

Supporting Information

Comparative Activities of Nickel(II) and Zinc(II) Complexes of Asymmetric [NN'O] Ligands as 26S Proteasome Inhibitors

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Figure S1. Human prostate C4-2B cells were treated with metal compounds, and salts for 18 h followed by measuring accumulated ubiquitinated proteins, PARP cleavage and AR disappearance by Western Blot analysis.

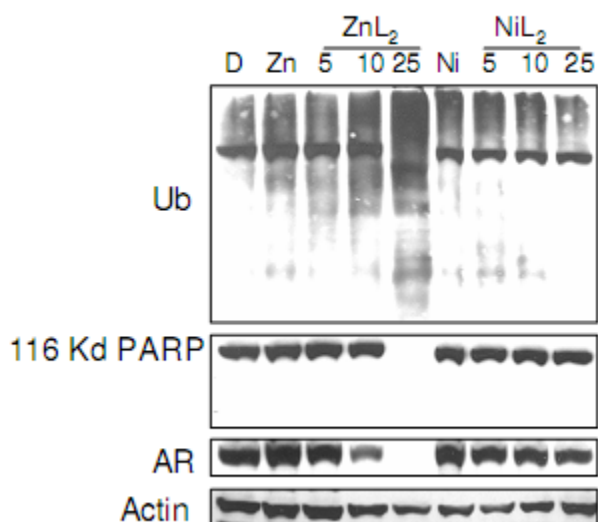


Figure S2. Human prostate cancer PC-3 cells were treated with metal compounds and salts for 18 h followed by measuring (A) accumulated ubiquitinated proteins (Ub), and disappearance of PARP by western blot analysis, and (B) apoptotic morphological changes. Magnification x100.

