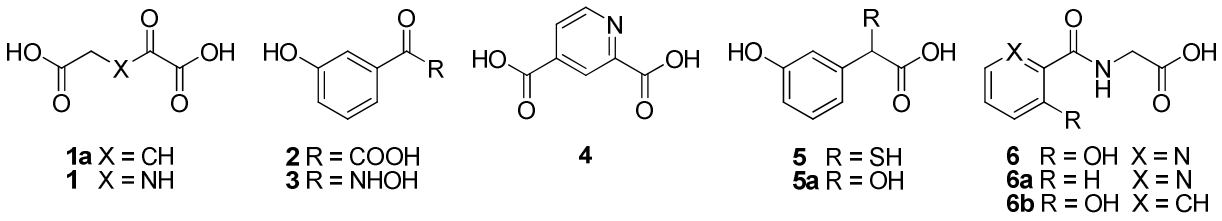
Figure Legends

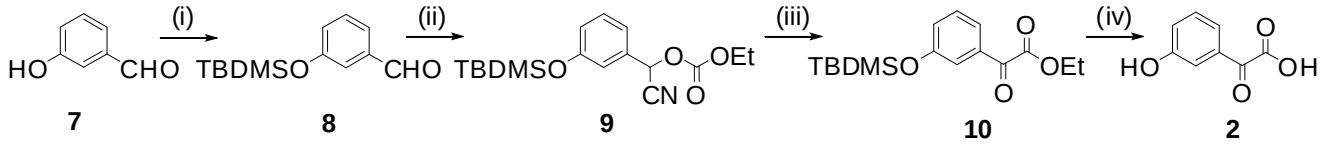
Figure 1: (a) The structures of the targeted 2OG analogues **1-9**.

Figure 2:
Crystal structures of FIH (green sticks) in complex with (a) **4** and (b) **2** (both as yellow sticks) with 2Fo-Fc electron density (grey mesh) contoured at 1σ. The active site iron atom (orange sphere) is apparently coordinated by a glycerol molecule (purple sticks) in the case of **4**. (c) Stereoview of the crystal structure of FIH (green sticks) in complex with **3** (yellow sticks) showing the two different binding modes observed for this inhibitor and the conformational change of the Asp201 side chain which no longer coordinates to the catalytic iron atom (orange sphere) in order to accommodate one of the binding modes of **3**. Comparison of the active site pocket of FIH (grey surface) with **2** and (d) *N*-oxalylglycine (NOG) (grey sticks) and (e) *N*-oxalyl-D-phenylalanine (NOFD) (grey sticks). The iron atom is an orange sphere.

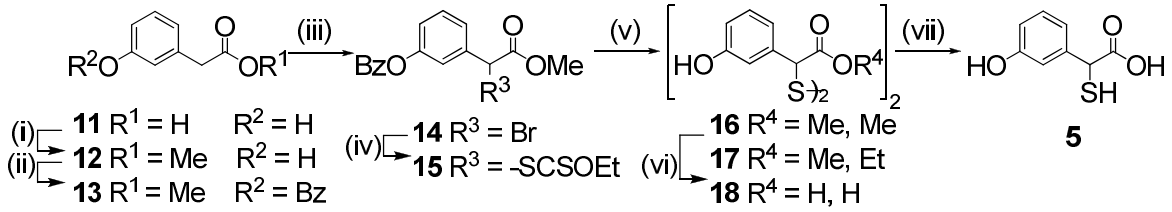
Figure 1.



Schemes 1 and 2.

