Supporting Information

for

On the Mechanism of Cytoprotection by Ferrostatin-1 and Liproxstatin-1 and the Role of Lipid Peroxidation in Ferroptotic Cell Death

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Rate constants and reaction stoichiometry determinations.

$$k_{inh} = \frac{k_{\text{BODIPY}}[\text{BODIPY}]R_i}{n[\text{RTA}]-\frac{\delta[\text{BODIPY}]}{\delta t}} \quad \textbf{(Eq. 1)}$$

k_{BODIPY} = rate constant of peroxyl addition to dye (M^{-1} s^{-1}), summarized in Table S1
[BODIPY] = dye concentration at (t = 0 s) (M)
R_i = rate of initiation (M s^{-1}), summarized Table S1
n = stoichiometry [a]
[RTA] = antioxidant concentration (M)
$\frac{\delta[\text{BODIPY}]}{\delta t}$ = slope of inhibited period (M s^{-1}), determined from slope of solid red line as in Figure S1A-C

[a] Stoichiometry for determining k_{inh} was assumed to be 2 for phenolic and aminic RTAs (Lip-1 and Fer-1) when the observed $n \geq 2$. When the observed $n < 2$, the observed n was used to determine k_{inh}.

$$n = \frac{t_{\text{inh}} \times R_i}{[\text{RTA}]} \quad \textbf{(Eq. 2)}$$

t_{inh} = inhibition time (s), determined from intersection of red lines as in Figure S1
R_i = rate of initiation (M s^{-1}), summarized Table S1
[RTA] = antioxidant concentration (M)

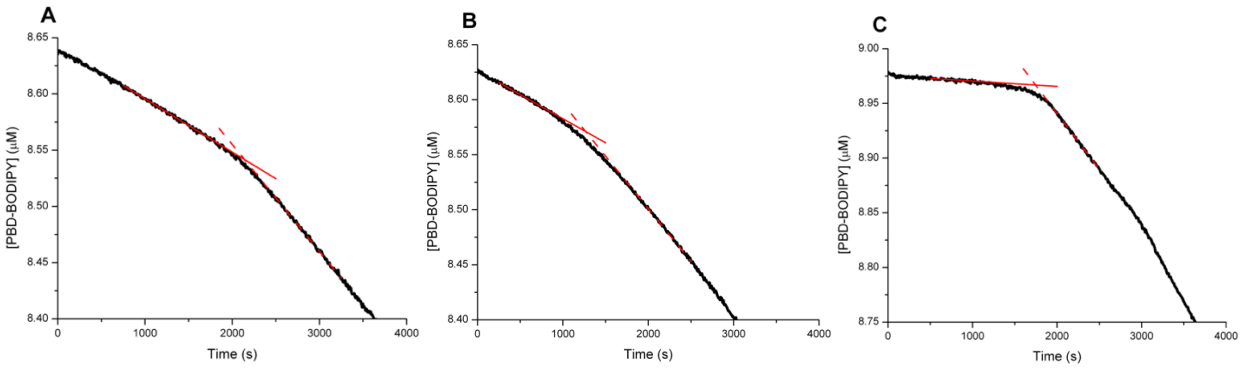
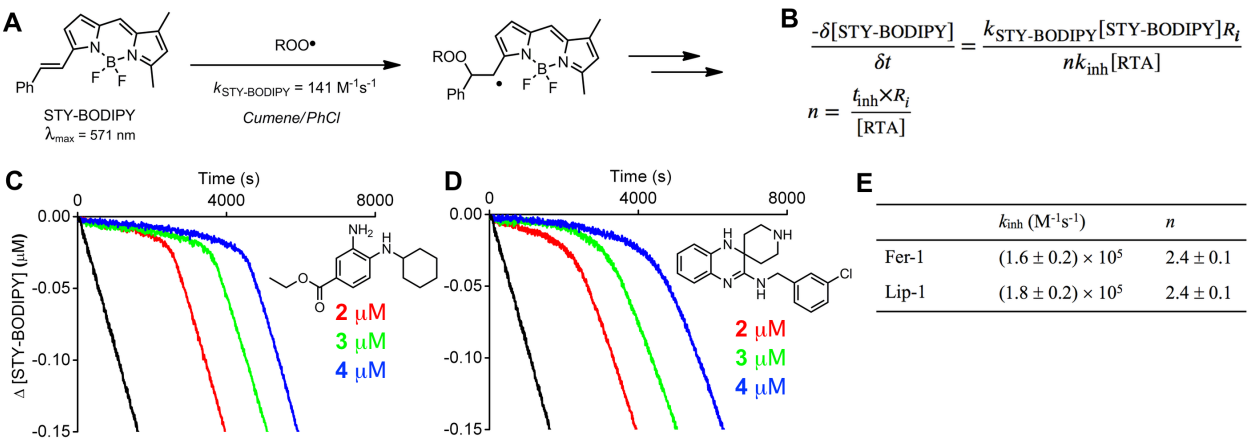


Figure S1. Sample coautoxidation plots for determining reaction stoichiometries and inhibition rate constants. Representative PBD-BODIPY and styrene coautoxidation plots initiated by AIBN (6 mM) and inhibited by Lip-1 (4 μM, **A**), Fer-1 (4 μM, **B**) and α-TOH (2 μM, **C**) at 37 °C. Reaction progress was monitored by loss of absorbance at 591 nm (ε = 139,000 M^{-1} cm^{-1}).

Table S1: Summary of $k_{\text{PBD- or STY-BODIPY}}$ and rate of initiation for each autoxidation media.

Media	$k_{\text{PBD- or STY-BODIPY}}$ (M^{-1} s^{-1})	R_i ($\times 10^{-9}$ M s^{-1})
Styrene in PhCl	$k_{\text{PBD-BODIPY}}$ = 2720	2.23
PC liposomes in pH 7.4 PBS	$k_{\text{STY-BODIPY}}$ = 894	2.55
THF in DMSO/PhCl	$k_{\text{PBD-BODIPY}}$ = 3623	2.78
Cumene in PhCl	$k_{\text{STY-BODIPY}}$ = 141	2.01

Coautoxidations of cumene in chlorobenzene and coautoxidations of THF in DMSO and chlorobenzene.



	k_{inh} ($M^{-1}s^{-1}$)	n
Fer-1	$(1.6 \pm 0.2) \times 10^5$	2.4 ± 0.1
Lip-1	$(1.8 \pm 0.2) \times 10^5$	2.4 ± 0.1

Figure S2: Coautoxidations of STY-BODIPY and cumene in chlorobenzene. STY-BODIPY serves as the signal carrier in cumene autoxidations (**A**), enabling determination of rate constants and reaction stoichiometries for reactions of inhibitors with chain-carrying peroxyl radicals (**B**). Coautoxidations of cumene (3.6 M) and STY-BODIPY (10 μM) initiated by AIBN (6 mM) in chlorobenzene at 37 °C (black trace) and inhibited by 2 μM (red trace), 3 μM (green trace), and 4 μM (blue trace) of Fer-1 (**C**) and Lip-1 (**D**). Average inhibition rate constants and stoichiometry summarized in (**E**). Reaction progress was monitored by absorbance at 571 nm (ε = 128,000 M^{-1} cm^{-1}).

