

Supporting Information

Chemical modification of the siRNA seed region suppresses off-target effects by steric hindrance to base-pairing with targets

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1. Results of luciferase reporter assays of passenger strand

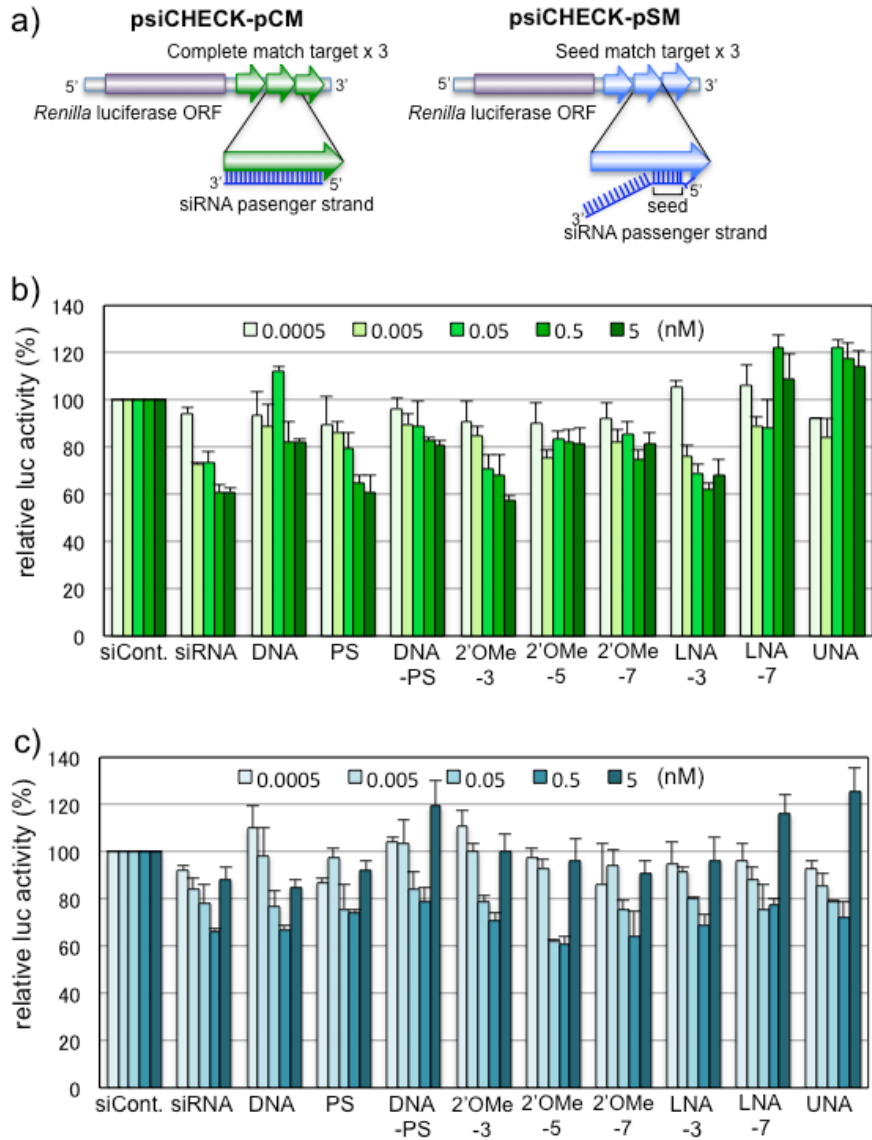


Figure S1. (a) Structures of reporter constructs for luciferase reporter assays. psiCHECK-pCM contains three tandem repeats of CM sequences of the siRNA passenger strand. psiCHECK-pSM contains three tandem repeats of SM sequences of the passenger strand. (b) Results of off-target effects on CM target using psiCHECK-pCM with unmodified or modified siRNA. (c) Results of seed-dependent off-target effects on SM target using psiCHECK-pSM with unmodified or modified siRNA. Each data shows an averaged value of three wells either of one or two independent experiments.

2. Additional information on microarray analyses

2.1 MA plots and cumulative distributions of the seed-matched off-target transcripts of siRNA guide strand.

a) RNA

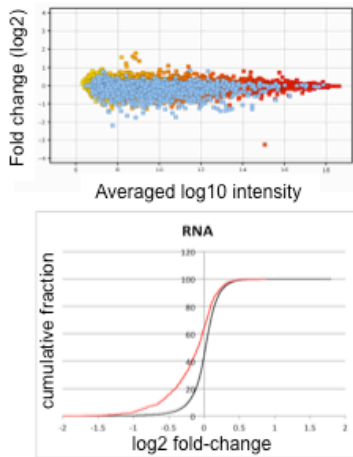
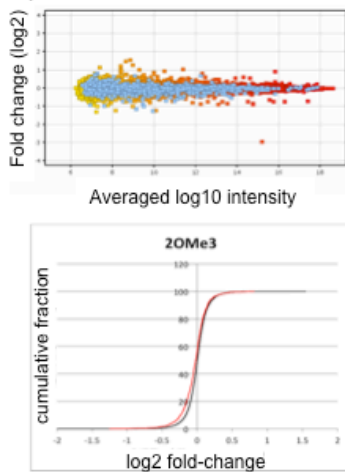
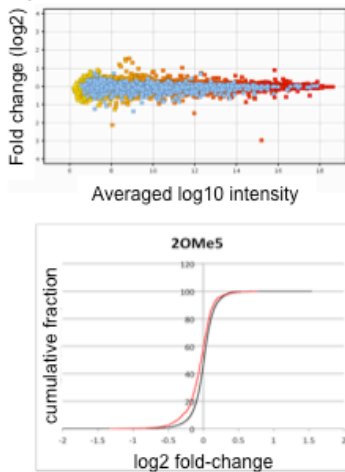


Figure S2. (a), 2'-OMe-3 (b), 2'-OMe-5 (c), 2'-OMe-7 (d), LNA-3 (e), or LNA-7 (f) siRNA. In the MA plots, the vertical bar indicates the mean \log_2 of signal intensities relative to those of mock transfection (M value), and the horizontal bar indicates the averaged \log_{10} signal intensities of mock and siRNA transfection (A value). Blue dots indicate mRNAs with guide strand SM sequences in their 3'UTRs, and red to yellow dots indicate non-SM mRNAs without guide strand SM sequences in their 3'UTRs. In the cumulative distributions, the horizontal axis indicates the M value of (a), and the vertical axis indicates the cumulative fraction of transcripts. The red line indicates the cumulative curve of SM transcripts of the guide strand, and black line indicates the cumulative curve of the other non-SM transcripts. The downregulation of SM transcripts was shown by the fold-change in the expression of SM transcripts compared to those of the other transcripts.

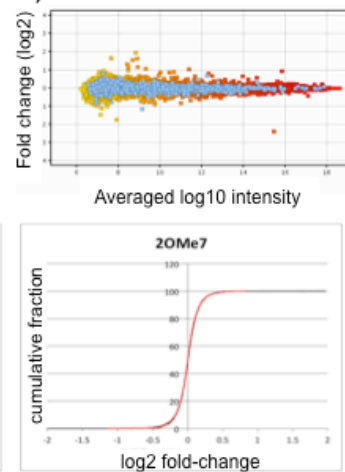
b) 2'-OMe-3



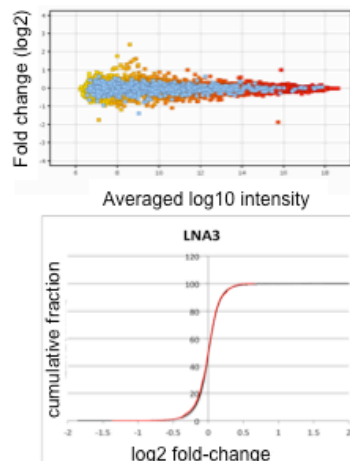
c) 2'-OMe-5



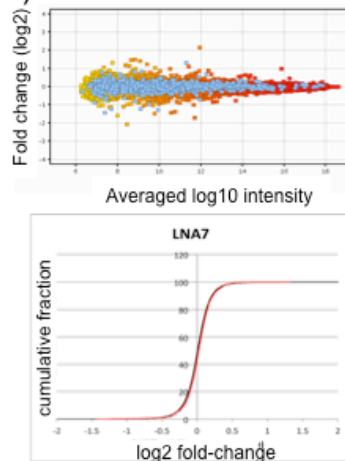
d) 2'-OMe-7



e) LNA-3



f) LNA-7



2.2 MA plots and cumulative distributions of the seed-matched off-target transcripts of siRNA passenger strand.

a) RNA

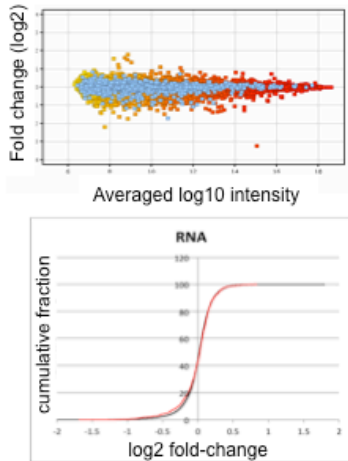
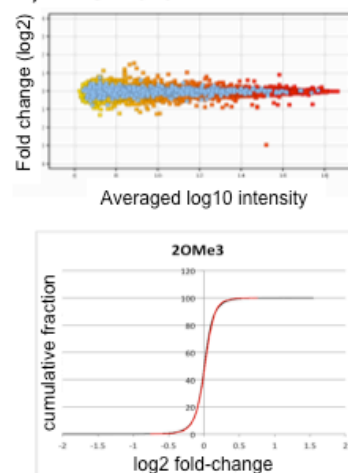
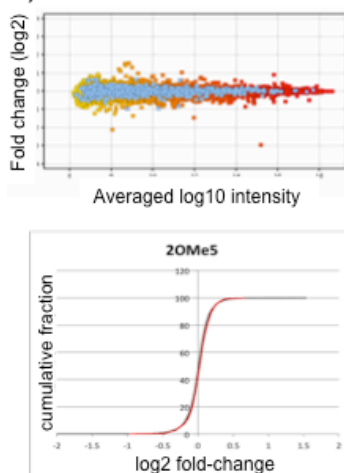


Figure S3. (a), 2'-OMe-3 (b), 2'-OMe-5 (c), 2'-OMe-7 (d), LNA-3 (e), or LNA-7 (f) siRNA. In the MA plots, the vertical bar indicates the mean log₂ of signal intensities relative to those of mock transfection (M value), and the horizontal bar indicates the averaged log₁₀ signal intensities of mock and siRNA transfection (A value). Blue dots indicate mRNAs with passenger strand SM sequences in their 3'UTRs, and red to yellow dots indicate non-SM mRNAs without passenger strand SM sequences in their 3'UTRs. In the cumulative distributions, the horizontal axis indicates the M value of (a), and the vertical axis indicates the cumulative fraction of transcripts. The red line indicates the cumulative curve of SM transcripts of the passenger strand, and black line indicates the cumulative curve of the other non-SM transcripts. The downregulation of SM transcripts was shown by the fold-change in the expression of SM transcripts compared to those of the other transcripts.

