Supporting Information

Unambiguious Evidence for Efficient Chemical Catalysis of Adenosine Ester Aminolysis by Its 2'-OH

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Contents

1. Design of the substrates

The computational model substrates **1** and **2** were designed to be enantiotopic rather than diastereotopic (they are prochiral rather than chiral compounds). This means that re and si attacks result in neither R nor S diastereomers but R and S enantiomers with the same physical and chemical properties including anchimeric catalysis by syn-2-OH (Figure SI 1).

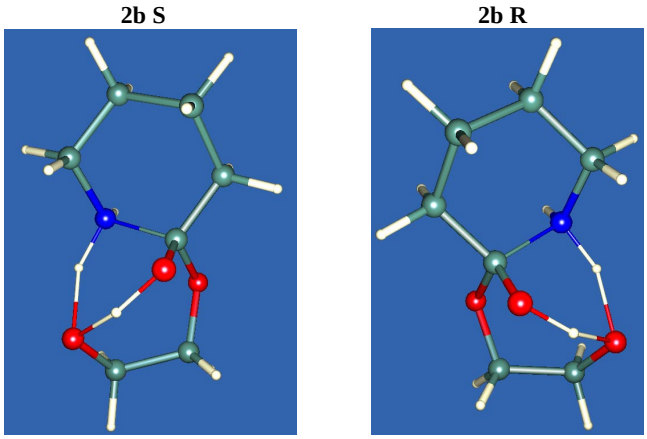
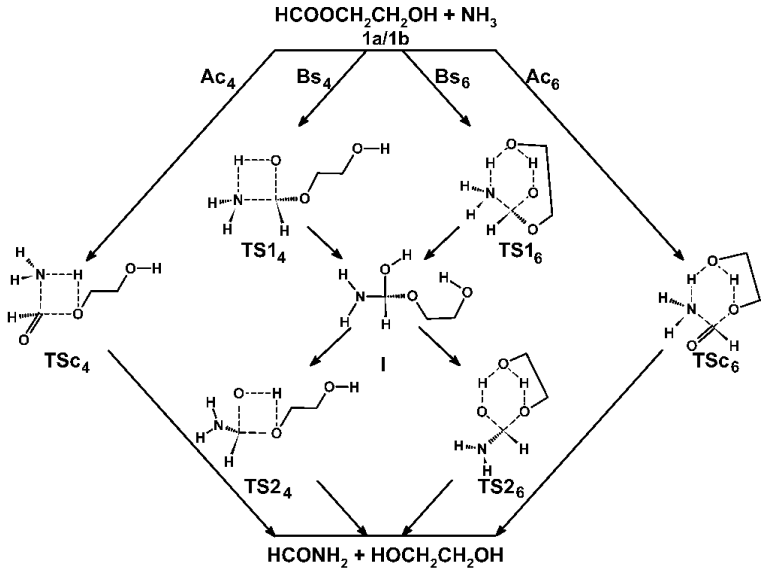


Figure SI 1 Calculated mirror-image structures of **2b S** and **2b R** enantiomers.

2'/3'-O-(α-N-p-nitrobenzoyl-L-ornithinyl) 5'-O-pivaloyl adenosine **3b** and its 2'-deoxy derivative **3a** (Figure 1) were designed to be soluble in organic solvents (hydrophobic protecting group pivaloyl (Piv) and p-nitrobenzoyl (nBz) groups) as well as functionalized with achromophoric group (p-nitrobenzoyl (nBz) group) to possess a suitable signal for HPLC monitoring and finally with a protecting group (pivaloyl (Piv) group) that survives the cleavage of the temporary protecting group t-butyloxycarbonyl (BOC) group.

2. Proposed reaction mechanisms

Scheme S1. Proposed mechanisms of aminolysis of 1-O-formyl 1,2-ethanediol with anti- (**Ac_4** and **Bs_4**) and syn- (**Ac_6** and **Bs_6**) oriented 2-OH; **Ac_4** and **Ac_6** – concerted pathways: **Bs_4** and **Bs_6** –stepwise pathways.



3. Computational details

All computations were carried out with the GAUSSIAN98W program package.[1] The calculations were performed at the B3LYP[2] level with 6-31G (d,p)[3] basis set. The use of B3LYP functional is motivated by its success in the evaluation of the reliable reaction enthalpies for the hydrolysis of neutral amides.[4] All obtained structures of the transition states and intermediates were further characterized by analytic computations of harmonic vibrational frequencies at the same level/basis set. These frequencies were used to verify the nature of the stationary points and allow evaluation of thermodynamic quantities such as zero-point vibrational energy, and thermal vibration contributions to the enthalpy, entropy and Gibbs free energy. All energies are calculated in relative to separated reactants.

4. Preparation and characterization of the substrates

*Trifluoroacetates of 2'/3'-O-(α-N-p-nitrobenzoyl-L-ornithinyl) 5'-O-pivaloyl adenosine **3b** and its 2'-deoxy derivative **3a*** were prepared by deprotection of their δ-N-t-butyloxycarbonyl (BOC) derivatives **4b** and **4a** by short treatment with CF_3COOH. The BOC derivatives **4a** and **4b** were prepared by transesterificationof α-N-p-nitrobenzoyl, δ-N-BOC-L-ornithinyl cyanomethyl ester **5** by 5'-O-pivaloyl adenosine **6b** and its 2'-deoxy derivative **6a** using the general procedure for monoacylation of vicinal diols and their deoxy derivatives described previously.[5] Cyanomethyl ester **5** was prepared by cyanomethylation of α-N-p-nitrobenzoyl, δ-BOC L-ornithine **7**. The latter was obtained by saponification of α-N-p-nitrobenzoyl, δ-BOC L-ornithine methyl ester **8**, prepared by p-nitrobenzoylation of δ-N-BOC ornithine methyl ester **9**. All new compounds were characterized by elemental, ^{1}H NMR and RP-HPLC analyses. ^{1}H NMR spectra of the δ –N-BOC derivatives of **3b** and **3a** are shown on Figure S1 and Figure S1. Details of the synthetic procedures and full characterization of the compounds and intermediates will be described elsewhere.