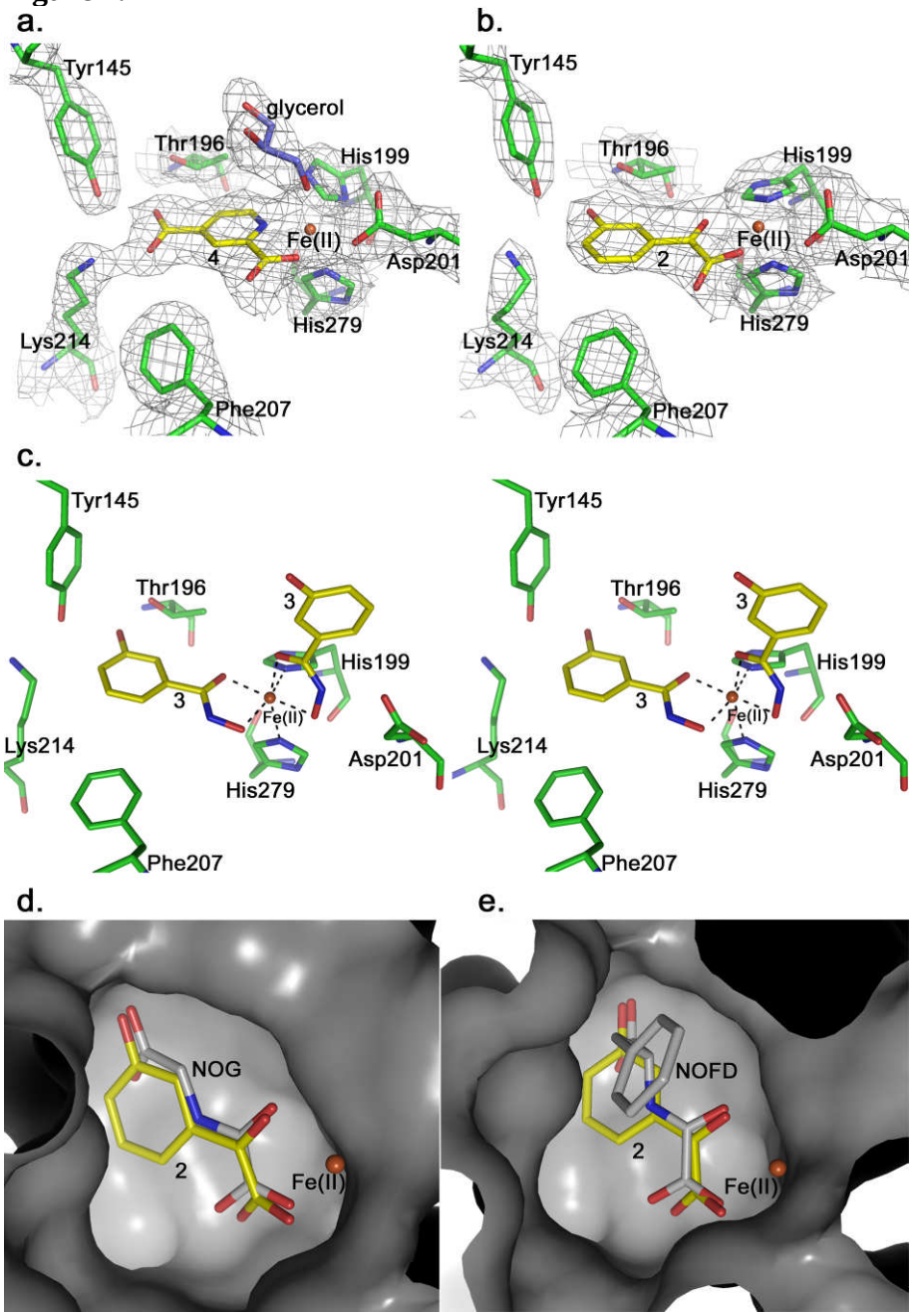


Scheme 1.- *Reagents and conditions:* (i) t-BuMe_2SiCl, dimethylaminopyridine, Et_3N, CH_2Cl_2; (ii) ClCOOEt, benzyltrimethylammonium chloride, THF, NaCN, H_2O; (iii) $LiN(iPr)_2$, THF, -78 ^oC room temp.; (iv) NaOH, MeOH.



Scheme 2.- *Reagents and conditions:* (i) *p*-toluenesulfonic acid, $HC(OCH)_3$, MeOH; (ii) benzoyl chloride, dimethylaminopyridine, Et_3N, CH_2Cl_2; (iii) *N*-bromosuccinimide, dibenzoyl peroxide, CCl_4; (iv) potassium *o*-ethyldithiocarbonate, MeOH, dioxane; (v) NH_4OH, MeOH; (vi) NaOH, MeOH, (vii) dithiothreitol.

Figure 2.


a.
Tyr145
glycerol
Thr196
His199
Fe(II)
4
Asp201
His279
Lys214
Phe207
b.
Tyr145
Thr196
His199
Fe(II)
2
Asp201
His279
Lys214
Phe207
c.
Tyr145
Thr196
3
His199
3
Fe(II)
Lys214
Asp201
His279
Phe207
Tyr145
Thr196
3
His199
3
Fe(II)
Lys214
Asp201
His279
Phe207
d.
NOG
2
Fe(II)
e.
NOFD
2
Fe(II)