Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

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

Ivo Vencato,[a]* Pedro H. Ferri,[b] Suzana C. Santos,[b] Maristela Pereira,[c] Carlito Lariucci,[a] Leon I. B. Homar[a] and Hamilton B. Napolitano[d]

[a]Instituto de Física–UFG, Caixa Postal 131, 74001-970 Goiânia, GO, Brazil, [b]Instituto de Química–UFG, Caixa Postal 131, 74001-970 Goiânia, GO, Brazil, [c]Instituto de Ciências Biológicas–UFG, Caixa Postal 131, 74001-970 Goiânia, GO, Brazil, and [d]Unidade Universitária de Ciências Exatas e Tecnológicas–UEG, BR 153, Km 98, 75133-050 Anápolis, GO, Brazil

Correspondence e-mail: vencato@if.ufg.br

Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.005 Å
R factor = 0.052
wR factor = 0.162
Data-to-parameter ratio = 12.1

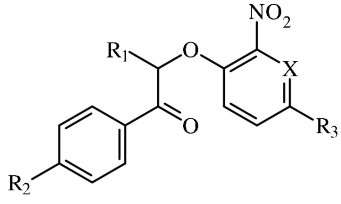
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 3 December 2004
Accepted 7 December 2004
Online 8 January 2005

The title compound, $C_{16}H_{16}N_2O_5$, is a β-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)°. The molecules are linked by two non-classical intermolecular C—H···O hydrogen bonds with distances between donors and acceptors of 3.441 (5) and 3.539 (5) Å, 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). β-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-aryloxypropiophenone 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) $R_1 = R_2 = R_3 =$ H, X = CH
(II) $R_1 = CH_3$, $R_2 = OCH_3$, $R_3 =$ H, X = CH
(III) $R_1 = R_3 = CH_3$, $R_2 = OCH_3$, X = 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-

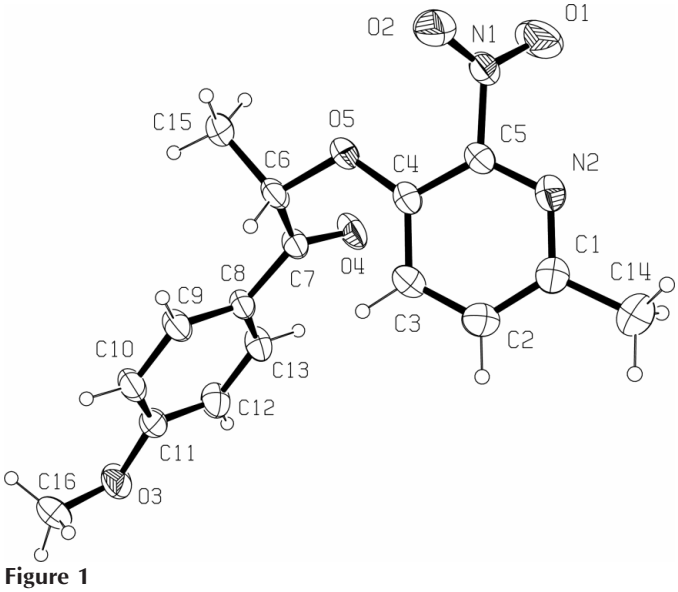


Figure 1
View of (III), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

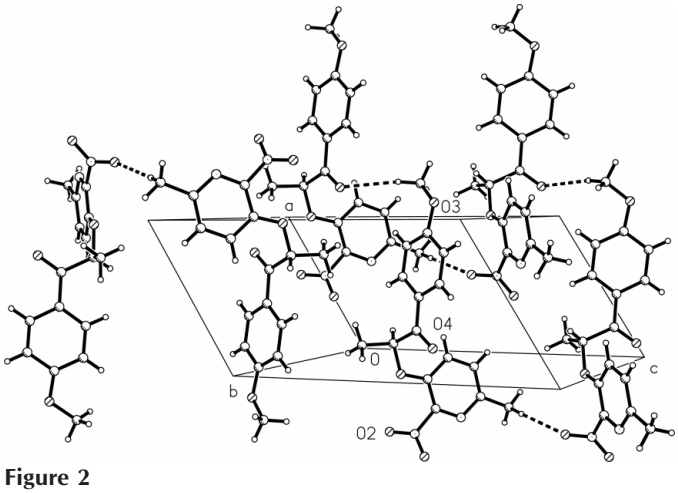


Figure 2
Packing diagram of (III), with intermolecular C—H···O non-classical hydrogen bonds shown as dashed lines.

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)°. The two exocyclic bond angles at C4 are significantly different [C3—C4—O5 = 126.6 (2)° and C5—C4—O5 = 117.8 (2)°], 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 (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 (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 prosmatic crystals (m.p. 403–405 K) were obtained from a solution in EtOH. FT–IR (Perkin–Elmer, KBr, cm^{-1}): 1687 (C═O), 1540 (C═N), 1475 and 1365 (O═N—O), 1234 (C—O); ^{1}H NMR (Varian Gemini, 300 MHz, $CDCl_3$/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}C NMR (Varian Gemini, 75 MHz, $CDCl_3$/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) [Ar-CO$^+$], 107 (8) [Ar$^+$].