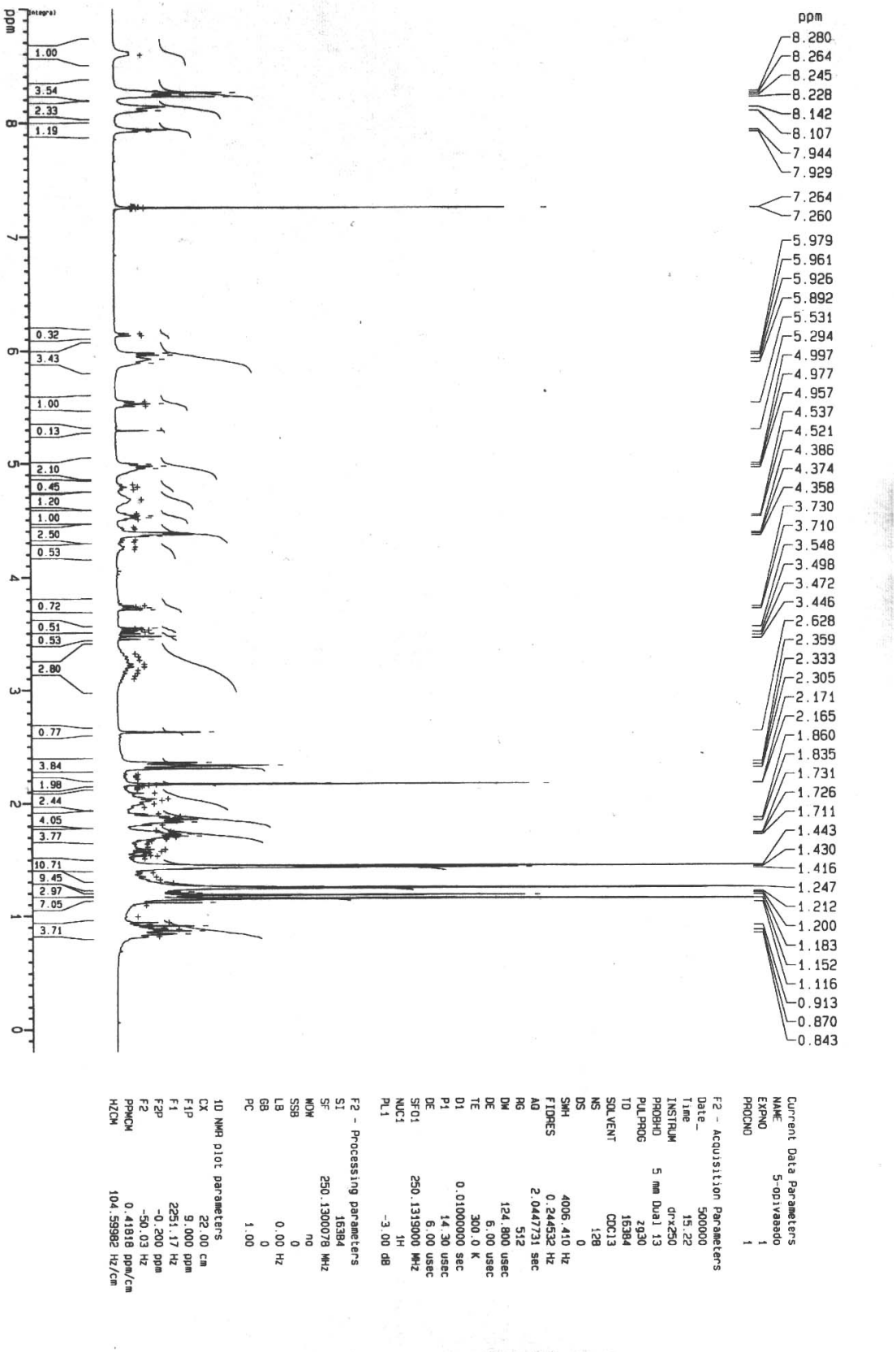


Figure SI 2. ^{1}H NMR spectrum of 2'/3'-O-(α-N-p-nitrobenzoyl, δ-N-tert-butyloxycarbonyl-L-ornithinyl) 5'-O-pivaloyl adenosine **3b** (250 MHz, $CDCl_3$, 25°C, TMS).

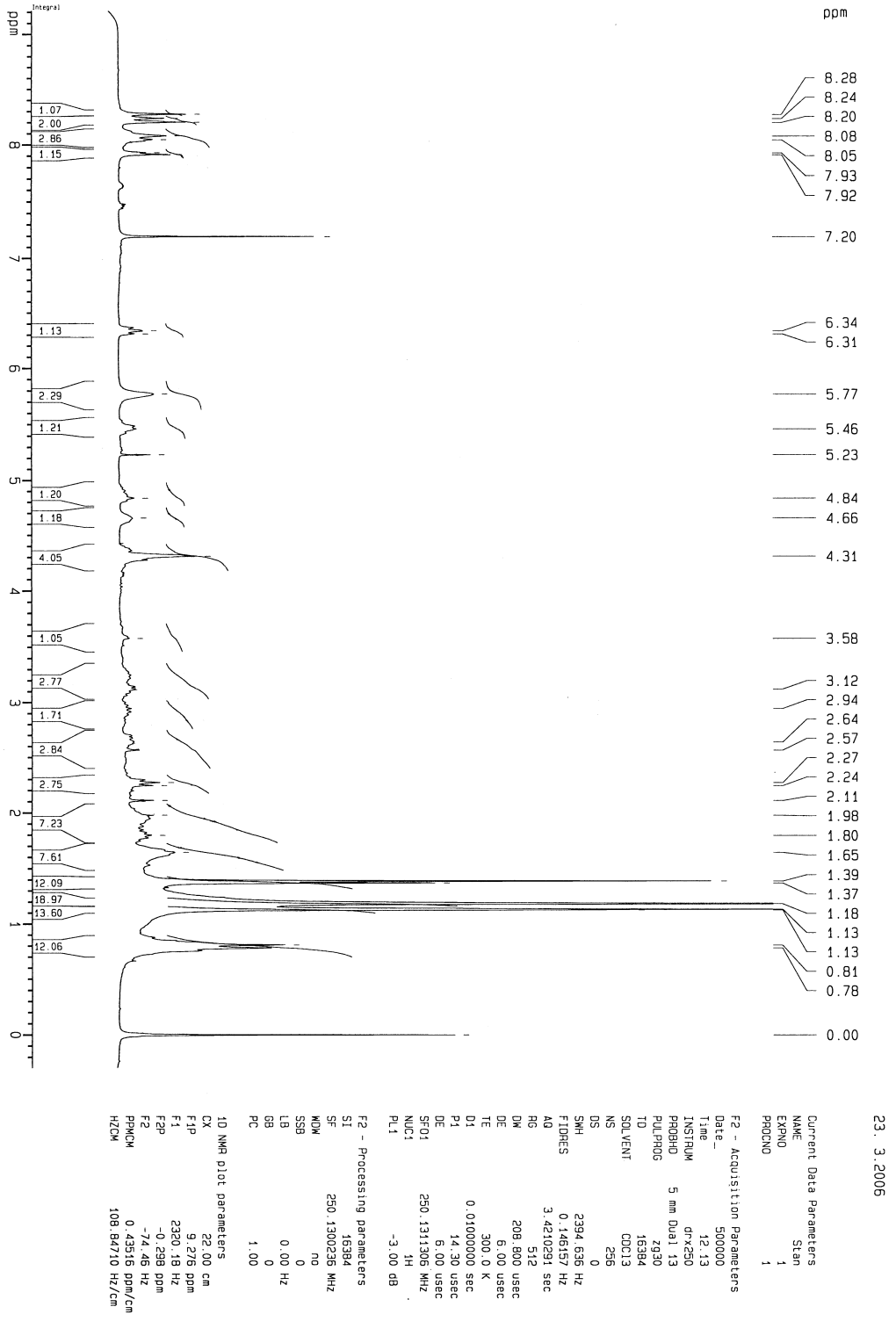


Figure SI 3. ^{1}H NMR spectrum of 3'-O-(α-N-p-nitrobenzoyl, δ-N-tert-butyloxycarbonyl-L-ornithinyl) 5'-O-pivaloyl deoxyadenosine **3a** (250 MHz, $CDCl_3$, 25°C, TMS).