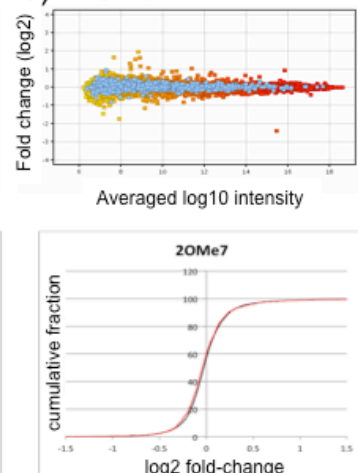
b) 2'-OMe-3



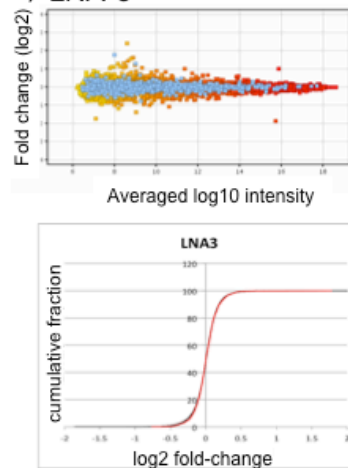
c) 2'-OMe-5



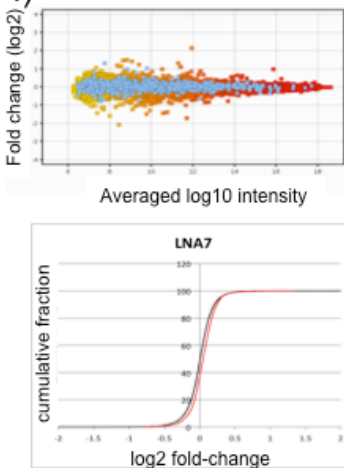
d) 2'-OMe-7



e) LNA-3



f) LNA-7



3. Supplementary computational data

3.1 Total energy and ZPE-corrected energy of 5'-GC-3' RNA

Table S1. Total energy and ZPE-corrected energy of 5'-GC-3' RNA

	Total energy (a.u)	Zero-point energy (a.u)	ZPE-corrected energy (a.u)	Relative energy (kJ mol ⁻¹)
unmodified RNA				
Structure 1 (Fig 4a) (*1)	-3632.733071	0.583801	-3632.149271	0
Structure 2 (Fig 4b) (*2)	-3632.718196	0.582579	-3632.135617	35.8
Structure 3 (Fig 4c) (*3)	-3632.712074	0.582627	-3632.129447	52
LNA				
Structure 1 (Fig 4d) (*4)	-3708.879704	0.595932	-3708.283772	0
Structure 3 (Fig 4f) (*5)	-3708.855978	0.594473	-3708.261505	58.4
2'-OMe				
Structure 1 (Fig 4g) (*6)	-3711.301628	0.640023	-3710.661605	0
Structure 2 (Fig 4h) (*7)	-3711.269529	0.636785	-3710.632744	75.7
Structure 4 (Fig 4i) (*8)	-3711.265146	0.637625	-3710.627521	89.4

(*1) Figure 4a

Unmodified 5'-GC-3' RNA (Structure 1), W-C face

Number of atoms = 78

Total charge = -3

C	-2.443964398	0.232242153	-1.774223145
C	-3.373884669	-1.736805695	-0.939829159
O	-3.619819344	-0.506362217	-1.641346728
H	-2.317712894	0.562354337	-2.809516552
C	-4.544768236	-2.049052985	-0.026240322
H	-4.298197934	-2.955698536	0.542755917
C	-1.291300156	-0.674386652	-1.354802021
C	-1.975163297	-1.587528259	-0.320158368
H	-0.430568885	-0.1191609	-0.97225461
O	-1.339139037	-2.844454615	-0.285727308
H	-2.013845644	-1.133763506	0.674962123
H	-5.418195628	-2.270314151	-0.653317192
O	-4.822702099	-0.972740486	0.83245293
P	-6.403029485	-0.823973972	1.371567567
O	-7.15201889	-0.545147498	-0.094275812
C	-6.789673034	0.636364652	-0.770953257
H	-6.722031603	1.482894882	-0.07638427
H	-5.825972385	0.52021765	-1.283827375
H	-7.565695094	0.847223321	-1.520033819
O	-6.910966061	-2.150996716	1.822558529
O	-6.410470729	0.43078353	2.178415168
P	-0.130071945	-3.123496227	0.860205629
O	-0.535219797	-2.460176416	2.129775662
O	0.255343816	-4.545196429	0.660269493
O	1.0691836	-2.13367626	0.262732664
C	1.890420706	-2.47626828	-0.823191387
C	2.908414112	-1.366452422	-1.03391229
H	1.296315447	-2.581579384	-1.740455306

H	2.419408396	-3.418665063	-0.636139392
C	3.914665428	-1.134534655	0.100327676
O	2.223763371	-0.120664765	-1.211549213
C	4.231288918	0.368457421	-0.061545787
C	2.897077905	0.926618789	-0.568450709
H	3.097467151	1.742280846	-1.262346879
O	5.16449147	0.602149304	-1.091237996
O	4.990611566	-2.02424797	-0.085038686
H	4.544423069	0.825933173	0.881756662
H	3.443243985	-1.303188369	1.075822831
N	-2.514863672	1.448495864	-0.950620283
C	-3.323825833	1.744412137	0.130749517
N	-3.067410707	2.922792357	0.645971942
C	-2.033680013	3.42072808	-0.119694099
C	-1.670303409	2.50730987	-1.098031499
N	-0.626305351	2.559002046	-1.96642092
C	0.128570521	3.604862553	-1.775277366
N	1.313663302	3.757842934	-2.476660653
N	-0.184736679	4.616125547	-0.90558031
C	-1.249287955	4.609581263	0.029376178
O	-1.360650765	5.538510368	0.822182584
H	0.537165514	5.292040929	-0.688486194
H	2.0820406	3.940721028	-1.821974459
H	1.501034777	2.890407477	-2.969132445
H	-4.064610679	1.037926016	0.490306058
N	2.028104266	1.504980573	0.479760506
C	2.032202491	2.899947662	0.665134397
O	2.818438278	3.599085014	0.004785876
N	1.132093373	3.437062753	1.526596187
C	0.235683421	2.665920853	2.126734282
N	-0.716451668	3.291244076	2.882657448
H	-0.849287478	4.261592349	2.611512965
H	-1.597953217	2.794745982	2.936785534
C	0.236686326	1.248420795	2.005097163
C	1.149759369	0.715642905	1.1560831
H	-0.469145696	0.60182558	2.512174619
H	1.183516109	-0.350554429	0.953256693
P	6.386056196	-1.915621561	0.813658955
O	6.1704097	-1.013905291	1.977882122
O	6.989606198	-3.276584009	0.847541397
O	7.284594646	-0.993015715	-0.292206607
C	7.614051727	-1.638421341	-1.501693919
H	8.342932333	-1.010426462	-2.029382848
H	6.724535945	-1.760992326	-2.135115916
H	8.046026731	-2.625634029	-1.304677665
O	-0.929226074	-1.45662249	-2.4753503
H	-3.307856616	-2.549776055	-1.677243666
H	-0.801754315	-2.345165048	-2.097581222
H	6.00044667	0.18431123	-0.803573879

H 3.486190935 -1.587398115 -1.94176854

(*2) Figure 4b

Unmodified 5'-GC-3' RNA (Structure 2), rigid strand 1

Number of atoms = 78

Total charge = -3

C	-2.403497345	0.196308102	-0.993885143
C	-2.463307104	-2.131182005	-0.903653225
O	-3.043311378	-0.946229572	-1.469466715
H	-2.035226381	0.808841573	-1.822145152
C	-3.563601642	-3.140008586	-0.636356483
H	-3.115091462	-4.022695288	-0.161296972
H	-1.758830256	-2.559517731	-1.629616981
C	-1.206491647	-0.248327913	-0.151934973
C	-1.636059777	-1.658828993	0.29729266
O	-0.132906546	-0.275805873	-1.053955307
H	0.641870225	-0.653559482	-0.603124714
H	-1.015272634	0.416741548	0.697086599
O	-0.584343651	-2.574111439	0.495784294
H	-2.263931512	-1.582578258	1.192735655
H	-3.998029221	-3.452423101	-1.595053107
O	-4.554510311	-2.570577483	0.184658979
P	-6.08471955	-3.24496004	0.117638095
O	-6.430552086	-2.950796324	-1.488806474
C	-6.496711739	-1.598897856	-1.87991055
H	-7.058030688	-1.002622569	-1.149621234
H	-5.493388656	-1.166409284	-1.991875137
H	-7.009842909	-1.553698417	-2.850373537
O	-5.993675257	-4.728556498	0.234600166
O	-6.92442233	-2.358601833	0.976125667
P	0.570675925	-2.316790454	1.664802052
O	0.139948908	-1.188279884	2.543000564
O	1.057039859	-3.650458305	2.103494779
O	1.753420185	-1.614639488	0.692770781
C	2.545334467	-2.3537323	-0.204920001
C	3.48661413	-1.379346935	-0.906940339
H	1.904148241	-2.849597945	-0.946808932
H	3.129474618	-3.117620832	0.321761552
H	4.001128012	-1.902414124	-1.724230372
C	4.565955056	-0.722709787	-0.034144223
O	2.708479656	-0.311378694	-1.452096825
C	4.715565975	0.672259373	-0.688913221
C	3.309830174	0.942860429	-1.242985275
H	3.379200778	1.489601431	-2.181748043
O	5.575053595	0.641247383	-1.804044044
O	5.710930996	-1.542965817	-0.05953213
H	5.029656435	1.425424709	0.04122475
H	4.219332254	-0.603735302	0.998698111
H	6.457726079	0.393301401	-1.464846407

