Theoretical study on the epimerization of azlactone rings: keto-enol tautomerism or base-mediated racemization?

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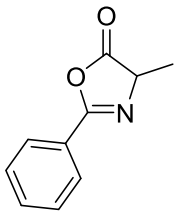
Supporting Information

Summary

1) Experimental and theoretical NMR data



4-methyl-2-phenyloxazolidin-5-one

Integral	**^{1}H Chemical shift (ppm)**			**Multiplicity**	**Coupling Constant (Hz)**	
	Experimental	Calculated	Error	Experimental	Experimental	Calculated
3	1.58	1.67	0.09	d	7.6	6.6
1	4.44	4.61	0.17	q	7.6	6.6
2	7.48	8.01	0.53	t	6.7	4.4 / 4.0
1	7.57	8.12	0.55	tt	7.5 / 1.2	4.0 / 0.9
2	7.99	8.69	0.70	m	-	4.0

Table S1. ^{1}H NMR data for alanine azlactone.

^{13}C chemical shift (ppm)		
Experimental	Calculated	Error
17.0	20.5	3.5
61.2	65.4	4.2
126.0	126.4	0.4
128.0	127.5	-0.5
128.9	127.8	-1.1
132.9	131.9	-1.0
161.7	162.6	0.9
179.1	181.3	2.2

Table S2. ^{13}C NMR data for alanine azlactone.

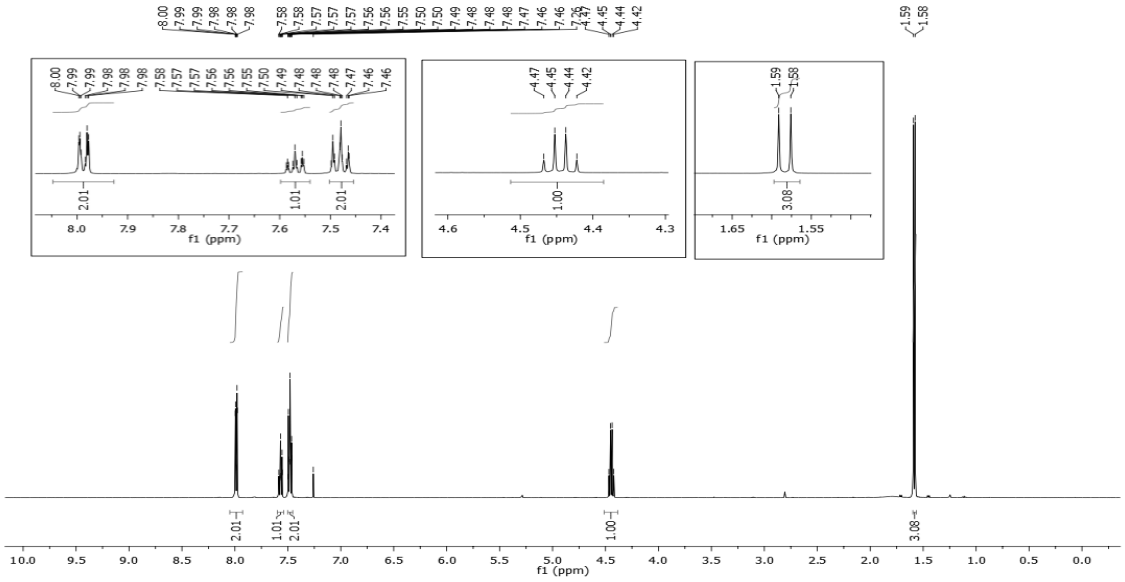


Figure S1. Experimental ^{1}H NMR of alanine-derived azlactone.

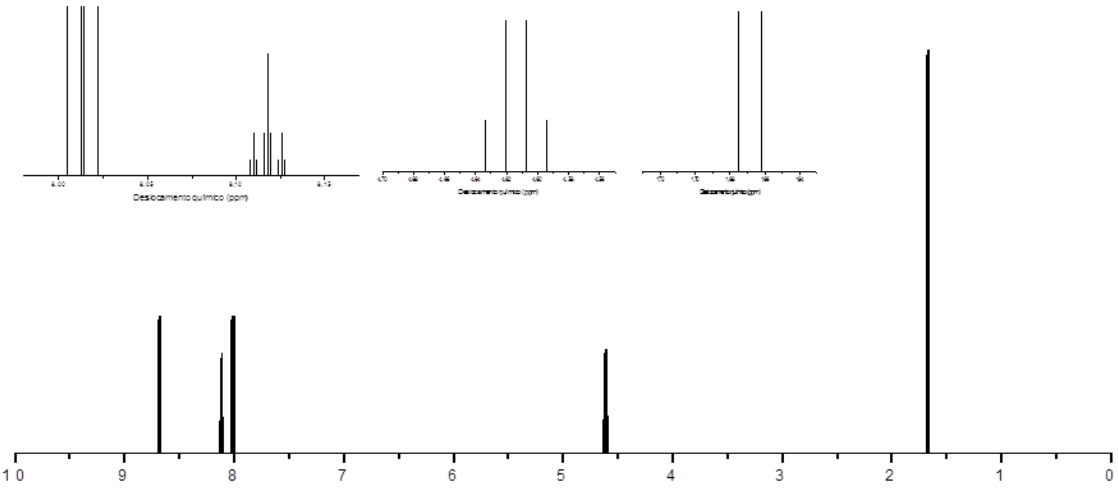


Figure S2. Calculated ^{1}H NMR of keto tautomer of alanine-derived azlactone.

