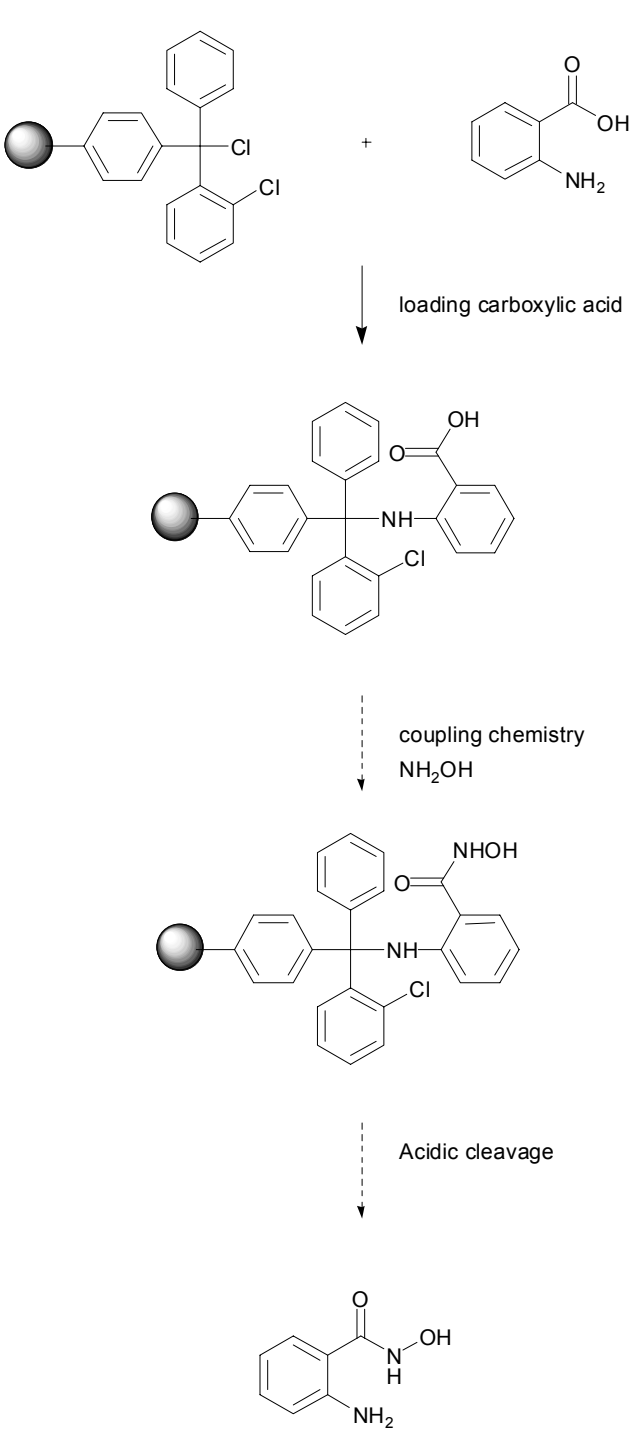


Fig. S1 2-chlorotrityl chloride polystyrene resin based method.

