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# 1-(4-Methoxyphenyl)-2-(2-nitrophenoxy)-propan-1-one

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**Key indicators**

Single-crystal X-ray study
$T$ = 293 K
Mean $\sigma$(C–C) = 0.003 Å
$R$ factor = 0.042
$wR$ factor = 0.129
Data-to-parameter ratio = 12.8

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



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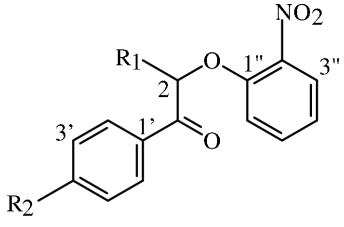
The title compound, $C_{16}H_{15}N_1O_5$, is a $\beta$-ketoether derivative, closely related to natural 8.4′-oxyneolignans, which are of interest because of their antiprotozoal activity. The nitro group is not coplanar with the aromatic ring, as is shown by a torsion angle of 49.4 (3)°. The molecules are connected in the crystal structure by two non-classical intermolecular hydrogen bonds with C···O distances of 3.363 (3) and 3.274 (2) Å; repetition of these hydrogen bonds leads to the formation of sheets of molecules parallel to the (001) plane.

## Comment

Neolignans, a class of widely distributed natural plant constituents (Gottlieb & Yoshida, 1990), have displayed activity against the protozoal disease leishmaniasis (Costa *et al.*, 1995, 1999), which is an important world health problem. $\beta$-Ketoether derivatives of natural 8.4′-oxyneolignans, such as compound (I), have shown significant activity against intracellular *Leishmania donovani* amastigotes in a mouse peritoneal macrophage model *in vitro*, although they were not active against extracellular promastigotes. This fact may be due to biochemical or metabolic differences between the two stages of the parasite, or to variations in the intracellular concentration of the compound by extracellular promastigotes and the macrophages (Barata *et al.*, 2000). In addition, the chain linking the aromatic rings in (I) constitutes a major type of structural element in lignins, although the 2-aryloxypropiophenone skeleton seems to occur only rarely in these polymers (Lundquist & von Unge, 1986). In this paper, the crystal structure of the title compound, (II), is described.




(I) $R_1 = R_2 = H$
(II) $R_1 = CH_3$, $R_2 = OMe$

In (II), the chain of atoms C6/O1/C7/C16/C8/O2/C9 is called an 8.O.4′ linkage, and compounds (I) and (II) can be called 8.4′-oxyneolignan derivatives, according to accepted neolignan nomenclature (Moss, 2000). The present crystal structure data will enable conclusions to be drawn about the geometry of these derivatives.

