

Electronic Supplementary Information

Synthesis, Cytotoxic and Hydrolytic Studies of Titanium Complexes Anchored by a Tripodal Diamine Bis(phenolate) Ligand

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Growth inhibition curves:

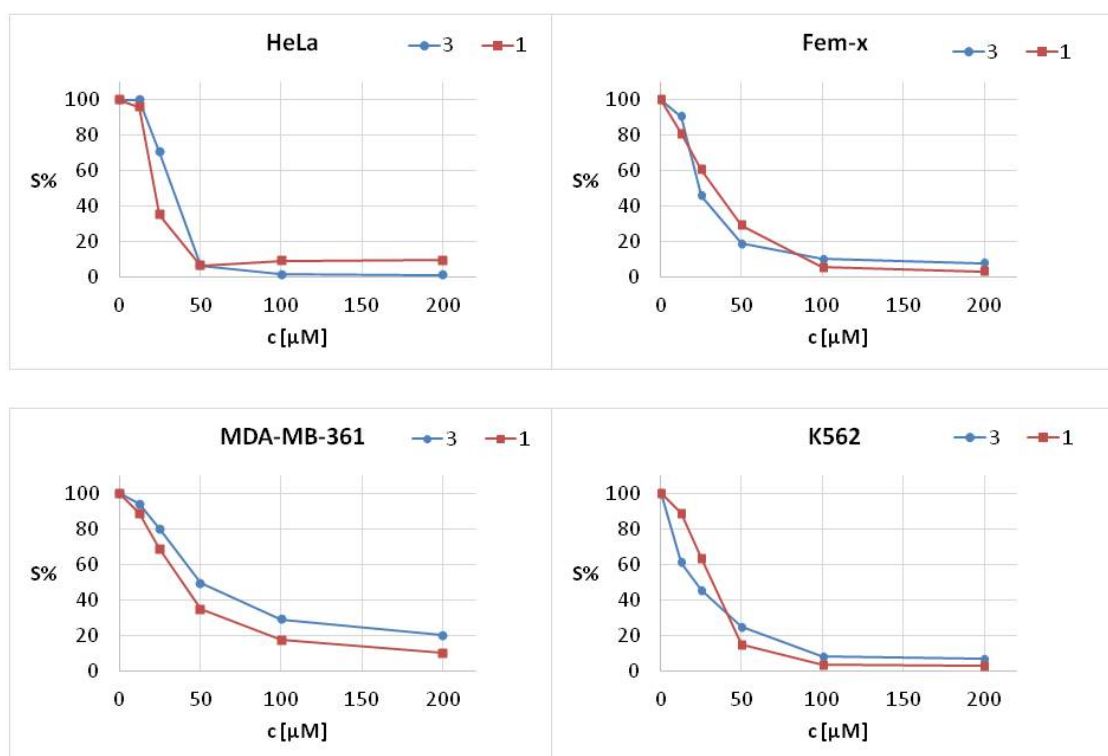


Figure S1. Growth inhibition curves of compounds 1 and 3 in HeLa, Fem-x, MDA-MB-361 and K562 cells

ESI-MS data for compounds 3, 4 and 5:

The mass spectrum of **3** shows four major peaks that are tentatively assigned to the following species:

$m/z = 524.5$ (free ligand, $\text{H}_2(\text{tBu}_2\text{O}_2\text{NN}')$)

$m/z = 587.5$ ($[\text{Ti}(\text{tBu}_2\text{O}_2\text{NN}')(\text{OH})]^+$)

$m/z = 601.8$ ($\text{H}_2(\text{tBu}_2\text{O}_2\text{NN}') + \text{HO}^i\text{Pr} + \text{H}_2\text{O}$)

$m/z = 629.5$ ($[\text{Ti}(\text{tBu}_2\text{O}_2\text{NN}')(\text{O}^i\text{Pr})]^+$)

