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5-(6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl)-4-phenyl-1,2,5-oxadiazole *N*-oxide

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.003 Å
R factor = 0.050
wR factor = 0.145
Data-to-parameter ratio = 14.8

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

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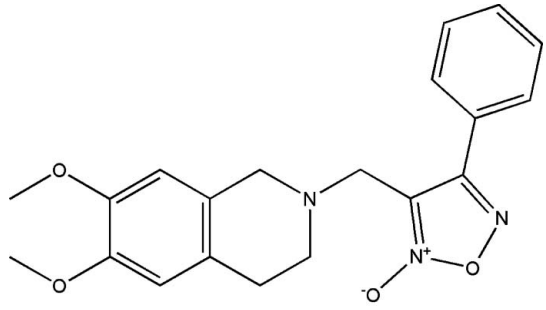
In the molecule of the title compound, $C_{20}H_{21}N_3O_4$, the six-membered heterocyclic ring has a flattened boat form. Intermolecular C—H···O hydrogen bonds link the molecules into dimers, which may be effective in the stabilization of the crystal structure.

Comment

In recent years, numerous researchers have focused on the study of furoxan derivatives, which were found to play an important pharmacological role, as they are able to activate the rat liver soluble guanylate cyclase and to release NO when treated with thiol compounds under physiological conditions (Feelisch *et al.*, 1992), resulting in a potent vasodilating effect (Ferioli *et al.*, 1995). It has also been shown to play a key role in exerting immune, anti-HIV1, nervous systems and cytotoxic activities (Cena *et al.*, 2003; Persichini *et al.*, 1999; Cerecetto *et al.*, 1999). In addition, recognition of the importance of tetrahydroisoquinolines as antihypertensive or antiarrhythmic agents has brought about escalating interest in related compounds (Harrold *et al.*, 1988). A combinatorial compound of tetrahydroisoquinoline and furoxan was prepared to search for a novel biological activity acting on calcium or potassium channels. We report here the crystal structure of the title compound, (I).



(I)

In the molecule of (I) (Fig. 1), the bond lengths and angles are within normal ranges (Allen *et al.*, 1987). Ring *B* (N1/C5–C9) is not planar, having a total puckering amplitude, Q_T, of 1.256 (4) Å and a flattened boat form [φ = 178.7 (2)° and θ = 131.2 (2)°; Cremer & Pople, 1975]. Rings *A* (C3–C5/C9–C11) and *D* (C15–C20) are, of course, planar. The dihedral angles between the planar rings are *A*/*C* = 71.9 (3)°, *A*/*D* = 57.3 (3)° and *C*/*D* = 28.1 (2)°.

As can be seen from the packing diagram (Fig. 2), intermolecular C—H···O hydrogen bonds (Table 1) link the molecules into dimers, which may be effective in the stabili-

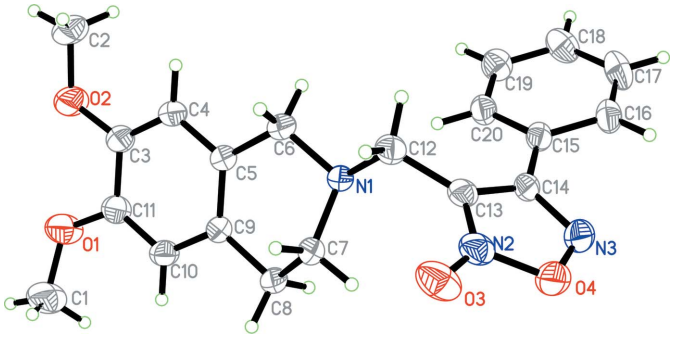


Figure 1
The molecular structure of (I), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

