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1,8-Dihydroxy-3-methyl-6-(oxiran-2-ylmethoxy)-9,10-dihydroanthracene-9,10-dione

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.003 Å
R factor = 0.052
wR factor = 0.169
Data-to-parameter ratio = 15.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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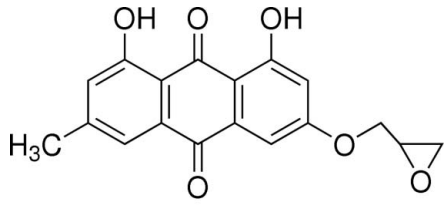
The title compound, $C_{18}H_{14}O_6$, was synthesized by the nucleophilic substitution of emodin (1,3,8-trihydroxy-6-methylanthraquinone) and epichlorohydrin in dilute KOH solution. The molecular structure is stabilized by two intramolecular O—H···O hydrogen-bonding interactions between the carbonyl group and the hydroxy groups.

Comment

Anthracycline compounds represent an important class of naturally occurring substances characterized by highly pronounced biological properties, especially the anthracycline pharmacophore, which plays a primary role in inhibiting the DNA replication of tumour cells and the synthesis of RNA-dependent RNA enzyme. Anthracycline analogues have been the subject of extensive study in the recent past (Li & Xu, 2006).



(I)

Emodin, an anthracycline analogue, is a major active component of the traditional Chinese medicine herb genus *Rhamnus* (Dahuang in Chinese). Emodin and its derivatives have been found to have diverse biological properties, such as antimicrobial, antiviral, anti-inflammatory, anti-oxidant, immunosuppressive, anti-ulcerogenic, fungicidal and chemopreventive activities (Teich *et al.*, 2004; Srinivas *et al.*, 2003).

Matrix metalloproteinases (MMPs), a family of zinc-dependent endopeptidases, have been suggested to be one of the important targets for cancer therapy (Li *et al.*, 2006). Up to now, at least 24 structurally related members in the mammal MMP gene family have been reported (Li & Xu, 2004), among which overexpression of IV gelatinase (MMP-2 and -9) has been found to be strongly associated with tumour growth, invasion and metastasis (Rundhaug, 2005; Singh *et al.*, 2004). Therefore, moderately manipulating the high expression of gelatinase may be useful in the control of cancer.

Because the hydroxyl and carbonyl of emodin derivatives are both zinc-binding groups, they can chelate with the active zinc ion at the catalytic centre of gelatinase. Thus, it is hoped that emodin and its derivatives will be potential gelatinase inhibitors. In fact, emodin analogues can prevent the degra-

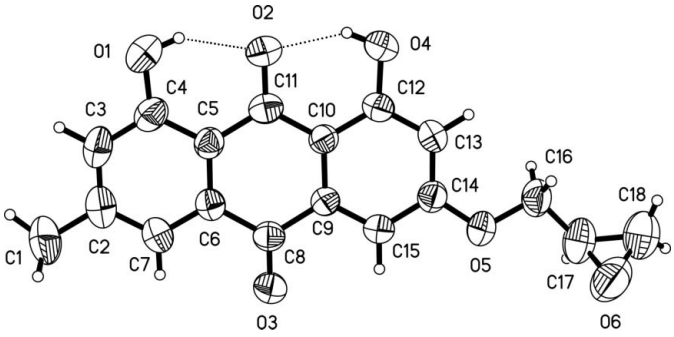


Figure 1
View of (I) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level. H atoms are represented as small spheres of arbitrary radii. Dotted lines indicate the hydrogen-bonding interactions.

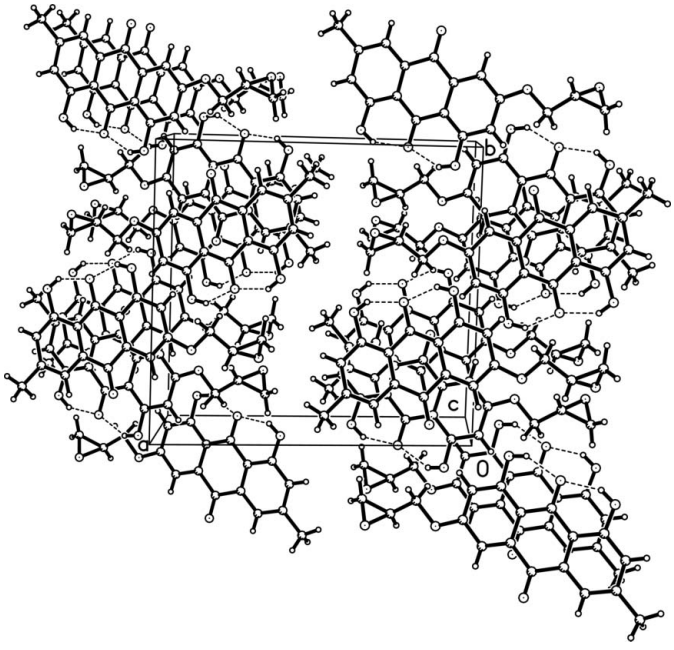


Figure 2
The molecular packing of (I) viewed along the *a* axis. Dashed lines indicate the hydrogen-bonding interactions.

dation of the ECM (extracelllular matrix) and cell migration by inhibiting the activities of gelatinases (Fang *et al.*, 2000).