N	-3.37465075	1.038928127	-0.277217265
C	-4.600366863	0.711594708	0.267730037
N	-5.270741053	1.763194625	0.677793771
C	-4.450607644	2.831043836	0.391987824
C	-3.265860463	2.391395427	-0.187605864
N	-2.190993559	3.119709834	-0.603788306
C	-2.335564978	4.391128331	-0.396994439
N	-1.290939376	5.285043794	-0.603848584
N	-3.478912625	4.941850731	0.133000774
C	-4.636131549	4.241598754	0.584390587
O	-5.563228268	4.884740801	1.05492237
H	-3.479295468	5.926529233	0.360179906
H	-1.497521818	6.045233812	-1.239599023
H	-0.406261864	4.807041565	-0.819619612
H	-4.926944458	-0.321409957	0.335948394
N	2.461595885	1.783037895	-0.372981915
C	2.058857665	3.063361119	-0.831382955
O	2.467411825	3.494940224	-1.901887557
N	1.213584634	3.784422232	-0.021484735
C	0.784533597	3.27845462	1.121818113
N	-0.015076853	4.07585189	1.904425062
H	-0.437826184	4.852604292	1.409257968
H	-0.642322628	3.580595848	2.521936293
C	1.135111575	1.984372371	1.58100563
C	1.967949068	1.274361048	0.782020482
H	0.723629164	1.522564033	2.470040166
H	2.222109141	0.250375439	1.023403936
P	7.130878682	-1.067988583	0.667549397
O	6.881070242	0.120002646	1.529341728
O	7.859037678	-2.306717674	1.058586802
O	7.885902122	-0.452696368	-0.720699609
C	8.219484935	-1.406335954	-1.70527046
H	8.813854417	-0.898249695	-2.474731881
H	7.314450493	-1.820972336	-2.169525903
H	8.798798794	-2.226047203	-1.266503319

(*3) Figure 4c

Unmodified 5'-GC-3' RNA (Structure 3), rigid strand 2

Number of atoms = 78

Total charge = -3

C	-2.632249834	0.420678559	-0.871013601
C	-2.61551079	-1.894425387	-0.604707828
O	-3.248668708	-0.76838536	-1.251984535
H	-2.39514606	1.026194567	-1.752310078
C	-3.662624674	-2.940169239	-0.277823753
H	-3.166522233	-3.761482379	0.256235956
C	-1.363199467	0.041672131	-0.117409392
C	-1.795255313	-1.281324128	0.536922749
O	-0.381788714	-0.184287658	-1.100743744

H	-1.056277151	0.788171618	0.621299904
O	-0.729322208	-2.132969724	0.870623312
H	-2.427683571	-1.078592658	1.409542757
H	-4.057220889	-3.339210894	-1.221233474
O	-4.706651477	-2.395265848	0.492242572
P	-6.198817945	-3.151730443	0.378858773
O	-6.509864334	-2.867020335	-1.236393241
C	-6.639388041	-1.519713434	-1.625675892
H	-7.239253412	-0.955407553	-0.900500387
H	-5.657206954	-1.038972989	-1.725208934
H	-7.142738662	-1.498636735	-2.602197329
O	-6.026358539	-4.628147936	0.490365908
O	-7.11337226	-2.319945103	1.213700015
P	0.432856649	-1.601824629	1.955054287
O	-0.021090179	-0.310868428	2.545033163
O	0.914508474	-2.797160672	2.695879925
O	1.620288638	-1.171662582	0.826111814
C	2.514053161	-2.187022341	0.40981274
C	3.639984118	-1.599222086	-0.418756169
H	1.975006168	-2.930226711	-0.194264544
H	2.940412173	-2.698067866	1.278985651
C	4.575515282	-0.598103915	0.272222242
O	3.083883393	-0.909597353	-1.54044735
C	5.043016582	0.273073755	-0.917926149
C	3.832778929	0.236388067	-1.858986201
H	4.183567308	0.204791732	-2.890293697
O	6.099795744	-0.327985451	-1.628869261
O	5.583214556	-1.317663584	0.942125593
H	5.295700981	1.289496828	-0.599867221
H	4.024452904	0.022816668	0.988005317
N	-3.560727404	1.217481574	-0.04254798
C	-4.706527977	0.79563196	0.610048906
N	-5.31412306	1.765006923	1.247660337
C	-4.532462864	2.872640946	1.020396294
C	-3.437988605	2.545358855	0.227298199
N	-2.436739691	3.366559322	-0.212119126
C	-2.530884506	4.583824275	0.248089983
N	-1.548493964	5.515568792	-0.009274938
N	-3.566974913	5.005188797	1.037310527
C	-4.668199088	4.218055497	1.495693279
O	-5.513724249	4.757089155	2.191490162
H	-3.529934128	5.926352563	1.451551752
H	-1.873650236	6.460273492	-0.157625804
H	-0.872002289	5.204613641	-0.709340807
H	-5.012509252	-0.245547555	0.585572514
N	2.941473213	1.407646178	-1.790739794
C	2.856090101	2.25715596	-2.925964066
O	3.71623729	2.202958049	-3.794374823
N	1.75503148	3.073190492	-3.007714147

C	0.925323127	3.144565331	-1.994081245
N	-0.234338034	3.89490896	-2.176517965
H	-0.378314142	4.078074001	-3.163345327
H	-1.046603688	3.456260523	-1.734056292
C	1.12188172	2.49427866	-0.75118395
C	2.106386136	1.559667165	-0.734507002
H	0.420109641	2.585880516	0.067164565
H	2.214782185	0.861484387	0.089606879
P	6.879709418	-0.539212164	1.639081434
O	6.624202021	0.927327731	1.674229186
O	7.347829132	-1.383542729	2.771806873
O	7.972205124	-0.758400246	0.359174231
C	8.34875902	-2.093135392	0.102044476
H	9.141997203	-2.077176624	-0.655729311
H	7.49784803	-2.670574647	-0.284236617
H	8.71548951	-2.572964086	1.016108457
H	-1.897695598	-2.337536324	-1.306732596
H	0.380491795	-0.59740714	-0.652890015
H	4.267657091	-2.427408454	-0.778260686
H	6.856957806	-0.37930589	-1.011901456

(*4) Figure 4d

LNA-modified 5'-GC-3' RNA (Structure 1), W-C face

Number of atoms = 80

Total charge = -3

C	-2.343059526	0.339273626	-1.412036399
C	-3.283190752	-1.651653001	-0.759120382
O	-3.573215791	-0.297451044	-1.178896223
H	-2.271363572	0.699688394	-2.443407456
C	-4.514154685	-2.258713598	-0.129557003
H	-4.233318793	-3.233188611	0.290268408
C	-1.318656602	-0.764509008	-1.150658786
C	-1.966674017	-1.49585271	0.031094456
H	-0.278349499	-0.458039774	-1.085483609
O	-1.391490848	-2.740505603	0.284568906
H	-2.070305551	-0.898063671	0.940953908
H	-5.261805595	-2.430886213	-0.915038733
O	-5.025228501	-1.409432416	0.867086828
P	-6.686333376	-1.442292279	1.083613282
O	-7.147518846	-0.697893926	-0.337163709
C	-6.769311233	0.650418716	-0.48760251
H	-6.989014744	1.224637701	0.421199969
H	-5.699703286	0.738663375	-0.7137994
H	-7.34267258	1.068763717	-1.326628217
O	-7.175281332	-2.847195195	0.963064566
O	-6.962038334	-0.529792249	2.231077785
P	-0.164766593	-2.86857977	1.418124813
O	-0.440842871	-1.906382432	2.524167393
O	0.099328939	-4.325822139	1.537129304

O	1.087253709	-2.133562614	0.599105982
C	1.685031181	-2.615770699	-0.576132564
C	2.616076683	-1.50831874	-1.028396014
H	0.924906928	-2.811431021	-1.346262996
H	2.258387097	-3.531346718	-0.388067102
C	3.774990243	-1.08766921	-0.093670862
O	1.824136121	-0.30512415	-1.163013535
C	4.04476815	0.152374623	-0.945580845
C	2.656385765	0.804314762	-0.953446676
H	2.55986841	1.519515452	-1.77085523
O	4.196238831	-0.381164383	-2.275018883
O	4.778470688	-2.056100908	-0.110589036
H	4.893473999	0.782455293	-0.697352902
H	3.456872615	-0.856095209	0.924667523
N	-2.239350241	1.517066212	-0.550503146
C	-2.92586904	1.80171668	0.610700404
N	-2.617151314	2.972254501	1.113690317
C	-1.679139611	3.483253151	0.240572063
C	-1.4275204	2.583710503	-0.78708032
N	-0.517630027	2.669554147	-1.79343722
C	0.195924729	3.75852665	-1.726561916
N	1.246252038	3.985752205	-2.605768937
N	-0.029445753	4.753346359	-0.814913286
C	-0.936310596	4.708506175	0.269624458
O	-0.976093407	5.647261763	1.058223493
H	0.649857042	5.50005549	-0.750667372
H	2.111946419	4.090429097	-2.062304146
H	1.342804139	3.162970267	-3.192374315
H	-3.647284268	1.098889583	1.010156391
N	2.202324777	1.501322757	0.270756245
C	2.406515244	2.887533335	0.36285866
O	3.12184514	3.442701303	-0.486905812
N	1.757316779	3.572311729	1.340875043
C	0.942060168	2.932928321	2.168246443
N	0.222700416	3.694291666	3.051438543
H	0.093374607	4.646994658	2.724976645
H	-0.655142845	3.273118136	3.329024029
C	0.775672306	1.522380324	2.156566135
C	1.403902933	0.848897262	1.16396755
H	0.126919849	0.982357183	2.835119325
H	1.26132061	-0.218968687	1.027451333
P	6.244241894	-1.708251004	0.638670309
O	5.998524882	-0.754684181	1.755197738
O	6.952127043	-3.017207708	0.738470202
O	6.95522387	-0.804748266	-0.569089022
C	7.251152875	-1.46894706	-1.771203177
H	7.942755102	-0.835565209	-2.3433492
H	6.343916274	-1.616881526	-2.370228579
H	7.723740167	-2.44058879	-1.57960876

