

The molecule mechanism of P450-catalyzed amination of the Pyrrolidine Derivative of Lidocaine: Insights from Multiscale Simulations

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(a) Substrate binding in the active site of the P450 variant

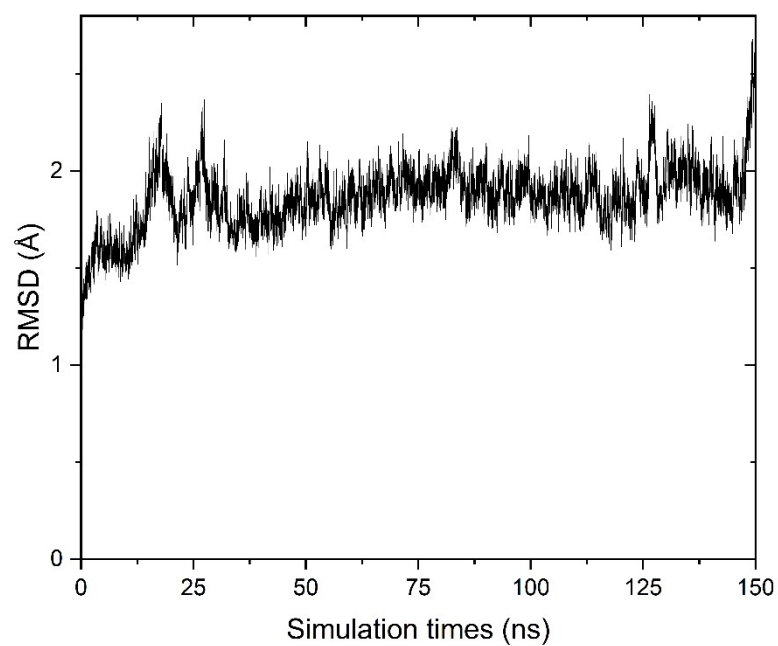


Fig. S1 Time evolution of the root mean square deviations (RMSD) for the protein backbone and substrate during the MD.

(b) MD simulation on two kinds of protonation state for Glu409

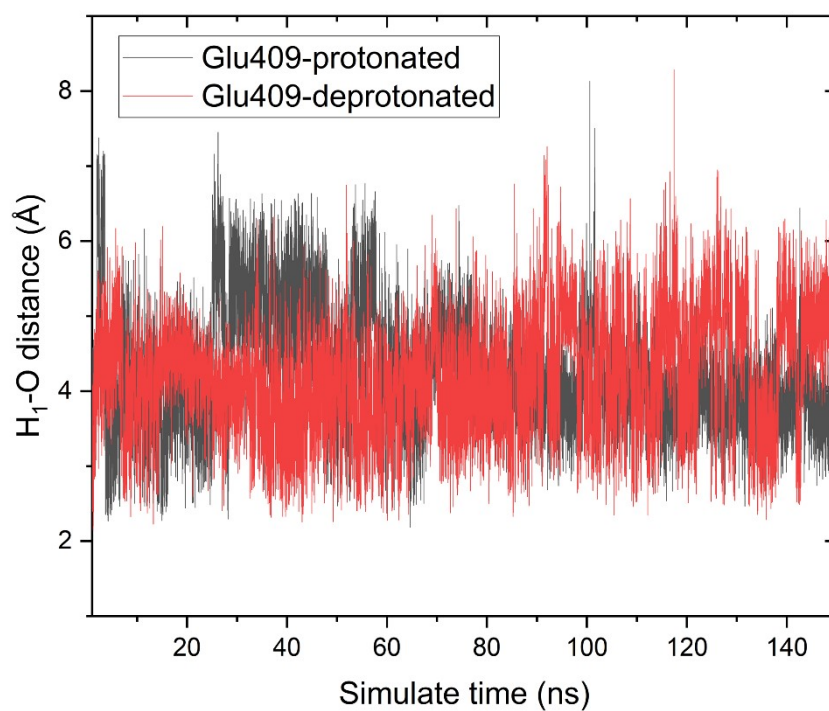


Fig. S2 Distance fluctuations between Cpd I-O and the H1 atom of the substrate throughout the MD trajectories of Glu409-protonated (black) and Glu409-deprotonated (red).

(c) QM/MM study on the hydroxylation of the pyrrolidine derivative of lidocaine in quartet state

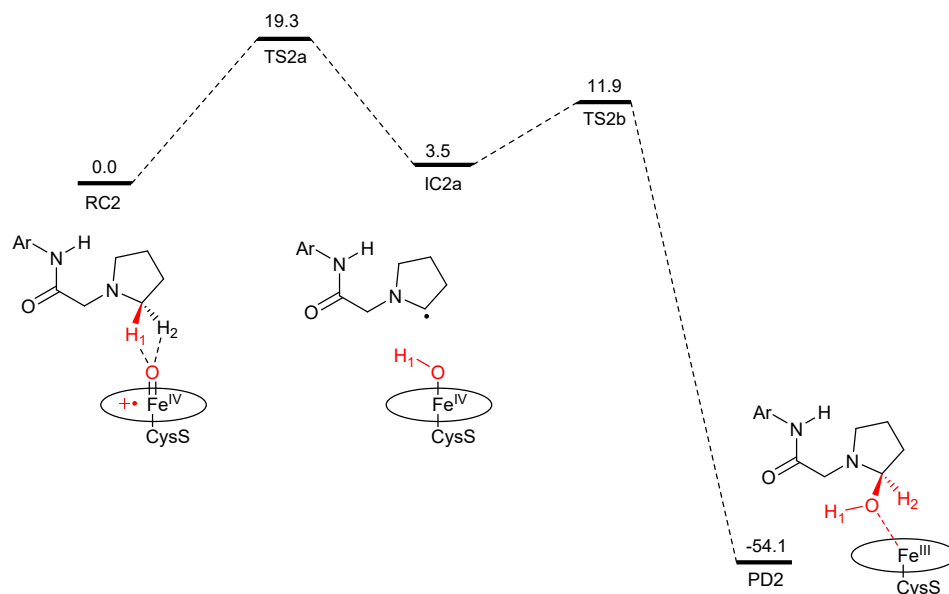


Fig. S3 QM(UB3LYP/B2//B1)/MM relative energies (kcal/mol) for the hydroxylation of the pyrrolidine derivative of lidocaine by the P450_{BM3} variant for quartet state. Key intermediates along the reaction energy profile are schematically drawn.

(d) QM(UB3LYP/def2-TZVP)/MM study on the hydroxylation of the pyrrolidine derivative of lidocaine

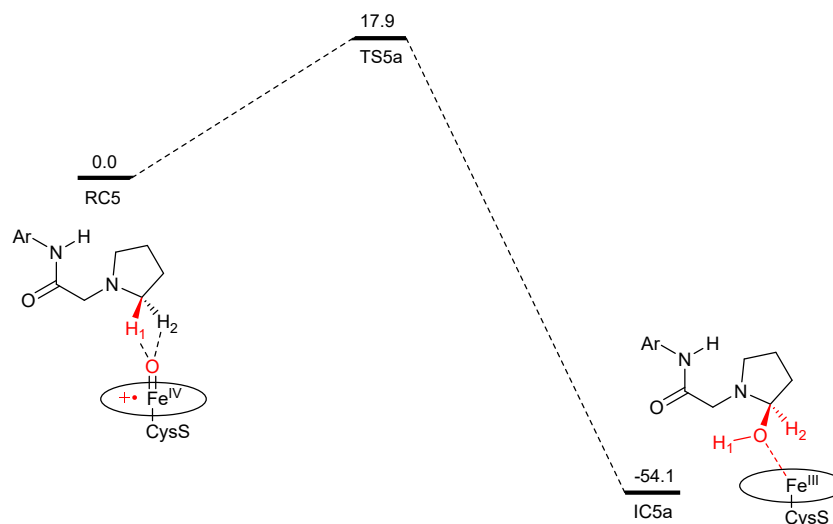
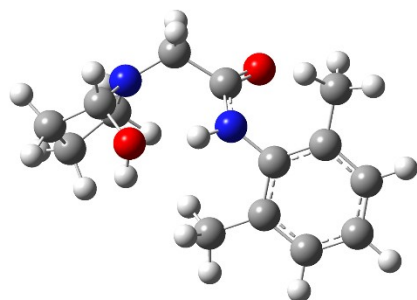


Fig. S4 QM(UB3LYP/def2-TZVP)/MM scanned energy barrier (kcal/mol) for the hydroxylation of the pyrrolidine derivative of lidocaine by the P450_{BM3} variant in the doublet state. Key intermediates along the reaction energy profile are schematically drawn.

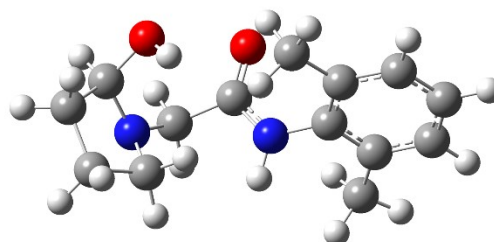
(e) QM study on the isomer of RC3

(a)



RC3 (0.0)

(b)



RC3' (3.6)

Fig. S5 (a) QM/B1 optimized structure of the hydroxylated intermediate RC3 with a well intramolecular hydrogen bond. (b) another QM optimized structure of the hydroxylated intermediate RC3' without a intramolecular hydrogen bond. The relative energies (in kcal/mol) are shown along the structure.