$m/z = 1215.8$ ($[(\text{Ti}(\text{tBu}_2\text{O}_2\text{NN}')(\text{O}^i\text{Pr}))-\mu\text{-O}-(\text{Ti}(\text{tBu}_2\text{O}_2\text{NN}'))]^+$)

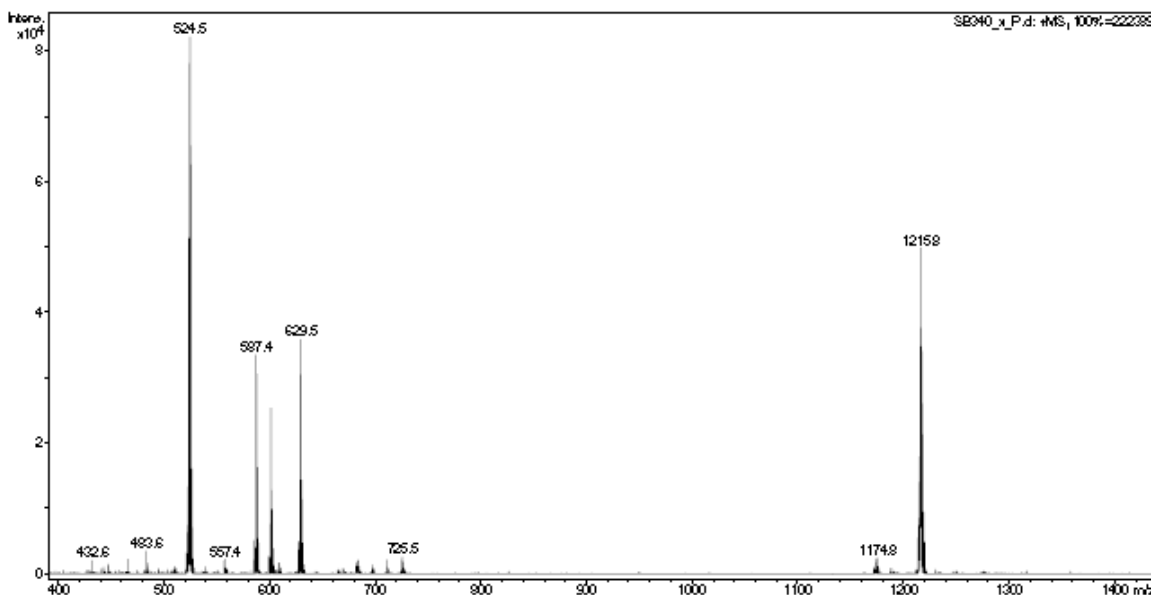


Figure S2. ESI-MS of **3** in CH_3CN .

The mass spectrum of **4** shows one major peak that was assigned to the following species:

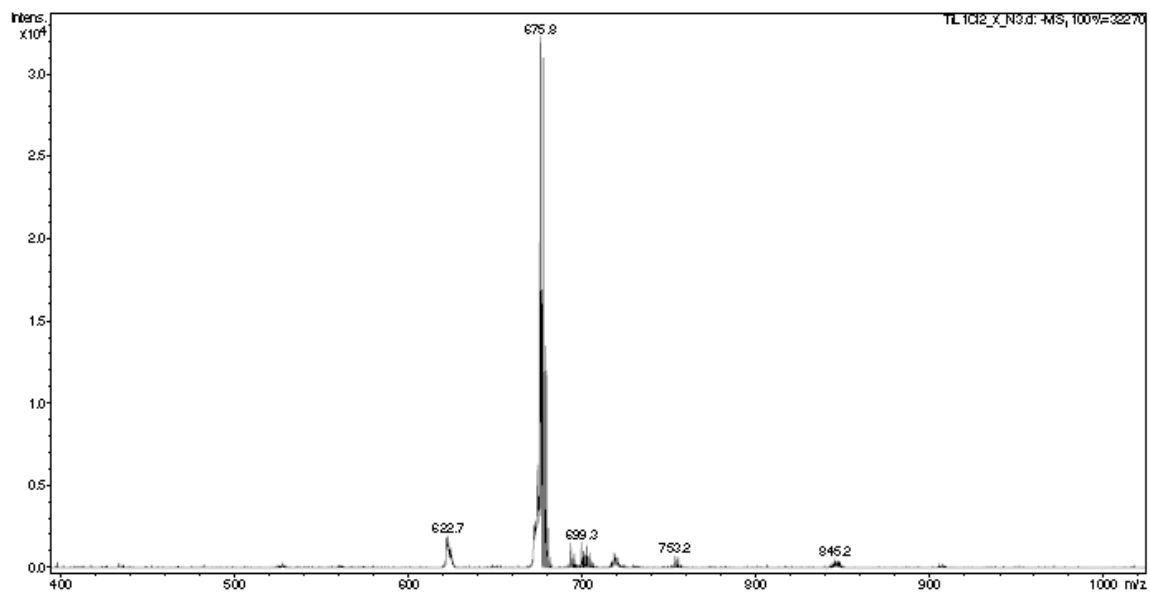
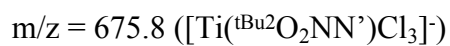