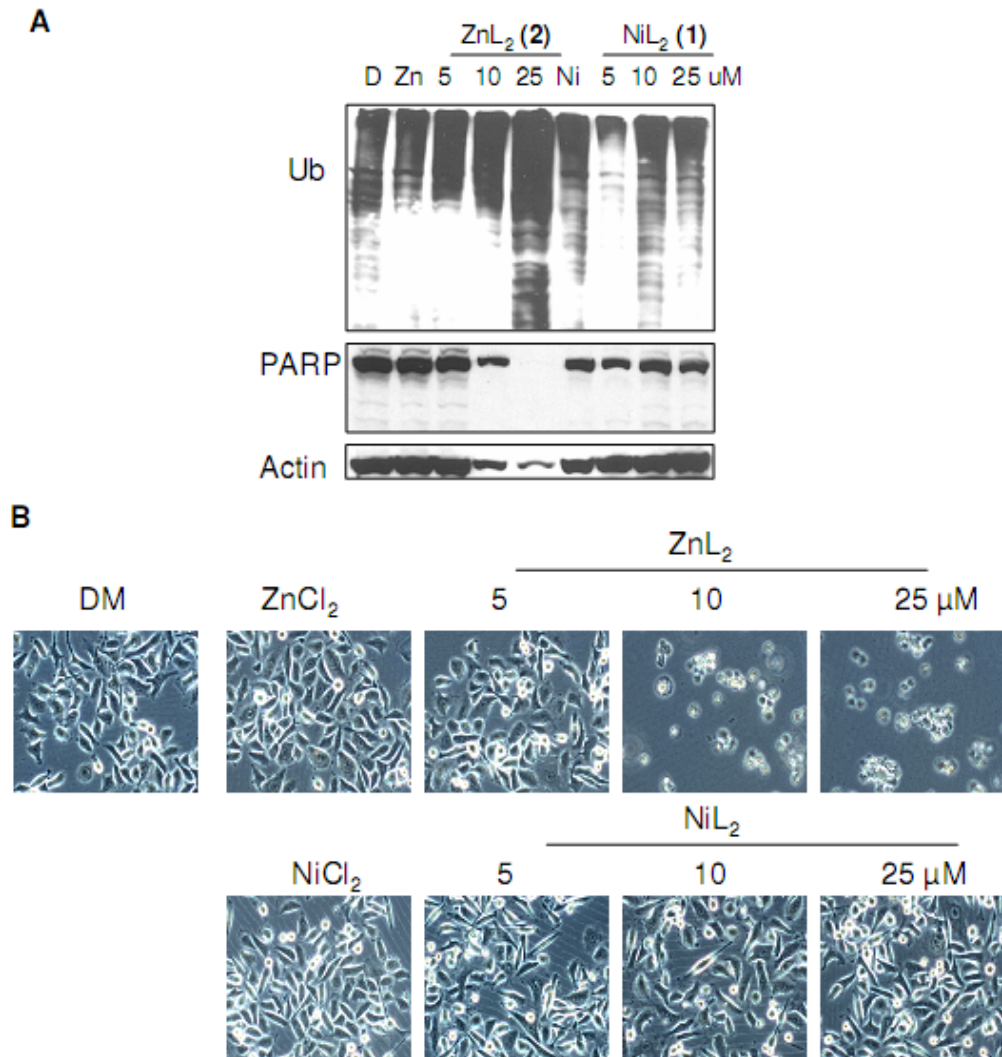


Figure S3. Human prostate C4-2B cells were treated with 15 $\mu\text{mol/L}$ of ZnL2 (**2**) for indicated time points, followed by measuring accumulated ubiquitinated proteins, decreased levels of AR, and PARP disappearance by Western Blot analysis. DMSO (DM) was used as solvent control.

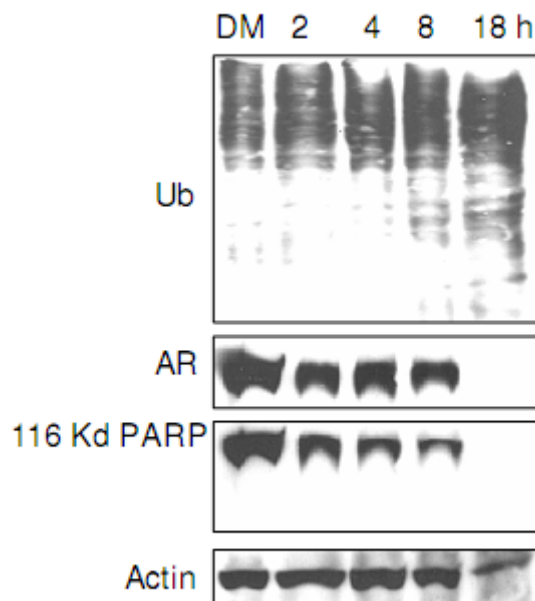
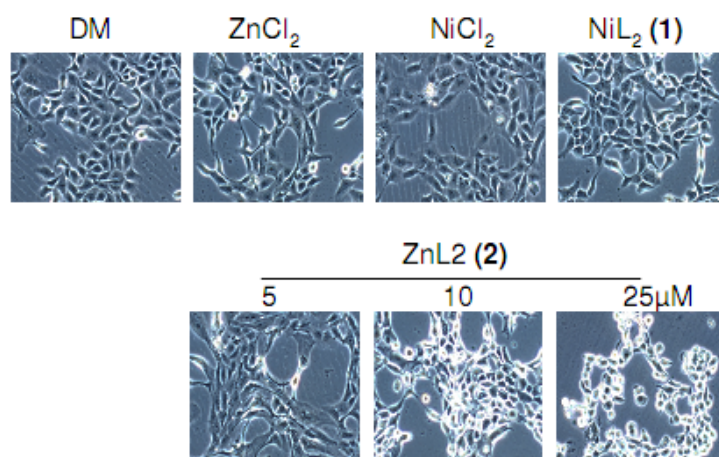


Figure S4. Normal breast cells (MCF-10A) were treated with 25 $\mu\text{mol/L}$ of ZnCl_2 , NiCl_2 , and NiL_2 (**1**), or indicated concentrations of ZnL2 (**2**) for 18h followed by visualization of morphological changes. DMSO (DM) was used as solvent control. Magnification x100.



Optimized Structures Cartesian Coordinates:

(1) E(UB+HF-LYP) = -1589.99416552

H	-2.39542500	-2.66437200	-1.80105500
H	2.49736100	-0.64903300	-4.65623000
H	-4.59847600	-2.35874600	-1.19377500
I	3.61044000	-3.41220600	-0.25917700
H	-0.03480700	-2.28022600	-1.08198800
H	-1.79582200	-3.44637900	0.48846800
H	-1.57688800	-1.21074000	-2.42211300
H	1.11770000	-1.39390100	-2.71683700
C	-1.99075400	-1.67941000	-1.51852100
C	2.23569800	0.05377200	-3.87214200
H	-0.10988000	-3.08432700	0.94157600
C	-4.41988300	-1.32151000	-0.92146300
N	-0.82127800	-1.85279000	-0.58787000
C	-1.06952800	-2.63674800	0.65391000
I	-7.48474000	-1.31582000	-0.43965400
C	1.45200900	-0.36413400	-2.78741800
C	-3.11212400	-0.81078000	-0.97941700
H	-2.67466000	-3.27449600	2.82436400
H	3.30047100	1.74787100	-4.71827200
C	-5.49221800	-0.50090500	-0.53427000
C	2.68183800	1.38866500	-3.90061500
H	6.09748400	-1.49131800	-0.08735800
C	3.96615300	-1.35257700	0.25925900
C	-1.53252900	-1.75270800	1.79629100
N	1.09574700	0.46633900	-1.77908000
C	-2.33012700	-2.24477700	2.84521200
C	5.27401900	-0.84983500	0.20631300
O	1.60298600	-1.05637300	0.66696700
C	-2.83660200	0.56242200	-0.63670700
Ni	-0.00009000	0.00014500	0.00034400
C	-5.27404500	0.84967300	-0.20675100
C	2.83669700	-0.56243300	0.63683300
O	-1.60292900	1.05653600	-0.66664800
C	2.33012200	2.24514900	-2.84444200
C	1.53262000	1.75298500	-1.79548400
N	-1.09571700	-0.46603100	1.77978700
C	-3.96622100	1.35253800	-0.25956200
H	-6.09763300	1.49113700	0.08661700
C	-2.68205300	-1.38816600	3.90121600
H	-3.30079200	-1.74729700	4.71882600
C	5.49240300	0.50064100	0.53411300
H	2.67473800	3.27483900	-2.82348600
I	7.48499900	1.31535500	0.43931800
C	3.11243000	0.81067300	0.97975000
C	-1.45218000	0.36456000	2.78795500
C	1.06977500	2.63695200	-0.65298500
C	4.42022700	1.32128300	0.92167700
C	-2.23600600	-0.05324800	3.87262200
N	0.82154500	1.85287700	0.58874500
H	0.11015200	3.08465400	-0.94055100
C	1.99120500	1.67926800	1.51917400

H	-1.11790600	1.39432900	2.71728600
I	-3.61083600	3.41233100	0.25844000
H	1.79615400	3.44649300	-0.48750000
H	1.57746400	1.21047200	2.42275600
H	0.03536000	2.28057300	1.08310300
H	4.59898400	2.35843900	1.19418600
H	-2.49784600	0.64965000	4.65656700
H	2.39595100	2.66417500	1.80178400

(1') E(UB+HF-LYP) = -1589.98833145

H	-2.76240700	2.04086400	4.90803600
H	-1.73300300	3.54168300	3.17428400
H	1.62613700	1.71919700	2.14107400
H	2.32017100	3.07711100	1.23065000
C	-2.24644300	1.61964100	4.04971100
C	-1.67488500	2.46152900	3.07986100
H	4.48839300	2.76279700	0.42644300
H	-0.08155100	3.70396900	1.28223800
C	1.96757100	2.03677000	1.14777900
H	-2.54606000	-0.46108700	4.62793100
C	-2.13110600	0.22546000	3.89744000
C	4.36777300	1.68268200	0.45129500
C	3.10315600	1.13693900	0.72347700
C	-1.02167600	1.89148700	1.97402600
C	5.47473500	0.84289300	0.24713500
C	-0.39498700	2.72950600	0.87534900
C	2.88828800	-0.28876400	0.76985000
C	-1.46055000	-0.26981700	2.76908900
C	5.33454000	-0.55115300	0.36086600
N	-0.93189300	0.54104900	1.82332000
O	1.66974100	-0.79225100	0.95920100
N	0.74868800	1.98801300	0.26563500
H	6.19245400	-1.20497700	0.24903800
C	4.06557500	-1.08995200	0.62806800
H	-1.14046500	2.89386800	0.09158300
H	-1.33567400	-1.33715600	2.62219900
H	0.96065700	2.37951200	-0.65479800
Ni	0.00000000	0.00003100	0.00004800
H	-6.19249300	1.20492400	-0.24911000
H	-0.96073200	-2.37943600	0.65486400
H	1.33564400	1.33718200	-2.62214800
H	1.14048500	-2.89375700	-0.09137800
C	-4.06559500	1.08996000	-0.62805000
C	-5.33456100	0.55112300	-0.36092600
N	-0.74868300	-1.98795000	-0.26555500
O	-1.66973800	0.79231800	-0.95911000
N	0.93191100	-0.54100800	-1.82321200
C	1.46055600	0.26984300	-2.76900000
C	-2.88828400	0.28880200	-0.76981700
C	-5.47473200	-0.84293000	-0.24725900
C	0.39503500	-2.72944600	-0.87518300
C	1.02174100	-1.89144900	-1.97386900
C	-3.10312800	-1.13690800	-0.72351300
C	-4.36774400	-1.68268700	-0.45140700
H	2.54608800	0.46108200	-4.62783200