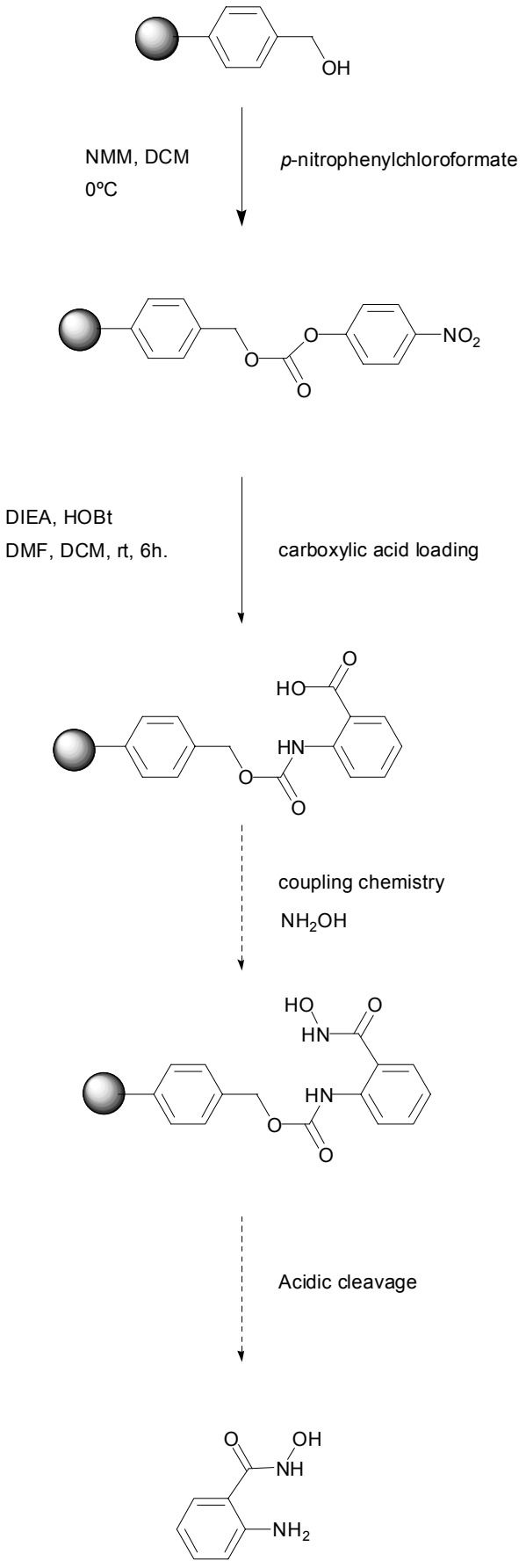


Fig. S2 *p*-nitrophenyl carbonate Wang resin based method.

Table S1 *Conditions for modified Wang resin method*

Reaction	Coupling Chemistry	Cleavage Protocol	% Yield	% Purity RP-HPLC
1	PyBop 5eq., DIEA 10eq., NH_2OH 5eq., (rt, 14 h)	50% TFA, 5% H_2O, 45% DCM, (rt, 2 h)	12%	7%
2	PyBop 5eq., DIEA 10eq., NH_2OBz 5eq., (rt, 14 h)	50% TFA, 5% H_2O, 45% DCM, (rt, 2 h)	19%	<3%
3	PyBop 5eq., HOBt 5eq., DIEA 10eq., NH_2OH 5eq., (37 °C, 14 h)	50% TFA, 5% H_2O, 45% DCM, (rt, 2 h)	14%	<3%
4	DIC 5eq., HOBt 5eq., DIEA 10eq., NH_2OH 5eq., (37 °C, 14 h)	50% TFA, 5% H_2O, 45% DCM, (rt, 2 h)	15%	-
5	HATU 2eq., HOAt 2eq., DIEA 4eq., $NH_2OTBDMS$ 2eq., (37 °C, 14 h)	50% TFA, 5% H_2O, 45% DCM, (rt, 2 h)	13%	15%
6	DIC 5eq., HOBt 2eq., DIEA 4eq., $NH_2OTBDMS$ 2eq., (rt, 14 h)	50% TFA, 5% H_2O, 45% DCM, (rt, 2 h)	15%	-
7	HATU 2eq., HOAt 2eq., DIEA 4eq., $NH_2OTBDMS$ 2eq., (rt, 3 h)	95% TFA, 5% H_2O (rt, 14 h)	62%	<3%
8	HATU 3eq., HOAt 3eq., DIEA 6eq., $NH_2OTBDMS$ 2eq., (rt, 3 h)	95% TFA, 5% H_2O (rt, 14 h)	49%	34%
9	DIC 2eq., HOBt 2eq., DIEA 4eq., $NH_2OTBDMS$ 1.2eq., (rt, 3 h)	95% TFA, 5% H_2O (rt, 14 h)	89%	<3%
10	DIC 2eq., HOBt 2eq., $NH_2OTBDMS$ 1.2eq., (rt, 3 h)	95% TFA, 5% H_2O (rt, 14 h)	83%	<3%
11	DCC 1.5eq., DIEA 3eq., $NH_2OTBDMS$ 1.5eq., (rt, 3 h)	95% TFA, 5% H_2O (rt, 14 h)	94%	<3%
12	HATU 1.2eq., DIEA 3.6eq., $NH_2OTBDMS$ 1.2eq., (rt, 14 h)	95% TFA, 5% H_2O (rt, 14 h)	41%	44%
13	DCC 4eq., HOBt 4eq., NH_2OH 4eq., (rt, 14 h)	50% TFA, 5% H_2O 45% DCM (rt, 2 h)	105%	<3%
14	DIC 4.5eq., HOBt 4.5eq., DMAP 0.8eq., NH_2OH 1.2eq., (rt, 4 h)	50% TFA, 5% H_2O, 45% DCM, (rt, 2 h)	49%	<3%
15	Ethylchloroformate 1.2eq., NMM 1.3eq., NH_2OH 1.5eq., (40 °C, 40 min)	50% TFA, 5% H_2O, 45% DCM, (rt, 2 h)	77%	33%
16	Ethylchloroformate 3.6eq., NMM 3.9eq., NH_2OH 3eq., (40 °C, 90 min)	50% TFA, 5% H_2O, 45% DCM, (rt, 2 h)	50%	42%
17	DIAD 3eq., PPh_3 3eq., *p*-nitrophenol 3eq. (rt, 14 h), NH_2OH 3eq., (rt, 4 h)	-	-	-