Figure S3. ESI-MS of **4** in THF.

The mass spectrum of **5** shows one major peak that was assigned to the following species:

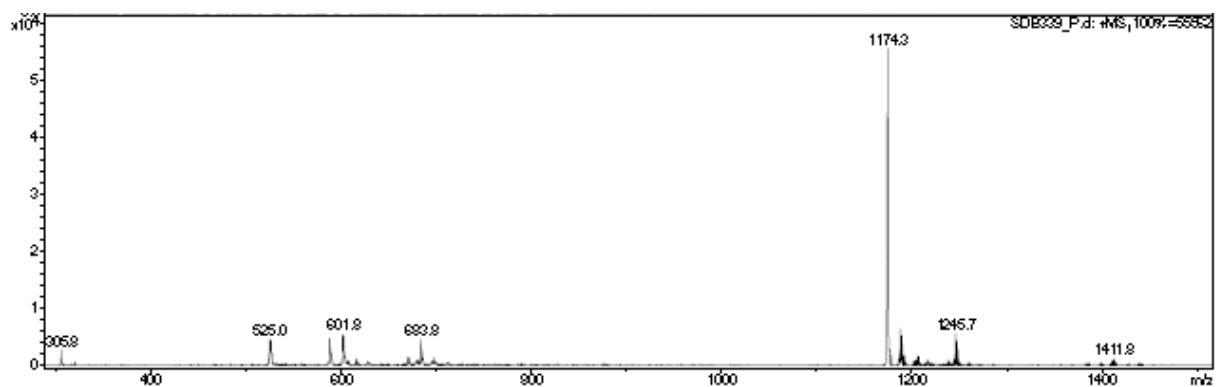


Figure S4. ESI-MS of **5** in CH₂Cl₂/CH₃CN.

X-ray data for compound 4:

The molecular structure of **4** is depicted in Figure S1. The compound crystallizes in the monoclinic system, space group $P2_1/a$. The titanium coordination geometry is distorted octahedral, with the two phenolate moieties *trans*-coordinated, with an angle of $159.0(2)^\circ$ between the planes containing the phenolate rings. The titanium atom is slightly away from the equatorial mean square plane ($0.198(1)^\circ$). The sidearm fragment is coordinated to the metal and the tripodal ligand forces the two chloride ligands to adopt mutually *cis* dispositions. The Ti-Cl distances compare well with the values reported for other titanium(IV) systems supported by O- and N-based ligands.¹