In this paper, the structure of the title compound, (I), which may be a gelatinase inhibitor, is reported. The molecular structure of (I) is illustrated in Fig. 1. It displays normal anthracycline geometry; the bond lengths and angles are unexceptional. There are two intramolecular O—H···O hydrogen-bonding interactions between the carbonyl group and the hydroxy groups (Fig. 2).

Experimental

A mixture of 1,3,8-trihydroxy-6-methylanthracene-9,10-dione (10 mmol) and epichlorohydrin (421 mmol, 33 ml) was stirred under reflux in a solution of potassium hydroxide (10 mmol) in water (3 ml) until the disappearance of the starting material, as evidenced by thin-layer chromatography (about 4 h). After the reaction was over, the solvent was removed *in vacuo* and the residue was partitioned between chloroform (50 ml) and distilled water (20 ml). The organic phase was washed with water (15 ml) and brine (15 ml), and dried over anhydrous sodium sulfate. The solvent was removed to give the crude product as a yellow oil, which was purified by flash chromatography (silica gel, petroleum ether–acetone 3:1). Yellow needle crystals were obtained by recrystallization from chloroform (1.56 g, 51% yield; m.p.473–474 K). IR (KBr, ν cm^{-1}): 3086.0, 2985.3, 1623.1, 1610.0 (C═O), 1308.2; ^{1}H NMR (DMSO-d_6, p.p.m.): δ 2.42 (*s*, 3H, Ph—CH$_3$), 2.76 (*dd*, 1H, J = 2.8 and 4.8 Hz, –CH$_2$), 2.88 (*t*, 1H, J = 4.8 Hz, –CH$_2$), 3.37–3.39 (*m*, 1H, –CH), 4.05 (*dd*, 1H, J = 6.0 and 11.2 Hz, O—CH$_2$), 4.59 (*dd*, 1H, J = 2.8 and 11.2 Hz, O—CH$_2$), 6.90–7.52 (*s*, 4H, ArH), 11.94 (*s*, 1H, –OH), 12.14 (*s*, 1H, –OH); ^{13}C NMR (DMSO-d_6, p.p.m.): δ 21.36 (C1), 43.24 (C18), 49.21 (C17), 68.49(C16), 107.35 (C13), 108.24 (C15), 110.15 (C10), 113.32 (C4), 120.55 (C7), 124.43 (C5), 132.88 (C3), 134.86 (C2), 148.57 (C9), 161.65 (C12), 164.42(C14), 165.53 (C6), 181.16 (C11), 190.08 (C8); ESI-MS (m/z): 327.3 [M+H]$^+$; Analysis found: C 66.78, H 4.01%; calculated for C$_{18}$H$_{14}$O$_6$: C 66.26, H 4.29%. Compound (I) (20 mg) was dissolved in methanol (15 ml); the solution was kept at room temperature for 15 d and natural evaporation gave yellow single crystals of (I), which were suitable for X-ray analysis.

Crystal data

C$_{18}$H$_{14}$O$_6$
M_r = 326.29
Monoclinic, $P2_1/c$
a = 14.6082 (5) Å
b = 13.5438 (6) Å
c = 7.6388 (3) Å
β = 99.838 (2)°
V = 1489.12 (10) Å^3
Z = 4
D_x = 1.455 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.11 mm^{-1}
T = 296 (2) K
Plate, yellow
0.49 × 0.38 × 0.03 mm

Data collection

Bruker APEXII CCD diffractometer
φ and ω scans
Absorption correction: multi-scan [*APEX2 Software Suite* (Bruker, 2005)]
T_{min} = 0.948, T_{max} = 0.997
9711 measured reflections
3395 independent reflections
1637 reflections with $I > 2\sigma(I)$
R_{int} = 0.037
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.053
$wR(F^2)$ = 0.169
S = 1.01
3395 reflections
220 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0764P)^2 + 0.163P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1D···O2	0.82	1.85	2.570 (2)	146
O4—H4A···O2	0.82	1.85	2.569 (2)	146

All H atoms were positioned geometrically (C—H = 0.93–0.98 Å and O—H = 0.82 Å). The methyl H atoms and hydroxyl H atoms were refined as rigid groups, which were allowed to rotate but not to tip, with U_{iso}(H) = 1.5U_{iso}(C,O). All other H atoms were allowed to ride on their parent atoms with U_{iso}(H) = 1.2U_{iso}(C).

Data collection: *APEX2 Software Suite* (Bruker, 2005); cell refinement: *APEX2 Software Suite*; data reduction: *APEX2 Software Suite*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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