Table S2 *Correlation between biological activity and electronic properties of substituted anthranilic hydroxamic acids (-AHA) MOPAC calculations**

AHA	pIC_{50}	IP (eV)	ΔH (kcal/mol)	O atom -H bond order	N atom -OH bond order	C atom -NOH bond order	H atom elec. dens.	O atom elec. dens.
3,5-I_2 (24)	5.14	8.61	18.6871	0.9401	0.9826	1.0758	0.7817	6.2772
3,5-Br_2 (23)	4.91	8.94	18.8830	0.9409	0.9828	1.0758	0.7817	6.2764
5-I (15)	4.76	8.66	18.6455	0.9511	0.9819	1.0791	0.7810	6.2796
5-Br (11)	4.85	8.81	18.5001	0.9403	0.9823	1.0754	0.7821	6.2776
3-CF_3 (6)	4.31	9.07	19.1267	0.9393	0.9827	1.0801	0.7799	6.2776
3-Cl (4)	4.84	8.71	18.4908	0.9403	0.9824	1.0719	0.7820	6.2781
3-Br-5-Me (26)	4.64	8.65	18.4219	0.9401	0.9823	1.0721	0.7818	6.2784
3,5-Cl_2 (22)	4.89	8.69	18.6180	0.9401	0.9826	1.0770	0.7816	6.2765
4,5-F_2 (29)	4.82	8.99	18.8119	0.9399	0.9830	1.0780	0.7813	6.2755
5-NO_2 (18)	4.54	9.40	19.3513	0.9399	0.9833	1.0919	0.7810	6.2730
4-Cl (7)	4.56	8.86	18.7216	0.9399	0.9821	1.0770	0.7811	6.2799
5-Cl (12)	4.54	8.70	19.1253	0.9405	0.9822	1.0756	0.7817	6.2787
4-F (8)	4.46	8.91	18.5935	0.9403	0.9825	1.0721	0.7819	6.2778
5-F (13)	4.16	8.83	18.8151	0.9397	0.9823	1.0810	0.7809	6.2784
AHA (3)	4.09	8.73	18.5392	0.9404	0.9818	1.0719	0.7818	6.2810
Nicotinic (31)	4.08	8.86	17.2940	0.9056	0.9814	1.1378	0.7630	6.3030
3,5-$(CH_3)_2$ (25)	4.08	8.49	18.2011	0.9401	0.9819	1.0704	0.7822	6.2802
3-OCH_3 (5)	3.93	8.46	18.4571	0.9400	0.9817	1.0748	0.7815	6.2816
5-CH_3 (17)	3.94	8.60	18.5393	0.9401	0.9816	1.0743	0.7816	6.2814
4-NO_2 (9)	4.16	9.20	18.9514	0.9394	0.9831	1.0824	0.7803	6.2737
4,5-$(OCH_3)_2$ (30)	3.69	8.59	18.0113	0.9406	0.9820	1.0697	0.7825	6.2802
6-F (20)	3.38	8.93	18.7427	0.9413	0.9824	1.0953	0.7843	6.2748
5- $NHCOCH_3$ (10)	3.60	8.24	17.7495	0.9415	0.9811	1.0830	0.7847	6.2788
5-OCH_3 (16)	3.41	8.41	18.0841	0.9404	0.9819	1.0731	0.7826	6.2791
6-CH_3 (21)	3.24	8.69	13.9162	0.9402	0.9798	1.0884	0.7829	6.2772
3,4,5-$(OCH_3)_3$ (27)	3.16	8.60	18.3131	0.9402	0.9824	1.0729	0.7823	6.2779