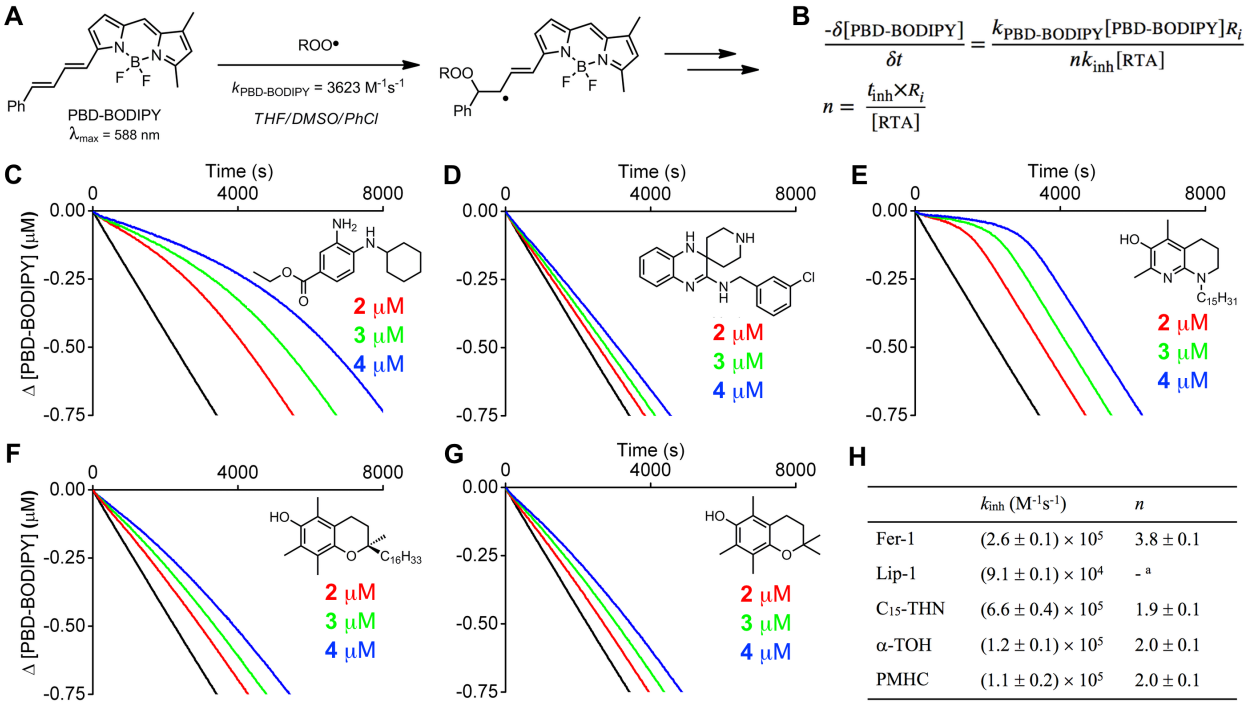


Figure S3: Coautoxidations of PBD-BODIPY and THF in DMSO and chlorobenzene. PBD-BODIPY serves as the signal carrier in THF autoxidations (**A**), enabling determination of rate constants and reaction stoichiometries for reactions of inhibitors with chain-carrying peroxyl radicals (**B**). Coautoxidations of THF (3.1 M) and PBD-BODIPY (10 μM) initiated by AIBN (6 mM) in DMSO (25 vol%) and chlorobenzene at 37°C (black trace) and inhibited by 2 μM (red trace), 3 μM (green trace), and 4 μM (blue trace) of Fer-1 (**C**), Lip-1 (**D**), C_{15}-THN (**E**), α-TOH (**F**), and PMHC (**G**). Average inhibition rate constants and stoichiometry summarized in (**H**). Reaction progress was monitored by absorbance at 588 nm (ε = 128,000 M^{-1} cm^{-1}). [a] The stoichiometry could not be determined from the data in panel **D** and stoichiometry was assumed to be 2 for calculation of k_{inh}.

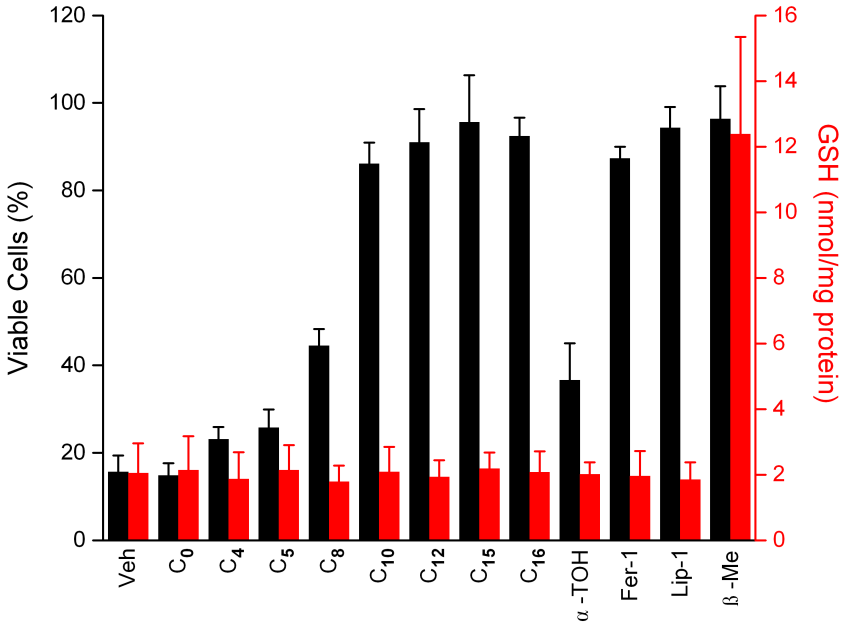


Figure S4. GSH levels in HT22 cells after glutamate-induced cell death. The viability of mouse HT22 hippocampal cells treated with THNs, Lip-1, Fer-1, and α-TOH was not associated with restoration of GSH. β-mercaptoethanol (β-Me) shown as positive control.