(f) Total QM/MM (or QM) Cartesian coordinates of all computed species

RC1				H	46.639091	45.414899	52.475495
C	49.461392	49.630723	53.264969	C	46.542681	47.019325	51.079209
H	48.750758	50.071250	53.983791	C	45.101485	47.066056	50.958028
H	49.410454	48.536482	53.317643	N	47.129520	47.988200	50.314334
S	49.002942	50.251546	51.624558	C	46.113446	48.670864	49.716100
N	48.708503	49.819013	48.770673	C	46.268534	49.773828	48.883082
C	47.471832	50.306581	48.443195	H	45.365059	50.238400	48.496373
C	49.606785	50.576972	48.083316	Fe	49.104011	48.267952	50.033187
C	47.578659	51.432013	47.539314	C	44.825444	48.099540	50.082045
C	48.927440	51.586173	47.280358	C	43.549284	48.559309	49.555851
C	50.987845	50.487625	48.231020	H	43.571780	49.522483	49.039287
H	51.605618	51.146287	47.620208	C	42.368676	47.914106	49.589481
C	51.646270	49.690219	49.154048	H	42.250308	46.928651	50.042769
N	51.053728	48.813729	50.031619	H	41.487911	48.368931	49.128791
C	52.084146	48.249982	50.752075	C	49.615518	52.540658	46.417605
C	53.364948	48.799796	50.332207	H	50.600800	52.219084	46.059140
C	53.079174	49.699903	49.338053	C	49.176426	53.749939	46.025144
C	51.926523	47.273214	51.724972	H	48.225601	54.167100	46.366289
H	52.826724	46.918386	52.227092	H	49.781609	54.367187	45.355202
C	50.716094	46.680549	52.086650	C	44.138064	46.196496	51.695937
C	50.597237	45.598876	53.050908	H	43.232312	46.763388	51.964337
C	48.602526	46.122917	52.123761	H	43.813162	45.330070	51.091293
N	49.498689	46.988042	51.541512	H	44.576791	45.806377	52.624203
C	49.275366	45.232755	53.050036	C	46.425102	52.241134	47.036847
C	47.232218	46.135024	51.911377	H	45.530036	51.617656	46.879223

H	46.157057	53.030438	47.762346	C	51.184985	38.988320	47.359975
H	46.670349	52.738096	46.085421	C	52.714939	38.902803	52.177088
C	54.036072	50.550742	48.569014	H	49.936472	42.376090	47.786836
H	55.062880	50.322468	48.881710	H	51.678577	42.027795	47.741338
H	53.952187	50.384275	47.480529	H	51.893830	44.157497	46.626168
H	53.858572	51.627413	48.744055	H	50.213650	44.564858	47.047420
C	48.655452	44.100617	53.808869	H	52.666058	44.942536	48.838649
H	48.663762	43.168412	53.214980	H	51.329907	46.109941	48.518579
H	49.233520	43.890549	54.722847	H	49.739714	44.685919	49.707957
H	47.608830	44.299761	54.091488	H	51.166613	44.672228	50.773047
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H	52.616296	45.550700	53.803734	H	50.192362	42.342998	51.359588
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C	54.721614	48.408715	50.835948	H	51.887101	36.344927	47.475645
H	54.689390	47.400157	51.263718	H	53.290140	36.303024	51.562806
H	55.409836	48.349604	49.974819	H	52.845557	35.099958	49.408876
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H	52.167771	43.646277	52.076052	H	51.822719	39.843860	47.075641
H	51.210410	42.857837	53.319960	H	51.068291	38.323503	46.491069
C	55.353420	49.341520	51.882385	H	53.013951	38.185083	52.954946
H	54.706810	49.396775	52.775156	H	53.455987	39.720746	52.154823
H	55.440342	50.369194	51.489541	H	51.755935	39.368459	52.457979
C	56.755083	48.863994	52.340174	H	50.460904	49.953287	53.556508
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O	53.806911	41.996338	52.886731				
O	56.953326	47.619084	52.369376	TS1a			
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O	57.585427	49.743549	52.666323	H	48.634267	50.053576	53.966551
O	49.255744	47.159056	48.861239	H	49.247299	48.477076	53.381013
C	50.933980	42.771831	48.066508	S	48.851043	50.080328	51.569526
N	51.018926	42.963071	49.537965	N	48.701995	49.585026	48.750077
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C	46.260508	49.605581	48.904885	O	54.078672	42.257541	52.804191
H	45.362934	50.077638	48.515499	O	56.970813	47.579260	52.382348
Fe	49.104204	48.134851	50.129264	O	53.807235	43.156919	54.846013
C	44.809357	47.991851	50.165953	O	57.564812	49.717279	52.654301
C	43.536233	48.461162	49.642972	O	49.156173	46.898625	48.990826
H	43.565211	49.422789	49.123532	C	50.642383	43.413993	47.680807
C	42.349495	47.829131	49.688355	N	50.623505	43.617568	49.131587
H	42.223771	46.848478	50.149307	O	49.249734	40.433418	49.805269
H	41.471260	48.291177	49.231091	C	51.016040	44.802545	47.121724
C	49.626791	52.257831	46.350342	N	51.479045	40.910910	49.690139
H	50.599830	51.913432	45.981318	C	51.707095	45.490125	48.310048
C	49.205676	53.470943	45.951870	C	50.854700	44.978137	49.460843
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H	49.809787	54.070314	45.265348	C	50.166062	41.247217	49.815059
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H	43.215937	46.717403	52.084781	C	51.685017	38.905811	48.297113
H	43.766454	45.262376	51.229775	C	52.486260	38.876481	50.624034
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H	46.186011	52.811840	47.758333	C	51.064529	39.643483	47.141765
H	46.673848	52.526772	46.073802	C	52.674136	39.564608	51.944750
C	54.028423	50.311091	48.514828	H	49.657239	43.057136	47.324105
H	55.059434	50.012947	48.746321	H	51.383865	42.635376	47.426805
H	53.865724	50.210572	47.428123	H	51.637186	44.744970	46.214979
H	53.925216	51.384083	48.755976	H	50.098456	45.368084	46.892884
C	48.639773	44.023910	53.909512	H	52.742101	45.130150	48.422513
H	48.612027	43.102773	53.299008	H	51.690150	46.585901	48.254031
H	49.237385	43.787141	54.803596	H	49.788934	45.754592	49.400340
H	47.605451	44.235363	54.224030	H	51.244216	45.101303	50.481654
C	51.696246	44.874955	53.897075	H	48.767438	42.833592	49.749421
H	52.540485	45.564443	54.031567	H	50.002628	43.032768	51.025623
H	51.373326	44.570926	54.903059	H	52.196947	41.627252	49.840320

H	51.808215	37.023689	47.242868	Fe	49.132952	48.117726	50.071528
H	53.244956	36.985262	51.316847	C	44.839361	48.007667	50.103080
H	52.777518	35.778887	49.168689	C	43.568702	48.490059	49.584190
H	50.059347	40.007656	47.406622	H	43.603158	49.452452	49.065830
H	51.674800	40.518378	46.858515	C	42.377662	47.866695	49.631549
H	50.973676	38.977268	46.272094	H	42.246577	46.884887	50.089128
H	52.947389	38.828662	52.715748	H	41.500365	48.335551	49.178369
H	53.458771	40.339015	51.928803	C	49.659666	52.406182	46.438716
H	51.742112	40.075260	52.236732	H	50.653285	52.098428	46.091218
H	50.336238	49.863048	53.514200	C	49.216288	53.617381	46.056205
TS1b				H	48.255990	54.020368	46.386916
C	49.444942	49.582809	53.225158	H	49.823896	54.249298	45.402002
H	48.727106	50.031276	53.931504	C	44.120722	46.161880	51.766973
H	49.397393	48.489307	53.298753	H	43.228853	46.756705	52.021761
S	48.978425	50.157854	51.567729	H	43.774675	45.285722	51.189115
N	48.739746	49.625102	48.724884	H	44.555937	45.789559	52.703684
C	47.506523	50.128198	48.402398	C	46.463830	52.091088	47.034495
C	49.638597	50.412346	48.070678	H	45.565634	51.474316	46.870161
C	47.616240	51.268602	47.518141	H	46.199602	52.867806	47.775254
C	48.965606	51.431879	47.274877	H	46.702933	52.606559	46.091818
C	51.014532	50.356934	48.263110	C	54.040645	50.492053	48.677462
H	51.636492	51.031021	47.674805	H	55.051212	50.368720	49.087614
C	51.660111	49.576918	49.208020	H	54.064953	50.265063	47.596555
N	51.066511	48.691534	50.076016	H	53.763126	51.557238	48.771290
C	52.092807	48.131227	50.802001	C	48.623460	44.023798	53.884764
C	53.371107	48.700119	50.400890	H	48.595626	43.093798	53.288378
C	53.087092	49.609845	49.416167	H	49.218780	43.796965	54.783365
C	51.926804	47.143293	51.765234	H	47.589191	44.246908	54.193672
H	52.823047	46.780117	52.270426	C	51.691221	44.814633	53.820513
C	50.710482	46.557812	52.122230	H	52.562057	45.478316	53.923361
C	50.576016	45.494038	53.099579	H	51.379147	44.542617	54.839810
C	48.586275	46.033171	52.184495	C	54.729933	48.322809	50.903526
N	49.490754	46.884969	51.594021	H	54.700966	47.322273	51.346364
C	49.251369	45.143591	53.114363	H	55.414669	48.251980	50.040908
C	47.216110	46.049092	51.972852	C	52.098301	43.541384	53.073074
H	46.618609	45.346876	52.555517	H	52.199047	43.769542	51.998270
C	46.538765	46.916362	51.114882	H	51.285950	42.793789	53.146193
C	45.099368	46.988474	51.000920	C	55.362367	49.276580	51.928978
N	47.143733	47.849737	50.318746	H	54.727404	49.335714	52.829195
C	46.135526	48.539443	49.714041	H	55.431415	50.301168	51.524742
C	46.300595	49.622522	48.859061	C	56.773442	48.820225	52.368064
H	45.401730	50.101645	48.481559	C	53.402325	42.862756	53.551253
				O	53.947157	42.129191	52.678628
				O	56.992503	47.577279	52.376757