*In general, no correlation was found between these properties and pIC_{50} values.

pIC_{50} = $-\log(IC_{50}*10^{-6})$. All of the compounds except for one exhibited pIC_{50}s less than 5, which signify low activity in the micromolar range.
IP = ionization potential. Although there is no direct correlation between pIC_{50} and IP, in general the tendency is that the higher the IP, the higher the pIC_{50}.
ΔH = heat of formation of the free radical (hydroxamate oxygen centered) minus the heat of formation of the parent compound.

The properties below refer to the hydrogen atom abstraction from the hydroxamate oxygen. These values were also computed for the hydrogen atom attached to all hetero atoms, but no correlation was found.
O-H = bond order of the O-H bond.
N-OH = bond order of the N-O bond.
C-NOH = bond order of the C-N bond.
H atom elec. dens. = electron density on the hydrogen atom
O atom elec. dens. = electron density on the oxygen atom.

QSAR analysis

The three compounds with PGHS-1 POX IC_{50} > 1000 µM (**19**, **21** and **27**) were excluded as their exact IC_{50} are not known, and would otherwise distort the analysis. The data was also weighted in favour of more stringent statistics (lower standard deviations) using the formula: \$weight = $[(1\text{-}SD/IC_{50})/\Sigma(SD/IC_{50})]$, where SD = standard deviation, both SD and IC_{50} are in µM. This led to the exclusion of another 3 compounds (**6**, **13** and **31**). All relevant (non-coordinate based) MOE QuaSAR descriptors (203) were calculated for all compounds, as described by others analysing COX site inhibitors[40].

No striking correlations (R^2 > 0.9) were found between the pIC_{50} values [$pIC_{50} = -\log(IC_{50}*10^{-6})$, IC_{50} in µM] and the descriptor values. The best associations had R^2 values ranging from 0.45 to 0.58. These included descriptors such as: hydrophobicity [logP(o/w), SlogP and SlogP_VASA9], molecular density (total atomic mass/volume, 2D and 3D based calculations) and water accessible surface area that is either negative (ASA-, FASA-, PEOE_VSA_NEG and Q_VSA_NEG) or positive (ASA+ and FASA+).