Supplementary Experimental

Inhibited autoxidation of cumene in chlorobenzene.
These experiments were carried out in a manner similar to that described in our previous work.[1] In brief, cumene was washed thrice with 1 M aqueous NaOH, dried over $MgSO_4$, filtered, distilled under vacuum and purified by percolating through silica, then basic alumina. To a cuvette of 1.25 mL cumene was added 1.18 mL chlorobenzene and the solution equilibrated for 5 minutes at 37°C. The cuvette was blanked and 12.5 μL of 2 mM STY-BODIPY in 1,2,4-trichlorobenzene was added followed by 50 μL of 0.3 M AIBN in chlorobenzene and the solution was thoroughly mixed. After 20 minutes, an aliquot of Lip-1, Fer-1, C_{15}-THN, PMHC or α-TOH stock solution (1 mM) in chlorobenzene was added and the loss of absorbance at 571 nm followed. The inhibition rate constant (k_{inh}) and stoichiometry (n) was determined for each experiment as shown above. Autoxidations were carried out in triplicate.

Inhibited autoxidation of THF in DMSO and chlorobenzene.
To a cuvette of 1.19 mL chlorobenzene was added 0.62 mL unstabilized THF and 0.62 mL DMSO and the solution equilibrated for 5 minutes at 37 °C. The cuvette was blanked and 12.5 μL of 2 mM PBD-BODIPY in 1,2,4-trichlorobenzene was added followed by 50 μL of 0.3 M AIBN in chlorobenzene and the solution was thoroughly mixed. After 5 minutes, an aliquot of Lip-1, Fer-1, C_{15}-THN, PMHC or α-TOH stock solution (1 mM) in DMSO was added and the loss of absorbance at 588 nm followed. The inhibition rate constant (k_{inh}) and stoichiometry (n) was determined for each experiment as shown above. Autoxidations were carried out in triplicate.

Inhibited autoxidation of styrene for determining KIEs.
Lip-1 and Fer-1 stocks (10 mM) were stirred in methanol or methanol-d_4 overnight under N_2 and complete deuterium exchange was confirmed by ^{1}H NMR. Autoxidations of proteated and deuterated RTAs were completed in parallel and identical to styrene autoxidations described in the main article with the inclusion of 1% MeOH (HPLC grade) or MeOD prior to blanking the cuvette.

EPR experiments.
Electron paramagnetic resonance spectra were recorded on a Bruker EMXplus spectrometer equipped with an ER 4119HS cavity at room temperature. Samples were diluted in benzene and degassed by at least 3 freeze-pump-thaw cycles. EPR spectra were simulated using EasySpin.[2]

Quantum chemical calculations.
Calculations of the bond dissociation energies were carried out using the CBS-QB3 complete basis set method[3] as it is implemented in the Gaussian 09 software.[4]

Synthesis of Lip-1.

1-(3'-((3-chlorobenzyl)amino)-1'H-spiro[piperidine-4,2'-quinoxalin]-1-yl)ethanone (*N*-acetyl Lip-1): *N*-acetyl Lip-1 was synthesized by modification of the procedure of Kysil *et. al.*[5] o-phenylenediamine (1.081 g, 10 mmol, 1 equiv.) and *N*-acetyl-4-piperidinone (1.412 g, 10 mmol, 1 equiv.) were heated to reflux in 15 mL dry methanol for 4 h under N_2. The reaction mixture was allowed to cool to 50°C, and a solution of TMSCl (1.27 mL, 10 mmol, 1 equiv.) in 7.5 mL dry acetonitrile was added dropwise over 15 min, followed by 1-chloro-3-isocyanomethylbenzene[6] (1.516 g, 10 mmol, 1 eq) in 7.5 mL dry methanol dropwise over 1 h. The reaction mixture was stirred for 4 h at 50°C, cooled, and concentrated *in vacuo*. The residue was triturated in 50 mL dry ether followed by sonication for 10 min. The precipitate was collected by filtration, air dried, and transferred portionwise to 50 mL of water. The mixture was stirred during addition of 1 M aqueous NaOH to pH 9, and extracted with 6 × 50 mL $CHCl_3$. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated to yield a brown oil which was purified by silica gel chromatography, 1:5:94 Et_3N:MeOH:CH_2Cl_2. The product was recrystallized from ethanol/hexanes to yield *N*-acetyl Lip-1 as granular crystals (1.53 g, 40%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.24-7.36 (m, 4H), 7.16 (t, J = 6.0 Hz, 1H), 6.80 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 6.73 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 6.69 (ddd, J = 7.6 Hz, 1.2 Hz, 1H), 6.54 (ddd, J = 7.6 Hz, 1.2 Hz, 1H), 6.12 (s, 1H), 4.47 (d, J = 5.6 Hz, 2H), 4.27 (d, J = 12.8 Hz, 1H), 3.68 (d, J = 12.8 Hz, 1H), 3.43 (t, J = 13.2 Hz, 1H), 2.93 (t, J = 12.0 Hz, 1H), 2.01 (s, 3H), 1.88 (dt, J = 12.8 Hz, 4.4 Hz, 1H) , 1.79 (dt, J = 12.8 Hz, 4.8 Hz, 1H), 1.52-1.60 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.1, 157.5, 143.0, 134.8, 134.4, 132.7, 130.0, 128.35, 128.31, 127.1, 126.3, 126.0, 122.7, 122.3, 117.9, 113.5, 50.8, 35.4, 31.6, 30.9, 21.3. HRMS (EI) calc. for $C_{21}H_{23}ClN_4O$ [M+] 382.1560; found 382.1530.

***N*-(3-chlorobenzyl)-1'H-spiro[piperidine-4,2'-quinoxalin]-3'-amine (Lip-1):** To a solution of *N*-acetyl Lip-1 (450 mg, 1.18 mmol, 1 equiv.) in 20 mL 99% ethanol was added aqueous KOH (5 mL, 4.0 M) and the mixture heated to reflux for 3 h. The solution was cooled and concentrated *in vacuo*. To the residue was added 10 mL water and the mixture extracted 4 × 25 mL $CHCl_3$. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated to yield Lip-1 (380 mg, 95%), which was recrystallized from degassed benzene to yield colourless needles. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.24-7.35 (m, 4H), 7.13 (t, J = 6.4 Hz, 1H), 6.82 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 6.69 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 6.65 (ddd, J = 7.6 Hz, 1.6 Hz, 1H), 6.50 (ddd, J = 7.6 Hz, 1.6 Hz, 1H), 5.88 (s, 1H), 4.49 (d, J = 6.4 Hz, 2H), 2.88 (t, J = 12.0 Hz, 2H), 2.68 (d, J = 12.0 Hz, 2H), 2.01 (bs, 1H), 1.75 (dt, J = 12.0 Hz, 4.8 Hz, 2H), 1.46 (d, J = 12.0 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.4, 143.3, 135.2, 134.7, 132.7, 129.9, 126.9, 126.2, 125.8, 122.4, 122.0, 117.6, 113.6, 50.9, 42.7, 31.9. HRMS (EI) calc. for $C_{19}H_{21}ClN_4$ [M+] 340.1455; found 340.1496.

Synthesis of dihydroquinoline 1 and the derived nitroxide.

