**N-(3-Chloro-5-fluorophenyl)-4-nitrobenzo[c][1,2,5]oxadiazol-5-amine**

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Category</th>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound</td>
<td>Additional names</td>
<td>Thomas H Scheuermann, Qiming Li, He-Wen Ma, Jason Key, Lei Zhang, Rui Chen, Joseph A Garcia, Jacinth Naikoo, Jamie Longgood, Doug E Frantz, Uttam K Tambar, Kevin H Gardner &amp; Richard K Bruick</td>
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<tr>
<td></td>
<td>Citation</td>
<td>Nature Chemical Biology, published online 24 February 2013, doi:10.1038/nchembio.1185</td>
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<td>Chemical descriptors</td>
<td>SMILES:</td>
<td>ClC1=CC(NC2=C([N+][O-])=O)C3=NON=C3C=C2)=CC(F)=C1</td>
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<td>InChIKey:</td>
<td>CDQUJZKBRAFWNG-UHFFFAOYSA-N</td>
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<td>Entries in chemical databases</td>
<td>Pub Chem SID: 160709351</td>
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<td>Availability</td>
<td></td>
<td>See Supplementary Note 1</td>
</tr>
<tr>
<td>Additional comments</td>
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<tr>
<td><strong>In vitro profiling</strong></td>
<td>Target</td>
<td>endothelial PAS domain protein 1 (EPAS1) / Hypoxia Inducible Factor-2α (HIF2A)</td>
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<td></td>
<td>Potency</td>
<td>(K_D = 81 \text{nM}) against HIF-2α PAS-B in ITC assay; see Figure 1d; (IC_{50} \approx 100 \text{nM}) against HIF-2α/ARNT PAS-B* heterodimerization in AlphaScreen assay; see Figure 3a</td>
</tr>
<tr>
<td></td>
<td>Selectivity</td>
<td>Profiled against HIF-1α-PAS-B and found (K_D \gg 5,000 \text{nM}); see Figure 4c</td>
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<td>Potential reactivities</td>
<td>no reactivity observed</td>
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<td>SAR</td>
<td></td>
<td>SAR information is available for HIF-2α PAS-B binding compounds (1) and (2) and related chemicals, all of which consist of two heterocyclic/aromatic rings and short connecting linker. These data provide some insight into the specific chemical groups required for high affinity binding and disruption of the HIF-2α-ARNT PAS-B interaction. Such information can be found in Supplementary Figure 5 from this work, along with the following literature references: Scheuermann et al., Proc. Natl. Acad. Sci. 106, 450-455 (2009); Key et al., J. Am. Chem. Soc. 131, 17647-17654 (2009); and forthcoming publications from our groups</td>
</tr>
<tr>
<td>Mechanism of inhibition</td>
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<td>allosteric</td>
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<td>Structure of target-probe complex</td>
<td>PDB code: 4GHI</td>
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</table>
### Additional comments

| Cellular profiling | Validation of cellular target | Dose-dependently inhibited HIF-2 at ~1 µM in 786-0 and Hep3B cells as determined by ChIP and mRNA accumulation from HIF-2 target genes; see [Figure 5](#).
| Validation of cellular specificity | | Did not antagonize HIF-1 heterodimerization or mRNA accumulation from HIF-1 selective target gene; see [Figure 5](#). |