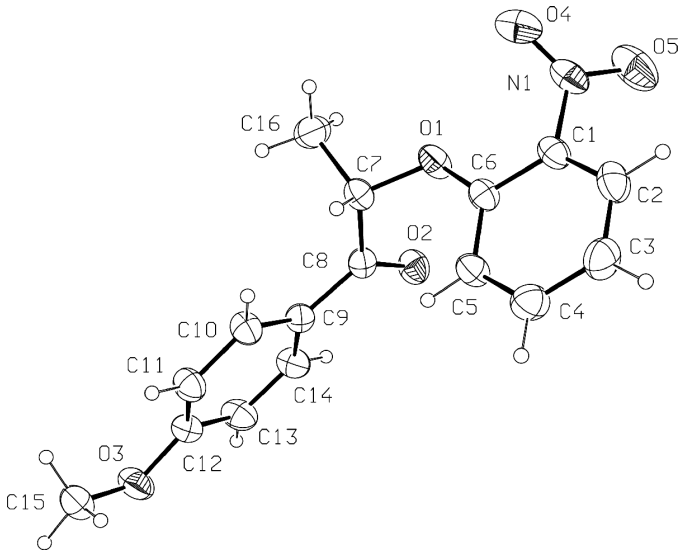



**Figure 1**
A view of (II) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

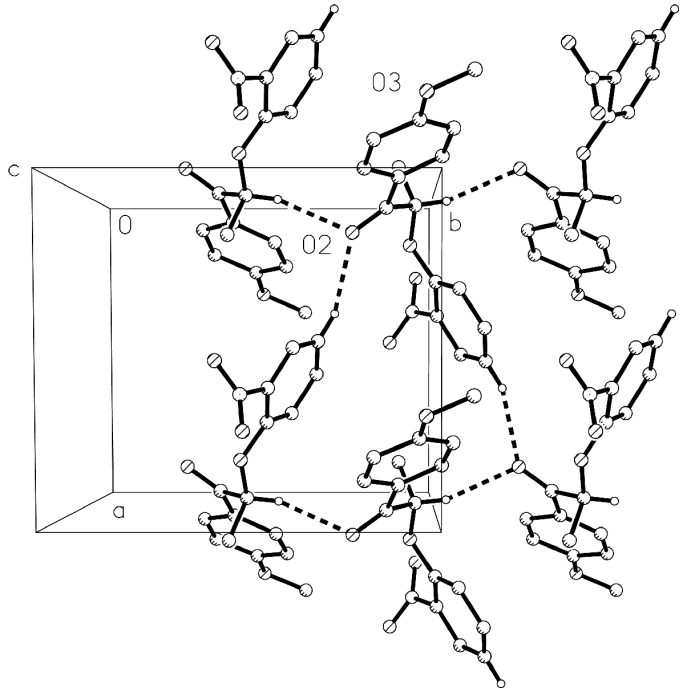



**Figure 2**
A packing diagram of (II), with intermolecular C—H···O non-classical hydrogen bonds shown as dashed lines. Only the H atoms involved in the hydrogen bonds are shown.

Fig. 1 shows a molecule of (II) with the atomic numbering scheme, and Table 1 shows selected bond distances and angles. The displacement ellipsoids for atoms O4 and O5 are large and highly anisotropic. The nitro group is twisted out of the plane of the aromatic ring, as can be seen from the C6—C1—N1—O4 torsion angle of 49.4 (3)°. The conformation of the nitro substituent presumably represents a compromise between the electronic preference of the nitro group to be coplanar with the aromatic ring and the need to minimize steric interaction with the neighbouring phenoxy atom O1.

A search of the November 2003 release of the Cambridge Structural Database (Allen, 2002) shows a compound similar to (II), *viz.* 3-hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1-propanone methanol solvate (Stomberg *et al.*, 1988), with the same 8.O.4′ linkage and two aromatic rings, but with different substituents. No significant differences were found in the bond distances and angles of the two molecules, except that, in the case of (II), keto atom O2 is 0.365 (3) Å out of the least-squares plane of the C9–C14 ring, while in the earlier structure it is essentially coplanar.

The parameters of the non-classical intermolecular C—H···O hydrogen bonds (Gu *et al.*, 1999) in (II) are given in Table 2. The H atoms on atoms C3 and C7 are involved in two intermolecular hydrogen bonds as donors, and atom O2 is involved in two hydrogen bonds as a dual acceptor. Thus, each molecule is linked to four others. Repetition of these linkages by crystal symmetry results in the formation of sheets of molecules parallel to the (001) plane, as can be seen in Fig. 2.

## Experimental

Compound (II) was obtained in quantitative yield using the method described previously by Barata *et al.* (1991). Prismatic crystals (m.p. 403–404 K) were obtained from a solution in EtOH. Spectroscopic analysis: FT–IR (Perkin–Elmer, KBr, $\nu$, cm$^{-1}$): 1675 (C═O), 1530 and 1365 (O═N—O), 860 (C—N); $^1$H NMR (Varian Gemini, 300 MHz, $CDCl_3$/TMS, $\delta$, p.p.m.): 1.79 (*d*, *J* = 6.9 Hz, Me-2, H-C16), 3.85 (*s*, OMe, H-C15), 5.41 (*q*, *J* = 6.9 Hz, H-C7), 6.90 (*d*, *J* = 8.7 Hz, H-C5), 6.93 (*d*, *J* = 9.0 Hz, H-C11 and H-C13), 6.98 (*dd*, *J* = 7.7 Hz, H4-C13), 7.38 (*dd*, *J* = 8.1 and 1.8 Hz, H-C4), 7.79 (*dd*, *J* = 1.8 and 8.1 Hz, H-C2), 8.13 (*d*, *J* = 9.0 Hz, H-C10 and H-C14); $^{13}$C NMR (Varian Gemini, 75 MHz, $CDCl_3$/TMS, $\delta$, p.p.m.): 126.1 (C9), 131.5 (C10 and C14), 114.0 (C11 and C13), 161.1 (C12), 196.3 (C8), 79.4 (C7), 19.2 (C16), 150.7 (C6), 140.1 (C1), 125.6 (C2), 120.9 (C3), 133.9 (C4), 115.2 (C5), 55.4 (C15); EI-MS [Varian MAT-311A, *m*/*z* (relative abundance)]: 302 (1) [$M^+$], 255 (1) [$M$-$NO_2$]$^+$, 135 (100) [Ar-CO$^+$], 107 (16) [Ar$^+$].