5. Kinetic studies

The aminolysis (lactamization) of 2'/3'-O-(α-N-p-nitrobenzoyl-L-ornithinyl) 5'-O-pivaloyl adenosine **3b** and its 2'-deoxy derivative **3a** was followed by monitoring the changes in the concentration of both the substrate and the two products, alpha-N-p-nitrobenzoyl cyclic L-ornithine and the corresponding 5'-O-pivaloyl adenosine/5'-O-pivaloyl 2'-deoxyadenosine using Waters Liquid Chromatograph equipped with absorbance detector model 441 set at 254 nm and analytical column Nucleosil 100-5C18 (12.5 cm x 4.6 mm). Reactions were carried out in stoppered tubes, which were immersed in a thermostated at 25° C water bath.

The lactamization reaction is a first-order reaction and in the case of adenosine ester **3b** is over during the mixing of the reagents and quenching the reaction in the analytical sample (ca 10 seconds). Attempts to slow it down by a decrease of the substrate concentration met the insurmountable impediment of HPLC determination of very low concentrations. However, the minimal rate constant ratio of the adenosine and deoxyadenosine ester lactamization can be estimated using the corresponding half-times

$$k = \ln 2 / \tau_{1/2}$$

and then

$$k_A / k_{dA} = \tau_{1/2dA} / \tau_{1/2A}$$

If we assume $\tau_{1/2A}$ = ca 2 sec (out of ca 10 sec for the reaction to be over) and $\tau_{1/2dA}$ = 120x60 sec, the estimated minimum rate constant ratio is ca 3600.

6. Typical kinetic experiment

To 1000 µl of a 2.746 mM solution of the adenosine **3b**/ deoxyadenosine **3a** ester in dry acetonitrile were added 19.1 µl 1 % solution of Et_3N in dry acetonitrile. Aliquots (20 µl) were withdrawn at appropriate time intervals, diluted with 500 µl mobile phase and subjected to RP-HPLC analysis with isocratic elution with 25 % acetonitrile in 20 mM TEAP buffer, pH 3, 0.8 ml/min flow at 298.2° K. The concentrations of the substrates and their reaction products were calculated from their peak areas.

7. Computational data

Calculated thermodynamic data (pro-S attack)

Reaction	TS1			TS2		
[Kcal/mol]	dG	dH	TdS	dG	dH	TdS
1a	52.8	40.7	-12.0	45.0	33.5	-11.5
1b	30.4	14.5	-15.8	36.9	23.3	-13.6
2a	46.3	41.8	-4.5	34.1	30.2	-3.8
2b	20.0	11.7	-8.4	28.1	21.7	-6.5

Calculated thermodynamic data (pro-R attack)

Reaction	TS1			TS2		
[Kcal/mol]	dG	dH	TdS	dG	dH	TdS
1a	52.8	40.7	-12.0	45.0	33.5	-11.5
1b	30.4	14.5	-15.8	36.9	23.3	-13.6
2a	46.3	41.8	-4.5	34.1	30.2	-3.8
2b	20.0	11.7	-8.4	28.1	21.7	-6.5

2 Initial

Energy = -556.2182544

O	-1.791020	-0.396420	0.001720
C	-3.052060	0.299740	0.011140
C	-0.684600	0.386090	0.019380
C	-4.136020	-0.763980	-0.023220
H	-3.135430	0.915400	0.911280
H	-3.123440	0.960680	-0.857260
O	-0.725230	1.596530	0.040310
C	0.573160	-0.459300	0.012910
O	-5.375670	-0.071440	-0.012180
H	-4.013190	-1.379600	-0.927240
H	-4.023900	-1.426630	0.848450
H	0.519150	-1.137100	-0.848330
H	0.541470	-1.109670	0.896920
C	1.855950	0.372710	-0.014810
H	-6.084810	-0.725120	-0.036190
C	3.119780	-0.493280	-0.007370
H	1.858240	1.054630	0.843510
H	1.846980	1.014120	-0.904090
C	4.409180	0.329690	-0.035620
H	3.125140	-1.173670	-0.867890
H	3.121490	-1.131920	0.888830
N	5.582700	-0.550450	-0.070740
H	4.423750	0.941470	-0.946450
H	4.402150	1.037710	0.813420
H	6.430460	0.007110	-0.144590
H	5.656120	-1.053700	0.811580

2a TS1 R

Energy = -556.1472419

O	-0.640760	0.327230	-0.724020
C	-1.883120	-0.382930	-0.681250
C	0.205750	0.171420	0.384380
C	-2.969250	0.456140	-0.020400
H	-2.155900	-0.591430	-1.720280
O	-0.342810	-0.179030	1.552600
C	1.183190	1.358230	0.401750
N	1.065170	-1.218900	0.260670
H	-1.789270	-1.329890	-0.139440
O	-4.193920	-0.254830	-0.185680
H	-2.704620	0.594220	1.034360
C	2.411240	-1.309340	-0.354260
H	0.436400	-1.876220	-0.201280
H	-3.002050	1.443740	-0.506880
H	1.523190	1.457360	1.437530
H	0.602410	2.253300	0.159980
C	2.395100	1.209740	-0.525480
H	0.607190	-1.108650	1.397070
H	-4.852890	0.154720	0.387160
C	3.214590	-0.027350	-0.137050
H	2.287640	-1.475340	-1.432340
H	2.929980	-2.183110	0.056020
H	3.518780	0.051020	0.914780
H	4.133580	-0.094760	-0.730020
H	3.020140	2.107390	-0.461530
H	2.064210	1.127640	-1.569120

