2-Phenylquinoline 1-oxide

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Key indicators

Single-crystal X-ray study
 $T = 293\text{ K}$
 Mean $\sigma(\text{C}—\text{C}) = 0.004\text{ Å}$
 R factor = 0.041
 wR factor = 0.115
 Data-to-parameter ratio = 9.6

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

The title compound, $\text{C}_{15}\text{H}_{11}\text{NO}$, is not planar, as seen in the dihedral angle of $41.92(12)^\circ$ formed between the quinoline and phenyl residues. This conformation allows the crystal structure to be stabilized by $\text{C}—\text{H}\cdots\text{O}$ interactions. Zigzag chains along the a direction, mediated by $\text{C}—\text{H}\cdots\text{O}$ interactions, may be discerned in the crystal structure and these stack along the c direction, again *via* $\text{C}—\text{H}\cdots\text{O}$ interactions. Interactions of the type $\text{C}—\text{H}\cdots\pi$ serve to stabilize the zigzag chains and to provide links between them.

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Comment

Quinolines substituted at the 2-position exhibit *in vivo* activity against *Leishmania infantum* and *Leishmania donovani* (Nakayama *et al.*, 2005). The title compound, (I), was synthesized as part of the generation of a series of 2-substituted quinolines and their corresponding *N*-oxides for testing as chemotherapeutic agents against this tropical parasite. This compound has been previously cocrystallized with 7,7,8,8-tetracyanoquinodimethane and its structure reported (Bocelli *et al.*, 1990). The molecule of (I) (Fig. 1) is not planar, as seen in the dihedral angle of $41.92(12)^\circ$ formed between the least-squares planes of the quinoline and phenyl residues. The geometric parameters (Table 1) are as expected (Allen *et al.*, 1987). The observed conformation in (I) no doubt allows for the close approach of two H atoms, derived from two different molecules, to atom O1, leading to the formation of $\text{C}—\text{H}\cdots\text{O}$ hydrogen bonds. The first of these leads to the formation of

zigzag chains parallel to the a direction as shown in Fig. 2. The parameters associated with this association are $\text{C24}\cdots\text{O1}^{\text{i}}$ of 2.58 Å , $\text{C24}\cdots\text{O1}^{\text{i}}$ of $3.471(4)\text{ Å}$, with an angle at H24 of 161° [symmetry code: (i) $-\frac{1}{2} + x, -\frac{1}{2} - y, 1 - z$]. Chains are stacked along the c direction *via* $\text{C26}—\text{H26}\cdots\text{O1}^{\text{ii}}$ interactions so that $\text{C26}—\text{H}\cdots\text{O1}^{\text{ii}}$ is 2.54 Å , $\text{C26}\cdots\text{O1}^{\text{ii}}$ is $3.423(4)\text{ Å}$ and the angle at H26 is 158° [symmetry code: (ii) $x, y, 1 + z$]. Additional stabilization in the crystal structure is afforded by $\text{C}—\text{H}\cdots\pi$ interactions. Thus, the $\text{N1/C2}—\text{C4/C9/C10}$ rings are linked so that the $\text{C3}—\text{H3}\cdots[\text{ring centroid of } (\text{N1/C2}—\text{C4/C9/C10})^{\text{i}}]$ distance is 2.89 Å with an angle at H of 126° . As indicated by the angle at atom H3, this atom is more

Figure 1
The molecular structure of (I) showing the crystallographic numbering scheme and displacement ellipsoids at the 35% probability level.

Figure 2
View of the zigzag chains in (I) formed by C—H...O interactions (dashed lines). Colour code: O (red), N (blue), C (grey) & H (green).

closely associated with atoms C4, C9 and C10 of the ring. These interactions serve to provide links between the zigzag chains along the *b* direction. The phenyl rings are also connected *via* C—H... π interactions so that the distance between C23—H23 and the ring centroid of (C21—C26)ⁱⁱⁱ is 2.95 Å with an angle of 143° [(iii) $-\frac{1}{2} - x, -y, \frac{1}{2} + z$]. These interactions provide stability within the zigzag chains.

Experimental

The procedure involved the addition of phenyl Grignard to quinoline-*N*-oxide. This yielded both the expected 2-phenylquinoline and, unexpectedly, (I). It is not clear whether the *N*-oxide survives the reaction or if the product is re-oxidized subsequent to arylation.