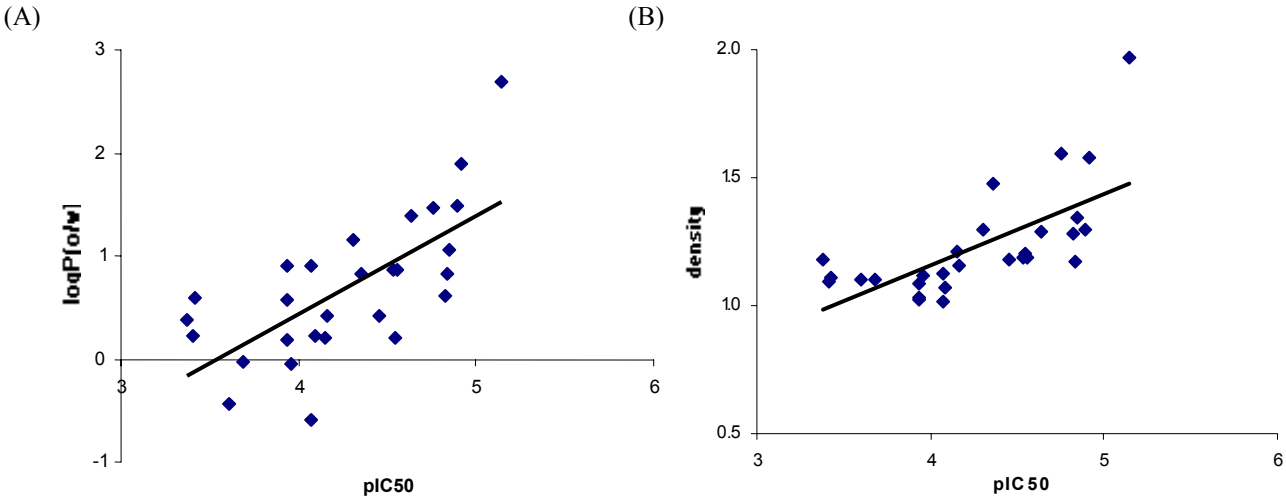
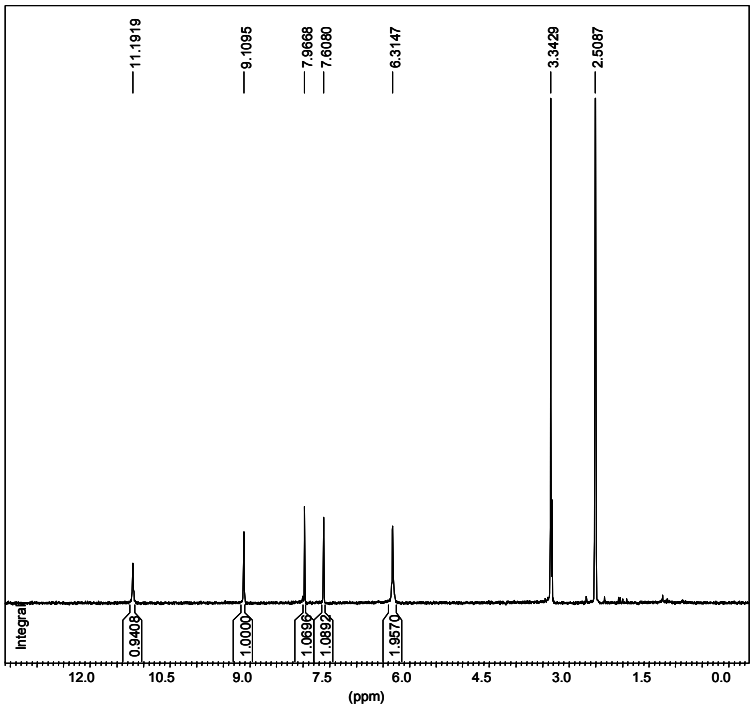
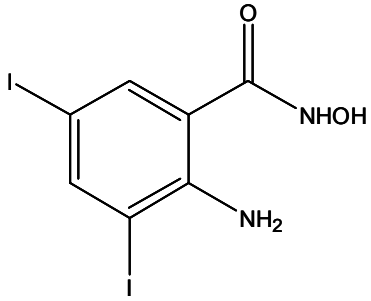
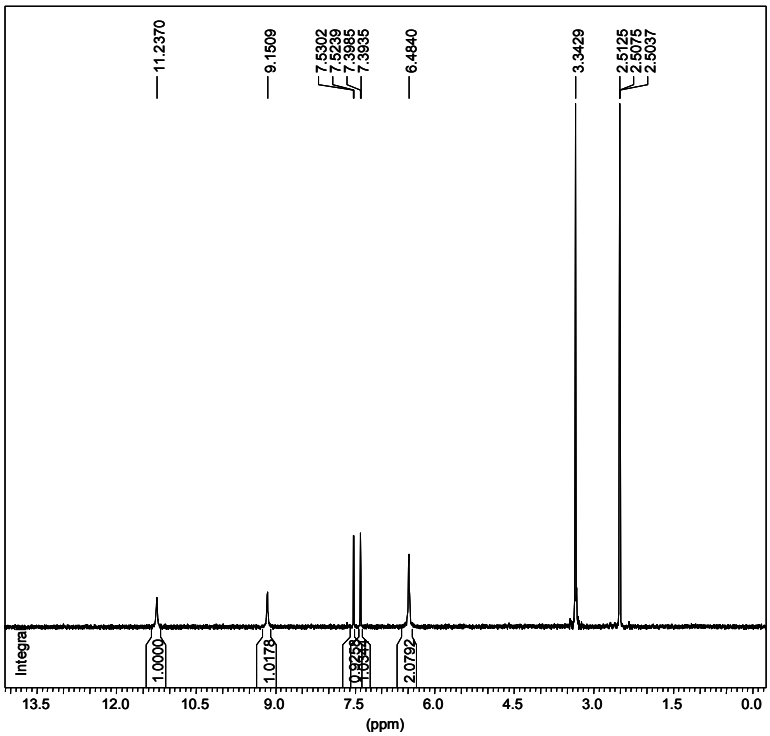