6-(*tert*-butyl)-2,2,4-trimethyl-1,2-dihydroquinoline (1): A 100 mL round bottom flask equipped with a Dean-Stark trap and condenser was charged with 4-*tert*-butyl aniline (13.5 g, 90 mmol, 1 equiv.) and *p*-toluenesulfonic acid (0.86 g, 4.5 mmol, 0.05 equiv.) in cyclohexane (20 mL) and purged with N_2. The solution was heated to a vigorous reflux and acetone (17 mL, 225 mmol, 2.5 equiv.) was added dropwise over 2 h. The solution was stirred at reflux overnight, at which point the theoretical amount of water was collected in the trap. The reaction mixture was cooled and diluted with diethyl ether, washed with saturated aqueous $NaHCO_3$ (2 x 100 mL), distilled water (2 × 100 mL) and brine (1 × 50mL), dried over $MgSO_4$, filtered and concentrated. The residue was distilled under vacuum (167°C) to yield **1** as a pale oil (11.6 g, 56%) which was further purified by flash chromatography (10% Et_2O/petroleum ether) prior to kinetic measurements. ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.90-6.93 (m, 2H), 6.38 (d, J = 8.4 Hz, 1H), 5.58 (s, 1H), 5.25 (s, 1H), 1.90 (s, 3H), 1.21 (s, 9H), 1.17 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 141.8, 137.2, 128.3, 127.7, 124.9, 119.6, 119.5, 111.9, 51.0, 33.5, 31.5, 30.8, 18.3. Spectra matched those reported in the literature.[7]

6-(*tert*-butyl)-2,2,4-trimethyl-1,2-dihydroquinoline-*N*-aminoxyl. A 100 mL round bottom flask was affixed with a condenser and charged with **1** (1.38 g, 6 mmol, 1 equiv.) and methanol (39 mL). The solution was heated to reflux and Na_2WO_4•$2H_2O$ (198 mg, 0.6 mmol, 0.1 equiv.) in 0.6 mL distilled H_2O was added in one portion and H_2O_2 (30%, 4.95 mL, 48 mmol, 8 equiv) in 18 mL MeOH was added dropwise until the majority of starting material was consumed by TLC. The solution was then cooled and concentrated *in vacuo*. The residue was taken up in ether and washed with saturated aqueous $NaHCO_3$ (2 × 100mL) and distilled water (1 × 100 mL), dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (5% Et_2O/petroleum ether) to yield a dark red oil (0.97 g, 66%) which was stored at -20°C under N_2 and as stock solutions in DMSO.

Generation of nitroxides.

Attempts to independently synthesize the nitroxides derived from Lip-1 and Fer-1 were challenging, and generally lead to intractable mixtures from which a single nitroxide could not be isolated. For example, UV irradiation of Lip-1 in the presence of dibenzothiophene S-oxide (mild conditions we have recently developed for the synthesis of nitroxides) led to a mixture of at least two nitroxides (Figure S5), as well as other (diamagnetic) products.

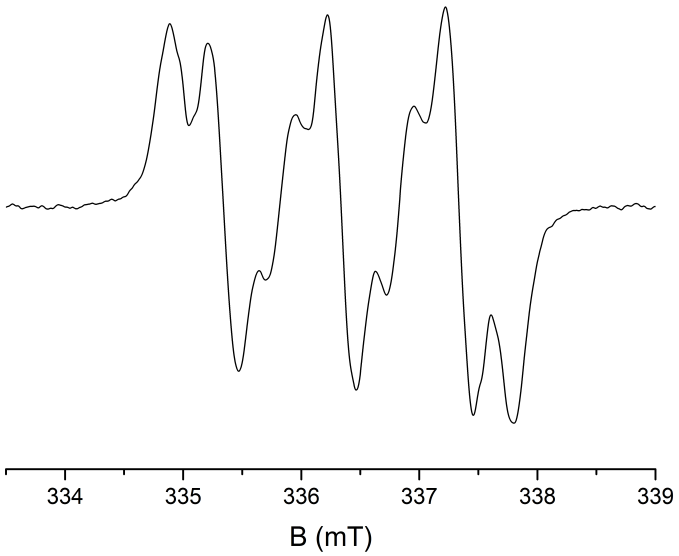


Figure S5. EPR spectrum of Lip-1 oxidation products.

NMR Spectra

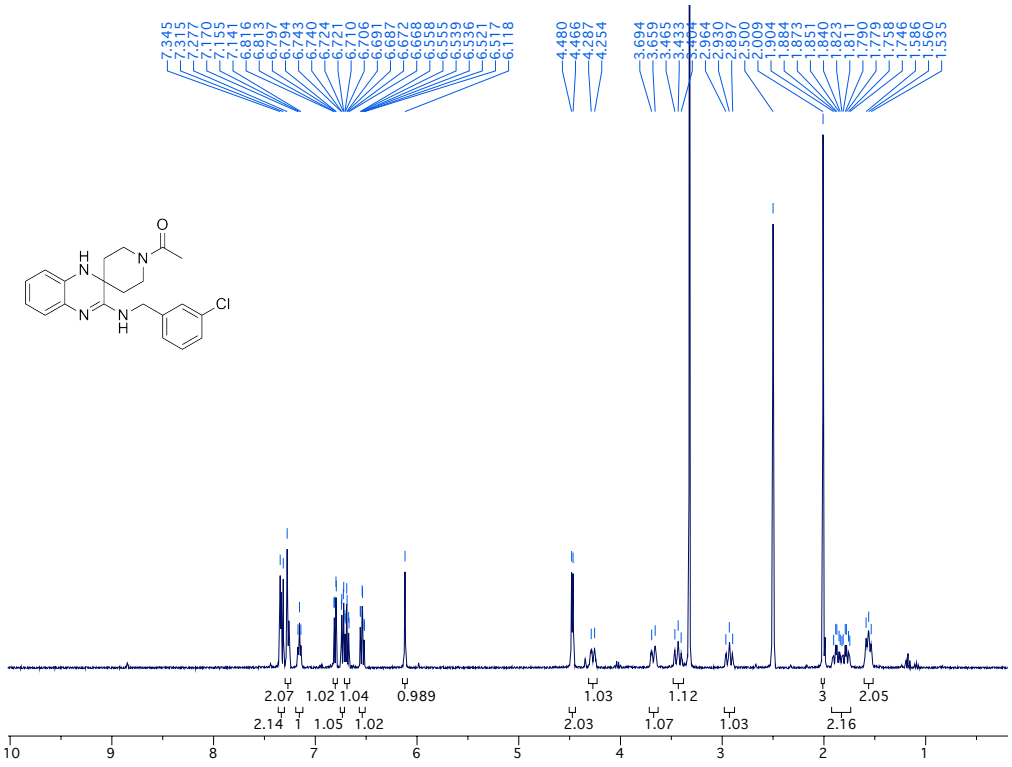


Figure S6. [1]H NMR of N-acetyl Lip-1.