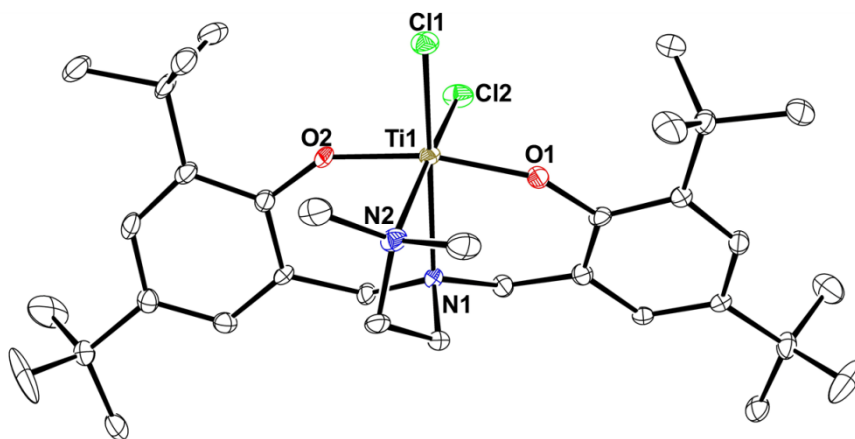


Figure S1. ORTEP diagram of **4** using 30 % probability level ellipsoids. Hydrogen atoms and disordered carbon atoms are omitted for clarity.

¹ a) G. J. Clarkson, V. C. Gibson, P. K. Y. Goh, M. L. Hammond, P. D. Knight, P. Scott, T. M. Smit, A. J. P. White, Williams, D. J. *Dalton Trans.* 2006, 5484-5491; b) K. J. Blackmore, N. Lal, J. W. Ziller, A. F. Heyduk, *Eur. J. Inorg. Chem.* 2009, 735-743; c) J. Saito, M. Mitani, S. Matsui, Y. Tohi, H. Makio, T. Nakano, H. Tanaka, N. Kashiwa, T. Fujita, *Macromol. Chem. Phys.* 2002, 203, 59-65.

Table S1. Selected structural parameters for **4**.

<i>Distances (Å)</i>			
Ti1-O1	1.839(2)	Ti1-N1	2.272(3)
Ti1-O2	1.829(2)	Ti1-N2	2.307(3)
Ti1-Cl2	2.307(1)	Ti1-Cl1	2.303(1)
Ti1-eq. plane ^a	0.198(1)		
<i>Angles (°)</i>			
O1-Ti1-O2	166.6(1)	O2-Ti1-Cl1	97.5(1)
O1-Ti1-Cl2	89.8(1)	N1-Ti1-Cl2	93.1(1)
O1-Ti1-N1	81.4(1)	N2-Ti1-Cl2	170.7(1)
O1-Ti1-N2	91.3(1)	N2-Ti1-Cl1	87.8(1)
O1-Ti1-Cl1	95.6(1)	N1-Ti1-N2	77.9(1)
O2-Ti1-Cl2	90.1(1)	N1-Ti1-Cl1	165.3(1)
O2-Ti1-N1	85.3(1)	Cl2-Ti1-Cl1	101.4(1)
O2-Ti1-N2	86.7(1)	θ^b	159.0(2)

^a The equatorial plane is defined by atoms O1, O2, N2 and Cl2.

^b θ is the dihedral angle between the planes containing the phenolate rings.

Atom coordinates for the optimized molecules:

1*

8	5.120048000	6.861504000	0.352839000	6	4.158588000	5.532259000	-5.590886000
8	3.753023000	7.281990000	2.659616000	6	8.348233000	11.824263000	0.985588000
8	3.046427000	5.301036000	-0.345238000	1	9.043346000	12.355909000	1.633491000
7	1.397690000	5.655163000	1.961953000	6	4.746717000	6.784795000	-3.588170000
7	4.135672000	4.619054000	2.146543000	6	7.555415000	12.555633000	0.096840000
6	5.496028000	5.708718000	5.423207000	6	6.856753000	8.791068000	-3.162269000
1	6.061068000	4.799912000	5.624077000	1	6.680564000	8.079690000	-3.974154000
6	1.671113000	4.252453000	2.318902000	1	6.687815000	9.797316000	-3.572045000
1	1.615969000	3.656239000	1.406925000	6	7.380461000	9.753315000	0.249920000
1	0.895209000	3.872506000	3.004230000	6	5.463209000	9.730161000	-1.357726000
6	3.639265000	1.731607000	-0.139897000	1	4.979943000	10.420248000	-2.065968000
1	4.194571000	1.030436000	0.481233000	1	4.691892000	9.409967000	-0.646493000
6	2.256356000	3.558805000	-1.752349000	6	5.477512000	4.470334000	-3.821566000
6	3.722495000	3.093805000	0.140719000	6	4.601167000	8.005006000	-2.732800000
6	4.261495000	7.084816000	3.872242000	1	3.901424000	7.808925000	-1.914125000
6	4.577111000	7.795014000	6.145344000	1	4.168919000	8.817486000	-3.336363000
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6	5.302978000	6.636876000	6.444115000	1	8.866979000	5.365501000	-2.576252000
6	2.207972000	2.188038000	-1.999242000	1	7.850903000	6.254410000	-3.714756000
1	1.623859000	1.838035000	-2.848963000	1	9.612560000	6.536863000	-3.701793000
6	4.995993000	5.921826000	4.138553000	6	9.812902000	7.472794000	-1.294721000
6	2.877742000	1.252383000	-1.206298000	1	9.683588000	8.189353000	-0.483543000
6	3.029527000	4.081992000	2.969083000	1	10.053558000	6.501555000	-0.861414000
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6	4.663246000	3.609021000	1.187554000	6	2.765177000	-0.220846000	-1.484890000
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1	5.521366000	4.082104000	0.696593000	1	3.600490000	-0.774960000	-1.047146000
6	4.048224000	8.042807000	4.882625000	1	1.841021000	-0.640297000	-1.068350000
6	5.295330000	4.968051000	3.022803000	6	3.486594000	5.445916000	-6.933193000
1	6.065527000	5.382640000	2.363681000	1	4.201157000	5.197269000	-7.726038000
1	5.702408000	4.037735000	3.446698000	1	2.712149000	4.670685000	-6.944997000
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8	6.077183000	5.759598000	-1.925123000	1	2.308394000	5.026957000	-3.314860000
8	7.317968000	8.425517000	0.275707000	1	0.823231000	4.061209000	-3.274063000
7	8.561899000	7.370239000	-2.058335000	1	1.102363000	5.353225000	-2.083068000
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1	3.596724000	7.573919000	-5.217930000	1	6.245283000	2.469236000	-3.978784000
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1	8.968452000	8.847522000	-3.530096000	1	8.484858000	9.036959000	2.702453000
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1	5.994875000	12.394735000	-1.375563000	1	9.684643000	10.347613000	2.710618000
6	8.284316000	10.436179000	1.084382000	6	3.286004000	9.293375000	4.563887000
6	6.543029000	10.464160000	-0.622638000	1	3.750410000	9.832240000	3.731635000
6	5.442169000	5.674516000	-3.089654000	1	2.261350000	9.069593000	4.248494000
6	4.834393000	4.430080000	-5.054834000	1	3.242187000	9.958413000	5.430112000
1	4.862412000	3.500342000	-5.620933000				