C	2.13114600	-0.22545200	-3.89732300
H	-4.48834300	-2.76280600	-0.42660400
C	-1.96750100	-2.03669900	-1.14778700
H	0.08164000	-3.70393200	-1.28204900
C	1.67499100	-2.46150800	-3.07967100
C	2.24653600	-1.61963400	-4.04954100
H	-2.32007400	-3.07704500	-1.23072200
H	-1.62601000	-1.71907600	-2.14104600
H	2.76253200	-2.04087000	-4.90784100
H	1.73314800	-3.54166400	-3.17405500
I	3.91541900	-3.22271700	0.90493000
I	7.40190000	1.69537500	-0.19913400
I	-3.91548300	3.22273800	-0.90482600
I	-7.40190000	-1.69547000	0.19888400

(2) E(UB+HF-LYP) = -1645.712414

H	5.74366200	-0.75991000	-0.54703100
I	4.43235700	1.90655200	-1.54198100
I	5.67013200	-3.68026500	0.68110600
I	-2.58721500	-2.08549700	-2.66489600
C	4.68653000	-0.94139600	-0.38948500
H	1.27602100	5.25176700	-2.73967900
C	3.74228000	0.04125500	-0.72046700
C	4.23713400	-2.15985900	0.15008700
H	1.16651500	2.83938600	-1.95823400
C	0.72793600	4.98716600	-1.84154500
C	2.33580700	-0.13470900	-0.53777900
C	0.66669700	3.64489000	-1.43186200
O	1.45386700	0.81129900	-0.84608100
C	2.86473700	-2.39087900	0.33891500
H	2.51959500	-3.34472100	0.73021400
C	1.92182200	-1.40298100	0.00620600
H	-0.04455600	-1.55551700	-0.85361900
H	0.09344100	7.00737600	-1.36409600
O	-1.74412400	0.63281300	-1.04581700
C	-3.57612300	-0.96106000	-1.12489000
C	0.06843600	5.96158000	-1.06951700
H	-5.26316000	-2.31178000	-1.05242000
C	0.44196800	-1.70317000	0.11673100
C	-2.94847100	0.23402900	-0.64469900
C	-4.82995000	-1.39632500	-0.66502300
N	-0.01437400	3.27715400	-0.31731700
H	0.30045300	-2.75289800	0.41751900
Zn	-0.23155700	1.22145100	0.17723700
C	-0.63173400	5.56736200	0.08736000
H	-2.95777600	2.92826800	-0.25503300
C	-0.65348400	4.20683300	0.43865300
N	-0.30938000	-0.80390300	1.07342200
C	-3.71573600	1.01226800	0.29604100
C	-5.51520100	-0.62952600	0.29483100
H	1.98248100	3.21377000	1.66550600
H	-1.30545700	-1.02634500	1.00456500
H	-1.15589600	6.29600500	0.69913900
C	-3.19061900	2.37848800	0.66590600
N	1.13208800	1.36015200	2.07506400

C	2.06969800	2.32062100	2.27579300
C	-4.97003600	0.57917700	0.75784900
H	0.53040100	-1.84641400	2.75566800
I	-7.42276300	-1.30196200	1.03632400
N	-1.91629200	2.33771000	1.45863000
C	0.14932900	-0.85109600	2.48213300
H	3.85496500	2.96064600	3.31088600
C	1.22517700	0.19052800	2.75956300
C	3.12078100	2.17055600	3.19156600
C	-1.35236500	3.69041300	1.69130600
H	-3.96015100	2.94677800	1.21510800
H	-5.52406100	1.19748800	1.45985000
C	2.25455500	-0.03703700	3.69357800
C	3.21139300	0.96662800	3.91746600
H	-2.12238200	4.41705600	2.00064600
H	-2.05583700	1.83947500	2.33958600
H	-0.62096400	3.61968600	2.50663700
H	2.31534000	-0.99048700	4.21023300
H	4.02211600	0.80600100	4.62268900
H	-0.71674800	-0.65025700	3.12975300