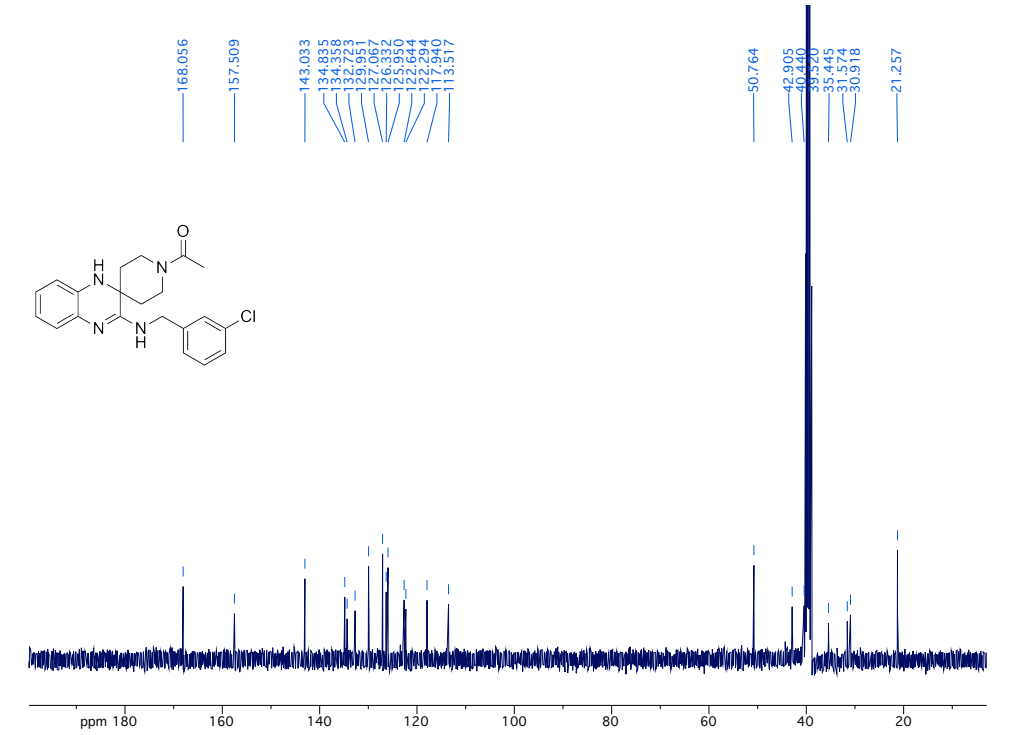


Figure S7. [13]C NMR of N-acetyl Lip-1.

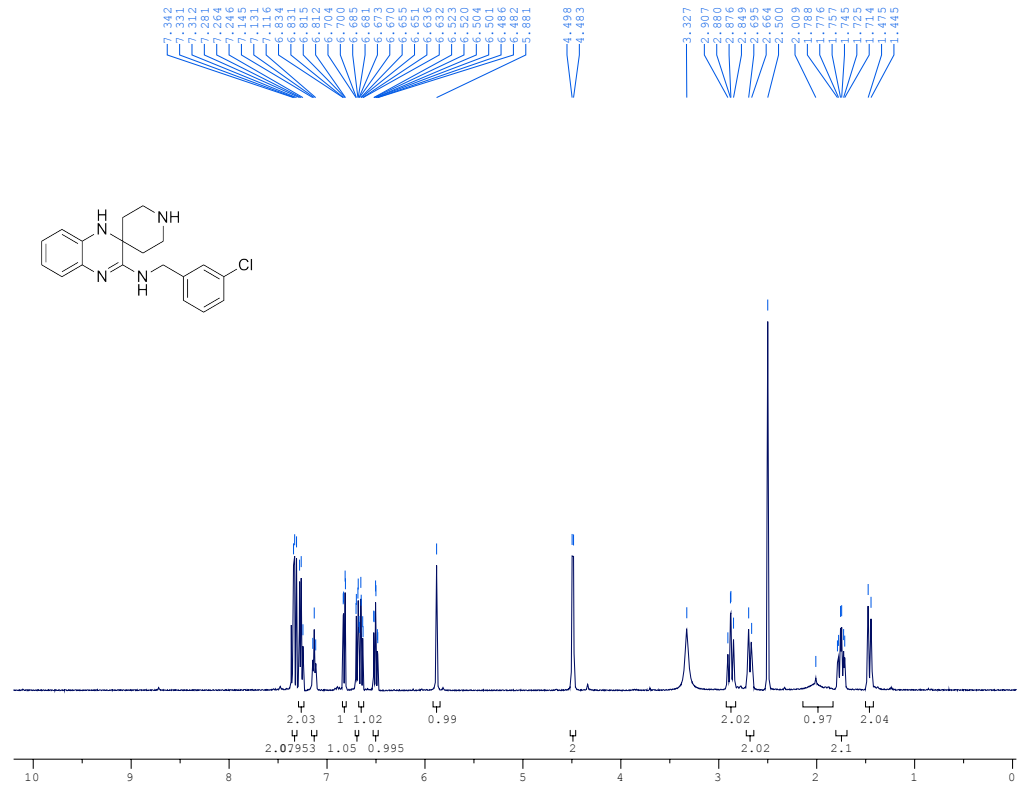


Figure S8. ^{1}H NMR of Lip-1.