O	53.784315	43.054954	54.725406	C	49.311900	49.678142	53.347149
O	57.593716	49.707658	52.699304	H	48.653885	50.160640	54.085077
O	49.371367	46.907027	48.951018	H	49.227080	48.588755	53.437748
C	51.127147	42.595974	47.619529	S	48.775411	50.250994	51.695354
N	50.750775	43.315729	48.873841	N	48.718442	49.869256	48.821339
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C	51.182625	43.655063	46.496630	C	49.619073	50.641592	48.144520
N	51.535871	40.571673	49.811904	C	47.594072	51.460917	47.540657
C	50.899737	44.974616	47.230889	C	48.945034	51.634553	47.315716
C	50.070501	44.527663	48.419317	C	50.996353	50.540521	48.284079
C	49.944999	42.499134	49.782326	H	51.617988	51.213536	47.693153
C	50.236268	40.984687	49.834947	C	51.650443	49.685700	49.158526
C	51.920615	39.191846	49.726981	N	51.056983	48.778300	50.008818
C	51.727264	38.485578	48.516216	C	52.096685	48.222402	50.730087
C	52.464829	38.555975	50.861821	C	53.373755	48.763628	50.300179
C	52.057976	37.120067	48.470485	C	53.083312	49.677781	49.319081
C	52.809094	37.196544	50.767422	C	51.950080	47.276921	51.736153
C	52.592849	36.472441	49.591487	H	52.853474	46.922336	52.232402
C	51.141151	39.153935	47.300937	C	50.735194	46.731593	52.135132
C	52.616096	39.295561	52.159197	C	50.605099	45.644226	53.088392
H	50.360830	41.835329	47.377606	C	48.610330	46.220837	52.197809
H	52.078960	42.060469	47.749607	N	49.513806	47.075294	51.603280
H	52.141202	43.640833	45.954417	C	49.277879	45.301242	53.098349
H	50.387198	43.456839	45.759155	C	47.240953	46.228264	51.974658
H	51.835473	45.427423	47.599268	H	46.643286	45.514012	52.541594
H	50.371577	45.721052	46.624489	C	46.567533	47.086591	51.110131
H	49.024955	44.285825	48.115845	C	45.130322	47.116940	50.969326
H	49.816695	45.707596	49.069277	N	47.167598	48.030356	50.306894
H	48.876399	42.538476	49.487587	C	46.136312	48.695682	49.691791
H	50.015207	42.902667	50.810118	C	46.278557	49.790240	48.853092
H	52.279255	41.268254	49.912831	H	45.375585	50.235063	48.444036
H	51.865140	36.557368	47.552481	Fe	49.103882	48.568311	50.328723
H	53.207356	36.699543	51.655351	C	44.854273	48.121809	50.061242
H	52.805132	35.399058	49.548674	C	43.576487	48.560578	49.519297
H	50.152566	39.582485	47.529568	H	43.595362	49.509575	48.977137
H	51.787407	39.976254	46.952773	C	42.397831	47.912686	49.569735
H	51.024490	38.422814	46.486954	H	42.279847	46.940163	50.049930
H	52.815081	38.580126	52.972138	H	41.515612	48.352384	49.097214
H	53.432885	40.037641	52.147352	C	49.637311	52.586322	46.453647
H	51.694131	39.857934	52.379292	H	50.632865	52.273637	46.116455
H	50.442353	49.908837	53.520019	C	49.190151	53.785770	46.040670
				H	48.227814	54.193339	46.360348
				H	49.798283	54.404236	45.374323
				C	44.163260	46.258570	51.716149

IC1a

H	43.259305	46.832734	51.975446	C	51.799595	38.274749	48.524595
H	43.835420	45.387679	51.119376	C	52.579905	38.246769	50.861121
H	44.595684	45.876338	52.650410	C	52.110433	36.907730	48.421199
C	46.439651	52.245380	47.003650	C	52.902592	36.888516	50.711578
H	45.559134	51.605876	46.829844	C	52.653086	36.212895	49.511981
H	46.139235	53.030667	47.721089	C	51.195219	39.021873	47.363879
H	46.696461	52.743355	46.055732	C	52.740809	38.953492	52.177479
C	54.039626	50.530740	48.550493	H	50.062639	42.270061	47.699416
H	55.065930	50.305265	48.866265	H	51.830511	42.111725	47.814234
H	53.957407	50.362427	47.462136	H	51.883063	44.209867	46.619384
H	53.859391	51.607135	48.722481	H	50.162241	44.491525	46.993532
C	48.649223	44.157119	53.832749	H	52.516755	45.022581	48.893286
H	48.617459	43.245854	53.207494	H	51.178414	46.143278	48.480664
H	49.245470	43.899890	54.722603	H	48.822775	44.913943	50.329435
H	47.615193	44.370170	54.149292	H	50.906342	44.726507	50.729977
C	51.718610	44.932778	53.790384	H	48.984317	42.259139	49.902311
H	52.613655	45.567277	53.852291	H	50.078324	42.350586	51.316894
H	51.423681	44.706753	54.826286	H	52.335284	40.991268	50.077523
C	54.733343	48.374870	50.797596	H	51.898227	36.380949	47.486628
H	54.708089	47.363698	51.219436	H	53.310933	36.352964	51.571033
H	55.422382	48.327844	49.936569	H	52.855575	35.140805	49.424900
C	52.070073	43.611988	53.092406	H	50.188624	39.391531	47.620972
H	52.212928	43.776606	52.013244	H	51.808877	39.900578	47.099268
H	51.218135	42.911048	53.177056	H	51.111972	38.362790	46.486833
C	55.355062	49.308473	51.849477	H	53.022995	38.233224	52.959190
H	54.702917	49.356226	52.738381	H	53.496743	39.757639	52.156222
H	55.433950	50.338176	51.460341	H	51.789407	39.438176	52.451467
C	56.757473	48.842199	52.313232	H	50.339067	49.962384	53.575621
C	53.322718	42.866086	53.615970				
O	53.815261	42.046781	52.789716				
O	56.964328	47.598266	52.341996	IC1b			
O	53.718964	43.094968	54.778880	C	49.393625	49.456365	53.202403
O	57.580343	49.726471	52.644702	H	48.693362	49.934739	53.902529
O	49.250152	44.732408	49.482922	H	49.346416	48.368106	53.328390
C	50.982902	42.774310	48.051052	S	48.894344	49.950679	51.513153
N	50.930268	43.009750	49.519718	N	48.781618	49.538341	48.698019
O	49.386747	39.829462	50.071044	C	47.547744	50.038360	48.370609
C	51.127811	44.179029	47.418901	C	49.680740	50.334011	48.052164
N	51.618854	40.280533	49.914950	C	47.656224	51.188561	47.497258
C	51.452628	45.087338	48.618429	C	49.005645	51.360420	47.262602
C	50.621050	44.433611	49.713716	C	51.057972	50.263894	48.219256
C	50.027785	42.122072	50.236535	H	51.671642	50.966844	47.656171
C	50.313449	40.633626	50.067817	C	51.720262	49.431457	49.110813
C	52.024290	38.921594	49.758746	N	51.145648	48.491202	49.933443