3*

8	5.167644000	6.724086000	0.274238000	1	10.809016000	7.956680000	-1.487474000
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8	7.274388000	8.380073000	0.491254000	6	4.063237000	5.295363000	-7.028268000
7	8.761628000	7.481349000	-1.814000000	1	4.798514000	5.011045000	-7.788995000
7	6.018547000	8.406476000	-2.076930000	1	3.268824000	4.540158000	-7.052115000
6	4.530394000	6.528376000	-4.871616000	1	3.620266000	6.247501000	-7.333353000
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6	6.594576000	11.765426000	-0.640042000	6	6.818331000	3.238562000	-3.336471000
1	5.989153000	12.273027000	-1.389861000	1	6.409612000	2.899109000	-2.378878000
6	8.105841000	10.443058000	1.305237000	1	6.812764000	2.396008000	-4.032862000
6	6.515198000	10.377013000	-0.538603000	1	7.861245000	3.518144000	-3.148910000
6	5.855593000	5.552005000	-3.094171000	6	8.870105000	9.723756000	2.376787000
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1	5.576016000	3.439030000	-5.736114000	1	9.595303000	9.016825000	1.959505000
6	4.687940000	5.395002000	-5.664363000	1	9.408154000	10.428845000	3.015637000
6	8.146520000	11.828323000	1.173994000	8	7.873711000	5.656546000	0.385465000
1	8.775033000	12.394100000	1.860234000	6	8.035255000	4.257297000	0.367637000
6	5.090306000	6.617852000	-3.596450000	6	6.965351000	3.594006000	1.222307000
6	7.412499000	12.516034000	0.202506000	1	7.065241000	3.905158000	2.267408000
6	7.046320000	8.745246000	-3.079001000	1	5.971285000	3.882583000	0.871129000
1	6.974353000	8.006357000	-3.882160000	1	7.052621000	2.503233000	1.175864000
1	6.838754000	9.728493000	-3.528034000	6	9.439541000	3.908628000	0.840519000
6	7.292778000	9.705400000	0.419677000	1	9.592893000	4.262782000	1.865123000
6	5.523650000	9.604346000	-1.356411000	1	9.598476000	2.825400000	0.821123000
1	5.055654000	10.285772000	-2.085559000	1	10.195781000	4.375103000	0.201310000
1	4.723401000	9.242669000	-0.698308000	1	7.908785000	3.914949000	-0.671328000
6	6.028195000	4.390798000	-3.879405000	6	4.592883000	7.272623000	1.437337000
6	4.821485000	7.808515000	-2.728162000	1	4.963163000	8.304307000	1.557219000
1	4.151873000	7.524181000	-1.908473000	6	5.013244000	6.475176000	2.663327000
1	4.312789000	8.580940000	-3.326902000	6	3.079674000	7.304902000	1.272072000
6	9.108307000	6.435302000	-2.780600000	1	2.794298000	7.890369000	0.392106000
1	9.267626000	5.495946000	-2.247420000	1	2.692799000	6.288901000	1.142793000
1	8.302138000	6.281050000	-3.497842000	1	2.600406000	7.751051000	2.149696000
1	10.028531000	6.699299000	-3.325486000	1	4.654793000	5.443416000	2.587294000
6	9.907981000	7.676698000	-0.920029000	1	4.599749000	6.919570000	3.574918000
1	9.678440000	8.460613000	-0.198935000	1	6.103153000	6.456021000	2.745674000
1	10.092475000	6.751350000	-0.372369000				

5*

8	5.123041000	6.899432000	0.348968000	6	2.861374000	1.318098000	-1.266763000
8	3.723531000	7.386769000	2.636050000	6	3.054475000	4.107422000	2.923299000
8	2.999149000	5.372748000	-0.409086000	1	3.091057000	4.615086000	3.891779000
7	1.418966000	5.697768000	1.961277000	1	3.228211000	3.037752000	3.115370000
7	4.140464000	4.663975000	2.093553000	6	2.979967000	4.078919000	-0.710545000
6	5.567971000	5.772830000	5.324227000	6	4.661939000	3.678526000	1.110856000
1	6.136790000	4.860485000	5.499033000	1	5.075363000	2.821581000	1.666352000
6	1.684401000	4.289363000	2.293048000	1	5.502128000	4.171724000	0.608365000
1	1.618388000	3.707685000	1.372446000	6	4.105642000	8.101420000	4.853968000
1	0.915782000	3.900008000	2.981592000	6	5.309127000	5.030058000	2.940254000
6	3.629165000	1.804138000	-0.208738000	1	6.055641000	5.442872000	2.252192000
1	4.195345000	1.106908000	0.407308000	1	5.737562000	4.109448000	3.368158000
6	2.219057000	3.619732000	-1.803971000	6	1.028155000	6.448774000	3.157282000
6	3.708066000	3.167229000	0.072577000	1	0.902059000	7.500725000	2.894164000
6	4.281888000	7.159090000	3.816675000	1	1.796777000	6.385611000	3.927524000
6	4.674039000	7.846795000	6.096759000	1	0.078480000	6.064908000	3.562155000
1	4.536268000	8.580012000	6.890202000	6	0.325743000	5.784483000	0.986379000
6	5.410144000	6.687219000	6.362148000	1	0.587273000	5.215558000	0.094536000
6	2.178049000	2.249713000	-2.052950000	1	0.191370000	6.829014000	0.699240000
1	1.589426000	1.896869000	-2.898499000	1	-0.612588000	5.391853000	1.407968000
6	5.028379000	5.993210000	4.055362000	22	3.446565000	6.587144000	0.942491000