Fig. S3 PGHS-1 peroxidase inhibition vs. hydrophobicity (A), molecular density (B)

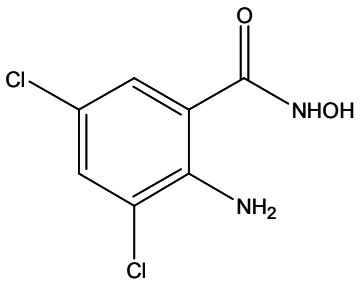


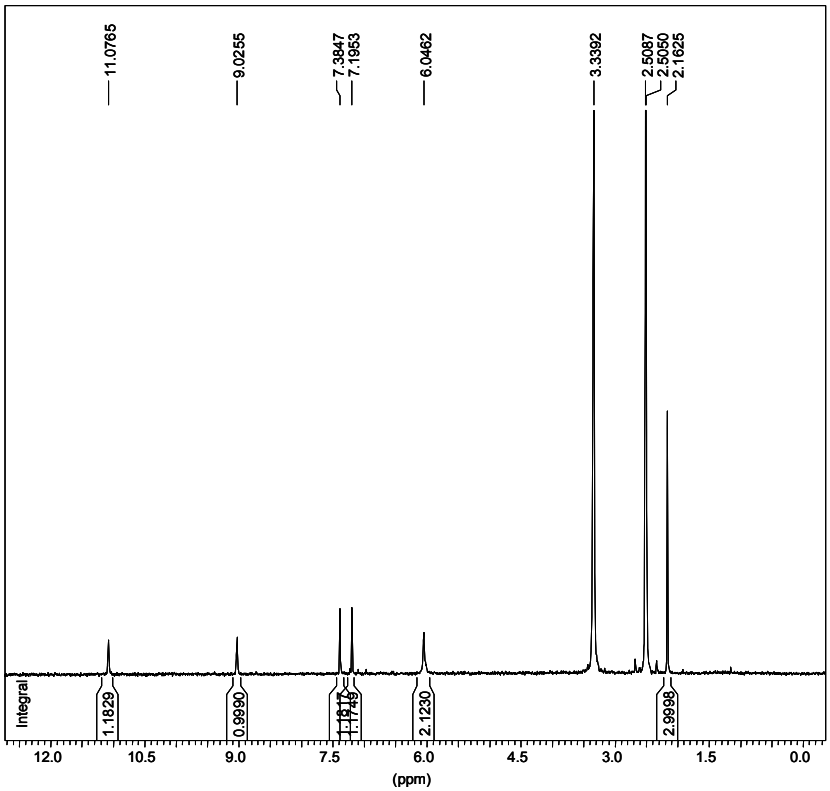
3,5-diiodoanthranilic hydroxamic acid



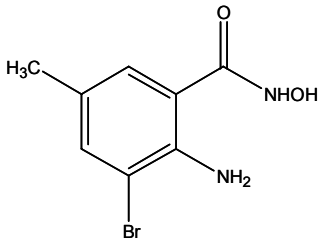


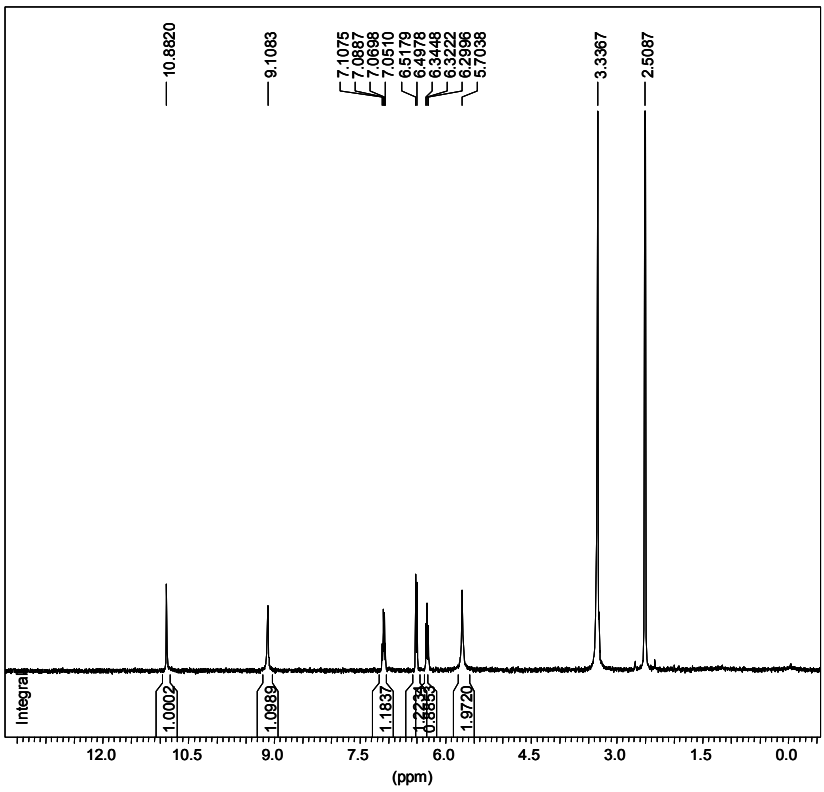
3,5-dichloroanthranilic hydroxamic acid