Crystal data

$C_{16}H_{16}N_2O_5$
M_r = 316.31
Monoclinic, $P2_1/c$
a = 8.185 (2) Å
b = 14.756 (3) Å
c = 15.092 (5) Å
β = 121.73 (2)°
V = 1550.3 (8) Å^3
Z = 4
D_x = 1.355 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 25 reflections
θ = 10.0–13.6°
μ = 0.10 mm^{-1}
T = 298 (2) K
Block, light brown
0.35 × 0.25 × 0.25 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Non–profiled ω/2θ scans
Absorption correction: none
3883 measured reflections
2729 independent reflections
1857 reflections with $I > 2\sigma(I)$
R_{int} = 0.024
θ_{max} = 28.0°
h = −10 → 10
k = −19 → 0
l = −10 → 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 $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.006
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.30 e Å^{-3}

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, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C14—H14*C*···O2^{i}	0.94 (3)	2.52 (3)	3.441 (5)	166 (4)
C16—H16*A*···O4^{ii}	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···H = 1.57 (4) Å and C—H = 0.96 (4) Å, and with U_{iso}(H) = 1.5U_{eq}(C). Atom H16*B* had the additional restraint O3···H16*B* = 1.95 (4) Å. 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 Å, and with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and U_{iso}(H) = 1.2U_{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).

This work was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico, CNPq, Fundação de Apoio à Pesquisa and FUNAPE/UFG. The authors thank the Departamento de Química, UFSC, for the X-ray single-crystal data collection.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Barata, L. E. S., Baker, P. M., Gottlieb, O. R. & Rúveda, E. A. (1978). *Phytochemistry*, **17**, 783–786.
Barata, L. E. S., Santos, L. S., Fernandes, A. M. A. P., Ferri, P. H., Paulo, M. Q., Neal, R. & Jourdan, M. C. (1991). Abstracts of II Braziliänisch-Deutsches Symposium für Naturstoffchemie, Hannover, July 28th, pp. 18–21.
Barata, L. E. S., Santos, L. S., Ferri, P. H., Phillipson, J. D., Paine, A. & Croft, S. L. (2000). *Phytochemistry*, **55**, 589–595.
Costa, E. O., Diniz, L. S. M., Netto, C. F., Arruda, C. & Dagli, M. L. Z. (1995). *J. Med. Vet. Mycol.* **33**, 39–42.
Enraf–Nonius (1994). *CAD-4 EXPRESS*. Version 5.1/1.2. Enraf–Nonius, Delft, The Netherlands.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Fonseca, C. A., Pereira, M., Soares, C. M. A., Jesuíno, R. S. A., Ferreira, H. D., Nalini, A. G., Oliveira, G. R., Vilela, E. C., Ricardo, A. F., Faria, L. C., Azevedo, N. R. & Ferri, P. H. (1995). Abstracts of XVII Brazilian Congress of Microbiology, São Paulo, September, pp. 174.
Gottlieb, O. R. & Yoshida, M. (1990). *Lignans: Chemical, Biological and Clinical Properties. Chemistry and Pharmacology of Natural Products*, edited by D. C. Ayres & J. D. Loike, pp. 150–181. Cambridge University Press.
Gu, Y., Kar, T. & Scheiner, S. (1999). *J. Am. Chem. Soc.* **121**, 9411–9422.
Harms, K. & Wocadlo, S. (1995). *XCAD4*. University of Marburg, Germany.
Hattori, M., Hada, S., Watahiki, A., Ihara, H., Shu, Y. Z., Kakiuchi, N., Mizuno, T. & Namba, T. (1986). *Chem. Pharm. Bull.* **34**, 3885–3893.
Lundquist, K. & von Unge, S. (1986). *Acta Chem. Scand. Ser. B*, **40**, 791–797.
Moss, G. P. (2000). *Pure Appl. Chem.* **72**, 1493–1523.
Paulino Filho, H. F. (1985). PhD thesis, USP, São Paulo, Brazil.
Pinheiro, A. A. C., Borges, R. S., Santos, L. S. & Alves, C. N. (2004). *Theochem*, **672**, 215–219.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Stomberg, R., Hauteville, M. & Lundquist, K. (1988). *Acta Chem. Scand. Ser. B*, **42**, 697–707.
Vencato, I., Ferri, P. H., Santos, S. C., Santos, L. S., Lariucci, C. & Napolitano, H. B. (2004). *Acta Cryst.* E**60**, o2498–o2500.
Zacchino, S., Rodríguez, G., Pezzenati, G. & Orellana, G. (1997). *J. Nat. Prod.* **60**, 659–662.