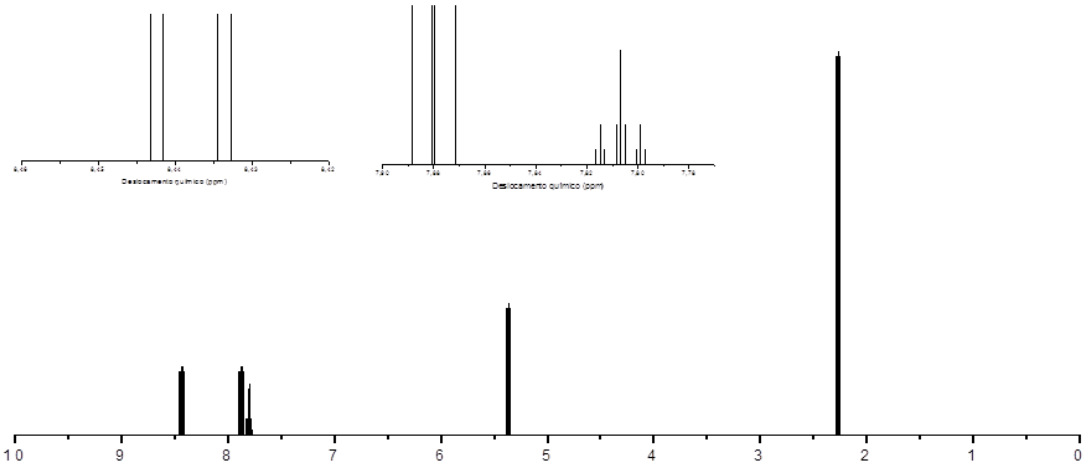


Figure S3. Calculated ^{1}H NMR of enol tautomer of alanine-derived azlactone.

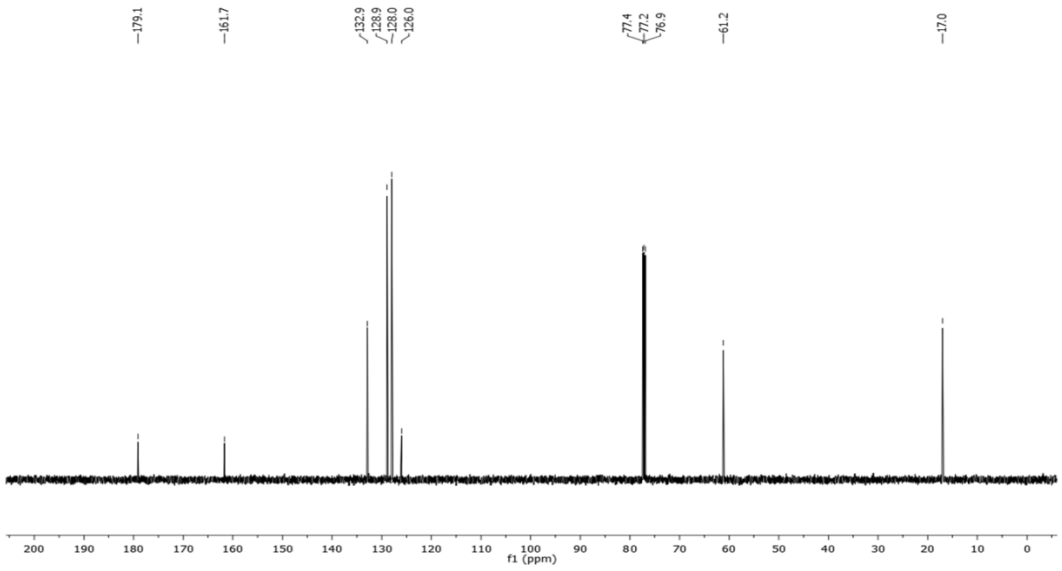


Figure S4. Experimental ^{13}C NMR of alanine-derived azlactone.