*Crystal data*

$C_{16}H_{15}NO_5$
$M_r$ = 301.29
Monoclinic, $P2_1/c$
$a$ = 8.851 (2) Å
$b$ = 9.858 (2) Å
$c$ = 17.255 (3) Å
$\beta$ = 94.99 (3)°
$V$ = 1499.8 (5) Å$^3$
$Z$ = 4
$D_x$ = 1.334 Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta$ = 10.4–13.6°
$\mu$ = 0.10 mm$^{-1}$
$T$ = 293 (2) K
Block, colourless
0.35 × 0.33 × 0.33 mm

*Data collection*

Enraf–Nonius CAD-4 diffractometer
Non-profiled $\omega/2\theta$ scans
Absorption correction: none
2738 measured reflections
2643 independent reflections
2080 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.023
$\theta_{max}$ = 25.0°
$h = -10 \rightarrow 10$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 20$
2 standard reflections
frequency: 120 min
intensity decay: <1%

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | $w = 1/[\sigma^2(F_o^2) + (0.0651P)^2 + 0.3965P]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $R[F^2 > 2\sigma(F^2)] = 0.042$ | $(\Delta/\sigma)_{max} < 0.001$ |
| $wR(F^2) = 0.129$ | $\Delta\rho_{max} = 0.25$ e Å$^{-3}$ |
| $S = 1.04$ | $\Delta\rho_{min} = -0.20$ e Å$^{-3}$ |
| 2643 reflections | Extinction correction: *SHELXL*97 (Sheldrick, 1997) |
| 206 parameters | Extinction coefficient: 0.056 (4) |
| H atoms treated by a mixture of independent and constrained refinement | |

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| O1—C6 | 1.358 (2) | O5—N1 | 1.234 (2) |
| O1—C7 | 1.432 (2) | N1—C1 | 1.460 (3) |
| O2—C8 | 1.220 (2) | C7—C8 | 1.527 (3) |
| O4—N1 | 1.198 (2) | C8—C9 | 1.476 (2) |
| | | | |
| C6—O1—C7 | 117.85 (13) | O1—C7—C8 | 111.22 (15) |
| O4—N1—O5 | 123.4 (2) | O2—C8—C9 | 121.82 (16) |
| O4—N1—C1 | 119.49 (19) | O2—C8—C7 | 118.95 (15) |
| O5—N1—C1 | 117.1 (2) | C9—C8—C7 | 119.14 (15) |
| | | | |
| O4—N1—C1—C6 | 49.4 (3) | O2—C8—C9—C10 | 164.16 (17) |
| C7—O1—C6—C5 | 15.1 (3) | C11—C12—O3—C15 | −0.6 (3) |

**Table 2**
Hydrogen-bonding geometry (Å, °).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| C3—H3···O2$^{i}$ | 0.95 (2) | 2.51 (2) | 3.363 (3) | 149.6 (19) |
| C7—H7···O2$^{ii}$ | 0.95 (2) | 2.39 (2) | 3.274 (2) | 153.7 (17) |

Symmetry codes: (i) $1-x, \frac{1}{2}+y, \frac{1}{2}-z$; (ii) $-x, \frac{1}{2}+y, \frac{1}{2}-z$.

Atoms H3 and H7 were located in a difference Fourier map and their positions were refined, with $U_{iso}(H) = 1.2U_{eq}(C)$. All other H atoms were positioned geometrically and allowed to ride on their parent atoms, with C—H distances in the range 0.93–0.96 Å, and with $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl H atoms and $1.2U_{eq}(C)$ for other atoms.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *XCAD*4 (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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