O	-1.487373556	-1.680359623	-2.240649034
C	-2.734857841	-2.35261185	-2.005169818
H	-2.556306427	-3.418918724	-1.834285623
H	-3.401444346	-2.205569161	-2.863069387
C	3.381974037	-1.568269422	-2.346096015
H	4.018371823	-2.455449184	-2.428285702
H	2.704971077	-1.491551428	-3.203417592

(*5) Figure 4f

LNA-modified 5'-GC-3' RNA (Structure 3), rigid strand 2

Number of atoms = 80

Total charge = -3

C	-2.473114195	0.542085995	-0.641614468
C	-2.310785859	-1.685887401	-1.209089108
O	-3.10218264	-0.476589862	-1.373359583
H	-2.194242383	1.381735234	-1.288637521
C	-3.147931054	-2.875490017	-1.609075056
H	-2.568696184	-3.786254759	-1.411550294
C	-1.223684933	-0.150141299	-0.098710137
C	-1.766388964	-1.541774252	0.224809151
O	-0.4215262	-0.346025043	-1.260144715
H	-0.670457908	0.353322473	0.686816598
O	-0.795172106	-2.504311326	0.497237492
H	-2.558366493	-1.528965353	0.97882649
H	-3.344094206	-2.821328321	-2.688450504
O	-4.351337639	-2.872667392	-0.881060087
P	-5.668526626	-3.610049491	-1.605690521
O	-5.906829645	-2.53613281	-2.860764111
C	-6.257537875	-1.220146564	-2.502120179
H	-7.030192502	-1.216303965	-1.7228059
H	-5.384257185	-0.663401623	-2.139570325
H	-6.64982251	-0.720900811	-3.398990496
O	-5.235995109	-4.881455378	-2.255072384
O	-6.784021606	-3.479106226	-0.623712625
P	0.21162887	-2.281791106	1.832725212
O	-0.367236326	-1.179396985	2.6540276
O	0.569941435	-3.647979172	2.302392226
O	1.548266044	-1.619936297	1.078214242
C	2.450791942	-2.501780172	0.448090385
C	3.3565838	-1.699854626	-0.454924983
H	1.912184752	-3.244978806	-0.155297364
H	3.057415109	-3.035997258	1.188401459
C	4.292478592	-0.61840209	0.133889173
O	2.531045722	-0.977491815	-1.388999675
C	4.656992367	-0.140694239	-1.275037159
C	3.266706435	0.117726678	-1.867520583
H	3.299382563	0.132232341	-2.958385054
O	5.106781197	-1.341576472	-1.926556701
O	5.33676207	-1.204854039	0.848602642

H	5.401038474	0.642564157	-1.385147166
H	3.781526251	0.136254428	0.733988514
N	-3.411260522	1.066206287	0.354639166
C	-4.564037619	0.474021206	0.830881814
N	-5.197351603	1.217677959	1.702704152
C	-4.422405579	2.350348907	1.81411786
C	-3.312239622	2.268122834	0.981213115
N	-2.322321768	3.189738779	0.789038968
C	-2.434274485	4.229474515	1.5685738
N	-1.462255545	5.203489293	1.580385199
N	-3.479621442	4.402631625	2.436465774
C	-4.578668551	3.510620788	2.64234803
O	-5.439247686	3.828057267	3.446512524
H	-3.458344306	5.172926131	3.090583828
H	-1.783393278	6.151471091	1.712189484
H	-0.77138868	5.10439199	0.835893497
H	-4.867064789	-0.5043308	0.476078525
N	2.568936498	1.359102211	-1.464956665
C	2.639644792	2.470154164	-2.340770225
O	3.481856289	2.478177235	-3.229057847
N	1.694402847	3.456258565	-2.177965659
C	0.879839606	3.397580402	-1.150740531
N	-0.141972874	4.35333487	-1.080433721
H	-0.221158366	4.835246351	-1.969584063
H	-1.019934962	3.909942568	-0.804584345
C	0.934860582	2.4140892	-0.138486307
C	1.742706009	1.350058522	-0.393631319
H	0.256708802	2.421767645	0.70358985
H	1.716506907	0.441476154	0.200915961
P	6.543493954	-0.203715694	1.456228541
O	5.955417251	1.130892781	1.759599595
O	7.318814477	-1.055325913	2.404156712
O	7.441226131	0.010613028	0.067809015
C	8.065633306	-1.130673988	-0.467200913
H	8.836592619	-0.791824737	-1.172851024
H	7.342620506	-1.750481772	-1.011879571
H	8.536803388	-1.727986545	0.323528886
C	-1.019276296	-1.426116098	-1.989389978
C	4.368393482	-2.42894907	-1.339997708
H	3.863458097	-2.993975766	-2.131191763
H	5.044224442	-3.075499828	-0.770849831
H	-1.230852937	-1.101599199	-3.014321114
H	-0.344992555	-2.287439293	-1.990103194

(*6) Figure 4g

2'-OMe-modified 5'-GC-3' RNA (Structure 1), W-C face

Number of atoms = 84

Total charge = -3

C	-2.447255234	0.130770154	-1.734932055
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C	-3.340115764	-1.818402669	-0.818698014
O	-3.610223417	-0.609715184	-1.556617308
H	-2.377352572	0.453599033	-2.778452955
C	-4.48716822	-2.087878869	0.139665679
H	-4.207972234	-2.942056781	0.770756319
C	-1.274663254	-0.778572728	-1.341830952
C	-1.930971275	-1.626825035	-0.241300343
H	-0.391387988	-0.226872373	-1.006753164
O	-1.314391145	-2.860416143	-0.0294716
H	-1.973627932	-1.043775615	0.687437065
H	-5.368358599	-2.373151782	-0.449043434
O	-4.769445407	-0.953198321	0.919284489
P	-6.350871948	-0.734421715	1.420732653
O	-7.083729397	-0.55618005	-0.06954376
C	-6.724828011	0.584032518	-0.814623593
H	-6.674800419	1.47263745	-0.173045772
H	-5.753696286	0.44580031	-1.306816228
H	-7.493856304	0.739093829	-1.584658391
O	-6.894425259	-2.008733666	1.970472251
O	-6.34063319	0.582811756	2.122946961
P	-0.222643769	-3.040149568	1.224639422
O	-0.594410545	-2.102081169	2.324868902
O	0.002543894	-4.50498926	1.3374509
O	1.130209264	-2.313887322	0.566511312
C	1.764065435	-2.760825622	-0.600233072
C	2.773580225	-1.704719648	-1.031277331
H	1.025204232	-2.908444243	-1.399285471
H	2.296462892	-3.705661487	-0.427190333
C	3.910317507	-1.384623362	-0.051567793
O	2.080847296	-0.45575303	-1.217035592
C	4.199652477	0.091805338	-0.365487439
C	2.808997138	0.634929014	-0.726601429
H	2.909483197	1.392911243	-1.50382098
O	4.994792881	0.192327643	-1.529248277
O	4.98071175	-2.260965698	-0.248684366
H	4.669340445	0.598438982	0.482749154
H	3.541596874	-1.442074487	0.979675889
N	-2.47451579	1.36717315	-0.937617646
C	-3.25028589	1.723254974	0.150320929
N	-2.948711854	2.912269515	0.615354005
C	-1.922407971	3.354286683	-0.191707269
C	-1.608274246	2.397183179	-1.145006104
N	-0.588298889	2.393531422	-2.046777517
C	0.183667189	3.437435823	-1.927525228
N	1.347327029	3.552425797	-2.675455774
N	-0.085927949	4.485752368	-1.090359099
C	-1.112546962	4.532695041	-0.115185301
O	-1.176333263	5.494244792	0.643168161
H	0.644017004	5.170746178	-0.9411348

H	2.141122227	3.70206981	-2.041336305
H	1.488735541	2.677241263	-3.169333327
H	-4.003214779	1.051906004	0.550986299
N	2.061583164	1.296169396	0.360507623
C	2.148352405	2.69374042	0.464766154
O	2.948666975	3.30712086	-0.268572587
N	1.314262007	3.328797662	1.321647235
C	0.415076579	2.637056697	2.014000817
N	-0.474970242	3.35213738	2.764160883
H	-0.590531373	4.306397085	2.434713707
H	-1.365029293	2.890666766	2.907760307
C	0.353213684	1.217001171	1.993063727
C	1.192610893	0.588700185	1.134529362
H	-0.347356827	0.62780935	2.57317332
H	1.179219971	-0.490314327	1.005865661
P	6.306106684	-2.164750351	0.776144269
O	5.902487414	-1.467129768	2.029936158
O	6.978980529	-3.493472701	0.686986989
O	7.229868888	-1.054954977	-0.064198423
C	7.663490957	-1.447907972	-1.340237755
H	8.342391746	-0.66994701	-1.717472925
H	6.815225785	-1.537111348	-2.030915074
H	8.196483647	-2.406973847	-1.29914038
O	-0.955896289	-1.619020814	-2.431417741
H	3.220436379	-2.004699579	-1.988759244
C	5.77822	1.359597371	-1.529509738
H	5.165794286	2.259095218	-1.365123809
H	6.552838971	1.296036161	-0.753564033
H	6.258629141	1.420435773	-2.512300132
H	-3.284166111	-2.656300783	-1.527126036
C	-0.157361057	-0.999317386	-3.410014728
H	-0.686609445	-0.187022795	-3.933247361
H	0.096278537	-1.776584198	-4.138168737
H	0.759384263	-0.590684081	-2.97135788