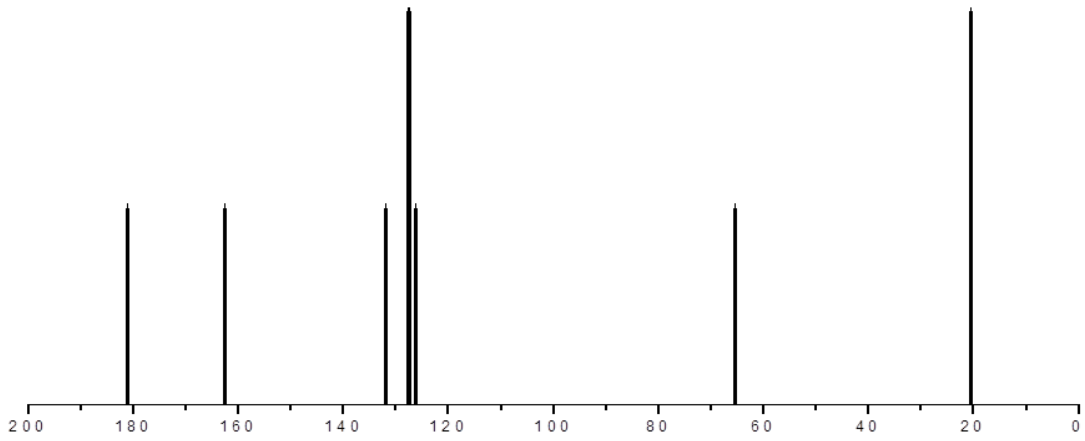


Figure S5. Calculated ^{13}C NMR of keto tautomer of alanine-derived azlactone.

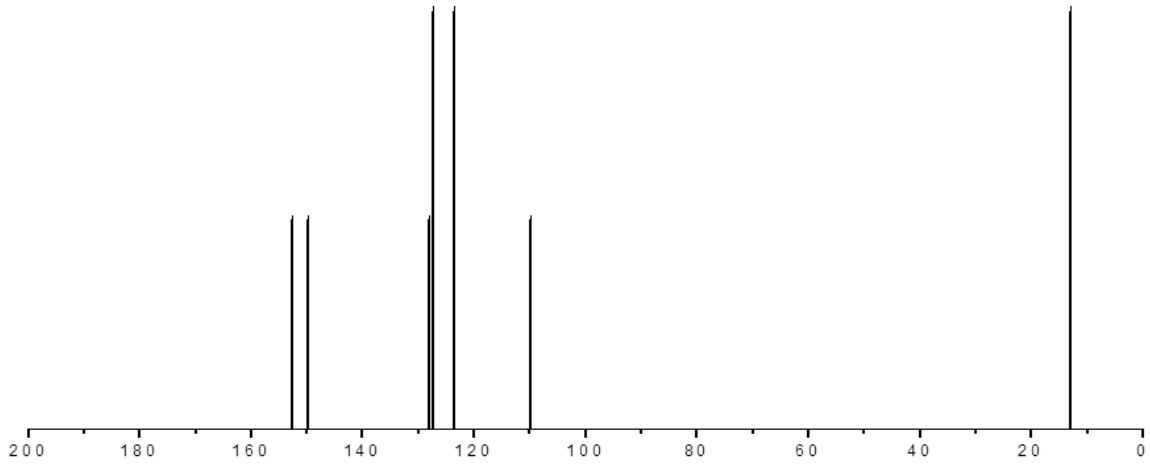
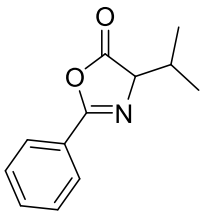


Figure S6. Calculated ^{13}C NMR of enol tautomer of alanine-derived azlactone.



4-isopropyl-2-phenyloxazolidin-5-one

Integral	^{1}H Chemical shift (ppm)			Multiplicity	Coupling Constant (Hz)	
	Experimental	Calculated	Error	Experimental	Experimental	Calculated
6	1.01 / 1.14	1.20	0.19 / 0.06	d / d	6.9 / 6.9	3.8
1	2.37	2.66	0.29	heptd	6.9 / 4.6	6.0 / 3.8
1	4.27	4.55	0.28	d	4.6	6.0
2	7.47	8.02	0.55	t	7.6	4.0 / 4.4
1	7.56	8.11	0.55	tt	7.5 / 1.3	4.0 / 0.9
2	8.00	8.68	0.68	m	-	4.4 / 0.9

Table S3. ^{1}H NMR data for valine azlactone.

^{13}C Chemical shift (ppm)		
Experimental	Calculated	Error
17.6	17.7	0.1
18.8	21.1	2.3
31.3	37.7	6.4
70.8	73.1	2.3
126.0	126.3	0.3
128.0	127.5	-0.5
128.8	127.8	-1.0
132.7	132.0	-0.7
161.7	162.8	1.1
177.9	179.4	1.5

Table S4. ^{13}C NMR data for valine azlactone.