C	52.173235	47.970472	50.690920	H	49.275973	43.773599	54.831144
C	53.438805	48.573787	50.306125	H	47.654947	44.252592	54.244891
C	53.143406	49.494790	49.331857	C	51.766094	44.846941	53.920729
C	52.011596	47.032899	51.710274	H	52.500272	45.611336	54.213310
H	52.907849	46.707230	52.240782	H	51.383833	44.395308	54.848231
C	50.792866	46.489908	52.116514	C	54.802537	48.249158	50.832012
C	50.649488	45.464709	53.141027	H	54.802112	47.254814	51.289163
C	48.667418	45.980555	52.190434	H	55.503784	48.193536	49.981120
N	49.573679	46.805504	51.576968	C	52.464046	43.769131	53.092837
C	49.327170	45.112605	53.152611	H	52.806408	44.244962	52.157563
C	47.296705	45.989609	51.971548	H	51.733776	42.994922	52.795833
H	46.697339	45.307244	52.574374	C	55.377854	49.239133	51.858282
C	46.617576	46.836630	51.096947	H	54.717224	49.284595	52.740660
C	45.176241	46.920418	51.007860	H	55.420274	50.259505	51.439734
N	47.215219	47.741652	50.253927	C	56.792183	48.843493	52.338974
C	46.192483	48.439539	49.667463	C	53.680419	43.035926	53.709318
C	46.341403	49.519354	48.810429	O	54.314680	42.324308	52.880020
H	45.439060	49.996605	48.437242	O	57.041282	47.607454	52.399787
Fe	49.175358	48.193028	50.188572	O	53.916954	43.172528	54.925706
C	44.903920	47.925116	50.098445	O	57.584759	49.762409	52.647387
C	43.623426	48.421528	49.615584	O	49.664919	46.407460	48.821713
H	43.658200	49.372601	49.076385	C	51.381009	44.084330	47.932561
C	42.419651	47.828291	49.721626	N	50.230459	44.032313	48.815416
H	42.281448	46.861558	50.208177	O	49.342301	41.215071	49.791287
H	41.537660	48.309591	49.290913	C	50.770108	44.502704	46.570270
C	49.697856	52.342694	46.435317	N	51.619093	41.318072	49.869871
H	50.695018	52.041432	46.092216	C	49.315335	44.931050	46.911073
C	49.252983	53.554653	46.056297	C	49.302590	45.046738	48.442700
H	48.289644	53.952887	46.383700	C	50.334059	43.405019	50.114284
H	49.863056	54.192411	45.409859	C	50.369708	41.868958	49.934988
C	44.203006	46.121225	51.808384	C	51.882420	39.936525	49.604829
H	43.340354	46.742751	52.097923	C	51.620401	39.408326	48.321066
H	43.806952	45.259096	51.241220	C	52.409499	39.128782	50.636528
H	44.660438	45.732283	52.727029	C	51.865793	38.045568	48.091690
C	46.502468	52.015966	47.024097	C	52.643571	37.768088	50.365942
H	45.602216	51.401534	46.860835	C	52.363396	37.223118	49.108381
H	46.241521	52.786728	47.772362	C	51.066083	40.278990	47.227151
H	46.738365	52.540446	46.085137	C	52.672429	39.702366	51.999814
C	54.085707	50.436725	48.649965	H	51.887326	43.107900	47.904941
H	55.023565	50.497972	49.218405	H	52.138367	44.826846	48.277347
H	54.322276	50.131991	47.614370	H	51.349678	45.315683	46.107098
H	53.659627	51.452827	48.586852	H	50.771987	43.655419	45.867636
C	48.683553	44.008210	53.932831	H	49.004205	45.877477	46.449500
H	48.630709	43.075868	53.340075	H	48.608011	44.142452	46.611536

H	48.321667	44.891346	48.912834
H	50.606363	46.565649	48.656568
H	49.441033	43.652116	50.704871
H	51.211763	43.757791	50.687815
H	52.424377	41.896208	50.126305
H	51.636692	37.618832	47.111255
H	53.017027	37.132668	51.174408
H	52.492051	36.150917	48.924373
H	50.055631	40.635737	47.486982
H	51.701332	41.166943	47.065876
H	51.010037	39.707905	46.289847
H	52.888702	38.894062	52.715367
H	53.524477	40.402744	52.020602
H	51.795001	40.276215	52.340232
H	50.401286	49.782330	53.460147

RC2

C	49.457631	49.620679	53.252487
H	48.745083	50.058966	53.970667
H	49.408878	48.526303	53.303378
S	48.998376	50.242469	51.612312
N	48.713524	49.810087	48.752346
C	47.475132	50.294787	48.424309
C	49.609255	50.574065	48.068590
C	47.579119	51.420961	47.520859
C	48.927537	51.581640	47.265636
C	50.990033	50.491295	48.220901
H	51.606859	51.154963	47.614608
C	51.648120	49.694452	49.144357
N	51.056435	48.810619	50.016291
C	52.088457	48.248755	50.738151
C	53.367432	48.803991	50.321424
C	53.080072	49.708368	49.331429
C	51.933979	47.269181	51.708054
H	52.835185	46.915347	52.208873
C	50.724297	46.675542	52.070834
C	50.605608	45.596673	53.037912
C	48.611081	46.118862	52.110049
N	49.507441	46.982132	51.524976
C	49.283578	45.231491	53.039132
C	47.240571	46.130779	51.899884
H	46.648604	45.411638	52.466483
C	46.549967	47.012592	51.066393

C	45.108637	47.058974	50.947245
N	47.135446	47.980861	50.299853
C	46.118974	48.662447	49.702898
C	46.272995	49.763634	48.867010
H	45.369151	50.227889	48.480968
Fe	49.113115	48.262342	50.014575
C	44.831259	48.092660	50.071885
C	43.554197	48.554565	49.550015
H	43.575858	49.518949	49.035533
C	42.373145	47.910306	49.585920
H	42.255078	46.923898	50.037203
H	41.491310	48.366770	49.129006
C	49.613182	52.542308	46.407739
H	50.601587	52.228279	46.051285
C	49.167418	53.750091	46.018676
H	48.211812	54.157976	46.357119
H	49.769622	54.374245	45.352415
C	44.146679	46.189257	51.686790
H	43.241840	46.756393	51.957912
H	43.819869	45.323663	51.081923
H	44.587227	45.797691	52.613639
C	46.423201	52.224646	47.016030
H	45.529545	51.598443	46.862909
H	46.152621	53.014681	47.739853
H	46.662359	52.718187	46.061446
C	54.035101	50.566134	48.567527
H	55.060839	50.352698	48.893747
H	53.965094	50.391867	47.479123
H	53.841715	51.641435	48.733556
C	48.663716	44.102416	53.802673
H	48.670388	43.168294	53.211692
H	49.243380	43.894869	54.716258
H	47.617918	44.303991	54.086848
C	51.723354	44.920632	53.772924
H	52.625361	45.548568	53.786980
H	51.439181	44.766719	54.825197
C	54.725060	48.413895	50.823531
H	54.696700	47.401122	51.241728
H	55.414741	48.365971	49.963006
C	52.058162	43.552622	53.158912
H	52.172453	43.640060	52.069362
H	51.210990	42.858515	53.313862
C	55.351470	49.339153	51.879697
H	54.702319	49.384479	52.771224

H	55.435669	50.370489	51.496173
C	56.753567	48.862202	52.336134
C	53.329248	42.841949	53.686404
O	53.799300	41.978190	52.894385
O	56.953174	47.617422	52.361230
O	53.761346	43.140634	54.821438
O	57.582986	49.741442	52.665524
O	49.243258	47.143980	48.848028
C	50.961656	42.757962	48.062225
N	51.021632	42.957030	49.534444
O	49.371605	39.838818	50.096332
C	51.166632	44.162774	47.442707
N	51.613856	40.235238	49.913046
C	51.581453	45.045324	48.632754
C	50.803496	44.395961	49.765560
C	50.093784	42.116349	50.269500
C	50.319817	40.617642	50.086866
C	52.004482	38.873245	49.755386
C	51.780528	38.229465	48.519621
C	52.561941	38.196631	50.855914
C	52.098145	36.864510	48.411139
C	52.893354	36.841381	50.700477
C	52.648337	36.169397	49.497711
C	51.174720	38.980137	47.361935
C	52.718527	38.900275	52.174764
H	49.979055	42.336384	47.768530
H	51.729859	42.031898	47.751023
H	51.894634	44.155395	46.616607
H	50.211159	44.539601	47.043801
H	52.660151	44.947890	48.835871
H	51.317763	46.103784	48.506098
H	49.731560	44.672768	49.688804
H	51.151755	44.671959	50.763080
H	49.044334	42.300131	49.961217
H	50.174825	42.339867	51.348059
H	52.342905	40.937718	50.054303
H	51.887048	36.339955	47.475247
H	53.307167	36.306293	51.557452
H	52.859677	35.099555	49.405069
H	50.180494	39.373851	47.630232
H	51.803735	39.843167	47.081322
H	51.065722	38.317639	46.490250
H	53.010422	38.180859	52.953778
H	53.465025	39.713067	52.155559

H	51.762052	39.372792	52.452658
H	50.456477	49.943391	53.546138

TS2a

C	49.342290	49.564193	53.277536
H	48.636093	50.065562	53.956475
H	49.268672	48.477996	53.413914
S	48.934981	50.051370	51.566588
N	48.701644	49.570969	48.745165
C	47.471115	50.100275	48.437936
C	49.615277	50.309225	48.041198
C	47.599512	51.212239	47.523469
C	48.947589	51.326578	47.241538
C	50.992811	50.208847	48.170192
H	51.608395	50.868006	47.558274
C	51.652417	49.417081	49.102198
N	51.069858	48.557167	49.984607
C	52.079885	48.070234	50.773335
C	53.363179	48.622985	50.351743
C	53.082480	49.473497	49.315301
C	51.910430	47.185243	51.831483
H	52.803834	46.866531	52.369077
C	50.690207	46.638485	52.232980
C	50.562598	45.557612	53.192461
C	48.570831	46.074811	52.257313
N	49.469634	46.943698	51.695826
C	49.243174	45.179289	53.178190
C	47.198812	46.072995	52.030844
H	46.606712	45.357133	52.601169
C	46.515287	46.938580	51.182525
C	45.072074	46.997087	51.061683
N	47.102642	47.884092	50.384624
C	46.092469	48.562243	49.776275
C	46.256126	49.630776	48.906659
H	45.362787	50.114349	48.520811
F	49.079090	48.174878	50.138755
C	44.801605	48.013136	50.166901
C	43.529147	48.481864	49.641081
H	43.560700	49.441158	49.116752
C	42.340420	47.852338	49.687484
H	42.212869	46.873440	50.152481
H	41.463349	48.314798	49.227413
C	49.645189	52.257577	46.359701

