

## 1-(4-Methoxyphenyl)-2-(6-methyl-2-nitro-3-pyridyloxy)propan-1-one

Ivo Vencato,<sup>a\*</sup> Pedro H. Ferri,<sup>b</sup>  
Suzana C. Santos,<sup>b</sup> Maristela  
Pereira,<sup>c</sup> Carlito Lariucci,<sup>a</sup>  
Leon I. B. Homar<sup>a</sup> and  
Hamilton B. Napolitano<sup>d</sup><sup>a</sup>Instituto de Física—UFG, Caixa Postal 131, 74001-970 Goiânia, GO, Brazil, <sup>b</sup>Instituto de Química—UFG, Caixa Postal 131, 74001-970 Goiânia, GO, Brazil, <sup>c</sup>Instituto de Ciências Biológicas—UFG, Caixa Postal 131, 74001-970 Goiânia, GO, Brazil, and <sup>d</sup>Unidade Universitária de Ciências Exatas e Tecnológicas—UEG, BR 153, Km 98, 75133-050 Anápolis, GO, BrazilCorrespondence e-mail: [vencato@if.ufg.br](mailto:vencato@if.ufg.br)

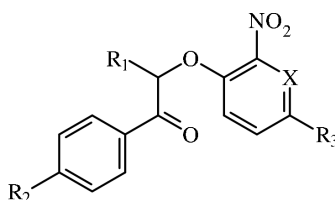
## Key indicators

Single-crystal X-ray study  
 $T = 298\text{ K}$   
Mean  $\sigma(\text{C}-\text{C}) = 0.005\text{ \AA}$   
 $R$  factor = 0.052  
 $wR$  factor = 0.162  
Data-to-parameter ratio = 12.1For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

The title compound,  $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_5$ , is a  $\beta$ -ketoether derivative closely related to natural 8,4'-oxyneolignans, which are of interest because of their moderate antifungal activity against systemic mycosis. The nitro group is not coplanar with the aromatic ring, as shown by a torsion angle of  $47.2(4)^\circ$ . The molecules are linked by two non-classical intermolecular  $\text{C}-\text{H}\cdots\text{O}$  hydrogen bonds with distances between donors and acceptors of  $3.441(5)$  and  $3.539(5)\text{ \AA}$ , leading to the formation of molecular stacking perpendicular to the  $bc$  plane.

## Comment

Neolignans belong to an important group of bioactive natural products widely distributed in terrestrial plants (Gottlieb & Yoshida, 1990). Within the great structural variety of neolignans, the 8,4'-oxyneolignans represent a small group, whose members have been isolated from plants of the Myristicaceae family (Paulino Filho, 1985). Regarding their reported biological activity, 8,4'-oxyneolignans show anti-protozoal (Barata *et al.*, 1978, 2000), antibacterial (Hattori *et al.*, 1986) and antifungal activities against dermatophytes (Zacchino *et al.*, 1997; Pinheiro *et al.*, 2004). Although the dermatophyte group of fungi is of particular concern in the tropics, many people have been exposed to a deep-seated fungal infection as paracoccidioidomycosis, the main systemic mycosis in Brazil (Costa *et al.*, 1995).  $\beta$ -Ketoether derivatives of 8,4'-oxyneolignans, such as compounds (I)–(III), have shown moderate *in vitro* activity against *Paracoccidioides brasiliensis*, the etiologic agent of this disease (Fonseca *et al.*, 1995). In addition, the chain linking the aromatic rings in (I)–(III) constitutes a major type of structural element in lignins, although the 2-aryloxypropiofenone skeleton seems to occur only rarely in these polymers (Lundquist & von Unge, 1986). In the present paper, the crystal structure of the title compound, (III), is described.



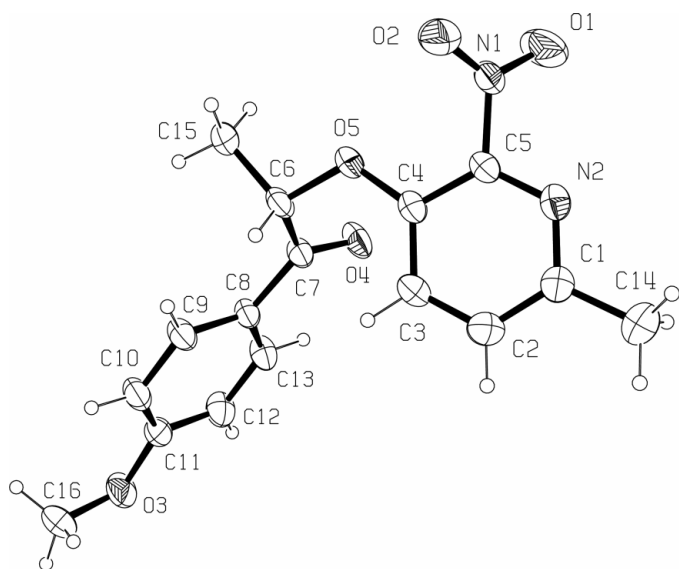
- (I)  $\text{R}_1 = \text{R}_2 = \text{R}_3 = \text{H}$ ,  $\text{X} = \text{CH}$   
(II)  $\text{R}_1 = \text{CH}_3$ ,  $\text{R}_2 = \text{OCH}_3$ ,  $\text{R}_3 = \text{H}$ ,  $\text{X} = \text{CH}$   
(III)  $\text{R}_1 = \text{R}_3 = \text{CH}_3$ ,  $\text{R}_2 = \text{OCH}_3$ ,  $\text{X} = \text{N}$