(*7) Figure 4h

2'-OMe-modified 5'-GC-3' RNA (Structure 2), rigid strand 1

Number of atoms = 84

Total charge = -3

C	-3.005016096	0.197304142	-1.354520518
C	-2.728239181	-2.113714916	-1.210035816
O	-3.605685139	-1.032741079	-1.584294237
H	-3.087020795	0.824652376	-2.247740025
C	-3.546123854	-3.205342735	-0.535067293
H	-2.849490782	-3.923671829	-0.081586255
H	-2.277621541	-2.524938433	-2.122732294
C	-1.530222217	-0.071175158	-1.068163599
C	-1.588689124	-1.463555107	-0.410936972
O	-0.93219575	-0.108696531	-2.342671859

H	-1.067884177	0.690997832	-0.43056962
O	-0.416691316	-2.221795137	-0.558116629
H	-1.859051959	-1.354823988	0.645230809
H	-4.129255208	-3.732462775	-1.300386785
O	-4.404241666	-2.644866561	0.426947877
P	-5.877315548	-3.384155946	0.700118599
O	-6.500192674	-3.356886898	-0.850650078
C	-6.827934748	-2.093926077	-1.379487024
H	-7.415485327	-1.506563423	-0.662685255
H	-5.926490888	-1.527114204	-1.646157579
H	-7.422783163	-2.25658923	-2.289223275
O	-5.683308776	-4.827417479	1.013877672
O	-6.629669723	-2.404250095	1.540447353
P	0.692320426	-2.357747054	0.690433746
O	0.246171811	-1.472246139	1.808547898
O	1.062274668	-3.795047196	0.78630561
O	1.984464777	-1.530929407	0.02462169
C	2.907539904	-2.084860983	-0.873476131
C	3.944095881	-1.017182442	-1.225477089
H	2.39943847	-2.409068815	-1.793117436
H	3.415982065	-2.951963374	-0.433385511
H	4.599741343	-1.410840957	-2.013899434
C	4.853230665	-0.534307203	-0.081691051
O	3.27826366	0.146802086	-1.729066248
C	5.046807427	0.96463045	-0.41703866
C	3.737207902	1.33061523	-1.129442928
H	3.93362394	2.076778507	-1.896201024
O	6.03637934	1.185843664	-1.399577216
O	6.033138425	-1.291677668	-0.075151214
H	5.241898217	1.560851249	0.480740205
H	4.332053114	-0.622890065	0.879463518
N	-3.700807328	0.930828553	-0.277466162
C	-4.802107962	0.565891868	0.473907207
N	-5.322490606	1.575025999	1.133050694
C	-4.532428002	2.650855149	0.804947371
C	-3.513137091	2.262073154	-0.056382787
N	-2.506955792	3.017253169	-0.589758228
C	-2.539088264	4.249250242	-0.189253324
N	-1.501082349	5.143669383	-0.447021177
N	-3.532315189	4.753561518	0.616276719
C	-4.615581005	4.031050568	1.194652676
O	-5.408694817	4.629134183	1.905931203
H	-3.430160598	5.697193655	0.963649172
H	-1.750686732	5.939674855	-1.0203009
H	-0.645544895	4.680895774	-0.763046793
H	-5.142502258	-0.463344499	0.521054256
N	2.696408717	1.942516763	-0.278925859
C	2.20893904	3.234358391	-0.620730643
O	2.699291348	3.849774047	-1.560782239

N	1.190431388	3.74757176	0.143448837
C	0.675543482	3.038741951	1.136351581
N	-0.26230397	3.653765734	1.92190485
H	-0.654562688	4.499860027	1.528494322
H	-0.914836163	3.050092275	2.400830898
C	1.071881277	1.710650461	1.43590091
C	2.092683869	1.215144252	0.696245004
H	0.581024227	1.071115322	2.159688799
H	2.411065757	0.190330111	0.824513525
P	6.952331525	-1.352742606	1.330219411
O	6.943954401	0.003178105	1.958254394
O	6.654608128	-2.61894169	2.058546917
O	8.418576461	-1.517849873	0.554540681
C	8.628263828	-2.728479617	-0.127214744
H	9.696298182	-2.796089193	-0.375875408
H	8.046685579	-2.765172172	-1.059883939
H	8.343443843	-3.586374959	0.493868741
C	0.439666501	0.21840128	-2.310365988
C	7.376118919	1.213066068	-0.949766045
H	0.859090116	-0.031579257	-3.288155144
H	0.580755037	1.296368931	-2.130131575
H	0.968319695	-0.341974801	-1.542379596
H	7.867660978	0.249544688	-1.110809256
H	7.891888914	1.99581962	-1.523843864
H	7.439653112	1.426225177	0.122087578

(*8) Figure 4i

2'-OMe-modified 5'-GC-3' RNA (Structure 4), stretch type

Number of atoms = 84

Total charge = -3

C	-3.413604308	0.408600816	-0.821026773
C	-2.621601187	-1.708612594	-0.245730537
O	-3.686238273	-0.95368055	-0.856618831
H	-3.537958348	0.850555974	-1.813681243
C	-3.222788542	-2.857680358	0.543790115
H	-2.410594151	-3.365593235	1.08048836
C	-1.958268832	0.568306151	-0.377128618
C	-1.778648006	-0.677261594	0.513627465
O	-1.233313261	0.502465321	-1.582880378
H	-1.757401331	1.500278041	0.161927524
O	-0.458119273	-1.128077862	0.629056173
H	-2.229254836	-0.487056964	1.497925663
H	-3.667375154	-3.571185574	-0.161375573
O	-4.198342523	-2.37993619	1.436292603
P	-5.471059553	-3.400225363	1.818250284
O	-6.153054076	-3.5608101	0.302990191
C	-6.72001484	-2.40187486	-0.261950309
H	-7.320550642	-1.855633602	0.476084273
H	-5.943264419	-1.732998489	-0.653748993

H	-7.366937946	-2.716414926	-1.092942954
O	-4.953800148	-4.755277624	2.157634156
O	-6.365993955	-2.567148855	2.674288283
P	0.513837161	-0.413940706	1.804306701
O	0.354748467	1.073689497	1.705370354
O	0.38866635	-1.187058105	3.067399614
O	1.965545678	-0.727537432	1.063749055
C	2.348081185	-1.998672777	0.600891486
C	3.502320671	-1.847213182	-0.381277693
H	1.504632393	-2.481921497	0.093457863
H	2.677246749	-2.638822793	1.429797662
C	4.833387617	-1.312599844	0.161316154
O	3.122463151	-0.917820818	-1.413107102
C	5.436803896	-0.667556991	-1.095414933
C	4.189951862	-0.091098445	-1.780154937
H	4.310758362	-0.092134969	-2.864246935
O	5.969356197	-1.662059603	-1.943524438
O	5.58562793	-2.341044224	0.732694778
H	6.188805918	0.084622243	-0.83994327
H	4.65082253	-0.516034242	0.893332088
N	-4.377010606	1.109040851	0.048158916
C	-5.150010901	0.641080544	1.095671179
N	-5.931337994	1.567339597	1.599262398
C	-5.661000123	2.693608127	0.859768532
C	-4.696229518	2.421001979	-0.103277629
N	-4.172192915	3.259508372	-1.046586955
C	-4.638357652	4.463588463	-0.956330567
N	-4.155384904	5.470038526	-1.796137971
N	-5.580621907	4.853075798	-0.044017106
C	-6.193535535	4.023439872	0.948149528
O	-7.02258074	4.525736295	1.689523832
H	-5.811123808	5.833142557	0.043635581
H	-4.887976954	5.987513559	-2.268075639
H	-3.513974278	5.060761595	-2.465557439
H	-5.087621851	-0.392107652	1.425715048
N	3.911778	1.318111877	-1.418554393
C	4.514100342	2.321576487	-2.214694196
O	5.281326341	1.993724454	-3.116595221
N	4.181300213	3.62339926	-1.947835601
C	3.378289523	3.896658851	-0.93799583
N	3.1073738	5.233623706	-0.714809338
H	3.306992545	5.814682058	-1.516763839
H	2.229551657	5.429643979	-0.256538852
C	2.806930436	2.919650062	-0.087467355
C	3.094488054	1.624408664	-0.385988591
H	2.131296314	3.137370033	0.730685043
H	2.658679511	0.796229676	0.168467427
P	7.052801172	-1.9516351	1.450479764
O	7.052452897	-0.501293922	1.796285856

O	7.35813801	-3.075036858	2.382520586
O	8.054799438	-2.085272251	0.12102187
C	8.154130758	-3.363434713	-0.452735609
H	8.884089771	-3.305714845	-1.272272725
H	7.189340165	-3.683109282	-0.866335036
H	8.492028253	-4.103996388	0.283909008
H	-1.984145051	-2.120483718	-1.039933205
H	3.697603016	-2.825952219	-0.840370133
C	0.132416191	0.871783892	-1.502899231
C	7.014816862	-1.164363585	-2.741009236
H	0.774566815	0.00755409	-1.317136374
H	0.2962899	1.59369205	-0.697507499
H	0.398312112	1.320416042	-2.468081214
H	7.289540454	-1.961259438	-3.440763765
H	7.883115549	-0.918249525	-2.114712369
H	6.705886123	-0.271892494	-3.30485298

