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## Key indicators

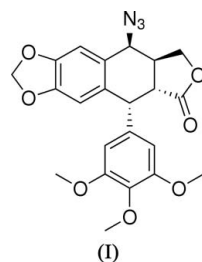
Single-crystal X-ray study  
 $T = 298$  K  
Mean  $\sigma(\text{C}-\text{C}) = 0.004$  Å  
Disorder in main residue  
 $R$  factor = 0.040  
 $wR$  factor = 0.112  
Data-to-parameter ratio = 8.8For details of how these key indicators were  
automatically derived from the article, see  
<http://journals.iucr.org/e>.4- $\beta$ -Azido-4-desoxypodophyllotoxin

The title compound,  $\text{C}_{22}\text{H}_{21}\text{N}_3\text{O}_7$ , was prepared by reaction of podophyllotoxin and hydrogen azide. Each of the five-membered rings displays an envelope conformation. Weak  $\text{C}-\text{H} \cdots \text{O}$  and  $\text{C}-\text{H} \cdots \text{N}$  hydrogen bonding helps to stabilize the crystal structure.

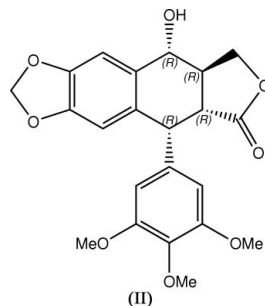
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## Comment

Podophyllotoxin is an effective intermediate in the synthesis of drugs with higher activity and lower toxicity against tumour cancer. Recently, we prepared the title podophyllotoxin derivative, (I), by substitution of an azide group at the 4-position of podophyllotoxin.



The molecular structure of (I) is shown in Fig. 1. Both five-membered rings display an envelope conformation. Within the O7-containing ring, atom C3 lies at the flap position and is 0.539 (4) Å out of the mean plane formed by the other four atoms; within the disordered O1-containing ring, atom C11A (C11B) lies at the flap position and is displaced from the mean plane formed by the other four atoms by 0.242 (9) Å [0.403 (8) Å]. The C1–C5/C10 ring displays a half-chair conformation, with atoms C2 and C3 deviating from the mean plane formed by the other four atoms by 0.415 (5) and –0.358 (5) Å, respectively. The bond distances and angles involving the azide group (Table 1) are comparable with those reported by Lautens *et al.* (2002).



We consider that the absolute configurations at atoms C1 and C2 are the same as the starting material, podophyllotoxin,

(II). The molecular structure shows that the configuration at C4 is *R*, which is different from the *S* configuration at C4 in (II).

Weak C—H···O and C—H···N hydrogen bonding (Table 2) helps to stabilize the crystal structure.

## Experimental

Podophyllotoxin (4.14 g, 10 mmol) and a benzene solution of hydrogen azide (10 ml, 1.2 mol l<sup>-1</sup>) were dissolved in a mixture of trifluoroborane/diethyl ether (2 ml) and dichloroethane (100 ml) at 258 K. The solution was stirred for 1 h and then quenched with pyridine (5 ml), giving a white deposit. The deposit was placed in water (50 ml). An organic layer was isolated, washed successively with hydrochloric acid (30 ml, 5%) and water (2 × 50 ml), and concentrated to dryness. Single crystals of (I) were obtained from an acetone/methanol solution after 1 d.

### Crystal data

C <sub>22</sub> H <sub>21</sub> N <sub>3</sub> O <sub>7</sub>	Z = 4
M <sub>r</sub> = 439.42	D <sub>x</sub> = 1.385 Mg m <sup>-3</sup>
Orthorhombic, P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	Mo Kα radiation
a = 8.998 (2) Å	μ = 0.11 mm <sup>-1</sup>
b = 12.880 (5) Å	T = 298 (1) K
c = 18.184 (5) Å	Chunk, colourless
V = 2107.4 (11) Å <sup>3</sup>	0.31 × 0.19 × 0.12 mm