In (III), the C4/O5/C6/C15/C7/C8/O4 chain of atoms is called an 8.O.4' linkage, and compounds (I)–(III) can be called 8,4'-oxyneolignan derivatives, according to accepted neo-

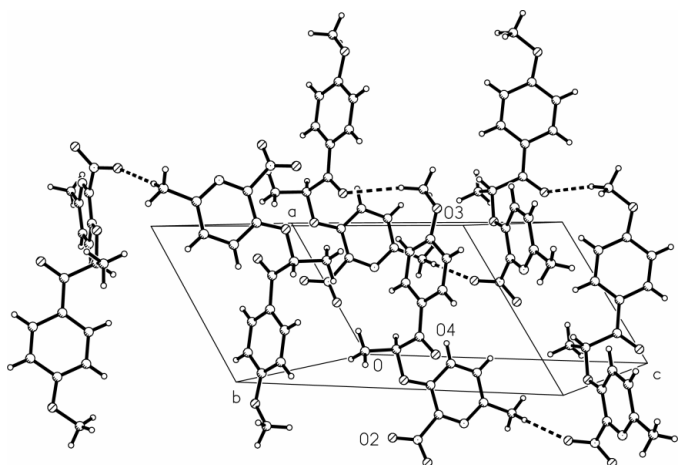
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**Figure 1**  
View of (III), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.



**Figure 2**  
Packing diagram of (III), with intermolecular C—H...O non-classical hydrogen bonds shown as dashed lines.

lignan nomenclature (Moss, 2000). The present crystal structure data will enable conclusions to be drawn about the geometry of these derivatives.

Fig. 1 shows a molecule of (III) with the atomic numbering scheme, and Table 1 shows selected bond distances and angles. The displacement ellipsoids for atoms O1 and O2 are large and highly anisotropic. The nitro group is twisted out of the plane of the aromatic ring, as can be seen from the O1—N1—C5—N2 torsion angle of  $47.2(4)^\circ$ . The two exocyclic bond angles at C4 are significantly different [ $C3—C4—O5 = 126.6(2)^\circ$  and  $C5—C4—O5 = 117.8(2)^\circ$ ], which could be a result of steric repulsion between the neighbouring phenoxy atom O5 and the nitro group.

A search of the November 2003 release of the Cambridge Structural Database (Allen, 2002) found a compound similar to (III), viz. 3-hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1-propanone methanol solvate (Stom-

berg *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 (III), keto atom O4 is  $0.201(5)$  Å out of the least-squares plane of the C8—C13 ring, while in the earlier structure it is essentially coplanar. A closely related structure to (III), viz. 1-(4-methoxyphenyl)-2-(2-nitrophenoxy)propan-1-one, was reported by Vencato *et al.*, (2004).

The molecular packing of (III) is stabilized through a non-classical hydrogen-bonded network (Gu *et al.*, 1999), as shown in Fig. 2, with the geometric parameters in Table 2. Repetition of these hydrogen bonds completes the packing, with molecules stacked in columns perpendicular to the *bc* plane (Fig. 2).

## Experimental

Compound (III) was obtained in quantitative yield from the condensation of 2-bromo-1-(4-methoxyphenyl)-1-propanone and 6-methyl-2-nitro-3-pyridinol, using the method described previously by Barata *et al.* (1991). Brown prismatic crystals (m.p. 403–405 K) were obtained from a solution in EtOH. FT-IR (Perkin-Elmer, KBr,  $\text{cm}^{-1}$ ): 1687 (C=O), 1540 (C=N), 1475 and 1365 (O=N—O), 1234 (C—O);  $^1\text{H}$  NMR (Varian Gemini, 300 MHz,  $\text{CDCl}_3/\text{TMS}$ , p.p.m.): 1.76 (*d*,  $J = 6.9$  Hz, H15), 2.46 (*s*, H14), 3.88 (*s*, H16), 5.47 (*q*,  $J = 6.9$  Hz, H6), 6.96 (*d*,  $J = 9.0$  Hz, H10 and H12), 7.24 (*d*,  $J = 0.8$  Hz, H2 and H3), 8.06 (*d*,  $J = 9.0$  Hz, H9 and H13);  $^{13}\text{C}$  NMR (Varian Gemini, 75 MHz,  $\text{CDCl}_3/\text{TMS}$ , p.p.m.): 125.9 (C8), 131.2 (C9, C13), 114.1 (C10, C12), 164.2 (C11), 195.4 (C7), 79.1 (C6), 19.0 (C15), 148.1 (C5), 143.4 (C4), 125.1 (C3), 128.0 (C2), 149.5 (C1), 22.7 (C14), 55.4 (C16); EI-MS (Varian MAT-311 A, *m/z*, relative abundance): 135 (100) [ $\text{ArCO}^+$ ], 107 (8) [ $\text{Ar}^+$ ].