2a TS2 R

Energy = -556.1656135

O	-0.816840	1.142440	-0.607380
C	-1.893420	0.674140	0.143710
C	-2.592030	-0.487190	-0.561480

H	-2.640960	1.465790	0.318610
H	-1.588850	0.324300	1.153660
O	0.865690	2.257880	0.483570
O	-3.638740	-0.959840	0.282860
H	-2.973100	-0.135070	-1.531750
H	-1.852080	-1.279120	-0.768890
C	1.043530	0.966350	0.222230
H	-0.080680	2.228820	-0.037280
H	-4.156770	-1.603290	-0.215540
C	1.752660	0.547490	-1.040280
N	1.063120	0.134630	1.273550
H	0.642280	0.519170	2.110770
C	1.181330	-1.324240	1.163460
C	1.705170	-0.965170	-1.272410
H	2.792840	0.887570	-0.928920
H	1.309790	1.106220	-1.865210
C	2.106600	-1.708370	0.007670
H	1.564870	-1.702870	2.115580
H	0.185440	-1.759650	1.007830
H	2.060420	-2.793280	-0.133280
H	3.141910	-1.459280	0.272220
H	2.364520	-1.241130	-2.101580
H	0.684650	-1.242470	-1.560780

2b TS1 R

Energy = -556.194875

H	2.399350	-1.372530	0.785030
C	2.338730	-0.932730	-0.216460
O	1.005140	-1.118820	-0.732660
C	2.757290	0.543140	-0.176330
H	2.984710	-1.503160	-0.890530
C	-0.037270	-0.575970	0.064680
O	1.837660	1.335430	0.547910
H	3.765320	0.598690	0.267290
H	2.847990	0.913050	-1.212520
N	-0.304080	0.835230	-0.642420
O	0.270610	-0.301370	1.333730
C	-1.280260	-1.441830	-0.108200
H	0.655320	1.330580	-0.280960
C	-1.530980	1.514920	-0.154330
H	1.101990	0.505050	1.195610
H	-1.096990	-2.371740	0.437770
C	-2.541220	-0.735540	0.408390
H	-1.383240	-1.700630	-1.169120
C	-2.756980	0.611620	-0.297130
H	-2.433060	-0.570240	1.486030
H	-3.415520	-1.379130	0.263670
H	-3.628680	1.130750	0.116670
H	-2.967740	0.446380	-1.363530
H	-1.345600	1.748210	0.897230
H	-1.646940	2.457370	-0.698320
H	-0.311430	0.697170	-1.652740

2b TS2 R

Energy = -556.1781578

N	0.925250	-1.317150	0.095180
O	-0.732280	-0.622760	1.506530
C	0.288610	-0.319310	0.752360
O	-0.747710	0.483190	-0.921400
O	-2.373430	-1.036020	-0.234460
C	-1.843160	1.263290	-0.528080
C	-3.013980	0.247060	-0.215140
H	0.368970	-2.153990	-0.034550
H	-1.545110	-0.983240	0.863150
C	1.082830	0.912160	1.097650
H	-1.501130	-0.638150	-0.798760
H	-2.140900	1.967420	-1.319890
H	-1.622860	1.860930	0.371980
H	-3.476650	0.425680	0.760120
H	-3.794630	0.269520	-0.984050
H	0.379160	1.724260	1.290770
H	1.581380	0.691290	2.052620
C	1.939750	-1.035860	-0.928810
C	2.895360	0.049950	-0.433810
C	2.108140	1.285610	0.019860
H	2.785880	2.056400	0.401590
H	1.567590	1.704600	-0.834010
H	3.493230	-0.344870	0.397450
H	3.589980	0.307440	-1.240380
H	1.444450	-0.711960	-1.852160
H	2.476050	-1.967990	-1.129660

1 Initial 1

Energy = -56.5577685

N	0.000000	0.119100	0.000000
H	-0.937310	-0.277850	0.000000
H	0.468660	-0.277920	0.811710
H	0.468660	-0.277920	-0.811710

1 Initial 2

Energy = -343.5948895

O	2.353990	-0.831990	-0.000150
C	2.009060	0.323520	-0.000040
O	0.741490	0.767910	0.000040
H	2.690380	1.188220	0.000010
C	-0.282160	-0.251750	-0.000020
C	-1.617390	0.472350	0.000110
H	-0.177400	-0.884610	0.885400
H	-0.177480	-0.884440	-0.885570
O	-2.614570	-0.537650	0.000030
H	-1.680690	1.118780	0.888500
H	-1.680750	1.118970	-0.888150
H	-3.478340	-0.107840	0.000140

1a TS1 R

Energy = -400.0854224

H	2.806010	0.219120	-0.526490
O	2.481260	-0.978080	-0.001210
C	1.480270	-0.226790	0.383430
N	2.090570	1.164360	-0.238980
H	2.451450	1.843030	0.431220

H	1.512570	1.625780	-0.941790
H	1.311740	-0.049960	1.465830
O	0.259500	-0.478720	-0.250160
C	-0.861350	0.207560	0.290710
C	-2.112140	-0.389030	-0.334110
H	-0.904470	0.099420	1.384040
H	-0.819240	1.285260	0.065160
O	-3.216420	0.343050	0.181060
H	-2.038870	-0.311420	-1.429240
H	-2.164220	-1.457090	-0.078120
H	-4.024500	-0.045080	-0.175500

1a TS2 4 R

Energy = -400.0971802

H	0.809360	1.099600	0.228420
O	1.838840	1.263460	-0.202240
C	1.879590	-0.033100	-0.412670
N	2.878120	-0.741470	0.144400
H	2.898920	-1.743690	0.029150
H	3.278890	-0.364970	0.992820
H	1.452770	-0.482000	-1.315700
O	0.180970	-0.048160	0.538660
C	-0.957740	-0.418380	-0.195350
C	-2.200580	0.234650	0.403210
H	-0.893820	-0.123480	-1.260210
H	-1.097880	-1.510510	-0.172830
O	-3.325920	-0.198370	-0.353770
H	-2.278350	-0.057400	1.461350
H	-2.081520	1.329320	0.368220
H	-4.113980	0.209010	0.025620

1b TS1 R

Energy = -400.1271379

H	0.385970	-1.263900	-0.544860
O	0.890100	0.017600	1.330760
C	1.149690	0.527470	0.142590
N	1.361710	-0.707780	-0.852920
H	2.197420	-1.235820	-0.605070
H	1.397440	-0.414420	-1.827340
H	2.058960	1.138510	0.086360
O	0.121990	1.260870	-0.500820
C	-1.201070	1.004450	0.008040
C	-1.660220	-0.438310	-0.238750
H	-1.224580	1.231850	1.079350
H	-1.850610	1.711150	-0.516230
O	-0.735870	-1.385160	0.280040
H	-2.650740	-0.572100	0.222180
H	-1.784980	-0.597430	-1.321820
H	-0.000970	-0.751500	1.046860