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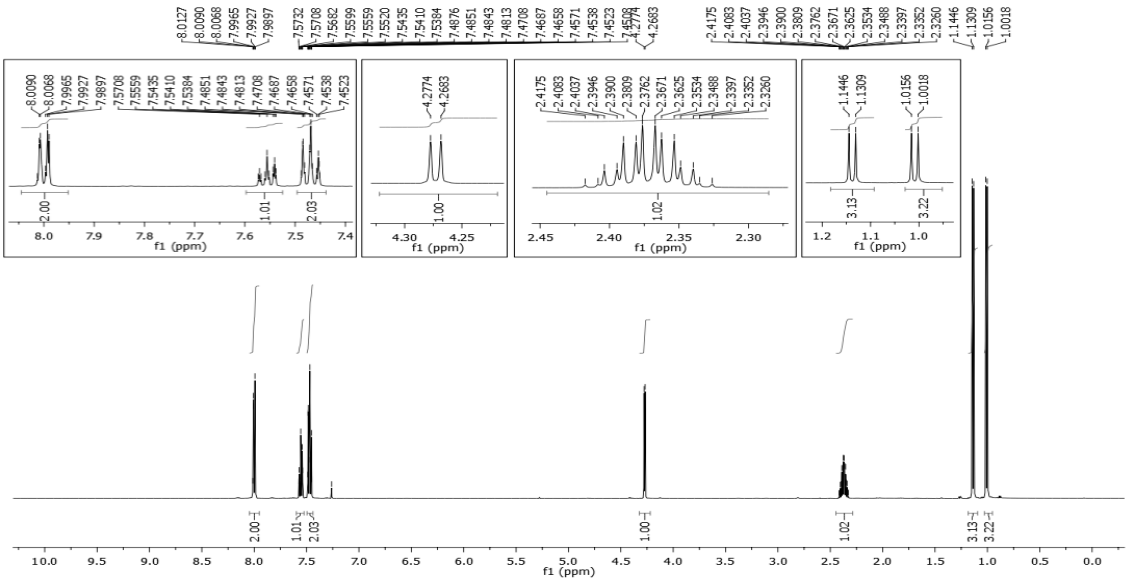

Figure S7. Experimental ^{1}H NMR of valine-derived azlactone.

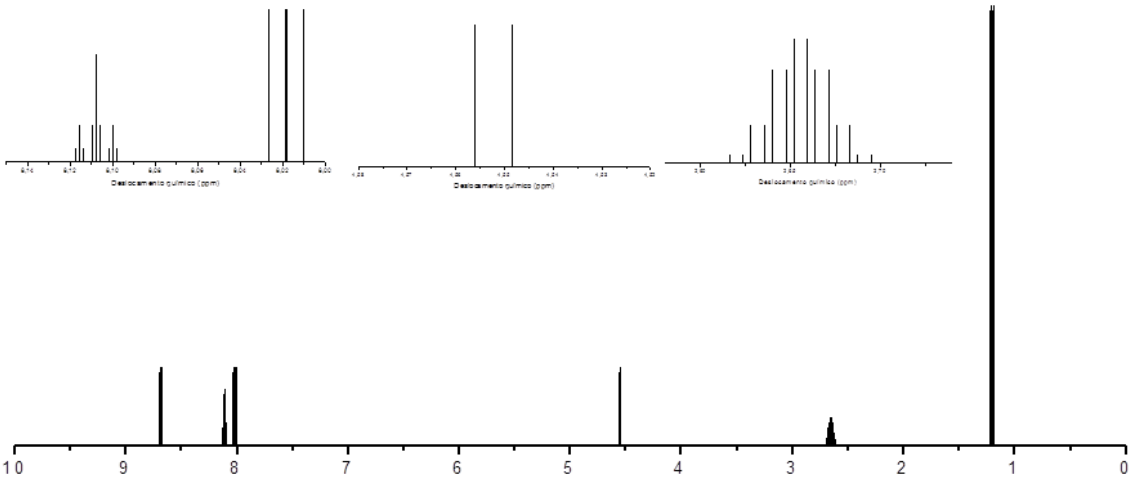

Figure S8. Calculated ^{1}H NMR of keto tautomer of valine-derived azlactone.

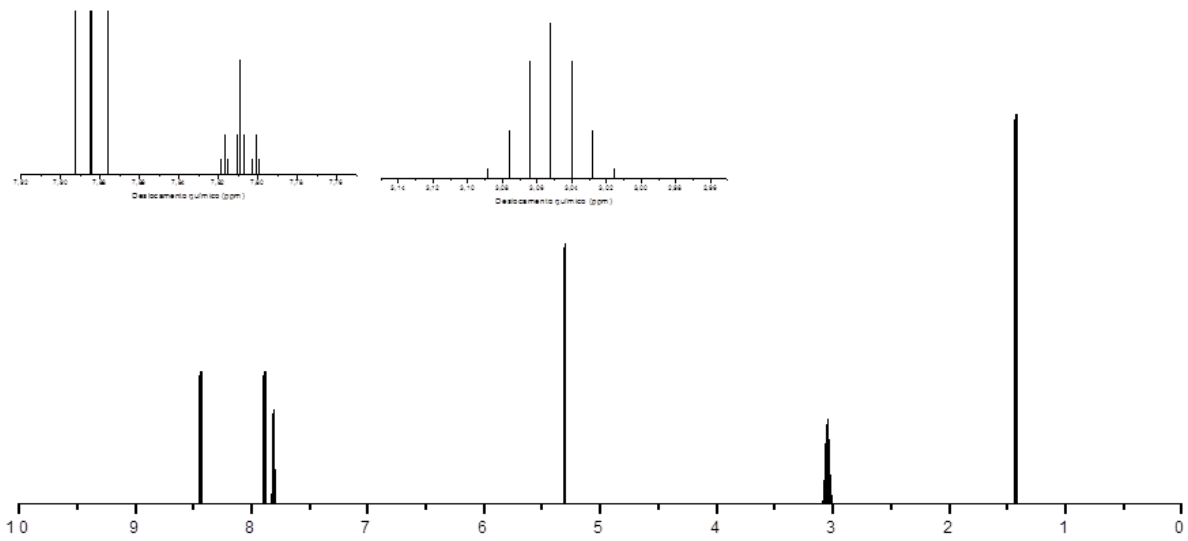

Figure S9. Calculated ^{1}H NMR of enol tautomer of valine-derived azlactone.