(2') E(UB+HF-LYP) = -1645.715538

H	2.75176500	1.08928200	-4.49775700
H	-2.37667200	2.46447400	-1.43144800
C	2.50273100	0.26635300	-3.83588500
H	1.18920100	1.44605600	-2.58036900
H	-1.52923800	1.08336300	-2.16474900
H	3.75886900	-1.20678400	-4.82116000
C	-1.97447900	1.46316700	-1.23524200
C	1.62106900	0.46704100	-2.76379000
C	3.06101800	-1.01425300	-4.01100700
H	-0.06737700	2.09841000	-0.64867100
H	-1.91628800	2.88560500	1.04399200
C	-4.42421800	0.90349900	-0.62589500
N	-0.83540100	1.55125600	-0.25273600
C	-3.08455300	0.51854600	-0.82158800
C	-1.15704000	2.09234400	1.09557200
H	-0.22910400	2.52681500	1.48970900
N	1.27690300	-0.52246500	-1.90641700
C	-5.46922400	-0.00433200	-0.36975800
H	6.15866800	1.30854100	0.19496700
C	2.71531600	-2.03680400	-3.11179500
C	-2.76617400	-0.89109300	-0.72929200
H	3.14361800	-3.03038800	-3.20709200
C	4.03548300	1.03546200	0.50729900
C	5.36060300	0.59680300	0.37403200
C	1.81515800	-1.75815300	-2.06631600
O	-1.50989600	-1.32726900	-0.86093200
C	-5.12894700	-1.37040800	-0.31781900
H	-2.92802500	2.29713600	3.20866800
C	-3.82151600	-1.82144200	-0.48941300
C	-1.61226200	1.01413800	2.06650500
O	1.68557400	0.57980700	0.85455200
C	2.93846100	0.14985700	0.74247400
C	5.63191500	-0.78020800	0.47200200

C	-2.50203400	1.30222000	3.11919100
H	0.41967100	-3.26523000	-1.50596900
C	1.35034800	-2.84222900	-1.10602400
N	-1.07781700	-0.22479100	1.91291500
C	3.26750000	-1.24998500	0.85027900
C	4.59352100	-1.69452400	0.71334200
H	2.10331300	-3.64400600	-1.06530900
N	1.03538300	-2.31547700	0.24815300
C	-2.84007100	0.28872100	4.03071500
H	4.81218300	-2.75518400	0.80903200
H	-3.52975300	0.48978800	4.84577000
H	0.26628900	-2.85967200	0.64442800
C	-1.41347300	-1.20485300	2.78426300
C	2.17885700	-2.23822200	1.22401100
C	-2.28410400	-0.99435300	3.86302100
H	1.72839900	-1.93167100	2.17802100
H	-0.97927000	-2.18502500	2.60864500
H	2.62313600	-3.23735900	1.36076800
H	-2.52581800	-1.80964400	4.53710700
Zn	0.08924100	-0.37491800	-0.00030900
H	-6.48771700	0.33109700	-0.22725400
H	-3.56413500	-2.87385800	-0.44771200
I	-6.69656100	-2.81089000	0.05554200
I	-5.04109100	2.99927800	-0.69992000
I	3.60564500	3.13818300	0.34623300
I	7.65538100	-1.48879600	0.25229600

Zn 1 mode rb3lyp/6-31g(d)

E = -2963.148768 a.u.

H	2.15219800	5.60140200	-1.07026000
C	2.37489100	4.58141100	-0.76286600
H	3.37374200	-0.08919100	-0.53050100
C	3.51435600	4.31857400	0.00540100
C	1.51873000	3.55309400	-1.13919200
C	3.77699700	3.00152700	0.37887100
H	4.66689700	2.77601200	0.96619500
C	1.75925000	2.21010800	-0.76203700
C	2.93485100	1.94907600	0.00443600
O	0.92995500	1.25421600	-1.14267400
H	4.24972700	0.49541800	0.89319600
C	3.28014300	0.53147300	0.37125000
H	3.53088900	-1.61574100	1.95819800
N	-1.52408800	-0.19741300	-1.06908000
N	2.22096100	-0.09514300	1.19981400
Zn	0.35016300	-0.16560900	0.05392000
C	2.49477000	-1.46917900	1.61352800
H	1.82873900	-1.69844400	2.45451200
C	2.19289600	-2.44774800	0.49026000
N	1.20158900	-2.10052000	-0.34931500
H	3.67584700	-3.90769500	1.04076600
C	2.87214800	-3.65955200	0.35392400
C	0.85435100	-2.93782000	-1.33688200
H	0.05063000	-2.59945000	-1.98417600
C	2.50600600	-4.53205700	-0.66853600