1b TS2 R

Energy = -400.1118269

H	-0.193010	-1.331780	-0.016990
O	0.904090	-1.258200	0.368520
C	1.286740	-0.023040	0.438960
N	2.465040	0.305300	-0.152340
H	2.671980	1.291600	-0.222590
H	2.698680	-0.243650	-0.969750
H	1.042270	0.587790	1.315370
O	-0.100550	0.967950	-0.563350
C	-1.210190	1.167580	0.281060
C	-1.990320	-0.206820	0.292320
H	-0.903400	1.446460	1.302040
H	-1.840500	1.980370	-0.103360
O	-1.253010	-1.029420	-0.621840
H	-2.001650	-0.669040	1.284260
H	-3.021240	-0.108060	-0.060110
H	-0.630010	-0.159700	-1.003130

I 2a TS1 R

Energy = -556.2037573

O	0.577540	0.094150	-0.449550
C	1.754920	-0.119470	0.328650
C	-0.508710	0.761720	0.171500
C	2.897190	-0.332900	-0.652900
H	1.967320	0.744040	0.965720
O	-0.023750	2.029460	0.576760
C	-1.075890	-0.031530	1.362150
N	-1.543120	0.968930	-0.815070
H	1.655820	-1.010300	0.964580
O	4.052790	-0.645200	0.115240
H	2.629220	-1.147470	-1.343280
C	-2.165600	-0.264660	-1.326740
H	-1.117570	1.489610	-1.579840
H	3.031060	0.581050	-1.250050
H	-1.816630	0.606030	1.859310
H	-0.275540	-0.213690	2.085220
C	-1.738160	-1.339250	0.908070
H	-0.806130	2.556730	0.788320
H	4.794510	-0.750130	-0.492450
C	-2.788770	-1.052930	-0.173390
H	-1.437950	-0.902280	-1.853280
H	-2.934500	0.026260	-2.050470
H	-3.610910	-0.467350	0.257450
H	-3.217600	-1.986080	-0.556090
H	-2.190450	-1.851490	1.764730
H	-0.971340	-2.010560	0.502030

I 2a TS2 R

Energy = -556.2046427

O	0.563290	0.243280	0.524410
C	1.700050	-0.058000	-0.276850
C	2.854230	-0.337350	0.673150
H	1.954780	0.781910	-0.934560
H	1.528700	-0.944510	-0.903510
O	-0.189970	2.077900	-0.693460
O	3.977710	-0.681580	-0.127110
H	3.042060	0.557560	1.285990
H	2.567580	-1.152140	1.355160

C	-0.562710	0.822910	-0.169110
H	0.222780	2.561720	0.035480
H	4.716410	-0.874620	0.462640
C	-1.660140	0.930920	0.896850
N	-1.041870	0.070500	-1.292660
H	-0.372300	0.105570	-2.054580
C	-1.487480	-1.289550	-0.978760
C	-2.213250	-0.448330	1.283350
H	-2.450180	1.558150	0.472540
H	-1.247530	1.444730	1.772250
C	-2.637370	-1.229340	0.031420
H	-1.821770	-1.755300	-1.911480
H	-0.678590	-1.918030	-0.567530
H	-2.948030	-2.246310	0.297430
H	-3.495340	-0.735010	-0.440970
H	-3.058350	-0.334970	1.971860
H	-1.435310	-1.006670	1.816960

I 2b TS1 R

Energy = -556.2203638

H	2.204100	-1.573330	-0.450720
C	1.840630	-0.724970	-1.043260
O	0.421170	-0.616370	-0.922370
C	2.605370	0.540620	-0.659880
H	2.017110	-0.949560	-2.100660
C	-0.144580	-0.566570	0.388980
O	2.455690	0.882260	0.715810
H	3.673550	0.369360	-0.839160
H	2.288270	1.373180	-1.304390
N	-0.302770	0.868970	0.747350
O	0.632360	-1.174270	1.366270
C	-1.488590	-1.298000	0.311620
H	1.536630	1.236360	0.795740
C	-1.251700	1.586780	-0.129770
H	1.445830	-0.634930	1.454470
H	-1.303550	-2.322720	-0.022910
C	-2.472300	-0.572440	-0.617650
H	-1.891410	-1.350920	1.330290
C	-2.623180	0.902330	-0.214370
H	-2.101460	-0.634160	-1.647060
H	-3.444810	-1.076520	-0.596360
H	-3.260200	1.436680	-0.929360
H	-3.121950	0.969230	0.763540
H	-0.797390	1.635620	-1.123780
H	-1.341800	2.612950	0.241130
H	-0.651130	0.886550	1.706110

I 2b TS2 R

Energy = -556.1805092

N	0.313000	0.613230	-0.934850
O	-0.581910	-1.537680	-0.968830
C	0.177750	-0.666490	-0.195530
O	-0.408590	-0.350820	1.070950
O	-2.443200	0.575550	-0.972010
C	-1.829900	-0.423580	1.195310
C	-2.596760	0.663660	0.443470
H	0.736370	0.379580	-1.832690
H	-1.410320	-1.059670	-1.201170
C	1.542200	-1.335650	0.091420
H	-1.523360	0.899740	-1.153180
H	-2.020370	-0.323780	2.269700
H	-2.182280	-1.413220	0.878420
H	-3.665780	0.547770	0.659190
H	-2.286830	1.655060	0.805680
H	1.676700	-2.146150	-0.631220
H	1.485300	-1.784930	1.087230
C	1.147240	1.626500	-0.240540
C	2.296840	1.019620	0.597930
C	2.713740	-0.336330	0.018430
H	3.580350	-0.740000	0.553730
H	3.033690	-0.204740	-1.025530
H	1.961060	0.876670	1.631220
H	3.143050	1.716240	0.625660
H	1.545780	2.284400	-1.020610
H	0.498620	2.237550	0.393770

I 1a TS1 R

Energy = -400.141977

H	2.690270	-0.992640	-0.800030
O	2.432800	-1.046470	0.133990
C	1.515780	-0.024300	0.320360
N	2.022220	1.182960	-0.310470
H	2.818630	1.535850	0.214760
H	1.315580	1.913470	-0.328060
H	1.368710	0.050840	1.412380
O	0.287690	-0.379780	-0.280000
C	-0.853290	0.301790	0.213390
C	-2.081800	-0.449570	-0.276040
H	-0.853160	0.331110	1.313840
H	-0.905490	1.340540	-0.149060
O	-3.216350	0.270610	0.187110
H	-2.048540	-0.509480	-1.374070
H	-2.051710	-1.476500	0.116490
H	-4.007230	-0.196370	-0.107950