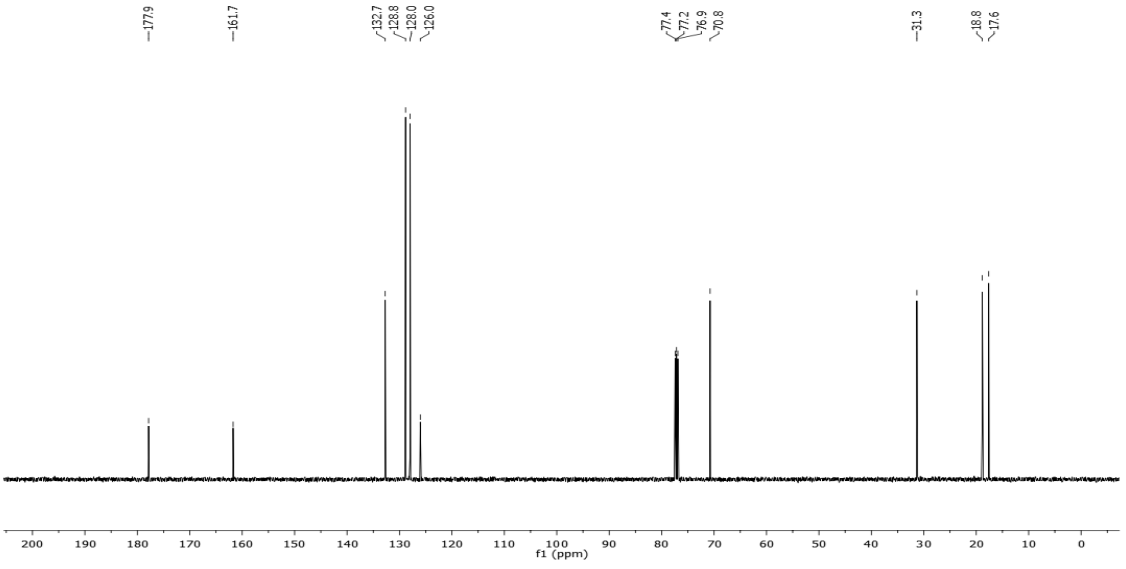

Figure S10. Experimental ^{13}C NMR of valine-derived azlactone.

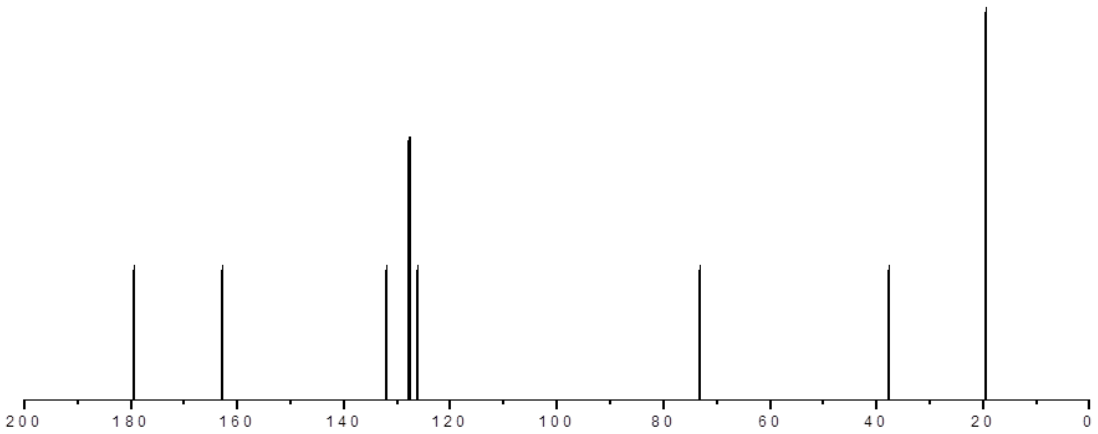

Figure S11. Calculated ^{13}C NMR of keto tautomer of valine-derived azlactone.