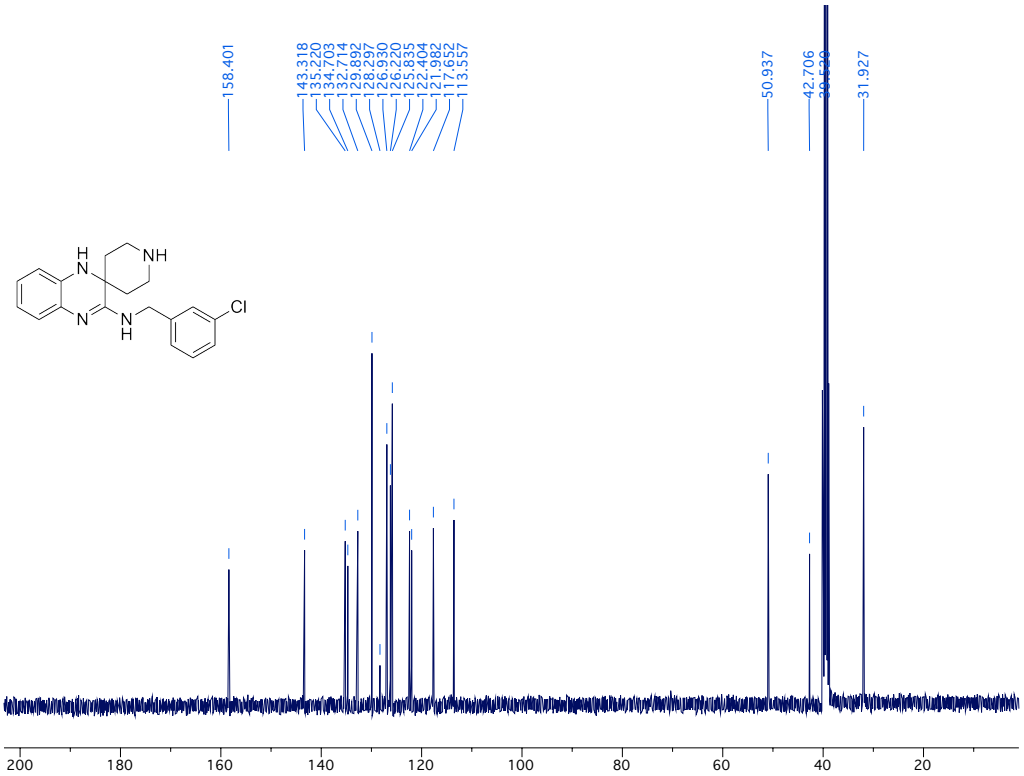


Figure S9. ^{13}C NMR of Lip-1.

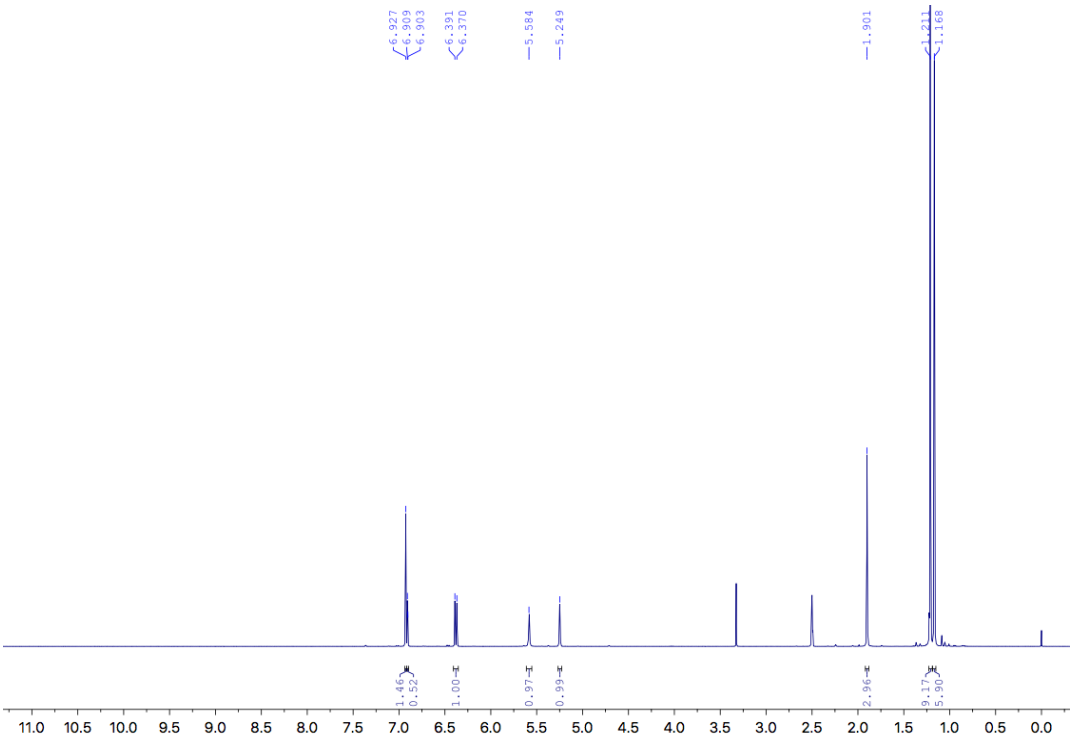


Figure S10. ^{1}H NMR of 1.

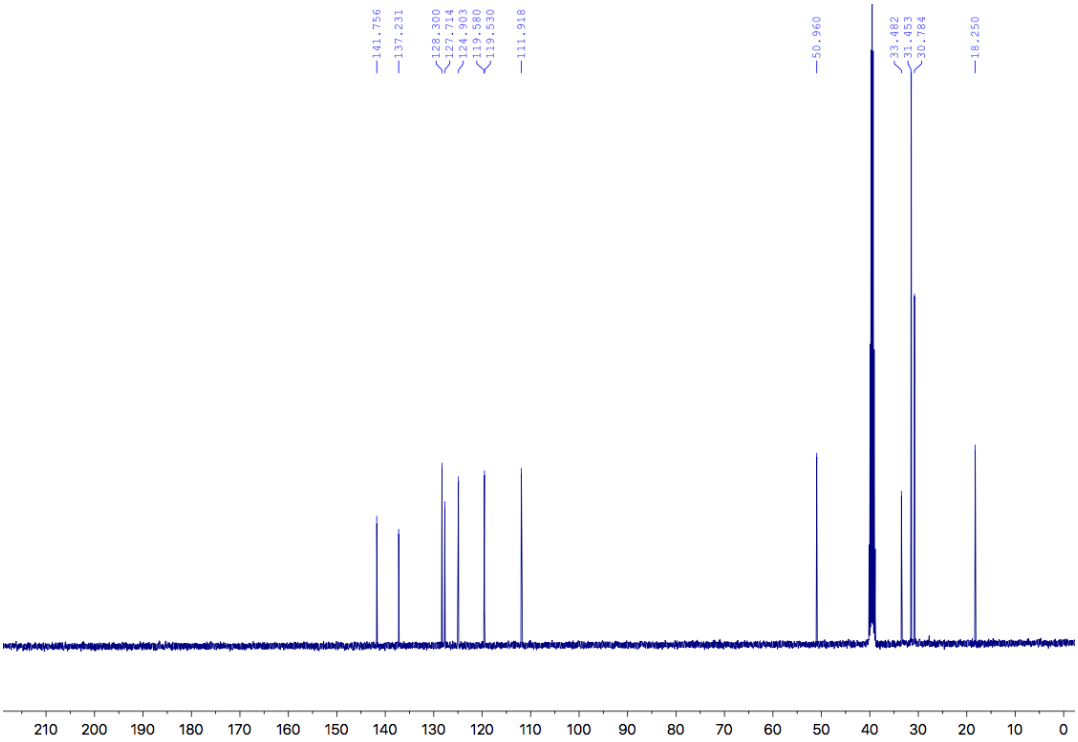
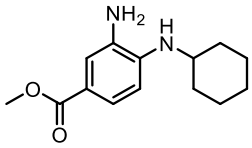


Figure S11. ^{13}C NMR of 1.