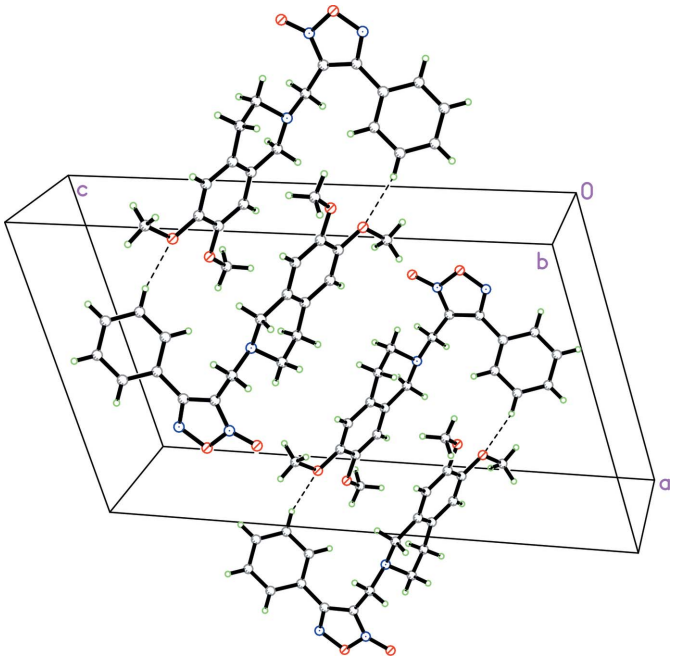


Figure 2
A packing diagram of (I). Hydrogen bonds are shown as dashed lines.

zation of the crystal structure. Dipole–dipole and van der Waals interactions are also effective in the molecular packing.

Experimental

Compound (I) was prepared from a mixture of 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (0.45 g, 2.3 mmol) (Smissman *et al.*, 1976) and 3-(chloromethyl)-4-phenyl-1,2,5-oxadiazole *N*-oxide (0.41 g, 1.9 mmol) (Gasco *et al.*, 1991) stirred in acetonitrile (50 ml) under reflux for 2 h. After filtering off the precipitate, the yellow solution was concentrated *in vacuo* and purified by column chromatography, eluting with EtOAc/petroleum ether (1:4), giving the title compound (yield 0.48 g, 69%; m.p. 389 K). Crystals were obtained by dissolving the white solid (0.3 g) in AcOEt/petroleum ether (1:1 20 ml) and evaporating the solvent slowly at room temperature for about 5 d.

Crystal data

$C_{20}H_{21}N_3O_4$
M_r = 367.40
Monoclinic, $P2_1/c$
a = 12.850 (3) Å
b = 6.8840 (14) Å
c = 21.723 (4) Å
β = 105.38 (3)°
V = 1852.8 (7) Å^3
Z = 4
D_x = 1.317 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 296 (2) K
Block, colorless
0.40 × 0.30 × 0.30 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.964, T_{max} = 0.973
3798 measured reflections
3630 independent reflections
2165 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 26.0°
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.145
S = 1.00
3630 reflections
245 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.07P)^2 + 0.11P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.039 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
C19—H19A···O1^{i}	0.93	2.49	3.349 (3)	154

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

H atoms were positioned geometrically, with C—H = 0.93, 0.97 and 0.96 Å for aromatic, methylene and methyl H atoms, respectively, and constrained to ride on their parent atoms, with U_{iso}(H) = xU_{eq}(C), where x = 1.5 for methyl and x = 1.2 for other H atoms.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; 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: *SHELXTL* (Bruker, 2000); 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.
Bruker (2000). *SHELXTL*. Bruker AXS Inc., Madison, Wisconsin, USA.
Cena, C., Lolli, M. L., Lazzarato, L., Guaita, E., Morini, G., Coruzzi, G., McElroy, S. P., Megson, I. L., Fruttero, R. & Gasco, A. (2003). *J. Med. Chem.* **46**, 747–754.
Cerecetto, H., Di Maio, R., Gonzalez, M., Risso, M., Saenz, P., Seoane, G., Denicola, A., Peluffo, G., Quijano, C. & Olea-Azar, C. (1999). *J. Med. Chem.* **42**, 1941–1950.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Enraf–Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.
Feelisch, M., Schönafingeri, K. & Noack, H. (1992). *Biochem. Pharmacol.* **44**, 1149–1157.
Ferioli, R., Folco, G. C., Ferrtti, C., Gasco, A. M., Medana, C., Fruttero, R., Civelli, M. & Gasco, A. (1995). *Br. J. Pharmocol.* **114**, 816–820.
Gasco, A. M., Fruttero, R., Sorba, G. & Gasco, A. (1991). *Liebigs Ann. Chem.* pp. 1211–1213.
Harms, K. & Wocadlo, S. (1995). *XCAD4*. University of Marburg, Germany.
Harrold, M. W., Grajzl, B., Shin, Y., Romstedt, K. J., Feller, D. R. & Miller, D. D. (1988). *J. Med. Chem.* **31**, 1506–1512.
North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.
Persichini, T., Colasanti, M., Fraziano, M., Colizzi, V., Medana, C., Polticelli, F., Venturini, G. & Ascenzi, P. (1999). *Biochem. Biophys. Res. Commun.* **258**, 624–627.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Smissman, E. E., Reid, J. R., Walsh, D. A. & Borchardt, R. T. (1976). *J. Med. Chem.* **19**, 127–131.