I 1a TS2 R

Energy = -400.1431119

H	2.007450	-1.799400	0.060220
O	2.482770	-0.959000	0.005430
C	1.554040	0.026630	0.327990
N	2.034990	1.255350	-0.212310
H	1.447120	2.038200	0.052990
H	2.081650	1.191690	-1.225930
H	1.427200	0.156700	1.418390
O	0.302090	-0.448370	-0.199380
C	-0.837270	0.259200	0.256130
C	-2.068610	-0.443460	-0.293590
H	-0.884310	0.278330	1.356430
H	-0.832780	1.302320	-0.094990
O	-3.198140	0.292900	0.154670
H	-2.002210	-0.473900	-1.391440
H	-2.080740	-1.482420	0.068840

H	-3.990960	-0.137450	-0.187350

I 1b TS1 R

Energy = -400.1596137

H	0.361370	-0.619730	1.353240
O	1.137180	-0.022680	1.311580
C	1.270370	0.355590	-0.012760
N	1.303780	-0.846110	-0.864410
H	2.125020	-1.402790	-0.634830
H	1.371720	-0.564510	-1.839760
H	2.191190	0.948640	-0.075660
O	0.251030	1.202620	-0.517520
C	-1.044200	1.105380	0.081400
C	-1.791000	-0.189310	-0.235350
H	-0.964350	1.232720	1.167820
H	-1.604140	1.955900	-0.321030
O	-1.155100	-1.345890	0.304730
H	-2.790850	-0.131220	0.210710
H	-1.915280	-0.285570	-1.323540
H	-0.377040	-1.512980	-0.276110

I 1b TS2 R

Energy = -400.1482448

H	-0.086920	-1.412110	-0.129420
O	0.810800	-1.360660	0.248480
C	1.162580	-0.012090	0.325050
N	2.529340	0.108160	-0.061790
H	2.790000	1.088330	-0.122880
H	2.649930	-0.320290	-0.976270
H	1.046720	0.379480	1.352130
O	0.313920	0.780600	-0.532740
C	-0.891350	1.248030	0.053240
C	-1.845490	0.131120	0.494730
H	-0.695460	1.906720	0.915310
H	-1.365400	1.859820	-0.723590
O	-1.910350	-0.936690	-0.452030
H	-1.500380	-0.332010	1.423340
H	-2.840950	0.558960	0.684810
H	-1.972400	-0.554480	-1.338660

I 1a TS1 S

Energy = -400.141977

H	-2.690270	-0.992650	-0.800030
O	-2.432800	-1.046470	0.133990
C	-1.515780	-0.024300	0.320360
N	-2.022230	1.182960	-0.310470
H	-2.818640	1.535850	0.214760
H	-1.315580	1.913470	-0.328070
H	-1.368720	0.050840	1.412380
O	-0.287700	-0.379780	-0.280010
C	0.853290	0.301790	0.213390
C	2.081810	-0.449570	-0.276040
H	0.853160	0.331120	1.313840
H	0.905500	1.340550	-0.149060
O	3.216340	0.270620	0.187110
H	2.048530	-0.509480	-1.374070
H	2.051710	-1.476500	0.116490
H	4.007240	-0.196370	-0.107940

I 1a TS2 S

Energy = -400.1431119

H	-2.007450	-1.799400	0.060230
O	-2.482770	-0.959000	0.005440
C	-1.554040	0.026630	0.327990
N	-2.034990	1.255350	-0.212310
H	-1.447120	2.038210	0.052990
H	-2.081650	1.191690	-1.225930
H	-1.427200	0.156690	1.418390
O	-0.302090	-0.448380	-0.199380
C	0.837280	0.259200	0.256130
C	2.068610	-0.443450	-0.293590
H	0.884310	0.278340	1.356430
H	0.832780	1.302320	-0.094990
O	3.198140	0.292900	0.154670
H	2.002210	-0.473900	-1.391430
H	2.080740	-1.482420	0.068840
H	3.990960	-0.137450	-0.187350

I 1b TS1 S

Energy = -400.1596138

H	-0.362310	-0.618910	1.354150
O	-1.137820	-0.021600	1.311430
C	-1.270400	0.355420	-0.013400
N	-1.302890	-0.847070	-0.863930
H	-2.124510	-1.403330	-0.634690
H	-1.370050	-0.566070	-1.839520
H	-2.191420	0.948040	-0.077310
O	-0.251010	1.202270	-0.518360
C	1.043920	1.105430	0.081300
C	1.791010	-0.189180	-0.234980
H	0.963250	1.232540	1.167680
H	1.603960	1.956140	-0.320570
O	1.155220	-1.345700	0.305280
H	2.790680	-0.130690	0.211380
H	1.915740	-0.285740	-1.323090
H	0.376500	-1.512280	-0.274880

I 1b TS2 S

Energy = -400.1482447

H	0.086660	-1.411700	-0.129830
O	-0.810310	-1.360310	0.249850
C	-1.162890	-0.011840	0.325190
N	-2.529370	0.107650	-0.062890
H	-2.790450	1.087680	-0.124480
H	-2.649000	-0.321120	-0.977340
H	-1.048100	0.380280	1.352160
O	-0.313920	0.780750	-0.532330
C	0.891320	1.247890	0.053960
C	1.845540	0.130690	0.494540
H	0.695350	1.905900	0.916530

H	1.365280	1.860300	-0.722430
O	1.910330	-0.936340	-0.453110
H	1.500480	-0.333180	1.422780
H	2.841000	0.558410	0.684850
H	1.971810	-0.553370	-1.339450

1a TS1 S

Energy = -400.0854224

H	-2.806000	0.219120	-0.526490
O	-2.481260	-0.978080	-0.001210
C	-1.480270	-0.226790	0.383440
N	-2.090570	1.164360	-0.238980
H	-2.451450	1.843020	0.431210
H	-1.512570	1.625780	-0.941800
H	-1.311730	-0.049960	1.465830
O	-0.259500	-0.478720	-0.250170
C	0.861340	0.207560	0.290720
C	2.112140	-0.389030	-0.334120
H	0.904480	0.099430	1.384030
H	0.819240	1.285260	0.065160
O	3.216410	0.343050	0.181070
H	2.038880	-0.311420	-1.429240
H	2.164220	-1.457090	-0.078130
H	4.024500	-0.045080	-0.175490

1a TS2 S

Energy = -400.0971802

H	-0.809360	1.099600	0.228420
O	-1.838840	1.263460	-0.202250
C	-1.879600	-0.033100	-0.412660
N	-2.878120	-0.741470	0.144400
H	-2.898920	-1.743690	0.029140
H	-3.278890	-0.364960	0.992820
H	-1.452770	-0.482000	-1.315700
O	-0.180970	-0.048160	0.538670
C	0.957740	-0.418380	-0.195350
C	2.200580	0.234650	0.403210
H	0.893820	-0.123480	-1.260200
H	1.097880	-1.510520	-0.172840
O	3.325920	-0.198370	-0.353770
H	2.278340	-0.057410	1.461360
H	2.081530	1.329320	0.368220
H	4.113980	0.209010	0.025620