H	50.604825	51.898475	45.969045	C	51.730698	45.384755	48.404986
C	49.242814	53.485967	45.988386	C	50.875250	44.880603	49.552394
H	48.320710	53.936230	46.364218	C	49.838638	42.666582	50.091763
H	49.847794	54.084783	45.301316	C	50.155565	41.166871	49.937138
C	44.100617	46.157193	51.821499	C	51.880609	39.457932	49.643586
H	43.205720	46.744193	52.083894	C	51.667355	38.814898	48.404621
H	43.757016	45.284491	51.236302	C	52.445862	38.775354	50.739325
H	44.541371	45.778956	52.753080	C	51.994395	37.453567	48.286456
C	46.459022	52.053171	47.042478	C	52.778229	37.418722	50.577548
H	45.556543	51.445303	46.867727	C	52.537888	36.752433	49.371611
H	46.196686	52.822158	47.791405	C	51.065222	39.560390	47.244021
H	46.708862	52.577092	46.107408	C	52.627341	39.461570	52.062053
C	54.035224	50.335656	48.552487	H	49.630434	42.990820	47.426415
H	55.064843	50.098927	48.852016	H	51.339143	42.508737	47.555845
H	53.940521	50.195582	47.461480	H	51.695655	44.589078	46.325847
H	53.864389	51.409250	48.750557	H	50.155553	45.266450	46.943510
C	48.626291	44.033188	53.919944	H	52.769442	45.033833	48.528010
H	48.606412	43.114384	53.305103	H	51.712782	46.480607	48.338403
H	49.218840	43.791774	54.816830	H	49.889240	45.733320	49.444796
H	47.588625	44.238608	54.228708	H	51.198890	45.030631	50.590488
C	51.685688	44.885981	53.916510	H	48.757141	42.753313	49.884228
H	52.533098	45.573194	54.048493	H	50.009307	42.960036	51.142468
H	51.365225	44.583438	54.924263	H	52.189649	41.534096	49.941719
C	54.716346	48.277031	50.893054	H	51.789887	36.933539	47.346065
H	54.672874	47.310400	51.403757	H	53.184745	36.876764	51.435544
H	55.409950	48.140484	50.044736	H	52.737127	35.679302	49.278533
C	52.155130	43.635631	53.163242	H	50.079997	39.973544	47.512713
H	52.296658	43.889831	52.098799	H	51.712469	40.401340	46.937452
H	51.358119	42.867415	53.183499	H	50.934094	38.884313	46.386826
C	55.359745	49.284727	51.857740	H	52.895138	38.724423	52.834288
H	54.723468	49.409577	52.750600	H	53.411965	40.236931	52.049471
H	55.445658	50.279739	51.387724	H	51.693536	39.972640	52.348386
C	56.763334	48.838302	52.333878	H	50.353785	49.870793	53.543882
C	53.458050	42.967437	53.671299				
O	54.043799	42.245722	52.815179				
O	56.977957	47.595793	52.389494	IC2a			
O	53.801185	43.156144	54.855889	C	49.320741	49.570148	53.264661
O	57.581868	49.733525	52.645659	H	48.633052	50.044574	53.979387
O	49.189557	46.755852	49.117600	H	49.253177	48.479439	53.358077
C	50.624167	43.317786	47.786880	S	48.854421	50.126792	51.591734
N	50.595032	43.544244	49.234800	N	48.681963	49.752061	48.760584
O	49.234975	40.357510	49.943718	C	47.442147	50.239202	48.426870
C	51.051391	44.685159	47.213149	C	49.588005	50.491500	48.054659
N	51.465511	40.822173	49.798560	C	47.558322	51.340982	47.501744

C	48.908597	51.484107	47.238034	H	55.048710	50.154165	48.705988
C	50.967880	50.390166	48.171871	H	53.876643	50.296690	47.361736
H	51.578917	51.047175	47.554428	H	53.883361	51.500596	48.664547
C	51.634659	49.569577	49.069182	C	48.640279	44.123531	53.837509
N	51.060718	48.699254	49.951171	H	48.632249	43.191764	53.242928
C	52.085110	48.155431	50.680775	H	49.230600	43.909793	54.742438
C	53.365175	48.693202	50.238322	H	47.599928	44.329532	54.134848
C	53.071255	49.578736	49.234424	C	51.695825	44.940214	53.806395
C	51.931270	47.223243	51.698076	H	52.566095	45.604903	53.890182
H	52.830595	46.874328	52.204701	H	51.376691	44.713160	54.834282
C	50.714243	46.678092	52.094557	C	54.723634	48.323345	50.751946
C	50.583400	45.609955	53.062177	H	54.707068	47.309562	51.168026
C	48.580781	46.146981	52.159506	H	55.423699	48.291769	49.899374
N	49.484843	47.000329	51.568571	C	52.114860	43.630034	53.128521
C	49.256775	45.252169	53.071194	H	52.267988	43.811058	52.054702
C	47.206465	46.160802	51.967569	H	51.291497	42.893962	53.196580
H	46.620520	45.441132	52.537954	C	55.320336	49.257683	51.818123
C	46.516282	47.037150	51.137503	H	54.657678	49.286979	52.700187
C	45.074470	47.075583	51.009687	H	55.388342	50.290630	51.436445
N	47.095077	47.995976	50.353158	C	56.723940	48.807807	52.292768
C	46.080862	48.658664	49.733921	C	53.396389	42.944184	53.665844
C	46.232272	49.731418	48.869345	O	53.957691	42.174496	52.837887
H	45.333563	50.185670	48.463197	O	56.938060	47.565558	52.336501
Fe	49.082213	48.323432	50.115178	O	53.746764	43.168150	54.842518
C	44.795899	48.085666	50.111041	O	57.540987	49.699002	52.618738
C	43.520396	48.526874	49.569838	O	49.160973	46.996304	48.875964
H	43.542061	49.476559	49.029411	C	50.559924	43.098029	47.775079
C	42.341869	47.879676	49.617373	N	50.728032	43.245823	49.229535
H	42.223888	46.906757	50.096422	O	49.303706	40.106427	49.943020
H	41.461520	48.321245	49.144006	C	50.801975	44.518460	47.219560
C	49.594957	52.418390	46.352428	N	51.534794	40.564246	49.757370
H	50.570388	52.080567	45.984378	C	51.611601	45.216356	48.331512
C	49.164557	53.628198	45.954538	C	51.046039	44.560944	49.552135
H	48.223676	54.059176	46.304617	C	49.955252	42.405565	50.109041
H	49.766656	54.231941	45.270331	C	50.230029	40.908981	49.929837
C	44.114454	46.214340	51.760226	C	51.948103	39.204163	49.613635
H	43.210548	46.785340	52.025067	C	51.723376	38.547008	48.385801
H	43.785586	45.342389	51.166292	C	52.513548	38.539872	50.718473
H	44.556632	45.833993	52.690390	C	52.037942	37.181407	48.289803
C	46.408403	52.146782	46.988707	C	52.836889	37.180474	50.577971
H	45.516300	51.521167	46.828319	C	52.582875	36.495897	49.384401
H	46.132729	52.932749	47.714382	C	51.116413	39.285940	47.223105
H	46.655313	52.644120	46.039005	C	52.689212	39.255047	52.027558
C	54.017285	50.425544	48.448639	H	49.546419	42.720351	47.544454

