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Methyl indole-3-carboxylate

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Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.003 Å
R factor = 0.056
wR factor = 0.152
Data-to-parameter ratio = 14.4

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

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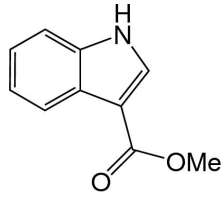
The title compound, $C_{10}H_9NO_2$, was isolated and characterized from an EtOAc extract of marine *Streptomyces sp.* 060524. All atoms, except the methyl H atoms, are nearly coplanar. There is an intermolecular N—H···O hydrogen bond in the crystal stucture. The compound is cytotoxic against K562 human chronic leukaemia.

Comment

Cancer continues to be one of the most difficult life-threatening diseases, but drugs derived from natural products could and have helped to ameliorate the situation (Nagle *et al.*, 2004). Since the discovery of penicillin from *Penicillium notatum* in the 1940s, terrestrial microorganisms, especially *Streptomyces*, have attracted attention for their ability to produce an immense number and variety of bioactive secondary metabolites (Watve *et al.*, 2001). Given that the rate of discovery of new biologically active compounds from common soil microorganisms has been falling (Bull *et al.*, 2000), marine microorganisms have more recently come into the focus of research as the source of several interesting new structures (Lopez *et al.*, 2003; Shu *et al.*, 2004; Jensen & Fenical, 2000; Liu *et al.*, 2002). In an ongoing programme to screen cytotoxic compounds from marine microorganisms, bioassay-guided fractionation of the EtOAc extract of marine *Streptomyces sp*. 060524 provided the title compound, (I), in 0.12% yield (22.8 mg). This isolated compound was identified as methyl indole-3-carboxylate (Bano *et al.*, 1987; Yue *et al.*, 2000). In this paper, we report the structure of (I).



(I)

Fig. 1 shows the molecular structure of (I). Bond lengths and angles (Table 1) in (I) are within normal ranges (Allen *et al.*, 1987). All non-H atoms are almost coplanar.

An intermolecular hydrogen bond between the N atom and the carbonyl O atom links the molecules to form a one-dimensional chain along the *b* axis (Fig. 2).

Experimental

The isolated *Streptomyces sp*. 060524 originated from a marine alga collected in the South China Sea, and showed a 99% similarity of its

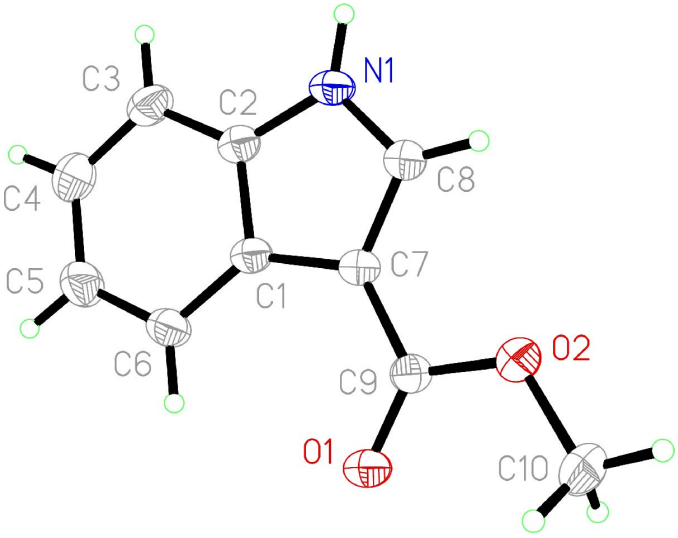


Figure 1
The structure of (I), showing 30% probability displacement ellipsoids and the atom-numbering scheme.

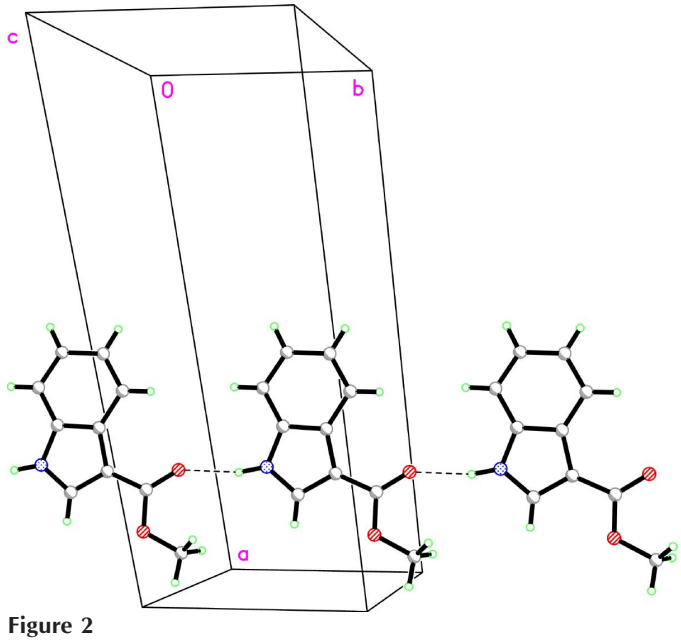


Figure 2
The one-dimensional chain of (I), running along the *b* axis. Dashed lines indicate hydrogen bonds.