1b TS1 S

Energy = -400.1271379

H	-0.385970	-1.263890	-0.544870
O	-0.890100	0.017600	1.330760
C	-1.149690	0.527480	0.142590
N	-1.361710	-0.707770	-0.852920
H	-2.197420	-1.235810	-0.605070
H	-1.397450	-0.414410	-1.827350
H	-2.058950	1.138510	0.086360
O	-0.121980	1.260870	-0.500820
C	1.201080	1.004450	0.008040
C	1.660210	-0.438320	-0.238750
H	1.224590	1.231830	1.079360
H	1.850620	1.711140	-0.516230
O	0.735870	-1.385160	0.280030
H	2.650740	-0.572110	0.222170
H	1.784980	-0.597440	-1.321820
H	0.000970	-0.751510	1.046850

1b TS2 S

Energy = -400.1118269

H	0.193350	-1.331180	-0.017060
O	-0.903020	-1.257320	0.371580
C	-1.286930	-0.022370	0.439360
N	-2.464660	0.304060	-0.154430
H	-2.671920	1.290150	-0.226870
H	-2.696140	-0.246250	-0.971550
H	-1.044800	0.589790	1.315540
O	0.100020	0.968500	-0.561990
C	1.210120	1.166950	0.282200
C	1.990680	-0.207190	0.290550
H	0.903670	1.443820	1.303810
H	1.839930	1.980640	-0.101060
O	1.251960	-1.029010	-0.623260
H	2.003970	-0.670590	1.281880
H	3.020870	-0.107720	-0.063780
H	0.628910	-0.158880	-1.003330

I 2a TS1 S

Energy = -556.2037585

O	-0.577700	0.094110	-0.449170
C	-1.755630	-0.115770	0.329100
C	0.509130	0.762520	0.170560
C	-2.896580	-0.336010	-0.652450
H	-1.969410	0.751380	0.960780
O	0.024900	2.030840	0.573990
C	1.076090	-0.029370	1.362250
N	1.543210	0.967150	-0.816810
H	-1.656810	-1.002720	0.970510
O	-4.052680	-0.644870	0.116020
H	-2.626710	-1.154280	-1.337780
C	2.165090	-0.267550	-1.326410
H	1.117500	1.486420	-1.582480
H	-3.030420	0.574330	-1.255210
H	1.817160	0.608700	1.858310
H	0.275650	-0.209820	2.085690
C	1.737510	-1.338210	0.910220
H	0.808010	2.559610	0.779430
H	-4.793930	-0.753140	-0.491790
C	2.788120	-1.054200	-0.171870
H	1.437060	-0.905830	-1.851680
H	2.933980	0.021740	-2.050860
H	3.610610	-0.468240	0.257840
H	3.216460	-1.988200	-0.553150
H	2.189680	-1.849360	1.767630
H	0.970220	-2.009730	0.505330

I 2a TS2 S

Energy = -556.2046427

O	-0.563290	0.243280	0.524410
C	-1.700050	-0.057990	-0.276850
C	-2.854230	-0.337340	0.673150
H	-1.954780	0.781920	-0.934550
H	-1.528700	-0.944510	-0.903510
O	0.189970	2.077900	-0.693460
O	-3.977710	-0.681580	-0.127110
H	-3.042050	0.557560	1.285990
H	-2.567570	-1.152140	1.355160
C	0.562710	0.822910	-0.169110
H	-0.222770	2.561720	0.035480
H	-4.716410	-0.874630	0.462640
C	1.660140	0.930920	0.896850
N	1.041870	0.070500	-1.292660
H	0.372290	0.105570	-2.054580
C	1.487470	-1.289540	-0.978760
C	2.213250	-0.448330	1.283350
H	2.450190	1.558150	0.472540
H	1.247530	1.444740	1.772250
C	2.637370	-1.229340	0.031420
H	1.821770	-1.755300	-1.911480
H	0.678600	-1.918030	-0.567530
H	2.948030	-2.246310	0.297420
H	3.495340	-0.735010	-0.440970
H	3.058350	-0.334970	1.971860
H	1.435310	-1.006670	1.816960

I 2b TS1 S

Energy = -556.2203638

H	-2.204090	-1.573340	-0.450720
C	-1.840630	-0.724980	-1.043260
O	-0.421160	-0.616380	-0.922370
C	-2.605370	0.540620	-0.659880
H	-2.017100	-0.949570	-2.100660
C	0.144580	-0.566570	0.388980
O	-2.455690	0.882270	0.715800
H	-3.673550	0.369350	-0.839160
H	-2.288280	1.373170	-1.304400
N	0.302770	0.868970	0.747350
O	-0.632360	-1.174260	1.366280
C	1.488590	-1.298000	0.311630
H	-1.536630	1.236360	0.795730
C	1.251700	1.586780	-0.129780
H	-1.445830	-0.634920	1.454470
H	1.303550	-2.322720	-0.022890
C	2.472300	-0.572440	-0.617640
H	1.891410	-1.350910	1.330300
C	2.623180	0.902330	-0.214370
H	2.101460	-0.634160	-1.647050
H	3.444810	-1.076520	-0.596350
H	3.260200	1.436680	-0.929360
H	3.121950	0.969230	0.763530
H	0.797390	1.635610	-1.123790
H	1.341800	2.612950	0.241110
H	0.651130	0.886560	1.706100

I 2b TS2 S

Energy = -556.2109332

N	-0.311670	0.607620	-0.939930
O	0.578440	-1.544910	-0.965340
C	-0.179750	-0.669460	-0.196800
O	0.405860	-0.352110	1.069960
O	2.442110	0.577800	-0.970250
C	1.827710	-0.423800	1.194330
C	2.593040	0.665170	0.444590
H	-0.736060	0.373070	-1.835510
H	1.402250	-1.071400	-1.204470
C	-1.545890	-1.333560	0.091920
H	1.523060	0.892070	-1.152260
H	2.020070	-0.326380	2.268150
H	2.181660	-1.411740	0.874890
H	3.661120	0.551490	0.665400
H	2.281010	1.654540	0.809550
H	-1.684340	-2.140820	-0.632350
H	-1.486860	-1.785060	1.085720
C	-1.140820	1.626130	-0.247770
C	-2.286430	1.025170	0.599660
C	-2.713030	-0.329220	0.024610
H	-3.578070	-0.727860	0.564320
H	-3.037890	-0.197310	-1.016910
H	-1.942670	0.881390	1.629340
H	-3.128290	1.725290	0.633320
H	-1.543510	2.280060	-1.028200
H	-0.490010	2.240570	0.380290