H	51.280822	42.357359	47.385860	N	49.498139	46.968591	51.627911
H	51.310429	44.505947	46.242937	C	49.275083	45.222622	53.128364
H	49.843359	45.050792	47.117024	C	47.225173	46.105103	51.995836
H	52.686708	44.979515	48.219407	H	46.638458	45.392803	52.575061
H	51.487013	46.308842	48.333929	C	46.537308	46.960587	51.142336
H	49.505971	46.176873	49.283671	C	45.094417	47.012128	51.024371
H	51.282176	44.804074	50.586122	N	47.120504	47.895972	50.331912
H	48.869925	42.536130	49.942126	C	46.106830	48.565051	49.718918
H	50.178819	42.680155	51.154049	C	46.260049	49.630939	48.846297
H	52.254762	41.281985	49.884498	H	45.361855	50.100883	48.456670
H	51.823298	36.647029	47.360456	Fe	49.109107	48.212124	50.097837
H	53.246511	36.651500	51.441346	C	44.819005	48.016438	50.118642
H	52.779065	35.421892	49.306775	C	43.543088	48.475197	49.592520
H	50.118559	39.671457	47.486608	H	43.569443	49.426604	49.054624
H	51.742006	40.149485	46.936614	C	42.356815	47.843318	49.654031
H	51.013289	38.617588	46.356096	H	42.233503	46.871252	50.133374
H	53.019145	38.549765	52.804100	H	41.476193	48.296296	49.192080
H	53.422354	40.077188	51.984267	C	49.617930	52.359531	46.372367
H	51.732447	39.712684	52.328831	H	50.599234	52.038250	46.004823
H	50.336669	49.871088	53.518820	C	49.181567	53.574318	45.995757
TS2b				H	48.234947	53.991150	46.346795
C	49.317216	49.563463	53.244203	H	49.783782	54.196720	45.328191
H	48.622311	50.049804	53.944091	C	44.128265	46.174044	51.792175
H	49.246299	48.474611	53.359845	H	43.237541	46.762941	52.063104
S	48.870367	50.079473	51.552267	H	43.777074	45.304564	51.207240
N	48.708889	49.618845	48.704767	H	44.574714	45.792606	52.719444
C	47.469662	50.124643	48.390863	C	46.433732	52.076866	47.010798
C	49.611825	50.386615	48.023402	H	45.532171	51.464112	46.853927
C	47.583146	51.249864	47.493369	H	46.177108	52.856271	47.750599
C	48.932264	51.399650	47.231070	H	46.671305	52.587248	46.065364
C	50.990335	50.305382	48.157740	C	54.030980	50.396764	48.483684
H	51.600080	50.977532	47.555480	H	55.063277	50.146801	48.758460
C	51.654884	49.497257	49.068617	H	53.911618	50.266869	47.394351
N	51.082043	48.624215	49.945860	H	53.873566	51.469274	48.696151
C	52.102147	48.104251	50.698150	C	48.661608	44.089594	53.890684
C	53.380993	48.655781	50.265285	H	48.643847	43.161748	53.290303
C	53.087965	49.533258	49.255181	H	49.257179	43.866269	54.789664
C	51.944893	47.194096	51.735867	H	47.624134	44.297123	54.197480
H	52.844912	46.858377	52.250524	C	51.717445	44.913121	53.841837
C	50.727147	46.655694	52.150056	H	52.588442	45.576547	53.923354
C	50.598696	45.588546	53.119680	H	51.412886	44.663470	54.868421
C	48.597910	46.109900	52.209432	C	54.740792	48.301826	50.782185
				H	54.731100	47.290012	51.201432
				H	55.440970	48.270858	49.929498

C	52.125634	43.619816	53.128421	H	50.089068	39.799959	47.471747
H	52.244772	43.826574	52.051076	H	51.714648	40.263403	46.912866
H	51.307402	42.878552	53.202382	H	50.976935	38.728886	46.352775
C	55.332759	49.243766	51.842535	H	52.951132	38.647944	52.800241
H	54.670898	49.275578	52.724744	H	53.410181	40.168073	51.996906
H	55.397414	50.275181	51.456200	H	51.706011	39.853469	52.318430
C	56.736828	48.797304	52.314364	H	50.331930	49.864153	53.503453
C	53.420749	42.938818	53.636787				
O	53.985567	42.189547	52.791888				
O	56.953108	47.554769	52.350231	PD2			
O	53.776826	43.147001	54.814345	C	49.305008	49.709873	53.394422
O	57.552540	49.687980	52.644177	H	48.680935	50.153973	54.182767
O	49.281450	46.746627	49.017198	H	49.221892	48.615202	53.423864
C	50.568161	43.153404	47.723631	S	48.764210	50.383164	51.780402
N	50.586071	43.426821	49.169099	N	48.733048	49.830641	48.757592
O	49.267534	40.235468	49.895949	C	47.491921	50.305498	48.403415
C	50.860409	44.529228	47.089367	C	49.634004	50.612199	48.086853
N	51.494794	40.701490	49.748649	C	47.601357	51.429781	47.504023
C	51.535722	45.311948	48.229882	C	48.954037	51.609348	47.275526
C	50.773393	44.789362	49.415275	C	51.012693	50.524307	48.228364
C	49.871596	42.545466	50.063591	H	51.629384	51.204630	47.641571
C	50.185820	41.046942	49.893980	C	51.669839	49.678941	49.109859
C	51.908379	39.335966	49.607631	N	51.081055	48.777024	49.964085
C	51.689718	38.676511	48.378903	C	52.114830	48.225171	50.689322
C	52.472744	38.666345	50.711201	C	53.393001	48.771842	50.264522
C	52.009333	37.311971	48.280403	C	53.102428	49.684953	49.282503
C	52.800268	37.307176	50.568249	C	51.966323	47.280607	51.695835
C	52.553011	36.624169	49.373548	H	52.867741	46.927824	52.196388
C	51.084629	39.407383	47.211137	C	50.750017	46.735974	52.094027
C	52.651565	39.368903	52.025207	C	50.621577	45.659349	53.053159
H	49.587235	42.740420	47.421896	C	48.618576	46.218153	52.166722
H	51.332672	42.395126	47.480876	N	49.522212	47.069983	51.563874
H	51.470611	44.452918	46.176303	C	49.291254	45.312978	53.069640
H	49.912691	45.035416	46.848171	C	47.246378	46.218131	51.952681
H	52.601021	45.024377	48.312986	H	46.654610	45.506001	52.527643
H	51.454422	46.400231	48.131147	C	46.568701	47.072462	51.088992
H	49.483720	45.884944	49.453993	C	45.130520	47.105188	50.950603
H	51.019365	45.046063	50.451164	N	47.164910	48.016228	50.287714
H	48.780989	42.624347	49.909564	C	46.140028	48.678113	49.665951
H	50.095003	42.835613	51.104961	C	46.285631	49.764114	48.816390
H	52.217537	41.413064	49.895877	H	45.383737	50.212371	48.409275
H	51.799235	36.779472	47.348728	Fe	49.110423	48.579674	50.304084
H	53.207447	36.776624	51.432432	C	44.855770	48.108597	50.040990
H	52.749671	35.549915	49.294889	C	43.578163	48.552615	49.503708

H	43.598113	49.503273	48.964597	C	50.985188	42.729002	48.060443
C	42.398358	47.907490	49.557964	N	50.926917	42.966112	49.528846
H	42.281326	46.933865	50.036314	O	49.392319	39.780761	50.066228
H	41.515108	48.350894	49.090850	C	51.121430	44.133895	47.426170
C	49.639989	52.577342	46.425995	N	51.623668	40.237784	49.919376
H	50.640309	52.279232	46.090707	C	51.430037	45.048548	48.625191
C	49.181861	53.776124	46.023953	C	50.601451	44.386589	49.718261
H	48.213988	54.170789	46.342139	C	50.028411	42.073121	50.245467
H	49.788093	54.408306	45.368987	C	50.317207	40.586891	50.070156
C	44.164841	46.250667	51.703291	C	52.033409	38.880668	49.762050
H	43.263621	46.828097	51.964752	C	51.810102	38.233627	48.527788
H	43.832436	45.379251	51.109931	C	52.591611	38.207809	50.864206
H	44.600993	45.869919	52.636661	C	52.126825	36.868178	48.423788
C	46.446852	52.225295	46.983922	C	52.922659	36.851948	50.712883
H	45.557154	51.595292	46.825348	C	52.675525	36.175761	49.513032
H	46.167058	53.013747	47.706278	C	51.200708	38.977982	47.367856
H	46.691555	52.718775	46.030880	C	52.745751	38.913348	52.182289
C	54.055279	50.551866	48.525946	H	50.069173	42.218254	47.707691
H	55.078546	50.354101	48.868218	H	51.837880	42.071831	47.826736
H	54.002484	50.372528	47.437631	H	51.882034	44.169793	46.632022
H	53.845118	51.624734	48.683907	H	50.156036	44.436658	46.993251
C	48.670757	44.175850	53.820892	H	52.494168	44.998637	48.903678
H	48.648903	43.255275	53.209204	H	51.143489	46.100808	48.483595
H	49.267984	43.938414	54.715316	H	48.802202	44.876912	50.324010
H	47.634586	44.385179	54.132410	H	50.878584	44.684482	50.735014
C	51.732172	44.953418	53.764797	H	48.984046	42.208877	49.914941
H	52.634489	45.578463	53.807395	H	50.081120	42.297555	51.326593
H	51.439757	44.754793	54.807118	H	52.337233	40.949182	50.090732
C	54.750930	48.385450	50.768658	H	51.915093	36.340792	47.489525
H	54.728273	47.368095	51.176383	H	53.335698	36.319132	51.571664
H	55.446364	48.354191	49.912171	H	52.884764	35.105153	49.424162
C	52.063480	43.613568	53.093016	H	50.189428	39.335266	47.623716
H	52.205036	43.755820	52.010625	H	51.804599	39.864873	47.108798
H	51.203548	42.924892	53.193478	H	51.127205	38.322138	46.487483
C	55.359879	49.306072	51.839583	H	53.019398	38.191441	52.965542
H	54.699502	49.339290	52.723285	H	53.504512	39.714906	52.167611
H	55.440200	50.340814	51.464460	H	51.794358	39.401216	52.450678
C	56.759672	48.835717	52.308453	H	50.340710	49.973453	53.608699
C	53.308491	42.860203	53.626072				
O	53.776808	42.008428	52.819070				
O	56.964419	47.591081	52.332010	RC3			
O	53.721273	43.116271	54.777440	O	1.785498	-3.713274	3.223160
O	57.581986	49.717090	52.648349	C	3.765742	-5.320124	5.167297
O	49.226722	44.665046	49.483275	H	4.230282	-5.888856	4.349130