16S rRNA gene sequence to *Streptomyces someliensis* (GenBank accession No. AY529644). The strain 060524 was cultured in a soybean medium containing 0.2% starch, 1.5% soybean powder, 0.2% yeast extract, 0.2% peptone, 0.4% $CaCO_3$, 75% seawater and 25% distilled water, pH 7.2–7.4, and incubated on a rotary shaker at 200 r.p.m. and 301 K for 5 d. The cultures were then harvested separately and centrifuged for 10 min. The broth supernatant was extracted with EtOAc and a brown residue (19.3 g) was obtained after depositing lipids, which was then subjected to column chromatography on silica gel (180 g, 200–300 mesh), eluting with chloroform–methanol (1:0–0:1), to give ten fractions (fraction 1 0.8 g, fraction 2 4.0 g, fraction 3 3.5 g, fraction 4 0.6 g, fraction 5 2.5 g, fraction 6 1.8 g, fraction 7 2.4 g, fraction 8 0.6 g, fraction 9 0.8 g, fraction 10 0.25 g). Fraction 5, showing pronounced antitumour activity, was re-chromatographed on a silica-gel column, eluting with chloroform–methanol (100:1–4:1), to afford four subfractions (fraction 5-1 0.5 g, fraction 5-2 1.0 g, fraction 5-3 0.4 g, fraction 5-4 0.6 g). Fraction 5-2 was subjected to gel filtration over Sephadex LH-20 with methanol, followed by repeated recrystallization, to give methyl indole-3-carboxylate, (I), a white crystalline solid (22.8 mg, m.p. 414–415 K). Spectroscopic analysis: ^{1}H NMR (500 MHz, $CDCl_3$, δ, p.p.m.): 7.93 (1H, *s*, H2), 8.20 (1H, *dd*, J = 8.0 and 2.5 Hz, H4), 7.41 (1H, *dd*, J = 8.0 and 2.5 Hz, H4), 7.28 (2H, *m*, H5, H6), 3.93 (3H, *s*, –OCH_3). The *in vitro* cytotoxicity was assessed using the MTT assay, performed as described by Mosmann (1983). The indicator cell line was K562 human chronic leukaemia, which was cultured in RPMI1640 (Gibcol) supplemented with 10% FBS. The results showed that methyl indole-3-carboxylate displayed significant growth inhibition against K562 with minimum inhibitory concentrations (MICs) of 14.0 μg ml^{-1}.

Crystal data

$C_{10}H_9NO_2$
M_r = 175.18
Monoclinic, $C2/c$
a = 21.382 (4) Å
b = 7.4070 (15) Å
c = 13.372 (3) Å
β = 125.34 (3)°
V = 1727.6 (6) Å^3
Z = 8
D_x = 1.347 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1009 reflections
θ = 2.9–26.5°
μ = 0.10 mm^{-1}
T = 298 (2) K
Prism, colourless
0.45 × 0.41 × 0.38 mm

Data collection

Siemens SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.959, T_{max} = 0.965
5009 measured reflections
1752 independent reflections
1315 reflections with $I > 2\sigma(I)$
R_{int} = 0.146
θ_{max} = 26.5°
$h = -26 \rightarrow 26$
$k = -9 \rightarrow 5$
$l = -16 \rightarrow 16$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.152
S = 1.06
1752 reflections
122 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0677P)^2 + 0.0691P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1^{i}	0.91 (1)	1.96 (1)	2.8381 (18)	162 (2)

Symmetry code: (i) $x, y+1, z$.

The coordinates of the H atom bonded to N were refined, but the displacement parameter was set to U_{iso}(H) = 1.2U_{eq}(N). H atoms bonded to C atoms were placed in geometric positions and constrained to ride on their parent atoms, with C—H distances of 0.96 Å and with U_{iso}(H) = 1.2U_{eq}(C). The methyl group was allowed to rotate but not to tip.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997*a*); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997*a*); molecular graphics:

SHELXTL (Sheldrick, 1997*b*); software used to prepare material for publication: *SHELXTL*.

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References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
Bano, S., Ahmad, V. U., Perveen, S., Bano, N., Shafiuddin & Shameel, M. (1987). *Planta Med.* **53**, 117–18.
Bull, A. T., Ward, A. C. & Goodfellow, M. (2000). *Microbiol. Mol. Biol. Rev.* **64**, 573–604.
Jensen, P. R. & Fenical, W. (2000). In *Drugs From the Sea*, edited by N. Fusetani, pp. 6–29. Basel: Karger.
Liu, J. Y., Liu, C. H., Zou, W. X., Tian, X. & Tan, R. X. (2002). *Helv. Chim. Acta*, **85**, 2664–2667.
Lopez, J. M. S., Insua, M. M., Baz, J. P., Puentes, J. L. F. & Hernandez, L. M. C. (2003). *J. Nat. Prod.* **66**, 863–864.
Mosmann, F. R. (1983). *J. Immunol. Methods*, **65**, 55–63.
Nagle, D. G., Zhou, Y. D., Mora, F. D., Mohammed, K. A. & Kim, Y. P. (2004). *Curr. Med. Chem.* **11**, 1725–1756.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (1997*a*). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Sheldrick, G. M. (1997*b*). *SHELXTL*. Version 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Siemens (1996). *SMART* and *SAINT*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Shu, R. G., Wang, F. W., Yang, Y. M., Liu, Y. X. & Tan, R. X. (2004). *Lipids*, **39**, 667–673.
Watve, M. G., Tickoo, R., Jog, M. M. & Bhole, B. D. (2001). *Arch. Microbiol.* **176**, 386–390.
Yue, Q., Miller, C. J., White, J. F. Jr & Richardson, M. D. (2000). *J. Agric. Food. Chem.* **48**, 4687–4692.