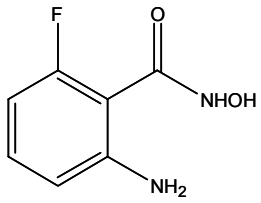


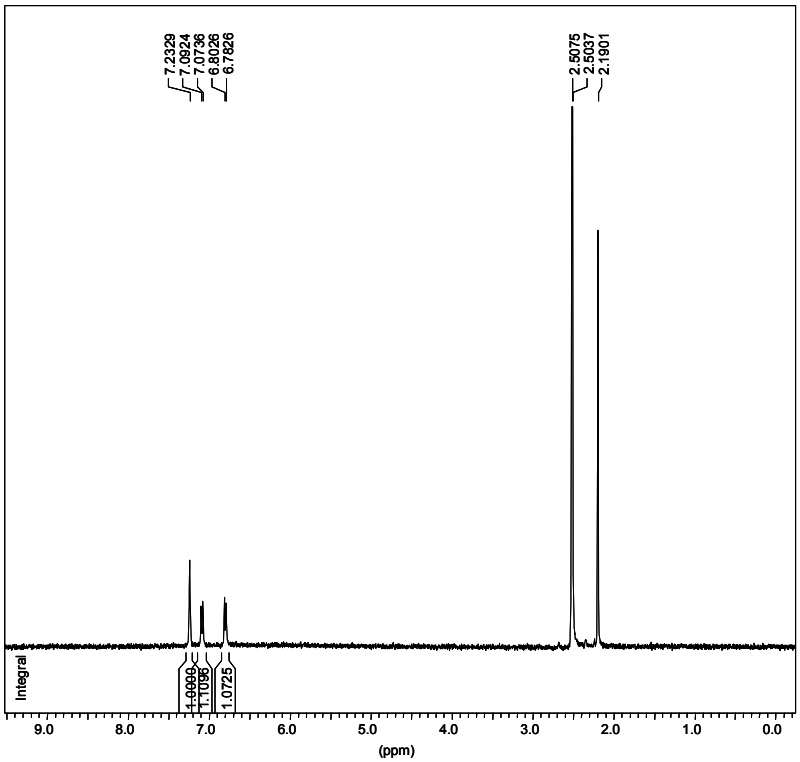
3,bromo-5-methylanthranilic hydroxamic acid





6-fluoroanthranilic hydroxamic acid





[1]H NMR recorded in DMSO-*d6*, therefore the signals at 2.5 ppm and 3.3 ppm (when present) are the signals for DMSO and water, respectively.

5-methylanthranilic hydroxamic acid