Computational Data

Optimized Gaussian Structures and CBS-QB3 Energies

Ferrostatin-1 (methyl ester)



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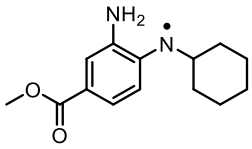
Ferrostatin-1 aminyl radical 1 (methyl ester)



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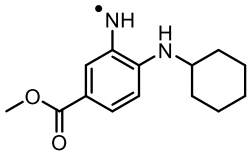
Ferrostatin-1 aminyl radical 2 (methyl ester)



CBS-QB3 Enthalpy = -803.451798
CBS-QB3 Free Energy = -803.516772

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 H                  1.67456600    1.85950100    0.11637200
 C                  2.61860400   -0.03004300   -0.25457000
 C                  3.02050500   -0.72659300    1.06143700
 C                  3.80769400    0.73717300   -0.85182900
 H                  2.31787700   -0.79867300   -0.97720700
 C                  4.23706000   -1.64234400    0.86451600
 H                  3.25371800    0.04831200    1.80182300
 H                  2.17013600   -1.29068700    1.45516500
 C                  5.03047100   -0.17170800   -1.04170900
 H                  4.06784800    1.56241600   -0.17536700
 H                  3.50909300    1.18784600   -1.80289900
 C                  5.42445100   -0.87775200    0.26320800
 H                  4.51918800   -2.09520600    1.81979600
 H                  3.96491300   -2.47119300    0.19800600
 H                  5.86977000    0.41555600   -1.42613300
 H                  4.80389000   -0.92505600   -1.80688700
 H                  6.26300500   -1.55803400    0.08512300
 H                  5.77587300   -0.13103700    0.98659700
 C                  0.18474100    0.56561100   -0.05581600
 C                 -0.73549600    1.68309100    0.19109100
 C                 -0.33766600   -0.72442900   -0.25848400
 C                 -2.13132300    1.39300500    0.19689500
 C                 -1.70391800   -0.94505200   -0.24174100
 H                  0.33198500   -1.55759800   -0.42857700
 C                 -2.61393200    0.11400900   -0.01385000
 H                 -2.83562700    2.19845100    0.37296400
 H                 -2.09035000   -1.94249300   -0.40154300
 N                 -0.18435400    2.86973900    0.38808600
 H                 -0.90437300    3.57432300    0.54871300
 C                 -4.08275300   -0.09144700    0.01173500
 O                 -4.90146100    0.77937100    0.20173000
 O                 -4.42629900   -1.38469500   -0.20441900
 C                 -5.83582100   -1.65908900   -0.19374000
 H                 -6.27023700   -1.40002800    0.77326900
 H                 -6.34412100   -1.08861000   -0.97291300
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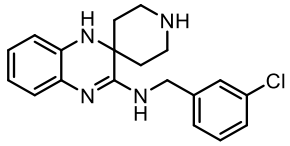
Liproxstatin-1



CBS-QB3 Enthalpy = -1413.675961
CBS-QB3 Free Energy = -1413.749082

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 C                  3.22979800   -2.70510000    0.87280100
 C                  2.67056900   -1.58600600    0.25242200
 C                  3.52084900   -0.54888700   -0.18703300
 C                  4.90208800   -0.66038600   -0.01479600
 C                  5.44162100   -1.78718700    0.60251200
 H                  5.02570300   -3.68243000    1.53912700
 H                  2.55821800   -3.49274500    1.19444000
 H                  5.55228500    0.13606000   -0.36531300
 H                  6.51538800   -1.86223200    0.73272000
 C                  0.77239500   -0.40888200   -0.35136800
 N                  2.91418800    0.52366200   -0.84258700
 H                  3.53089400    1.30242500   -1.02069100
 N                  1.29611600   -1.52974600    0.00619600
 N                 -0.57877000   -0.34188100   -0.57561700
 H                 -0.92271200    0.43048700   -1.12202500
 C                 -1.39670600   -1.55024600   -0.58739400
 H                 -1.10448000   -2.14419600    0.28199200
 H                 -1.17638900   -2.16944000   -1.46557100
 C                  1.56246500    0.91222600   -0.41557700
 C                  1.01319700    1.92902500   -1.44142800
 C                  1.53573300    1.56778600    0.99928400
 C                  1.72464400    3.28455500   -1.34545100
 H                 -0.04232500    2.12772900   -1.23615500
 H                  1.10896500    1.51598200   -2.44933300
 C                  2.21706500    2.93790300    1.00327000
 H                  0.49454200    1.68875800    1.31161600
 H                  2.02492600    0.90019600    1.71344500
 H                  1.25837700    3.98386700   -2.04446100
 H                  2.78086000    3.18452100   -1.66265800
 H                  2.10997500    3.39603000    1.98973000
 H                  3.30157800    2.81156200    0.82543400
 N                  1.58436600    3.80767100    0.01032100
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 C                 -2.87102700   -1.21531600   -0.54476200
 C                 -3.75322500   -1.74977500   -1.48583500
 C                 -3.37372200   -0.37797300    0.45809100
 C                 -5.11560100   -1.46157800   -1.42558600
 H                 -3.37226700   -2.39599400   -2.26898300
 C                 -4.73264100   -0.09652800    0.50131500
 H                 -2.70728300    0.04848400    1.19698100
 C                 -5.61883100   -0.62982700   -0.43058200
 H                 -5.79162400   -1.88273700   -2.16082100
 H                 -6.67376200   -0.39544600   -0.37472600
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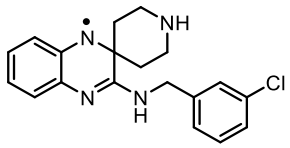
Liproxstatin-1 aminyl radical