H	4.046830	-5.820012	6.103931
C	4.196027	-3.837493	5.136908
H	4.941632	-3.601509	5.900226
H	4.635436	-3.595218	4.162295
C	2.877546	-3.057980	5.334117
H	2.635610	-2.961060	6.397486
H	2.889163	-2.059204	4.889725
C	1.848520	-3.970352	4.664794
H	2.687404	-3.509660	2.918351
H	0.816526	-3.814661	4.987970
N	2.301142	-5.273941	5.050873
C	1.598084	-6.483617	4.684322
H	0.527301	-6.258703	4.613086
H	1.728139	-7.238605	5.468182
C	2.027437	-7.185084	3.381102
O	2.312092	-8.392104	3.380051
N	2.039052	-6.406910	2.272068
H	1.912921	-5.402171	2.428985
C	2.457696	-6.846756	0.981293
C	1.738243	-7.853148	0.306553
C	3.572040	-6.216990	0.389812
C	2.183579	-8.245494	-0.963159
C	3.975118	-6.631385	-0.884078
C	3.292457	-7.645364	-1.556307
H	1.638656	-9.022548	-1.493349
H	4.836489	-6.155884	-1.346177
H	3.619626	-7.960557	-2.543450
C	0.509157	-8.489322	0.904520
H	0.777578	-9.256158	1.639394
H	-0.106209	-7.750751	1.429915
H	-0.100570	-8.959319	0.126904
C	4.310877	-5.111766	1.103731
H	3.726698	-4.182045	1.102685
H	4.510180	-5.365904	2.150515
H	5.264380	-4.899607	0.611184

TS3a

O	1.614566	-4.029585	2.828386
C	3.844854	-5.165549	5.199665
H	4.407189	-5.759152	4.473347
H	4.125506	-5.495266	6.205712
C	4.006648	-3.648702	4.991777
H	4.719544	-3.207716	5.690948

H	4.356355	-3.450931	3.973796
C	2.575760	-3.093967	5.170017
H	2.355345	-2.874655	6.222739
H	2.362369	-2.198129	4.585037
C	1.730285	-4.268360	4.765303
H	2.398206	-3.507037	2.580582
H	0.649435	-4.282637	4.826800
N	2.394010	-5.388956	5.017614
C	1.888710	-6.732862	4.777949
H	0.799924	-6.722983	4.892337
H	2.304001	-7.402870	5.534358
C	2.245174	-7.308102	3.391527
O	2.484662	-8.542032	3.327290
N	2.236543	-6.430964	2.393642
H	1.909658	-5.106190	2.585249
C	2.544050	-6.839541	1.071590
C	1.651134	-7.636963	0.322755
C	3.731065	-6.348705	0.485271
C	1.976040	-7.948967	-1.003947
C	4.020840	-6.679032	-0.843438
C	3.151889	-7.478101	-1.588343
H	1.290827	-8.563375	-1.583915
H	4.938341	-6.307174	-1.293937
H	3.387289	-7.727510	-2.619710
C	0.365645	-8.133811	0.935486
H	0.562097	-8.899446	1.695126
H	-0.171695	-7.322493	1.440770
H	-0.293616	-8.565183	0.175704
C	4.676674	-5.496519	1.296969
H	4.184067	-4.590716	1.670287
H	5.042214	-6.037473	2.178586
H	5.542776	-5.191885	0.700716

IC3a

O	1.630732	-3.800509	2.264610
C	3.851100	-5.150915	5.169698
H	4.403868	-5.729019	4.428092
H	4.143127	-5.481653	6.170962
C	3.930519	-3.629021	4.972638
H	4.660079	-3.168032	5.639725
H	4.212319	-3.407056	3.939557
C	2.486560	-3.139447	5.235800
H	2.329385	-2.820513	6.275901

H	2.159554	-2.324652	4.586689
C	1.682032	-4.369696	5.010875
H	2.474879	-3.330071	2.349106
H	0.603552	-4.429829	4.918715
N	2.400283	-5.436392	5.010910
C	1.936341	-6.806670	4.808008
H	0.853629	-6.830252	4.956056
H	2.410526	-7.433389	5.565675
C	2.288880	-7.362798	3.409779
O	2.478787	-8.611397	3.355595
N	2.321140	-6.463641	2.446780
H	1.892130	-4.759703	2.388235
C	2.589938	-6.868325	1.121266
C	1.656836	-7.620247	0.368794
C	3.777682	-6.401851	0.510829
C	1.943209	-7.914239	-0.970640
C	4.029773	-6.715928	-0.829003
C	3.121960	-7.472674	-1.572383
H	1.224580	-8.492877	-1.547552
H	4.948513	-6.361518	-1.291653
H	3.327616	-7.708477	-2.613318
C	0.363766	-8.080079	0.994665
H	0.542704	-8.857378	1.746900
H	-0.138365	-7.254557	1.514023
H	-0.320768	-8.481891	0.240769
C	4.757621	-5.579759	1.311874
H	4.282184	-4.675031	1.710302
H	5.138650	-6.137541	2.176553
H	5.613061	-5.276502	0.699219

TS3b

O	3.766401	-3.740959	1.899194
C	3.456090	-4.607038	5.296783
H	4.253214	-4.685285	4.547343
H	3.909641	-4.557284	6.288105
C	2.480045	-3.460461	4.995457
H	2.035789	-3.092684	5.924437
H	2.975792	-2.625400	4.497163
C	1.389439	-4.116035	4.108266
H	0.369425	-3.822105	4.374936
H	1.526758	-3.895346	3.046290
C	1.594112	-5.577583	4.344332
H	4.215335	-3.294736	2.634980

H	0.820090	-6.321854	4.222859
N	2.588613	-5.805591	5.200299
C	3.187016	-7.125463	5.057859
H	2.554238	-7.889385	5.520694
H	4.165205	-7.151832	5.540351
C	3.305448	-7.451598	3.552550
O	3.885453	-8.520816	3.239622
N	2.705097	-6.555030	2.775812
H	3.493119	-4.589495	2.294911
C	2.621701	-6.726805	1.375626
C	1.344500	-6.799806	0.770462
C	3.791093	-6.753539	0.571889
C	1.252130	-6.914867	-0.620276
C	3.650283	-6.870041	-0.817464
C	2.395730	-6.951648	-1.418159
H	0.267818	-6.979279	-1.078264
H	4.546859	-6.890097	-1.432973
H	2.308992	-7.038798	-2.497904
C	0.091615	-6.764115	1.609673
H	0.124918	-7.508138	2.414464
H	-0.048666	-5.784779	2.083471
H	-0.792973	-6.965261	0.997289
C	5.173702	-6.655497	1.169199
H	5.224256	-5.889152	1.949093
H	5.470200	-7.599894	1.637083
H	5.909906	-6.405833	0.398592

PD3

O	3.663032	-3.033723	0.822097
C	3.612924	-5.039110	5.280795
H	4.443980	-5.462582	4.696782
H	3.976142	-4.872818	6.298610
C	3.078365	-3.772134	4.609270
H	2.630947	-3.105233	5.352810
H	3.873903	-3.219339	4.100326
C	1.996158	-4.286244	3.625608
H	1.060682	-3.730065	3.727677
H	2.311085	-4.200310	2.583886
C	1.779967	-5.752593	4.009583
H	4.157943	-3.231564	1.633810
H	0.723546	-6.025521	4.071975
N	2.443029	-5.958186	5.309584
C	2.858119	-7.368977	5.290017

H	2.070308	-8.020539	5.688532	O	0.617895	-9.152983	2.576048
H	3.766611	-7.540100	5.870501	N	2.409281	-7.916790	3.263135
C	3.065706	-7.712733	3.817230	H	2.868149	-7.539762	4.085611
O	3.650232	-8.701418	3.360661	C	3.220085	-8.114006	2.102719
N	2.465194	-6.726484	3.103774	C	4.414722	-8.844247	2.246492
H	3.469108	-3.920186	0.472438	C	2.834213	-7.555543	0.870433
C	2.427376	-6.677525	1.678146	C	5.224131	-9.023206	1.119327
C	1.216285	-6.922327	1.006032	C	3.664493	-7.772273	-0.237084
C	3.613036	-6.367058	0.980698	C	4.849048	-8.498293	-0.117669
C	1.203884	-6.830976	-0.392051	H	6.148446	-9.586908	1.215784
C	3.558912	-6.294004	-0.417286	H	3.380041	-7.351305	-1.198014
C	2.361965	-6.517158	-1.100168	H	5.482926	-8.649983	-0.987132
H	0.274529	-7.017835	-0.923766	C	4.800299	-9.422212	3.585183
H	4.464633	-6.055235	-0.968502	H	4.981341	-8.634419	4.328440
H	2.335771	-6.452317	-2.184368	H	4.002298	10.058190	3.987346
C	-0.041841	-7.275051	1.759140	H	5.711545	10.021688	3.503923
H	0.168065	-7.950670	2.595371	C	1.583361	-6.724769	0.741768
H	-0.520823	-6.380413	2.176647	H	0.683755	-7.333816	0.879787
H	-0.766611	-7.757651	1.096809	H	1.557517	-5.935881	1.504054
C	4.903456	-6.102377	1.714310	H	1.530721	-6.251277	-0.242899
H	4.769925	-5.334737	2.484537				
H	5.263430	-7.005024	2.220180				
H	5.679410	-5.763315	1.022354	RC4			
				O	1.813790	-3.677656	3.190436
				C	3.793144	-5.293962	5.219103
RC3'				H	4.347077	-5.884526	4.473896
O	-1.150466	-6.642778	2.914873	H	3.989362	-5.749431	6.201410
C	0.910729	-5.717520	5.007922	C	4.192912	-3.803556	5.176809
H	1.379336	-5.590311	4.018991	H	4.925102	-3.542915	5.945588
H	1.716685	-5.840791	5.739422	H	4.642897	-3.559313	4.206155
C	-0.030049	-4.543882	5.313882	C	2.852344	-3.058514	5.349651
H	-0.089723	-4.382438	6.394467	H	2.577598	-2.998817	6.408403
H	0.316714	-3.613860	4.855081	H	2.853006	-2.045641	4.936622
C	-1.404404	-5.009613	4.759567	C	1.865465	-3.979959	4.626278
H	-2.189408	-4.924194	5.516440	H	2.716340	-3.443201	2.911203
H	-1.724806	-4.432066	3.887791	H	0.822267	-3.866306	4.934288
C	-1.206018	-6.484894	4.348534	N	2.355714	-5.275542	4.954142
H	-0.475034	-6.033895	2.571033	C	1.649418	-6.501563	4.682293
H	-2.031417	-7.139430	4.640596	H	0.573099	-6.287513	4.655434
N	-0.001650	-6.868502	5.059059	H	1.825591	-7.225815	5.486895
C	0.540202	-8.200903	4.816152	C	2.028404	-7.235445	3.376657
H	-0.269580	-8.927313	4.924851	O	2.269664	-8.439724	3.370132
H	1.289416	-8.406994	5.590704	N	2.044180	-6.437647	2.267781
C	1.179126	-8.472778	3.444445	H	1.919083	-5.435809	2.428898