## Crystal data

$\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_5$

$M_r = 316.31$

Monoclinic,  $P2_1/c$

$a = 8.185(2)$  Å

$b = 14.756(3)$  Å

$c = 15.092(5)$  Å

$\beta = 121.73(2)^\circ$

$V = 1550.3(8)$  Å<sup>3</sup>

$Z = 4$

$D_x = 1.355$  Mg m<sup>-3</sup>

Mo  $K\alpha$  radiation

Cell parameters from 25

reflections

$\theta = 10.0\text{--}13.6^\circ$

$\mu = 0.10$  mm<sup>-1</sup>

$T = 298(2)$  K

Block, light brown

$0.35 \times 0.25 \times 0.25$  mm

## Data collection

Enraf-Nonius CAD-4

diffractometer

Non-profiled  $\omega/2\theta$  scans

Absorption correction: none

3883 measured reflections

2729 independent reflections

1857 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.024$

$\theta_{\text{max}} = 28.0^\circ$

$h = -10 \rightarrow 10$

$k = -19 \rightarrow 0$

$l = -10 \rightarrow 19$

2 standard reflections

every 120 min

intensity decay: <1%

## Refinement

Refinement on  $F^2$

$R[F^2 > 2\sigma(F^2)] = 0.052$

$wR(F^2) = 0.162$

$S = 1.04$

2729 reflections

226 parameters

H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0812P)^2 + 0.4785P]$

where  $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\text{max}} = 0.006$

$\Delta\rho_{\text{max}} = 0.38$  e Å<sup>-3</sup>

$\Delta\rho_{\text{min}} = -0.30$  e Å<sup>-3</sup>

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

O1—N1	1.202 (3)	N1—C5	1.472 (3)
O2—N1	1.198 (3)	N2—C5	1.313 (3)
O4—C7	1.211 (3)	N2—C1	1.335 (4)
O5—C4	1.354 (3)	C6—C7	1.521 (4)
O5—C6	1.442 (3)	C7—C8	1.476 (4)
C4—O5—C6	118.6 (2)	N2—C5—N1	113.6 (2)
O2—N1—O1	123.1 (3)	C4—C5—N1	120.7 (2)
O2—N1—C5	118.5 (2)	O5—C6—C7	111.2 (2)
O1—N1—C5	118.3 (3)	O4—C7—C8	122.0 (3)
O5—C4—C3	126.6 (2)	O4—C7—C6	119.6 (2)
O5—C4—C5	117.8 (2)	C8—C7—C6	118.3 (2)
C6—O5—C4—C3	−5.7 (4)	O4—C7—C8—C9	175.1 (3)
O1—N1—C5—N2	47.2 (4)	C16—O3—C11—C10	−6.8 (5)

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

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
C14—H14C...O2 <sup>i</sup>	0.94 (3)	2.52 (3)	3.441 (5)	166 (4)
C16—H16A...O4 <sup>ii</sup>	0.98 (3)	2.57 (3)	3.539 (5)	169 (3)

Symmetry codes: (i)  $x, -y + \frac{3}{2}, z + \frac{1}{2}$ ; (ii)  $x + 1, y, z$ .

The H atoms of methyl atoms C14 and C16 were found in a difference Fourier map and their positions were refined with restraints  $H \cdots H = 1.57 (4) \text{ \AA}$  and  $C-H = 0.96 (4) \text{ \AA}$ , and with  $U_{\text{iso}}(H) = 1.5U_{\text{eq}}(C)$ . Atom H16B had the additional restraint  $O3 \cdots H16B = 1.95 (4) \text{ \AA}$ . These restraints ensure a reasonable geometry for the methyl groups, which were refined because they have H atoms involved in hydrogen bonding. All other H atoms were positioned geometrically and allowed to ride on their parent atoms, with  $C-H$  distances in the range  $0.93-0.98 \text{ \AA}$ , and with  $U_{\text{iso}}(H) = 1.5U_{\text{eq}}(C)$  for methyl H atoms and  $U_{\text{iso}}(H) = 1.2U_{\text{eq}}(C)$  for other H atoms.

Data collection: *CAD-4 EXPRESS* (Enraf–Nonius, 1994); cell refinement: *SET4* in *CAD-4 EXPRESS*; data reduction: *XCAD4* (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure:

*SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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