C	1.47518700	-4.16682600	-1.53456300
H	3.02216000	-5.47993400	-0.79194600
H	1.16150900	-4.81253800	-2.34794200
H	2.01967700	0.48645500	2.01042900
H	4.18267700	5.12103800	0.30435500
H	0.63380700	3.75366200	-1.73775300
O	-0.74599200	-0.03746400	1.60957300
C	-2.08704300	-0.23030400	1.35640900
H	-2.70042900	0.33395400	2.08540800
C	-2.49304800	-1.71122300	1.47574000
H	-3.57227600	-1.87029600	1.36279000
H	-1.97674200	-2.32162300	0.72458100
H	-2.18918900	-2.07351500	2.46325400
C	-2.44932200	0.36698800	-0.06395800
H	-2.24119200	1.43841100	-0.00447300
H	-1.31859900	0.49499600	-1.78800000
H	-2.02316600	-0.96749900	-1.52139300
C	-3.89341800	0.08942300	-0.49703800
O	-4.11468500	-0.83162000	-1.29059600
N	-4.90840100	0.83085900	0.04494000
C	-4.75460300	1.96918500	0.93765200
H	-5.28627200	1.78817800	1.88103100
H	-3.70956000	2.15922500	1.17144400
H	-5.17931400	2.87215200	0.47759300
C	-6.28383300	0.51948300	-0.32081200
H	-6.74655500	1.37187500	-0.83619900
H	-6.27967400	-0.34641000	-0.98060700
H	-6.87491900	0.29849500	0.57745200

Zn 2 mode rb3lyp/6-31g(d)

E = -2963.093592 a.u.

H	-5.29602400	-3.37652400	-1.43657300
C	-4.82023100	-2.49318800	-1.01557700
H	-2.73728900	1.73363600	-0.25488100
C	-5.46510000	-1.77265800	-0.00309100
C	-3.57580600	-2.09750500	-1.49246200
C	-4.83857000	-0.64107300	0.51510300
H	-5.33198400	-0.05816000	1.29250100
C	-2.91864400	-0.95925700	-0.97135500
C	-3.58976400	-0.22052600	0.04401900
O	-1.73712000	-0.59287400	-1.44025200
H	-3.62379300	1.54555500	1.26850500
C	-2.95152500	1.03390100	0.56387000
H	-1.83049400	2.58197900	2.33346800
N	1.36187400	-0.50533500	-1.31790000
N	-1.64199400	0.75909500	1.23166300
C	-1.06199600	1.94714500	1.86850700
H	-0.39298100	1.60801800	2.66994000
C	-0.23699300	2.76450800	0.88793500
N	0.37859200	2.06872100	-0.08192000
H	-0.58195000	4.67709900	1.81734600
C	-0.05537300	4.13899400	1.03461600
C	1.24824500	2.69359800	-0.89737000
H	1.79798200	2.06864500	-1.59943700
C	0.81697800	4.79759600	0.16874500

C	1.49430500	4.06116600	-0.80210900
H	0.97414900	5.86866700	0.26054800
H	2.20440600	4.52778600	-1.47629400
H	-1.78445700	0.02752700	1.92619400
H	-6.43639800	-2.08485400	0.36950200
H	-3.07326300	-2.65339100	-2.27910000
O	3.56547100	0.25131000	-2.19126100
C	3.78714700	-0.66437100	-1.23035400
H	4.64415200	-0.40417600	-0.55957600
C	4.04439300	-2.08665200	-1.78599500
H	4.25807200	-2.84491300	-1.01881500
H	3.18783500	-2.43053800	-2.38012800
H	4.89963400	-2.03201700	-2.46709900
C	2.45366400	-0.59160800	-0.31279700
H	1.19388100	-1.44319900	-1.69128400
H	1.94888300	-0.01251500	-2.07331400
C	1.89949100	-1.44158800	0.83642400
O	0.65036600	-1.39340300	1.02378600
N	2.66901100	-2.16218800	1.67588600
H	2.53624500	0.41299200	0.12828200
C	4.12683700	-2.15454700	1.70084700
H	4.51993300	-3.15432000	1.48254600
H	4.52599600	-1.44963200	0.97606600
H	4.46592300	-1.86172400	2.70261800
C	2.04210100	-2.92788200	2.75099000
H	0.97558800	-3.01753100	2.55599000
H	2.49850600	-3.92264600	2.79476300
H	2.19502800	-2.43255300	3.71894500
Zn	-0.31115500	0.01893900	-0.33042200