C	2.446757	-6.860309	0.968491
C	1.719439	-7.855510	0.285326
C	3.560046	-6.230341	0.375621
C	2.153885	-8.233010	-0.991705
C	3.952191	-6.628283	-0.906763
C	3.260382	-7.629971	-1.586418
H	1.603317	-9.002612	-1.527689
H	4.813498	-6.151964	-1.369331
H	3.579336	-7.934993	-2.579848
C	0.492911	-8.488387	0.889831
H	0.769438	-9.214786	1.661212
H	-0.139210	-7.736060	1.376523
H	-0.102747	-8.996888	0.124828
C	4.312991	-5.139008	1.099228
H	3.771464	-4.183475	1.052073
H	4.464163	-5.383125	2.156894
H	5.294062	-4.971961	0.643701

TS4a

O	1.614212	-4.023047	2.791153
C	3.822511	-5.181368	5.240367
H	4.401652	-5.790328	4.541174
H	4.059926	-5.500535	6.261813
C	4.002627	-3.667281	5.021904
H	4.715271	-3.226844	5.722251
H	4.366883	-3.481517	4.006535
C	2.574768	-3.099420	5.183810
H	2.350703	-2.866769	6.233830
H	2.370196	-2.204936	4.592852
C	1.725398	-4.271115	4.781476
H	2.371775	-3.476688	2.518214
H	0.643130	-4.276030	4.802086
N	2.379114	-5.393110	5.007395
C	1.858932	-6.734249	4.774385
H	0.769141	-6.705794	4.879040
H	2.257598	-7.402598	5.541232
C	2.223541	-7.333082	3.389356
O	2.372507	-8.565045	3.338707
N	2.309621	-6.431493	2.403152
H	1.927467	-5.080264	2.568770
C	2.581933	-6.842586	1.077219
C	1.678028	-7.644116	0.342485
C	3.748330	-6.341852	0.455659

C	1.975285	-7.951005	-0.991130
C	4.009667	-6.665564	-0.879785
C	3.132083	-7.472037	-1.604846
H	1.280442	-8.569566	-1.556090
H	4.913257	-6.284707	-1.351811
H	3.344597	-7.719275	-2.642159
C	0.404706	-8.142703	0.976158
H	0.621786	-8.914289	1.723157
H	-0.113260	-7.331327	1.503507
H	-0.277599	-8.557045	0.226095
C	4.709343	-5.480463	1.239782
H	4.227880	-4.563516	1.603739
H	5.086781	-6.006580	2.125282
H	5.568148	-5.185392	0.627279

IC4a

O	1.400117	-3.925458	2.554300
C	3.843969	-5.158824	5.145281
H	4.378643	-5.756054	4.406047
H	4.145653	-5.471508	6.150908
C	3.942924	-3.641412	4.916705
H	4.710180	-3.177202	5.538951
H	4.181156	-3.445933	3.867268
C	2.518732	-3.126108	5.227264
H	2.403179	-2.826469	6.279105
H	2.192323	-2.292251	4.603735
C	1.688965	-4.342231	4.994224
H	2.109680	-3.389120	2.166317
H	0.608796	-4.381939	4.937089
N	2.390006	-5.424093	5.006862
C	1.903679	-6.787809	4.810409
H	0.819071	-6.788438	4.951280
H	2.357086	-7.420794	5.576353
C	2.253231	-7.382465	3.413280
O	2.328135	-8.624552	3.370562
N	2.403943	-6.465554	2.462593
H	1.752081	-4.867905	2.480526
C	2.648526	-6.866760	1.134163
C	1.699209	-7.597885	0.378764
C	3.834885	-6.410496	0.511560
C	1.974434	-7.887991	-0.962948
C	4.074453	-6.717652	-0.831503
C	3.154246	-7.460704	-1.571932

H	1.243735	-8.453282	-1.538930
H	4.994538	-6.371570	-1.299149
H	3.349813	-7.695258	-2.615566
C	0.398735	-8.032520	1.004411
H	0.571014	-8.810838	1.756242
H	-0.082132	-7.193679	1.525101
H	-0.298593	-8.414296	0.250613
C	4.833101	-5.603734	1.306326
H	4.371808	-4.701430	1.729396
H	5.229454	-6.176393	2.154602
H	5.679609	-5.292923	0.683843

TS4b

O	3.857067	-3.834522	2.299699
C	3.403786	-4.564684	5.398173
H	4.247231	-4.573812	4.698028
H	3.791593	-4.545318	6.419461
C	2.403548	-3.437754	5.086627
H	1.925820	-3.091415	6.007945
H	2.895434	-2.591817	4.605271
C	1.354065	-4.102126	4.157337
H	0.319738	-3.827298	4.388476
H	1.537570	-3.861695	3.105960
C	1.585763	-5.563611	4.371466
H	3.941576	-3.886114	1.334197
H	0.839054	-6.329217	4.217939
N	2.593204	-5.787012	5.201334
C	3.211705	-7.096742	5.064130
H	2.592653	-7.867315	5.535810
H	4.191396	-7.103810	5.545205
C	3.339043	-7.436412	3.550716
O	3.921316	-8.490470	3.256291
N	2.739192	-6.526817	2.767289
H	3.524927	-4.726971	2.533535
C	2.651760	-6.706400	1.367807
C	1.375293	-6.765326	0.759845
C	3.819785	-6.742454	0.560705
C	1.279832	-6.866607	-0.631786
C	3.675978	-6.845523	-0.829027
C	2.421045	-6.906829	-1.431051
H	0.294316	-6.919401	-1.089705
H	4.572053	-6.876403	-1.445502
H	2.333132	-6.984710	-2.511752

C	0.120558	-6.731197	1.597438
H	0.147941	-7.486705	2.392149
H	-0.020096	-5.756092	2.080894
H	-0.765205	-6.922677	0.982864
C	5.203319	-6.670753	1.160954
H	5.291381	-5.842695	1.872956
H	5.433182	-7.588331	1.711538
H	5.958430	-6.526493	0.380831

PD4

O	3.615708	-3.175342	0.691719
C	3.536769	-4.980739	5.409550
H	4.424863	-5.264299	4.816341
H	3.849840	-4.873613	6.453061
C	2.883109	-3.726130	4.830376
H	2.238085	-3.263329	5.585000
H	3.616297	-2.980879	4.507846
C	2.036411	-4.274906	3.657929
H	1.085325	-3.745169	3.553110
H	2.563000	-4.173556	2.705086
C	1.812396	-5.758746	4.009112
H	4.454697	-3.475342	1.075279
H	0.753004	-6.026493	4.062227
N	2.460336	-5.986545	5.309222
C	2.933282	-7.370968	5.281202
H	2.180490	-8.057469	5.692520
H	3.857182	-7.503754	5.849455
C	3.144724	-7.704582	3.799776
O	3.750162	-8.662651	3.338192
N	2.502951	-6.717645	3.094950
H	3.266752	-3.986755	0.286771
C	2.445242	-6.667185	1.672581
C	1.218183	-6.865724	1.009363
C	3.631263	-6.405920	0.954126
C	1.191068	-6.767565	-0.387440
C	3.563118	-6.331648	-0.443556
C	2.350227	-6.500799	-1.112344
H	0.248266	-6.917196	-0.907725
H	4.471678	-6.133135	-1.007002
H	2.312476	-6.433282	-2.196281
C	-0.046375	-7.190268	1.766188
H	0.149605	-7.873405	2.599553
H	-0.512202	-6.288300	2.183665

H	-0.781925	-7.660019	1.105836	H	5.307807	-7.137128	2.091751
C	4.944898	-6.196332	1.664031	H	5.706620	-5.816228	0.975526
H	4.843049	-5.490485	2.497055				