8	6.089933000	5.653543000	-1.873829000	1	10.645961000	7.582179000	-1.935343000
8	7.419946000	8.374048000	0.299999000	22	6.671521000	6.852280000	-0.567732000
7	8.543479000	7.291076000	-2.080357000	6	2.758707000	-0.155729000	-1.546370000
7	5.876653000	8.455218000	-2.090169000	1	2.787363000	-0.362440000	-2.621009000
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1	3.704660000	7.506630000	-5.224453000	1	1.820380000	-0.575541000	-1.163085000
6	8.303793000	8.625906000	-2.647832000	6	3.612027000	5.383886000	-6.945837000
1	8.522108000	9.364160000	-1.874724000	1	4.347438000	5.147684000	-7.723577000
1	8.990474000	8.819269000	-3.489350000	1	2.842041000	4.605118000	-6.986283000
6	6.555963000	11.786144000	-0.607288000	1	3.137986000	6.331653000	-7.215662000
1	5.867843000	12.309021000	-1.270507000	6	7.489976000	14.023306000	0.107087000
6	8.281841000	10.422850000	1.111796000	1	7.666231000	14.468629000	1.091346000
6	6.514069000	10.393088000	-0.562067000	1	8.298699000	14.365585000	-0.550668000
6	5.473686000	5.585803000	-3.048330000	1	6.556022000	14.437268000	-0.284197000
6	4.894681000	4.348482000	-5.032103000	6	6.016731000	6.449600000	7.717321000
1	4.923371000	3.417298000	-5.596010000	1	5.278808000	6.574105000	8.517383000
6	4.248939000	5.459458000	-5.585836000	1	6.426847000	5.438941000	7.797553000
6	8.278045000	11.813076000	1.044175000	1	6.833006000	7.152632000	7.921834000
1	8.959771000	12.364215000	1.690398000	6	1.521250000	4.604908000	-2.693484000
6	4.802107000	6.705332000	-3.565278000	1	2.248609000	5.159963000	-3.297053000
6	7.435406000	12.522685000	0.184409000	1	0.830778000	4.098260000	-3.373167000
6	6.872330000	8.786713000	-3.129272000	1	0.963496000	5.349268000	-2.117276000
1	6.690690000	8.120087000	-3.977630000	6	6.164941000	3.175020000	-3.187819000
1	6.723029000	9.815165000	-3.489335000	1	5.609149000	2.827516000	-2.309526000
6	7.397563000	9.700014000	0.284003000	1	6.210779000	2.355656000	-3.909948000
6	5.451111000	9.646352000	-1.311803000	1	7.180427000	3.400026000	-2.846719000
1	4.944510000	10.345828000	-1.996301000	6	9.177196000	9.682646000	2.060611000
1	4.694533000	9.278366000	-0.608287000	1	8.596493000	9.015753000	2.707052000
6	5.506600000	4.382174000	-3.783441000	1	9.903494000	9.053297000	1.532740000
6	4.632950000	7.930648000	-2.719154000	1	9.735253000	10.376852000	2.694326000
1	3.936010000	7.722502000	-1.900110000	6	3.329240000	9.353819000	4.578057000
1	4.183280000	8.728393000	-3.331684000	1	3.783092000	9.923354000	3.759430000
6	8.676301000	6.283217000	-3.136287000	1	2.301860000	9.128391000	4.270860000
1	8.773847000	5.297649000	-2.677292000	1	3.288468000	9.995637000	5.461978000
1	7.795455000	6.267127000	-3.778086000	8	2.454633000	8.014350000	0.335392000
1	9.565441000	6.483957000	-3.754653000	1	2.524410000	8.787288000	0.906876000
6	9.786970000	7.305354000	-1.304306000	8	7.739744000	5.673720000	0.359383000
1	9.690863000	8.019498000	-0.485889000	1	8.227560000	6.090906000	1.078378000
1	9.954009000	6.310717000	-0.886391000				