CBS-QB3 Enthalpy= -1413.047153
CBS-QB3 Free Energy= -1413.122441

0 2

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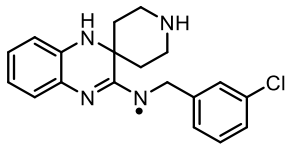
C	3.02713200	-2.99311100	0.04700900
C	2.52448800	-1.69108100	-0.03112300
C	3.36845900	-0.58095100	0.34270500
C	4.69889800	-0.86467500	0.79156000
C	5.16146500	-2.15686500	0.85776800
H	4.69684100	-4.24678600	0.53761300
H	2.37229600	-3.80739200	-0.24068200
H	5.31642900	-0.01910600	1.07077600
H	6.17139300	-2.35646700	1.19774700
C	0.78924100	-0.26504600	-0.51450800
N	2.96408300	0.68112300	0.28728500
N	1.23030900	-1.48524500	-0.45812300
N	-0.50351300	-0.05980300	-0.88866100
H	-0.81492300	0.88677200	-1.03387900
C	-1.39603400	-1.12890300	-1.32353600
H	-1.05149600	-2.04078500	-0.83246400
H	-1.30117800	-1.29768600	-2.40282700
C	1.62287800	0.98027300	-0.18413900
C	1.77704100	1.86411600	-1.46753800
C	0.92630600	1.83147100	0.92619800
C	2.43131100	3.21019500	-1.15543700
H	0.79047200	2.05368200	-1.90157700
H	2.36705100	1.31220800	-2.20428600
C	1.62072500	3.17837000	1.12857100
H	-0.11458000	2.01984100	0.64904600
H	0.92530100	1.25811000	1.85721600
H	2.44926400	3.81764500	-2.06511900
H	3.47121800	3.04006600	-0.83947400
H	1.05678000	3.76412100	1.86026500
H	2.62889200	3.00670300	1.53354200
N	1.63488800	3.90941000	-0.14269400
H	2.00736600	4.84137500	0.00240500
C	-2.83883100	-0.83091700	-0.97762700
C	-3.82774100	-0.84377400	-1.96274900
C	-3.20104100	-0.55715200	0.34638600
C	-5.15932000	-0.59420900	-1.63425100
H	-3.55562600	-1.05114900	-2.99191200
C	-4.53080500	-0.30664300	0.65666500
H	-2.45051900	-0.54107200	1.12664900
C	-5.52340700	-0.32180800	-0.31990000
H	-5.91963200	-0.60671600	-2.40665200
H	-6.55281900	-0.12303700	-0.05216300
Cl	-4.97324700	0.03390000	2.32336900

Liproxstatin-1 amidinyl radical



CBS-QB3 Enthalpy= -1413.041457
CBS-QB3 Free Energy = -1413.115752

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 C                  3.49486600   -2.70535900    0.34748600
 C                  2.77852400   -1.51226000    0.04611900
 C                  3.53500200   -0.34402800   -0.32839000
 C                  4.93471200   -0.42704100   -0.44209400
 C                  5.58559300   -1.61155300   -0.15268600
 H                  5.39492500   -3.67292100    0.48391000
 H                  2.90711200   -3.56886700    0.63406900
 H                  5.49687400    0.45045500   -0.74535500
 H                  6.66550800   -1.65886500   -0.23397500
 C                  0.74119800   -0.37637100   -0.20178100
 N                  2.83894800    0.78826800   -0.59964800
 H                  3.36593300    1.61580200   -0.83463600
 N                  1.43704000   -1.52701800    0.05327800
 N                 -0.53222500   -0.36986900   -0.41521400
 C                 -1.25252500   -1.62746500   -0.38620000
 H                 -0.82443600   -2.32712900    0.34041700
 H                 -1.13427100   -2.11527700   -1.36526300
 C                  1.45360600    0.98854700   -0.13742300
 C                  0.78404100    2.04926900   -1.03164800
 C                  1.43320000    1.48384700    1.33850600
 C                  1.35349900    3.45249300   -0.79734800
 H                 -0.27953400    2.05365400   -0.79926100
 H                  0.89389600    1.75846900   -2.07995700
 C                  1.98259200    2.90486400    1.47796300
 H                  0.39282000    1.47050000    1.67448000
 H                  2.00032300    0.79163600    1.96769800
 H                  0.78744000    4.17136000   -1.39517100
 H                  2.40261300    3.51073100   -1.15716300
 H                  1.87375500    3.23591300    2.51395300
 H                  3.06754000    2.90783300    1.25417600
 N                  1.22720400    3.80784000    0.61284400
 H                  1.51333200    4.76822300    0.76485200
 C                 -2.73720400   -1.44619600   -0.12479300
 C                 -3.51334400   -2.55725100    0.22159000
 C                 -3.35534600   -0.20105000   -0.24465400
 C                 -4.88176500   -2.42942400    0.43686700
 H                 -3.04086000   -3.52878800    0.32585400
 C                 -4.72368800   -0.09122000   -0.02363700
 H                 -2.76340100    0.66552700   -0.50120800
 C                 -5.50489200   -1.18871700    0.31602500
 H                 -5.47216700   -3.29798400    0.70644400
 H                 -6.56755400   -1.07375900    0.48471500
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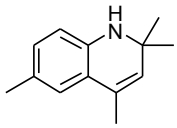
Dihydroquinoline (simplified **1** – methyl group)



CBS-QB3 Enthalpy= -559.272557
CBS-QB3 Free Energy= -559.327742

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 C                 -0.11223700   -0.88139800   -0.23308300
 C                 -1.10577300   -1.86710100   -0.25416000
 C                 -2.44674600   -1.52631900   -0.11900800
 C                 -2.84720600   -0.19750000    0.04607600
 C                  0.57076500    1.49033400   -0.10295000
 C                  1.85540800    1.10421100   -0.06329200
 C                  2.30146900   -0.33640700    0.07021500
 N                  1.22154500   -1.19473000   -0.43866800
 C                  3.55055000   -0.59279200   -0.78984300
 C                  2.61478000   -0.64971100    1.55452300
 C                  0.19887400    2.94940700   -0.17583300
 C                 -4.30126300    0.16729200    0.23239000
 H                 -4.95848700   -0.54928300   -0.26675200
 H                 -4.58076100    0.18168200    1.29229900
 H                 -4.51944500    1.15843500   -0.17386400
 H                 -2.14276500    1.81820200    0.17120200
 H                 -0.82170700   -2.90685300   -0.38658300
 H                 -3.19484300   -2.31283600   -0.13997400
 H                  2.64739600    1.84752100   -0.07450000
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 H                  3.34415000   -0.36131300   -1.83620000
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 H                  3.85843800   -1.64153900   -0.72144700
 H                  3.39246200    0.01657000    1.93972200
 H                  1.71976900   -0.51983400    2.16675900
 H                  2.96687200   -1.68151300    1.66553200
 H                  1.09136400    3.57483400   -0.23009300
 H                 -0.42075300    3.15912500   -1.05353400
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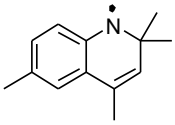
Dihydroquinoline aminyl radical (simplified – methyl group)



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CBS-QB3 Free Energy= -558.698440

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 C                  0.73962900   -0.52911200    0.00000000
 C                  2.16506600   -0.37643900    0.00000000
 C                  2.75198500    0.86351100    0.00000000
 C                  1.96831900    2.04152800    0.00000000
 C                 -1.51310300    0.52202500    0.00000000
 C                 -2.02159500   -0.72388400    0.00000000
 C                 -1.18399700   -1.97460000    0.00000000
 N                  0.25633700   -1.76511900    0.00000000
 C                 -1.51310300   -2.81742500    1.26093200
 C                 -1.51310300   -2.81742500   -1.26093200
 C                 -2.40282500    1.73896900    0.00000000
 C                  2.63204600    3.39355200    0.00000000
 H                  3.27173900    3.52022000    0.87995200
 H                  3.27173900    3.52022000   -0.87995200
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 H                 -0.91346200   -3.72969800    1.25593000
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 H                 -2.22530600    2.36455000   -0.88087100
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Supplementary References

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