1′)—C(1″) | 111.3 (4) | O(9)—C(9)—C(10) | 120.7 (4) |
| O(1′)—C(1′)—C(1″) | 124.2 (4) | C(8)—C(9)—C(10) | 116.8 (3) |
| C(1)—C(2)—C(3) | 117.0 (3) | O(10)—C(10)—C(9) | 113.8 (3) |
| C(2)—C(3)—C(4) | 110.9 (3) | O(10)—C(10)—C(11) | 115.8 (3) |
| C(2)—C(3)—C(8) | 114.6 (3) | C(9)—C(10)—C(11) | 97.0 (3) |
| C(4)—C(3)—C(8) | 105.3 (3) | C(10)—C(11)—C(12) | 115.5 (3) |
| O(4′)—C(4′)—N(1) | 124.7 (4) | C(10)—C(11)—C(15) | 122.1 (4) |
| O(4′)—C(4′)—C(4) | 127.3 (4) | C(12)—C(11)—C(15) | 120.1 (4) |
| N(1)—C(4′)—C(4) | 108.0 (4) | C(11)—C(12)—C(13) | 111.2 (3) |
| C(3)—C(4)—C(4′) | 112.4 (3) | C(12)—C(13)—C(14) | 109.2 (3) |
| C(3)—C(4)—C(5) | 113.3 (3) | C(1)—C(14)—C(13) | 113.9 (3) |
| C(4′)—C(4)—C(5) | 103.9 (3) | Br(1)—C(15)—C(1) | 114.3 (3) |
| O(5′)—C(5′)—N(1) | 124.8 (4) | Br(1)—C(15)—C(11) | 122.0 (4) |
| O(5′)—C(5′)—C(5) | 128.3 (4) | C(1)—C(15)—C(11) | 121.5 (4) |
| N(1)—C(5′)—C(5) | 106.8 (4) | | |

The $\theta$-scan width used was $(1.30 + 0.3\tan\theta)°$ at a speed of 32.0° min$^{-1}$ (in $\omega$). The weak reflections were rescanned a maximum of four times and the counts accumulated to ensure good counting statistics. Stationary background counts were made on each side of the reflection with a 2:1 ratio of peak-to-background counting time. H atoms were located from a difference map and fixed at ideal position with $U_{iso}$ = $1.2U_{eq}(C)$. The structure was solved by Patterson methods and expanded using Fourier techniques (Beurskens *et al.*, 1992).

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1991). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1985). Program(s) used to solve structure: *PATTY, DIRDIF92* (Beurskens *et al.*, 1992). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

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# Specific Structural Features and Photochemical Properties of Three Benzo-Annulated 2,2-Diphenyl[2*H*]chromenes

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## Abstract

The crystal structures of 3,3-diphenylbenzo[*f*]chromene, $C_{25}H_{18}O$, 1,3,3-triphenylbenzo[*f*]chromene, $C_{31}H_{22}O$, and 2,2-diphenylbenzofuro[2,3-g]chromene, $C_{27}H_{18}O_2$, have been determined. Annulated 2,2-diphenylchromenes are of interest because of the influence of steric strain energy in the pyran ring on the photochromic properties of these compounds.

## Comment

We presented previously (Aldoshin *et al.*, 1995), the results of an X-ray investigation of the 2*H*-chromene derivative (I).

(I)
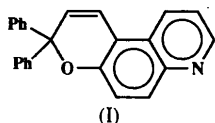
Our interest in this class of compounds is due to the fact that, in contrast to other classes of photochromic compounds like spiropyrans and spirooxazines, 2*H*-chromenes do not contain a spiro-heterocyclic fragment. Nevertheless, some chromenes do possess photo-, thermo- or solvatochromic properties in solution.

The breaking of the C1—O1 bond is responsible for the photochromic properties of chromenes. The X-ray study of the photochromic diphenylchromene (I)

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(Aldoshin *et al.*, 1995) has shown that the C1—O1 bond in this compound is elongated due to steric interactions. In order to analyse the influence of substitution on the structure of the pyran ring and to establish a relationship with their photochromic properties, we have determined the X-ray structures of three new compounds, namely, 3,3-diphenylbenzo[*f*]chromene, (II), 1,3,3-triphenylbenzo[*f*]chromene, (III), and 2,2-diphenylbenzofuro[2,3-g]chromene, (IV) (Pozzo, 1994).

(II)

(III)                                      (IV)
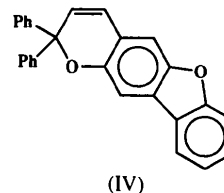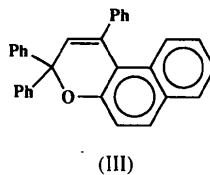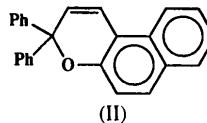
The main characteristic parameters of compounds (II)–(IV) are reported for comparison in Table 5. In compound (II), the pyran ring is only slightly flattened compared to compound (I), whereas for compounds (III) and (IV) the pyran rings are more non-planar.

The phenyl groups for all three compounds are quite orthogonal. The relative orientations of these phenyl groups with respect to the pyran ring are different; one ring is eclipsed with respect to the O1—C1 bond [(II) O1—C1—C14—C15 14.2 (2); (III) O1—C1—C26—C27 18.2 (3); (IV) O1—C1—C22—C27 14.5 (1)°] and the other is eclipsed with respect to the C1—C2 bonds of the pyran ring [(II) C2—C1—C20—C25 3.2 (2); (III) C2—C1—C20—C25 7.1 (3); (IV) C2—C1—C16—C17 4.5 (1)°]. In compound (I), the O1—C1 and C1—C2 bonds of the pyran ring are in a screw conformation with respect to the phenyl rings [corresponding values are 32.6 (2) and 24.1 (2)°].
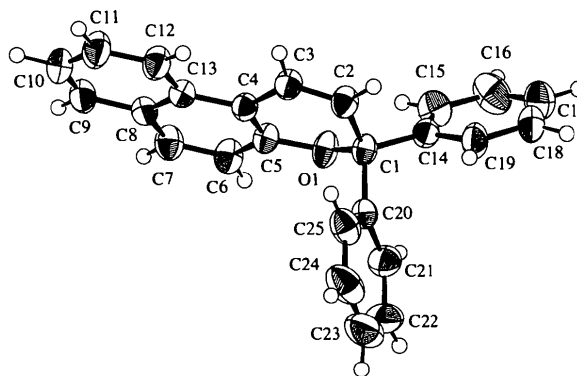
Fig. 1. *ORTEP*II drawing (Johnson, 1976) of compound (II) with displacement ellipsoids at the 50% probability level.

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