3.2 Modeling of 5'-AAA-3' RNA with AGO protein binding pocket

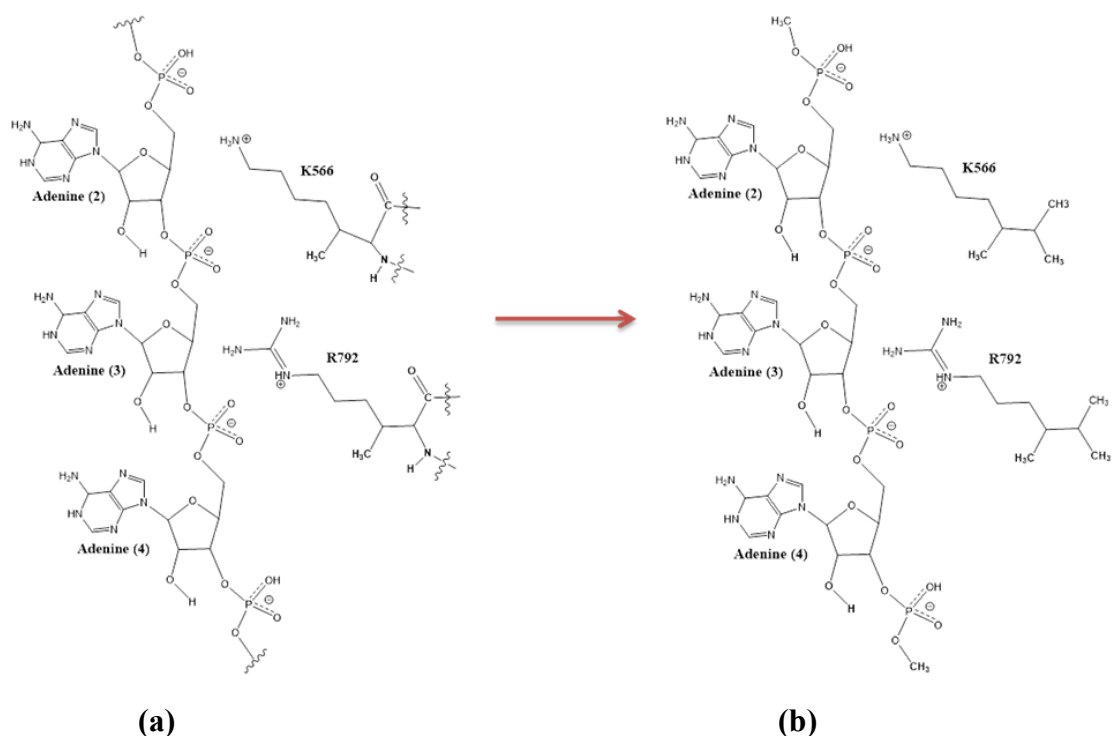


Figure S4.

(a) Schematic drawing of a part of AGO protein binding pocket (5'-AAA-3' RNA with R792 and K566) taken from crystal structure of Schirle *et al.*¹² This structure is shown in Figure 5(a).

(b) Schematic drawing of a structure used in the geometry optimization. Each of 5'- and 3'-terminal phosphates was capped with a methyl group, and the parts of main chain (C=O and N-H) of R792 and K566 were replaced with methyl groups in order to avoid artificial interactions. The full geometry optimization of this binding pocket model was performed for each of unmodified, 2'-OMe-modified and LNA-modified RNA, and the optimized structure is shown in Figure 5 (b), (c) and (d), respectively.

3.3 Total energy of the model of 5'-AAA-3' RNA with AGO protein binding pocket

Table S2. Total energy of 5'-AAA-3' RNA with AGO protein

	Total energy (a.u)
unmodified RNA (Fig 5b) (*1)	-5782.749051
2'-OMe-modified RNA (Fig 5c) (*2)	-5822.029741
LNA-modified RNA (Fig 5d) (*3)	-5820.815823

(*1) Figure 5b

Unmodified 5'-AAA-3' RNA on AGO protein

Number of atoms = 165

Total charge = -2

C	-16.24967915	32.92274267	35.33229002
C	-17.59590745	33.66001733	35.27139222
C	-18.81101583	32.79135858	35.5954309
C	-20.15121381	33.53279814	35.56981851
C	-20.53639593	34.1640575	34.23437517
N	-20.62638412	33.18033917	33.1315648
C	-21.36160614	32.91104565	40.13820666
C	-20.90725687	31.4491401	40.07278831
C	-19.9323011	31.14790912	38.93346769
C	-19.77305486	29.64416077	38.66829266
N	-20.97174174	29.01085281	38.14506164
C	-21.42524405	29.21840108	36.907786
N	-20.65100277	29.81752092	35.97152193
N	-22.62535848	28.77836976	36.54230765
O	-23.5670215	34.83717675	30.99097317
C	-23.49206704	35.70702661	32.09638017
C	-24.53057699	35.36865623	33.14204527
O	-25.81147416	35.84619566	32.72368773
C	-24.77625388	33.88932907	33.41351451
O	-23.71991032	33.32842715	34.17261985
C	-26.14011531	33.95520765	34.11515314
O	-26.0397906	34.49592261	35.40488645
C	-26.82889757	35.03650065	33.26557135
N	-27.63223218	34.50707177	32.17362567
C	-27.21060368	33.98781912	30.96925184
N	-28.18496388	33.53411928	30.22118897
C	-29.3153312	33.76875057	30.97805917
C	-30.67637914	33.50230817	30.77014716
N	-31.12482694	32.91569488	29.62270698
N	-31.56566593	33.85029999	31.70958078
C	-31.10612837	34.46621311	32.81586071
N	-29.8546281	34.76077244	33.14027033
C	-28.99560478	34.37828165	32.18846049
P	-23.70253331	31.69244715	34.35998512
O	-22.2152041	31.35031031	34.32952182
O	-24.68864512	31.00770191	33.50002929
O	-24.20281135	31.53390654	35.90800201
C	-23.5528723	32.19984818	36.97143992

C	-24.51817544	32.28454538	38.1337041
O	-25.66027489	33.0364464	37.72843699
C	-25.06121582	30.94179128	38.61882849
O	-24.16661208	30.39197765	39.55033292
C	-26.43580373	31.33804495	39.18156399
O	-26.32662819	31.89690549	40.46030325
C	-26.86000836	32.45145718	38.21121183
N	-27.67221067	32.01654265	37.08914225
C	-27.34846313	31.1484916	36.06416837
N	-28.28706167	31.02268258	35.16329567
C	-29.28966319	31.85696508	35.6129867
C	-30.56468418	32.14606286	35.11616285
N	-31.04724203	31.503784	34.00019726
N	-31.33928273	33.01523508	35.76630486
C	-30.85724122	33.55294277	36.89753844
N	-29.68510024	33.34718319	37.48863542
C	-28.93388365	32.48598366	36.79859156
P	-24.04683018	28.74804918	39.71468111
O	-22.65047588	28.52488688	40.22594937
O	-24.49689308	28.10503388	38.43286617
O	-25.16591097	28.42172017	40.82700105
C	-25.04569258	28.95234431	42.14981514
C	-26.42295649	28.93426009	42.77773238
O	-27.28583641	29.77705988	41.98155168
C	-27.11322296	27.55608821	42.8110938
O	-27.06208603	26.87136798	44.03242894
C	-28.59442937	27.90846348	42.56796124
O	-29.21017244	28.22224057	43.78867361
C	-28.53516612	29.18209501	41.7222898
N	-28.72156683	28.95575069	40.29619635
C	-27.96667029	28.20726555	39.41040223
N	-28.43723435	28.20703153	38.19013244
C	-29.5710966	28.9918625	38.26662376
C	-30.53643034	29.37179705	37.31568961
N	-30.50701206	28.92728544	36.02855435
N	-31.53977373	30.17257758	37.70099556
C	-31.57800445	30.57211914	38.97933547
N	-30.75133227	30.27156858	39.97492378
C	-29.7612816	29.4738703	39.55811358
P	-25.60011565	26.57384947	44.84135763
O	-25.95508355	25.567106	45.87603114
O	-24.92844404	27.88045449	45.09339602
O	-24.780584	25.87643204	43.58840661
H	-16.29889367	32.07678078	34.63068711
H	-17.70737896	34.09095561	34.26671629
H	-17.56903567	34.51214533	35.9671424
H	-18.6923275	32.36657956	36.59910477
H	-18.83920192	31.93443487	34.90442658
H	-20.94831478	32.83770456	35.85147597

H	-20.13582337	34.33015087	36.32360956
H	-19.84173491	34.9482855	33.92097992
H	-21.53187943	34.60336646	34.3195492
H	-21.31658857	32.4364953	33.40037926
H	-19.72955778	32.72738496	32.96228794
H	-20.89883515	33.7111906	32.19475651
H	-21.83564273	33.15116193	39.17364246
H	-20.44234219	31.16921633	41.02938068
H	-21.79275238	30.81330271	39.9742443
H	-18.93914108	31.56742617	39.14563774
H	-20.28916639	31.64316678	38.01852752
H	-19.54718749	29.13094797	39.60698508
H	-18.92726235	29.44612629	37.99569952
H	-21.63976739	28.67325814	38.87344852
H	-21.17044948	30.3119672	35.2288011
H	-19.83358514	30.30316683	36.30280664
H	-23.32549734	28.43919904	37.23708241
H	-22.96851744	29.04310766	35.62995401
H	-23.65372191	36.74855566	31.78037379
H	-22.49929254	35.64963335	32.55486416
H	-24.25325767	35.86011711	34.08548997
H	-24.86556322	33.349812	32.46730244
H	-26.67734226	33.00053923	34.0912349
H	-25.79349446	33.80943555	36.04831488
H	-27.50850281	35.61623354	33.89533887
H	-26.16313249	34.0029546	30.69348267
H	-32.05297015	32.5232629	29.65896063
H	-30.43810009	32.43025104	29.06517763
H	-31.86127273	34.71955024	33.55516074
H	-23.25126805	33.20914086	36.6645363
H	-22.66265448	31.64144169	37.2924826
H	-24.03323997	32.79256494	38.97459476
H	-25.19045031	30.25220557	37.77937693
H	-27.14430234	30.50891366	39.15510325
H	-26.60031487	31.20903744	41.09513404
H	-27.45187351	33.20202275	38.73701661
H	-26.38241668	30.6683044	36.00989419
H	-31.80859757	31.98517147	33.53817263
H	-30.3232619	31.18758188	33.36694478
H	-31.52189902	34.25387873	37.39721119
H	-24.67825618	29.98397624	42.10132251
H	-24.36480476	28.34565903	42.74803014
H	-26.35709816	29.33412475	43.79198062
H	-26.7234997	26.93122447	41.99835599
H	-29.13421779	27.1089689	42.04195629
H	-28.69102722	27.72360656	44.44738485
H	-29.33895936	29.86269068	42.01126083
H	-27.04298107	27.73547538	39.7188959
H	-31.04374961	29.4928533	35.37962107