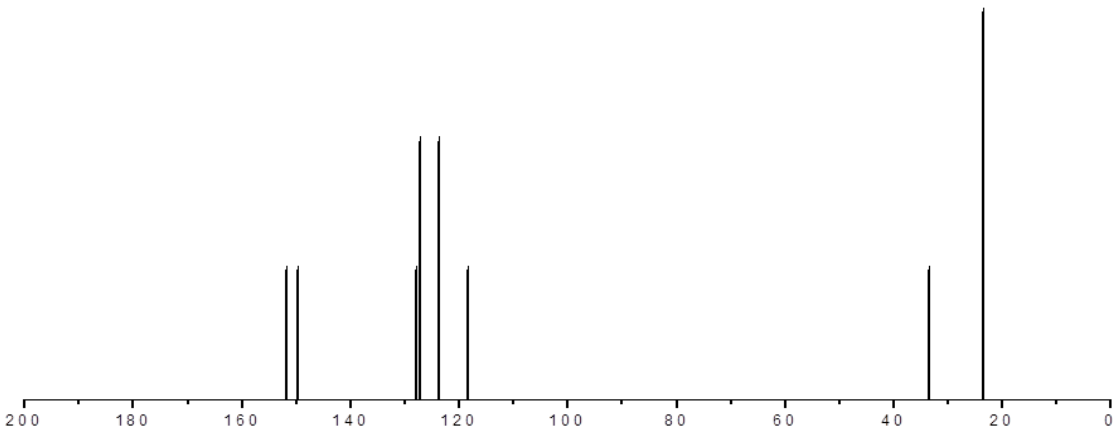

Figure S12. Calculated ^{13}C NMR of enol tautomer of valine-derived azlactone.

2) Experimental and theoretical IR data

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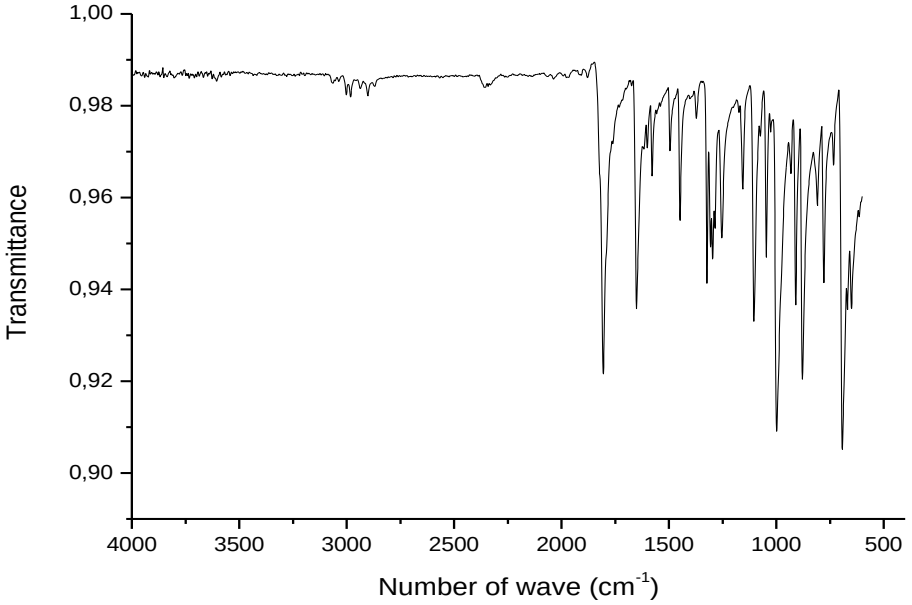


Figure S13. Experimental IR alanine-derived azlactone

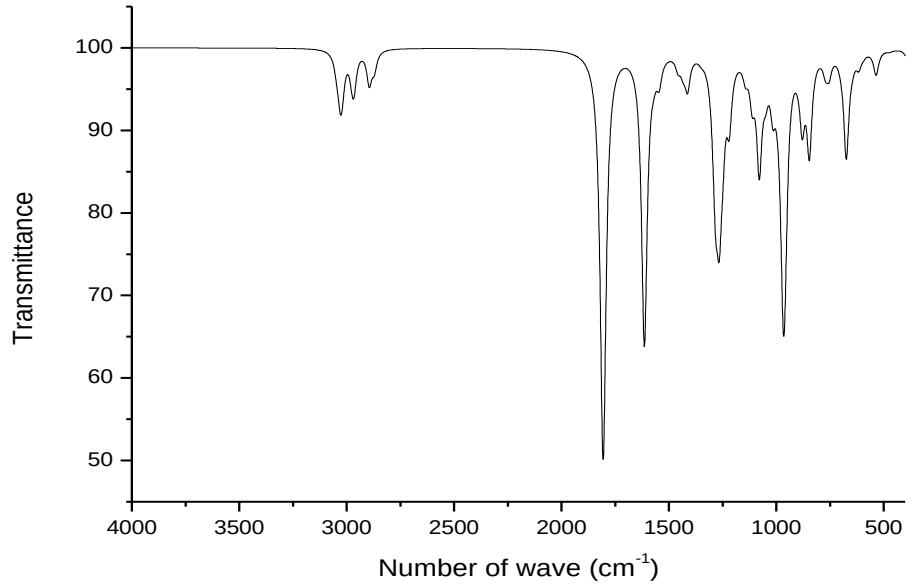


Figure S14. Calculated IR of keto tautomer of alanine-derived azlactone.