Magnesium turnings (0.45 g, 18.4 mmol) were activated with a small crystal of iodine and bromobenzene (2.72 g, 17.2 mmol) in dry THF (5.7 ml) was added slowly over a period of 30 min under a nitrogen atmosphere. When most of the magnesium had dissolved, quinoline-*N*-oxide (0.5 g, 3.44 mmol) in dry THF (5.0 ml) was added over a period of 15 min and the reaction was refluxed for 1 h. After this period, the reaction was quenched with water and extracted with CH₂Cl₂ (3 × 20 ml), and the combined organic phases washed with brine, dried (MgSO₄) and condensed. The crude product was subjected to flash column chromatography on silica with a solvent gradient from neat *n*-hexane to *n*-hexane/EtOAc (4:1) to provide 2-phenylquinoline (289 mg, 41% yield) and 2-phenylquinoline-*N*-oxide (120 mg, 16% yield). The latter was crystallized from hexane/ethyl acetate (4:1) overnight at room temperature to provide pale-yellow block-shaped crystals of (I) [m.p. 315–316 K; literature 315–316 K (Endo *et al.*, 1981)].

Crystal data

C ₁₅ H ₁₁ NO	<i>Z</i> = 4
<i>M_r</i> = 221.25	<i>D_x</i> = 1.339 Mg m ^{−3}
Orthorhombic, <i>P</i> 2 ₁ 2 ₁ 2 ₁	Mo <i>K</i> α radiation
<i>a</i> = 7.754 (3) Å	μ = 0.08 mm ^{−1}
<i>b</i> = 21.436 (6) Å	<i>T</i> = 293 (2) K
<i>c</i> = 6.603 (2) Å	Block, pale yellow
<i>V</i> = 1097.5 (6) Å ³	0.50 × 0.30 × 0.20 mm

Data collection

Rigaku AFC-7R diffractometer	<i>R</i> _{int} = 0.011
ω scans	$\theta_{\max}$ = 27.5°
Absorption correction: none	3 standard reflections
1772 measured reflections	every 150 reflections
1486 independent reflections	intensity decay: 1.5%
996 reflections with <i>I</i> > 2σ(<i>I</i>)	

Refinement

Refinement on <i>F</i> ²	$w = 1/[\sigma^2(F_o^2) + (0.0562P)^2 + 0.0354P]$
$R[F^2 > 2\sigma(F^2)] = 0.041$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.115$	(Δ/σ) _{max} < 0.001
<i>S</i> = 1.04	$\Delta\rho_{\max} = 0.16 \text{ e Å}^{-3}$
1486 reflections	$\Delta\rho_{\min} = -0.23 \text{ e Å}^{-3}$
154 parameters	
H-atom parameters constrained	

Table 1

Selected geometric parameters (Å, °).

O1—N1	1.301 (3)	N1—C9	1.411 (3)
N1—C2	1.352 (3)		
O1—N1—C2	121.5 (2)	C2—N1—C9	120.6 (2)
O1—N1—C9	117.8 (2)		

H atoms were included in the riding-model approximation with distances C—H = 0.93 Å and with *U*_{iso}(H) = 1.2*U*_{eq}(C). In the absence of significant anomalous scattering effects, 67 Friedel pairs were averaged in the final refinement.

Data collection: *MSC/AFC7 Diffractometer Control Software* (Molecular Structure Corporation, 1999); cell refinement: *MSC/AFC7 Diffractometer Control Software*; data reduction: *TEXSAN for Windows* (Molecular Structure Corporation, 1999); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976) and *DIAMOND* (Crystal Impact, 2006); software used to prepare material for publication: *TEXSAN for Windows*.

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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.
- Altomare, A., Cascarano, M., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.
- Bocelli, G., Cantoni, A., Giorgini, E. & Tosi, G. (1990). *J. Crystallogr. Spectrosc. Res.* **20**, 419–423.
- Crystal Impact (2006). *DIAMOND*. Version 3.1. Crystal Impact GbR, Bonn, Germany.
- Endo, T., Saeki, S. & Hamana, M. (1981). *Chem. Pharm. Bull.* **29**, 3105–3111.
- Johnson, C. K. (1976). *ORTEP II*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- Molecular Structure Corporation (1999). *MSC/AFC7 Diffractometer Control Software for Windows* (Version 1.02) and *TEXSAN for Windows*. (Version 1.05). MSC, The Woodlands, Texas, USA.
- Nakayama, H., Loiseau, P. M., Bories, C., Torres de Ortiz, S., Schinini, A., Serna, E., Rojas de Arias, A., Fakhfakh, M. A., Franck, X., Figadere, B., Hocquemiller, R. & Fournet, A. (2005). *Antimicrob. Agents Chemother.* **49**, 4950–4956.
- Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.