H	-29.58942701	28.66848736	35.68983415
H	-32.40344538	31.23467804	39.23066008
C	-25.20013642	24.59516951	43.17808342
H	-24.49774854	24.25168141	42.41227254
H	-25.20787593	23.89498798	44.02095419
H	-26.21020892	24.62164155	42.74452385
P	-22.18952639	34.57923466	30.09195013
O	-21.01400141	34.63563111	31.07903985
O	-22.41481749	33.38839044	29.23450512
C	-22.10656837	36.12146302	29.12007527
H	-21.21028548	36.10922657	28.49328502
H	-22.06023136	36.99643959	29.7763866
H	-22.98702067	36.19973709	28.47682641
C	-20.19390828	33.88338187	40.32787032
C	-22.41141206	33.08624101	41.23802228
H	-19.48342669	33.83940833	39.49322184
H	-20.55298451	34.91645852	40.40278779
H	-19.6445099	33.65141647	41.24979723
H	-23.25699014	32.4063121	41.09085911
H	-22.79736805	34.11222633	41.25824279
H	-21.97574061	32.87059865	42.22194079
C	-15.9522485	32.3651176	36.72777494
C	-15.11909566	33.84942698	34.87695056
H	-14.9660489	31.88847844	36.75466836
H	-15.95594545	33.1706058	37.47331423
H	-16.68612186	31.61593246	37.04141647
H	-14.15515032	33.3283065	34.87239011
H	-15.03158602	34.70949029	35.55292854
H	-15.30212817	34.23427613	33.86744757

(*2) Figure 5c

2'-OMe-modified 5'-AAA-3' RNA on AGO protein

Number of atoms = 168

Total charge = -2

C	4.114111161	-8.210275134	-0.233711796
C	4.225825873	-6.844435995	0.459739766
C	3.189829015	-5.815642806	0.007571555
C	3.312820985	-4.446293978	0.683296454
C	4.629149931	-3.709593654	0.45031359
N	4.89868762	-3.446697062	-0.981927751
C	-0.533788123	-4.125929109	3.125586604
C	-1.328660231	-4.660273227	1.929051797
C	-0.479362813	-5.408625388	0.900929823
C	-1.204096478	-5.630510302	-0.433977024
N	-1.446031491	-4.40632333	-1.178537251
C	-0.479884805	-3.709642837	-1.778606678
N	0.750923535	-4.24221284	-1.979604866
N	-0.721319798	-2.492765497	-2.253474602

O	7.018016398	-0.146091285	-0.718486744
C	6.672266322	-0.383198656	0.625950589
C	5.492462519	0.462314119	1.046916495
O	5.919359477	1.812211214	1.236412272
C	4.34392801	0.586092405	0.051599916
O	3.557254199	-0.592630034	0.030191239
C	3.640581129	1.839376994	0.589207297
O	2.968069069	1.588521588	1.794125381
C	4.855140406	2.697415417	0.976395191
N	5.267149271	3.640388919	-0.051389136
C	5.882255823	3.387574596	-1.258212451
N	6.047399095	4.454215745	-1.999385053
C	5.511030568	5.470473801	-1.234457309
C	5.343340446	6.845176134	-1.454343186
N	5.770710567	7.445585717	-2.601640386
N	4.764796087	7.596888792	-0.507381427
C	4.389936036	6.991903277	0.636198439
N	4.478292942	5.710070897	0.961962031
C	5.032132205	4.989135464	-0.018957318
P	2.447871189	-0.750661904	-1.182357221
O	2.565618205	-2.217778161	-1.586153043
O	2.530371835	0.34879291	-2.165346297
O	1.043367583	-0.586209285	-0.363176438
C	0.733513527	-1.403587196	0.747233509
C	-0.21641222	-0.640514441	1.645976946
O	0.421108865	0.564787881	2.061417926
C	-1.532404814	-0.216943136	0.987498042
O	-2.478137707	-1.245477285	1.138095399
C	-1.862949487	1.084463963	1.739742813
C	-0.467709329	1.666961339	2.004768451
N	-0.003607776	2.629492814	1.021728449
C	0.196919656	2.470773449	-0.336002163
N	0.69331796	3.530018573	-0.921144286
C	0.840245425	4.439130084	0.107022261
C	1.27785024	5.771245002	0.128729539
N	1.677439161	6.407457393	-1.008954082
N	1.250137102	6.442042816	1.286973211
C	0.826446396	5.788420641	2.380595955
N	0.394474167	4.537535546	2.494707677
C	0.416693066	3.906100656	1.317751538
P	-3.442556089	-1.708930323	-0.128437209
O	-3.574930552	-3.201780246	-0.015161233
O	-2.889020962	-1.089430148	-1.383780056
O	-4.830615452	-0.968821952	0.199242377
C	-5.90039506	-1.586528307	0.920219748
C	-7.071689533	-0.627077936	0.864244001
O	-6.696278116	0.606849105	1.499624415
C	-7.508218386	-0.2685637	-0.57285171
O	-8.695530686	-0.871874631	-1.012971555

C	-7.775054088	1.249235793	-0.497344235
O	-9.11502887	1.482955851	-0.151083926
C	-6.893222038	1.711436773	0.666491741
N	-5.629011537	2.317056404	0.238593931
C	-4.691318736	1.879239487	-0.67440367
N	-3.68209903	2.698918636	-0.83322308
C	-3.965698791	3.742343977	0.02557647
C	-3.290309068	4.939631476	0.321337169
N	-2.159876072	5.307645194	-0.326405134
N	-3.805550271	5.762044132	1.248020395
C	-4.958214346	5.405003336	1.831776839
N	-5.706558358	4.326695613	1.626376899
C	-5.157714805	3.52119153	0.706173137
P	-8.847532995	-2.559822556	-1.074695446
O	-10.06266149	-2.788413008	-1.901246879
O	-8.610518115	-3.106980109	0.291717646
O	-7.474131799	-2.883347422	-1.935519511
H	4.213125463	-8.043888466	-1.316671595
H	5.237153604	-6.453234522	0.283443419
H	4.13830674	-6.986038917	1.547465715
H	2.185199394	-6.198391962	0.222369967
H	3.242104108	-5.704857047	-1.086839083
H	2.504322263	-3.796854118	0.331820878
H	3.181536325	-4.566169528	1.7662426
H	5.492022329	-4.246254357	0.853863463
H	4.582631964	-2.728751428	0.927288967
H	4.122595453	-2.852584515	-1.362783433
H	4.924769766	-4.310876392	-1.521389299
H	5.907145271	-2.988349551	-1.087332348
H	0.221604364	-3.42668435	2.734435431
H	-2.126858434	-5.325075587	2.290097027
H	-1.842469903	-3.823097317	1.444743169
H	-0.169584317	-6.387869246	1.291201394
H	0.443235234	-4.839427764	0.720314544
H	-2.188685874	-6.068401118	-0.248722528
H	-0.660896815	-6.34708257	-1.064865252
H	-2.325056998	-3.909664986	-0.915850409
H	1.511598572	-3.546436801	-1.998909616
H	0.967370815	-5.081059566	-1.465761926
H	-1.582760182	-1.963134439	-1.994474432
H	0.059424016	-1.964032143	-2.615154938
H	7.515513983	-0.1468961	1.292344537
H	6.420582408	-1.438838062	0.7728188
H	5.097211015	0.0691799	1.99454232
H	4.740065383	0.776597858	-0.948734908
H	3.0050509	2.322252362	-0.161910513
H	2.159432109	1.072975115	1.631577884
H	4.609783496	3.296814115	1.856972103
H	6.213838564	2.38912176	-1.515422863

H	5.39139957	8.359300503	-2.795613995
H	5.958578221	6.841843914	-3.387767321
H	3.920695032	7.638503991	1.372490708
H	1.643812292	-1.657926711	1.304506096
H	0.244730439	-2.331400542	0.42045169
H	-0.449150835	-1.246084735	2.52900888
H	-1.384746616	-0.001333677	-0.074822583
H	-2.477077351	1.768783064	1.146000909
H	-0.457319386	2.193651673	2.960195509
H	-0.007024498	1.535482998	-0.83600083
H	2.264896069	7.220045706	-0.878871536
H	1.931269061	5.802534506	-1.777423462
H	0.834109038	6.372267483	3.298224982
H	-5.59467029	-1.750135092	1.959985
H	-6.182188431	-2.537103694	0.463880116
H	-7.913913395	-1.069091291	1.401304142
H	-6.689989143	-0.483592083	-1.269957633
H	-7.514087601	1.767323428	-1.430807652
H	-9.5763887	0.672428626	-0.437848279
H	-7.396716424	2.500101493	1.229414217
H	-4.780964175	0.921500369	-1.166732782
H	-1.613407128	6.050198722	0.082794806
H	-1.667097897	4.617905321	-0.876371572
H	-5.330709584	6.103278591	2.579156664
C	-7.460909538	-2.502735373	-3.292466159
H	-6.529699686	-2.877341611	-3.728733034
H	-8.321022879	-2.921738912	-3.826820383
H	-7.486525948	-1.409050572	-3.404277386
P	7.851150452	-1.329279053	-1.540525879
O	7.318004	-2.669937074	-1.012017351
O	7.805524604	-1.002209682	-2.987942369
C	9.52670485	-1.138952914	-0.84456593
H	10.1910475	-1.885019097	-1.289740367
H	9.521152026	-1.281627026	0.240720994
H	9.909415099	-0.141428252	-1.075742781
O	-2.4368334	0.817769383	2.992658802
C	-3.852113226	0.90844803	2.977285189
H	-4.174637119	1.957574554	2.91207415
H	-4.207252796	0.482946549	3.918286537
H	-4.288443669	0.355508469	2.143944078
C	5.25923431	-9.123930827	0.211061792
C	2.763096324	-8.886116084	0.020567736
C	0.213395721	-5.228982267	3.880549397
C	-1.461657793	-3.346908028	4.060793868
H	6.234678713	-8.666807454	0.010748823
H	5.222844277	-10.08782563	-0.308931554
H	5.19645539	-9.322549208	1.288523959
H	1.926160862	-8.303667014	-0.377732225
H	2.596069691	-9.020469334	1.097048672