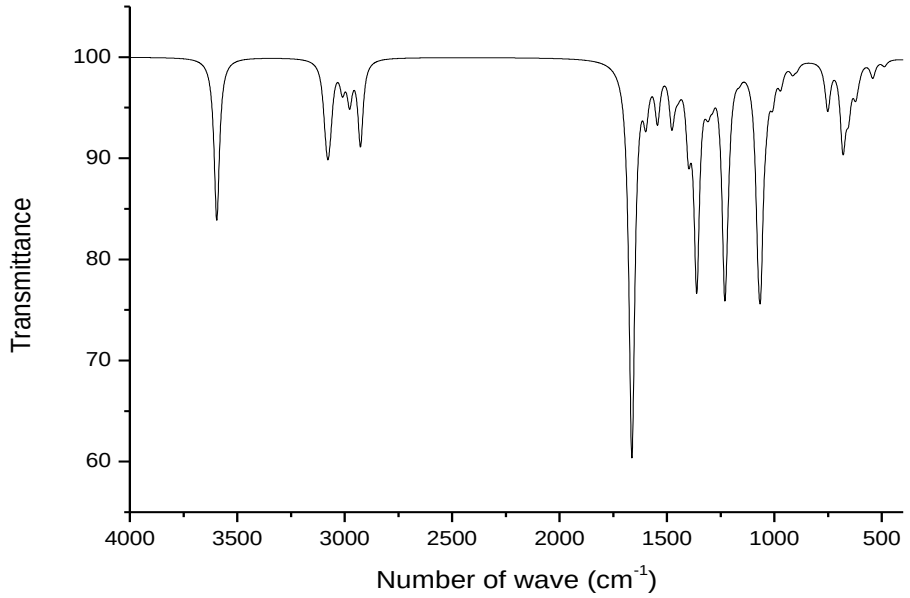
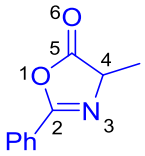


Figure S15. Calculated IR of enol tautomer of alanine-derived azlactone.

3) Eletrostatic potential and NBO calculations



Alanine Azlactone						
	Keto		Enolate		Enol	
	B.O.	Bond length. (Å)	B.O.	Bond length (Å)	B.O.	Bond length (Å)
O-H	----	----	---	---	0.73	0.971
C^4-H	0.86	1.099	---	---	---	---
C^5-O^6	1.84	1.198	1.56	1.233	1.04	1.346
C^4-C^5	0.96	1.529	1.26	1.422	1.55	1.361
C^4-N^3	1.00	1.461	1.31	1.361	1.18	1.392
O^1-C^5	0.93	1.392	0.88	1.428	1.00	1.363
C^2-N^3	1.77	1.278	1.47	1.320	1.61	1.299
O^1-C^2	0.94	1.394	0.99	1.376	0.97	1.384

Table S5. Bond order and bond length for alanine azlactone keto, enol and enolate forms.

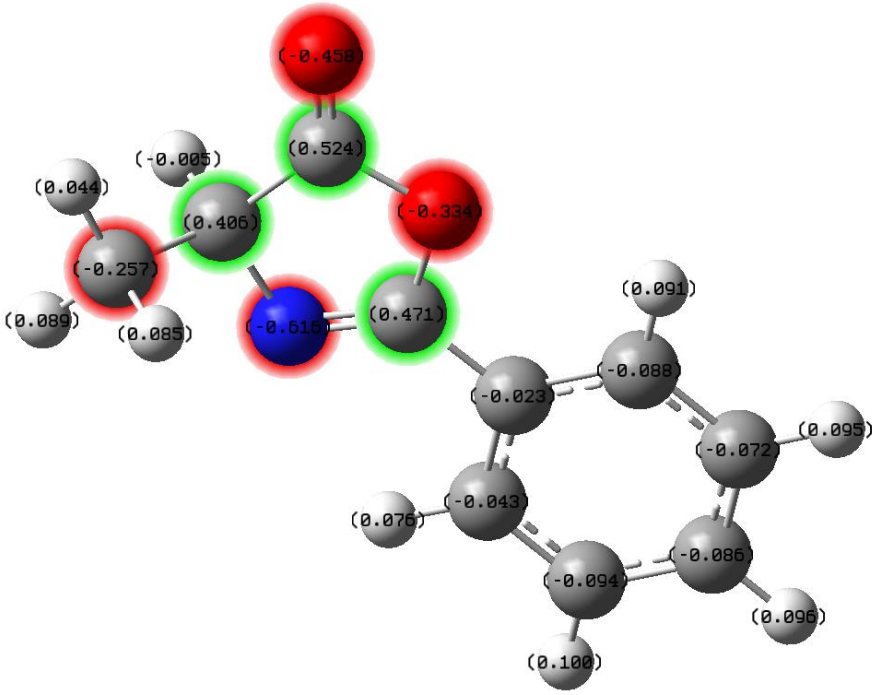


Figure S16. Eletrostatic potential for azlactone (keto).