### Data collection

Rigaku R-Axis RAPID diffractometer	2735 independent reflections
ω scans	2050 reflections with I > 2σ(I)
Absorption correction: none	R <sub>int</sub> = 0.035
20804 measured reflections	θ <sub>max</sub> = 27.5°

### Refinement

Refinement on F <sup>2</sup>	w = 1/[σ <sup>2</sup> (F <sub>o</sub> <sup>2</sup> ) + (0.0578P) <sup>2</sup> + 0.1971P]
R[F <sup>2</sup> > 2σ(F <sup>2</sup> )] = 0.040	where P = (F <sub>o</sub> <sup>2</sup> + 2F <sub>c</sub> <sup>2</sup> )/3
wR(F <sup>2</sup> ) = 0.112	(Δ/σ) <sub>max</sub> < 0.001
S = 1.05	Δρ <sub>max</sub> = 0.14 e Å <sup>-3</sup>
2735 reflections	Δρ <sub>min</sub> = -0.17 e Å <sup>-3</sup>
311 parameters	Extinction correction: SHELXL97
H-atom parameters constrained	Extinction coefficient: 0.0117 (17)

**Table 1**

Selected geometric parameters (Å, °).

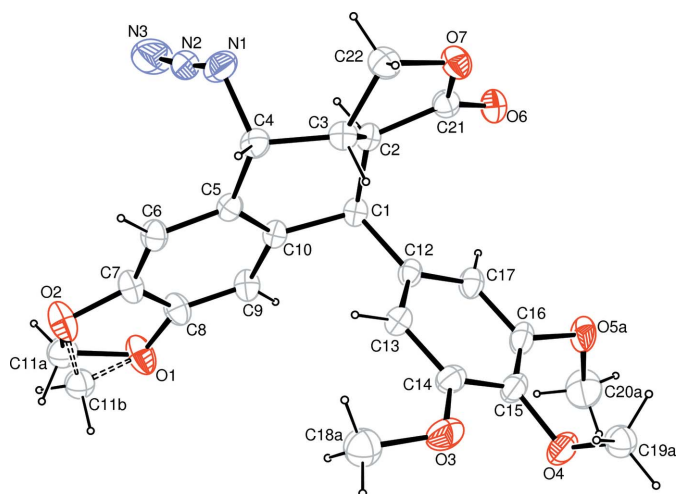
C4—N1	1.505 (4)	N2—N3	1.118 (5)
N1—N2	1.201 (4)		
N2—N1—C4	118.1 (3)	N1—N2—N3	173.0 (4)

**Table 2**

Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C6—H6···O6 <sup>i</sup>	0.93	2.54	3.433 (4)	161
C18A—H18A···O7 <sup>ii</sup>	0.96	2.56	3.517 (11)	176
C18A—H18C···N3 <sup>iii</sup>	0.96	2.52	3.349 (11)	145

Symmetry codes: (i) x + 1, y, z; (ii) x + ½, -y + ½, -z + 1; (iii) -x + ½, -y + 1, z - ½.



**Figure 1**

The molecular structure of (I), shown with 25% probability displacement ellipsoids (arbitrary spheres for H atoms). For each methoxy group, only one disorder component is shown. For C11, both disordered components are shown.

The three methoxy groups are disordered: C18, C19 and C20 each over two sites and O5 over two sites. C11 is also disordered over two sites. For all disordered atoms, site occupancies were initially refined but later fixed at 0.5. Disordered non-H atoms were refined isotropically. H atoms were placed in calculated positions with C—H = 0.93 Å (aromatic), 0.96 Å (methyl group), 0.97 Å (methylene group) and 0.98 Å (methine). Torsion angles were refined for methyl groups to fit the electron density,  $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ . Other H atoms were refined in riding mode with  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ . The absolute configuration was assigned by reference to the unchanging C1 and C2 chiral centres in the synthetic procedure. In the absence of significant anomalous scattering effects, Friedel pairs were averaged.

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *CrystalStructure* (Rigaku/MS, 2004); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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