2a TS1 S

Energy = -556.1386745

O	-0.874390	1.032670	0.080180
C	-1.589790	-0.192510	0.107400
C	0.524890	1.003530	0.247500
C	-3.052360	0.138280	-0.148960
H	-1.499510	-0.704760	1.073980
O	1.060980	2.207170	0.144380
C	1.020010	0.131640	1.427150
N	1.186720	0.466080	-1.186680
H	-1.232110	-0.883750	-0.671900
O	-3.759450	-1.095340	-0.147840
H	-3.139220	0.664880	-1.111120
C	1.917590	-0.807910	-1.363640
H	0.457880	0.582390	-1.891300
H	-3.405820	0.821180	0.637150
H	1.853250	0.698250	1.851350
H	0.237810	0.101650	2.193650
C	1.505580	-1.284480	1.080580
H	1.605170	1.584110	-0.892840
H	-4.697310	-0.901820	-0.264930
C	2.547060	-1.258430	-0.045070
H	1.221290	-1.581640	-1.712320
H	2.677940	-0.677060	-2.142580
H	3.369140	-0.583900	0.226840
H	2.985020	-2.251700	-0.193560

H	1.937780	-1.740180	1.978540
H	0.666630	-1.926910	0.782290

2a TS2 S

Energy = -556.1656135

O	0.816840	1.142430	-0.607380
C	1.893420	0.674130	0.143710
C	2.592030	-0.487200	-0.561480
H	2.640960	1.465790	0.318600
H	1.588860	0.324300	1.153660
O	-0.865680	2.257880	0.483560
O	3.638750	-0.959830	0.282860
H	2.973090	-0.135080	-1.531750
H	1.852080	-1.279130	-0.768880
C	-1.043530	0.966350	0.222230
H	0.080680	2.228820	-0.037280
H	4.156770	-1.603290	-0.215540
C	-1.752650	0.547490	-1.040280
N	-1.063130	0.134630	1.273550
H	-0.642290	0.519170	2.110770
C	-1.181340	-1.324230	1.163460
C	-1.705170	-0.965170	-1.272410
H	-2.792840	0.887570	-0.928920
H	-1.309780	1.106220	-1.865210
C	-2.106600	-1.708370	0.007670
H	-1.564880	-1.702870	2.115580
H	-0.185440	-1.759650	1.007830
H	-2.060430	-2.793270	-0.133280
H	-3.141920	-1.459270	0.272220
H	-2.364520	-1.241130	-2.101580
H	-0.684660	-1.242470	-1.560780

2b TS1 S

Energy = -556.194875

H	-2.399340	-1.372530	0.785030
C	-2.338730	-0.932730	-0.216470
O	-1.005140	-1.118820	-0.732670
C	-2.757280	0.543140	-0.176330
H	-2.984710	-1.503160	-0.890530
C	0.037270	-0.575970	0.064680
O	-1.837660	1.335430	0.547910
H	-3.765320	0.598690	0.267290
H	-2.847990	0.913050	-1.212520
N	0.304080	0.835230	-0.642430
O	-0.270610	-0.301370	1.333730
C	1.280260	-1.441830	-0.108190
H	-0.655320	1.330570	-0.280960
C	1.530980	1.514920	-0.154340
H	-1.101990	0.505050	1.195610
H	1.096990	-2.371750	0.437780
C	2.541220	-0.735540	0.408390
H	1.383240	-1.700640	-1.169120
C	2.756980	0.611620	-0.297140
H	2.433060	-0.570240	1.486030
H	3.415520	-1.379140	0.263670
H	3.628680	1.130750	0.116670
H	2.967730	0.446380	-1.363530
H	1.345600	1.748210	0.897230
H	1.646940	2.457360	-0.698320
H	0.311430	0.697170	-1.652740

2b TS2 S

Energy = -556.1781578

N	-0.925260	-1.317150	0.095180
O	0.732280	-0.622750	1.506530
C	-0.288610	-0.319320	0.752360
O	0.747710	0.483190	-0.921400
O	2.373440	-1.036020	-0.234460
C	1.843160	1.263290	-0.528080
C	3.013990	0.247060	-0.215140
H	-0.368970	-2.153990	-0.034560
H	1.545110	-0.983240	0.863150
C	-1.082830	0.912160	1.097640
H	1.501130	-0.638150	-0.798760
H	2.140900	1.967420	-1.319880
H	1.622870	1.860930	0.371980
H	3.476650	0.425670	0.760130
H	3.794630	0.269510	-0.984050
H	-0.379160	1.724260	1.290770
H	-1.581380	0.691290	2.052620
C	-1.939740	-1.035860	-0.928810
C	-2.895360	0.049950	-0.433810
C	-2.108140	1.285610	0.019860
H	-2.785880	2.056390	0.401600
H	-1.567590	1.704600	-0.834010
H	-3.493230	-0.344870	0.397440
H	-3.589980	0.307440	-1.240370
H	-1.444440	-0.711970	-1.852160
H	-2.476050	-1.967990	-1.129660

2 products

Energy = -556.2407323

N	1.056180	-0.635450	-0.120520
O	0.079590	1.409280	-0.241450
C	1.105490	0.718230	-0.135890
O	-4.605000	-0.185920	-0.672490
O	-1.859530	-0.483140	-0.334390
C	-3.973590	0.367980	0.467470
C	-2.709640	-0.413970	0.811400
H	0.110530	-1.016870	-0.158370
H	-1.347210	0.359980	-0.387360
C	2.471580	1.385480	-0.071950
H	-3.879370	-0.358860	-1.292810
H	-4.688490	0.324610	1.297430
H	-3.712700	1.428810	0.308040
H	-2.192530	0.036740	1.671050
H	-2.976590	-1.444810	1.068390
H	2.358340	2.283820	0.540870
H	2.686400	1.736170	-1.089970
C	2.176990	-1.554790	0.072980
C	3.511340	-0.889270	-0.260570
C	3.601570	0.476330	0.426510

H	4.572440	0.946330	0.238620
H	3.522100	0.343030	1.513380
H	3.598650	-0.762500	-1.347030
H	4.326830	-1.548170	0.054990
H	2.191570	-1.909100	1.114470
H	2.013800	-2.432820	-0.561120

2 Products 1

Energy = -169.8970272

N	1.085500	-0.158730	-0.000210
O	-1.199420	-0.245420	0.000040
C	-0.161300	0.388140	0.000000
H	-0.128500	1.496490	0.000020
H	1.178480	-1.163900	0.000420
H	1.914680	0.413030	0.000760

2 Products 2

Energy = -230.2573838

O	-1.318990	-0.575400	0.222280
O	1.422460	-0.582180	-0.189600
C	0.740400	0.572150	0.265510
C	-0.684680	0.609930	-0.262760
H	-2.131200	-0.717240	-0.278190
H	0.824440	-1.319970	0.001380
H	1.295220	1.444900	-0.094430
H	0.713830	0.618750	1.366420
H	-1.200840	1.516850	0.088700
H	-0.663480	0.624850	-1.361900

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