H	2.72730604	-9.875097925	-0.449765686
H	-0.48744566	-5.995745015	4.236384308
H	0.959102469	-5.725491112	3.247901762
H	0.73573719	-4.821457887	4.753807075
H	-0.90126212	-2.874370395	4.876014978
H	-2.205074421	-4.019027976	4.508177301
H	-2.004742292	-2.566135659	3.517736764

(*3) Figure 5d

LNA-modified 5'-AAA-3' RNA on AGO protein

Number of atoms = 166

Total charge = -2

C	5.171041416	6.978922038	0.920963657
C	5.441188284	5.930059692	-0.168091598
C	4.433051264	4.781103134	-0.196399881
C	4.778029032	3.638239164	-1.152718605
C	6.078482756	2.897689496	-0.849271707
N	6.185513995	2.455495256	0.561523753
C	-0.435230345	5.3844742	-2.227296782
C	-0.822517225	5.616246642	-0.763916679
C	0.352991032	5.95818722	0.151752935
C	-0.003869088	5.850795148	1.641518896
N	-0.300960652	4.49854497	2.082749396
C	0.637010159	3.561978297	2.250329074
N	1.949754007	3.885217388	2.220847299
N	0.295789384	2.308446361	2.533539252
O	7.224751885	-1.420437521	-0.068646198
C	6.973964272	-0.968922243	-1.377392804
C	5.551355539	-1.246303425	-1.811086054
O	5.421969425	-2.621045968	-2.208119345
C	4.455173405	-1.099433549	-0.762146889
O	4.170224051	0.243828073	-0.436901636
C	3.316267059	-1.845867108	-1.461642002
O	2.821129875	-1.091115763	-2.537295565
C	4.101185641	-3.055196245	-2.000043589
N	4.097151672	-4.158574968	-1.046116677
C	4.89290156	-4.340535055	0.065888815
N	4.464560232	-5.280779222	0.869340242
C	3.30630958	-5.727115374	0.265973662
C	2.312939941	-6.63364765	0.66365641
N	2.401794472	-7.329402775	1.833195238
N	1.257862929	-6.833384142	-0.136548704
C	1.188132306	-6.136771153	-1.286112687
N	2.025561622	-5.223127088	-1.751119072
C	3.06338399	-5.04804435	-0.922925463
P	3.241706691	0.48200873	0.904977672
O	3.60895168	1.912067312	1.285684007
O	3.307341804	-0.643642393	1.858319158

O	1.717523467	0.502784956	0.304369446
C	1.365941421	1.328843385	-0.786614712
C	0.088780905	0.793167163	-1.378629056
O	0.261963064	-0.596311445	-1.725455097
C	-1.187791216	0.758731686	-0.523879347
O	-1.622751625	2.063675443	-0.265592433
C	-1.951311274	0.04581012	-1.642844986
C	-1.036453478	-1.156095944	-1.902649385
N	-1.158906209	-2.311833703	-1.034593991
C	-0.362556494	-2.691550217	0.02856579
N	-0.554231301	-3.925265228	0.414776919
C	-1.530488694	-4.398726666	-0.443789255
C	-2.130194767	-5.655720234	-0.631547635
N	-1.78760348	-6.759699996	0.104288826
N	-3.081716307	-5.785333787	-1.566037422
C	-3.404463629	-4.716918048	-2.30592295
N	-2.863029647	-3.502315982	-2.28552374
C	-1.930314608	-3.407014765	-1.335686404
P	-2.714497846	2.304248168	0.971097352
O	-2.766301943	3.796867484	1.120467234
O	-2.281846769	1.4369993	2.118972626
O	-4.061093397	1.663126768	0.376723761
C	-4.686078575	2.144104891	-0.819995336
C	-5.790629791	1.173581515	-1.186435872
O	-5.190433895	-0.105210584	-1.480690834
C	-6.825085237	0.884214721	-0.079056422
O	-8.006972803	1.639266925	-0.103272744
C	-7.223795878	-0.571718568	-0.384292974
O	-8.21473056	-0.58667841	-1.37869733
C	-5.942899529	-1.168140424	-0.969650589
N	-5.145093121	-1.900902213	0.016493848
C	-4.122113259	-1.430241767	0.811650054
N	-3.560337549	-2.352432489	1.551649534
C	-4.266711672	-3.493685234	1.242744737
C	-4.118894075	-4.826795673	1.647697519
N	-3.129593831	-5.204176578	2.515041232
N	-4.958398437	-5.751651369	1.164596405
C	-5.875439131	-5.354705988	0.269124979
N	-6.090938656	-4.143903522	-0.234773419
C	-5.252066741	-3.241039531	0.292075794
P	-8.009909519	3.326174393	-0.262331407
O	-9.378252865	3.73499989	0.152868847
O	-7.354751827	3.678033199	-1.555198062
O	-6.902464092	3.679625523	0.910853263
H	5.210563584	6.465304922	1.893133202
H	6.455376874	5.532871515	-0.013726145
H	5.458993765	6.425554171	-1.150354269
H	3.447189153	5.166460934	-0.482693515
H	4.315537565	4.365906757	0.812957712

H	3.964885059	2.908405301	-1.123795761
H	4.842747299	4.015829908	-2.181275708
H	6.967425445	3.493516377	-1.074519685
H	6.125095588	1.991934827	-1.455292652
H	5.261739094	2.088326932	0.894730053
H	6.428965952	3.231416023	1.175019994
H	6.993231408	1.700857619	0.631086446
H	0.293706657	4.558087577	-2.246380423
H	-1.568815617	6.422258988	-0.709630539
H	-1.328004554	4.720870863	-0.389255198
H	0.718669217	6.975767239	-0.040153575
H	1.18990926	5.279624573	-0.072806479
H	-0.904506383	6.438451408	1.840777086
H	0.7897546	6.27390311	2.271494191
H	-1.276034053	4.186103684	1.894534872
H	2.611337543	3.116580396	2.024911155
H	2.192654841	4.755056543	1.775741821
H	-0.692069348	1.981466864	2.48024446
H	1.010043935	1.595043095	2.497146978
H	7.647995981	-1.46412888	-2.092780795
H	7.154011545	0.109206499	-1.442284357
H	5.318543261	-0.604413554	-2.672918333
H	4.754205847	-1.630397901	0.144912623
H	2.522901801	-2.150854737	-0.773324341
H	1.861133683	-1.0021914	-2.410054501
H	3.654706135	-3.427507186	-2.925309031
H	5.783725641	-3.742554008	0.214083002
H	1.532064744	-7.700985586	2.185218188
H	3.029544529	-6.942116235	2.523218015
H	0.31441821	-6.344298365	-1.899040349
H	2.161036178	1.314875643	-1.542019446
H	1.191777465	2.362116503	-0.457543312
H	-1.078422966	0.172073827	0.392898855
H	-3.011236318	-0.174840383	-1.528617774
H	-1.16944212	-1.508929791	-2.928788396
H	0.344182871	-1.999705306	0.468669569
H	-2.193717411	-7.607579679	-0.268190988
H	-0.798944801	-6.836110028	0.342047784
H	-4.202410302	-4.87184602	-3.027486725
H	-3.944557905	2.175593841	-1.62717944
H	-5.111651516	3.134833613	-0.65678345
H	-6.301128596	1.555080518	-2.074313012
H	-6.335357024	0.953874604	0.900101757
H	-7.546046242	-1.120350464	0.510982042
H	-8.679809611	0.261385289	-1.256902023
H	-6.186550261	-1.885938662	-1.757434596
H	-3.852941035	-0.383679579	0.806057037
H	-2.828089956	-6.157557755	2.357449238
H	-2.358492836	-4.546544893	2.550119181

H	-6.526006785	-6.143130325	-0.10442357
C	-7.280145918	3.465486314	2.251202541
H	-6.443341661	3.786303114	2.878862281
H	-8.181092389	4.037304618	2.502528861
H	-7.482122718	2.402976879	2.44745252
P	8.331112403	-0.57861756	0.854406613
O	8.20139206	0.896516667	0.448503093
O	8.177598004	-1.007075434	2.266291656
C	9.902375654	-1.161218852	0.129431852
H	10.73828447	-0.656966464	0.622709841
H	9.948647338	-0.943681212	-0.942655839
H	10.00087312	-2.239200644	0.282789977
C	-0.449201217	1.469935269	-2.637803863
O	-1.759147219	0.907685348	-2.769738329
H	0.15953354	1.216052312	-3.513006871
H	-0.518405257	2.555071314	-2.529986469
C	6.260995024	8.053503644	0.909538927
C	3.785676001	7.616303469	0.783619218
C	-1.666928306	4.95519635	-3.027700896
C	0.237593158	6.605175338	-2.861869229
H	-2.143858543	4.077784609	-2.578175888
H	-1.406951431	4.711883951	-4.064800162
H	-2.413149217	5.758688078	-3.046258743
H	-0.42481909	7.479286233	-2.809382203
H	0.467445094	6.423655509	-3.918369238
H	1.175934762	6.863786032	-2.356639792
H	3.663386279	8.076703693	-0.205391485
H	3.636802863	8.395748015	1.539024042
H	2.982152468	6.883495745	0.905418708
H	7.256299358	7.612185027	1.035470815
H	6.110234064	8.782108133	1.714080433
H	6.254535434	8.599712989	-0.042321534