HO¹Pr

6	-0.199582000	1.645863000	-3.769580000
1	-0.194533000	2.722534000	-3.524950000
6	1.099138000	1.026990000	-3.270732000
6	-1.419533000	1.012998000	-3.128596000
1	-2.333265000	1.460647000	-3.527992000
1	-1.442148000	-0.060035000	-3.344083000
1	-1.406796000	1.151487000	-2.043586000
1	1.116773000	-0.043383000	-3.499752000
1	1.210772000	1.153989000	-2.189110000
1	1.968832000	1.492511000	-3.749279000
8	-0.347237000	1.468672000	-5.169328000
1	0.422033000	1.859800000	-5.595565000

H₂O

8	4.479911000	0.000000000	-0.886318000
1	4.479911000	0.756923000	-0.294232000
1	4.479911000	-0.756923000	-0.294232000

NET₃·HCl

Net₃

7	-0.255382000	-0.663862000	-0.117696000
6	-1.515703000	-1.007495000	0.526388000
1	-1.477594000	-0.870830000	1.624517000
1	-2.273346000	-0.304903000	0.159111000
6	-1.979681000	-2.422431000	0.206836000
1	-1.306157000	-3.183785000	0.611514000
1	-2.038194000	-2.564690000	-0.875868000
1	-2.969413000	-2.604080000	0.637921000
6	0.883978000	-1.290403000	0.535730000
1	1.034422000	-0.913673000	1.566773000
1	0.653935000	-2.356006000	0.639125000
6	2.180636000	-1.159014000	-0.248733000
1	2.554882000	-0.130937000	-0.268326000
1	2.035203000	-1.488930000	-1.281789000
1	2.959287000	-1.778870000	0.205896000
6	-0.106320000	0.768562000	-0.337969000
1	0.761780000	0.926330000	-0.987678000
1	-0.976357000	1.095213000	-0.921036000
6	0.026204000	1.651858000	0.904700000
1	0.922128000	1.409808000	1.485595000
1	-0.839101000	1.550086000	1.567653000
1	0.098646000	2.704856000	0.614020000

7	-0.032561000	-0.225083000	-0.082345000
6	-1.224661000	-0.963417000	0.431610000
1	-0.945393000	-1.466976000	1.363628000
1	-1.983128000	-0.218743000	0.688555000
6	-1.796245000	-1.940823000	-0.582196000
1	-1.092885000	-2.739265000	-0.825637000
1	-2.043709000	-1.432545000	-1.517097000
1	-2.702979000	-2.393358000	-0.170195000
6	1.266592000	-0.742259000	0.418052000
1	2.031921000	-0.093245000	-0.018080000
1	1.295937000	-0.627523000	1.507307000
6	1.526544000	-2.179008000	0.006711000
1	1.451939000	-2.279861000	-1.079696000
1	0.835525000	-2.878942000	0.484988000
1	2.538726000	-2.457427000	0.312384000
6	-0.148916000	1.249839000	0.069241000
1	0.663958000	1.676729000	-0.525369000
1	-1.077618000	1.528709000	-0.436946000
6	-0.125721000	1.758261000	1.498533000
1	0.832697000	1.573425000	1.991029000
1	-0.917846000	1.314195000	2.109469000
1	-0.284927000	2.839971000	1.493088000
1	0.037586000	-0.336586000	-1.226547000
17	0.318654000	-0.295707000	-2.908392000