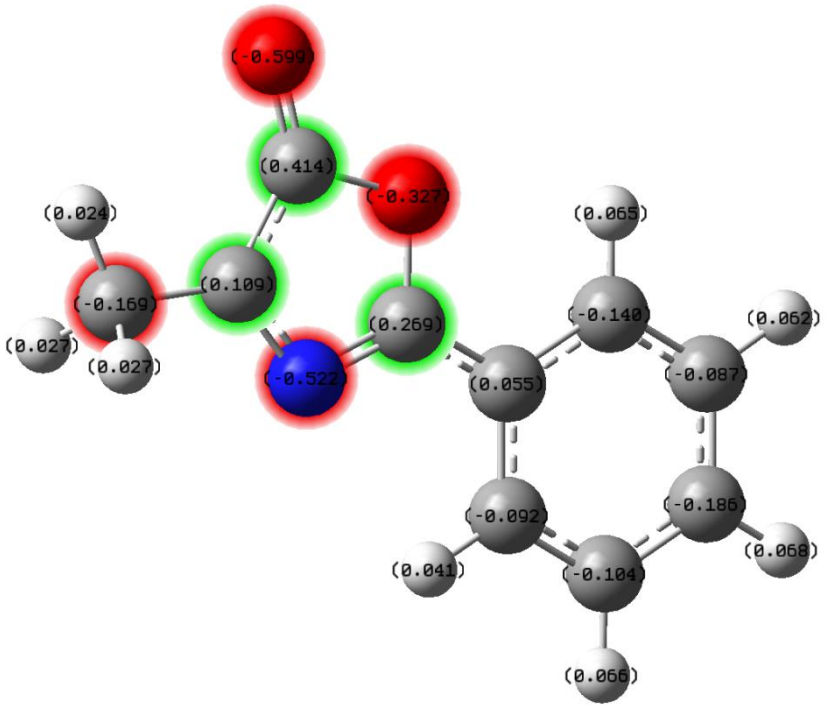


Figure S17. Eletrostatic potential for azlactone (enolate).

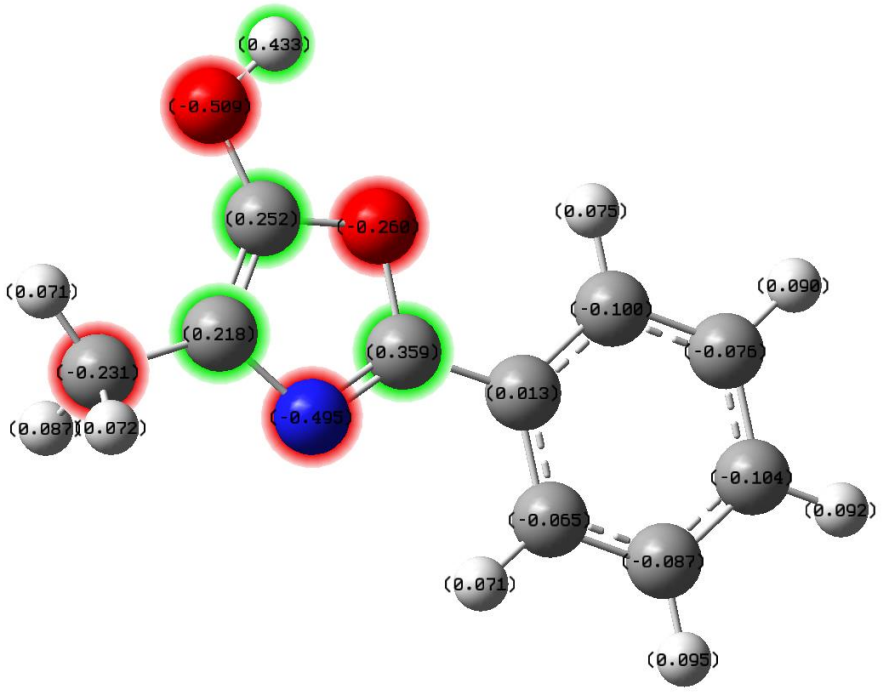
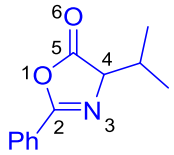


Figure S18. Eletrostatic potential for azlactone (enol).



Valine Azlactone						
	Keto		Enolate		Enol	
	B.O.	Bond length. (Å)	B.O.	Bond length (Å)	B.O.	Bond length (Å)
O-H	---	---	---	---	0.7243	0.9713
C^4-H	0.86	1.100	---	---	---	---
C^5-O^6	1.84	1.199	1.55	1.236	1.04	1.347
C^4-C^5	0.97	1.531	1.26	1.422	1.55	1.364
C^4-N^3	1.00	1.461	1.31	1.361	1.19	1.394
O^1-C^5	0.94	1.392	0.89	1.424	1.00	1.365
C^2-N^3	1.77	1.277	1.47	1.320	1.61	1.298
O^1-C^2	0.94	1.392	0.98	1.378	0.97	1.382

Table S6. Bond order and bond length for alanine azlactone keto, enol and enolate forms.

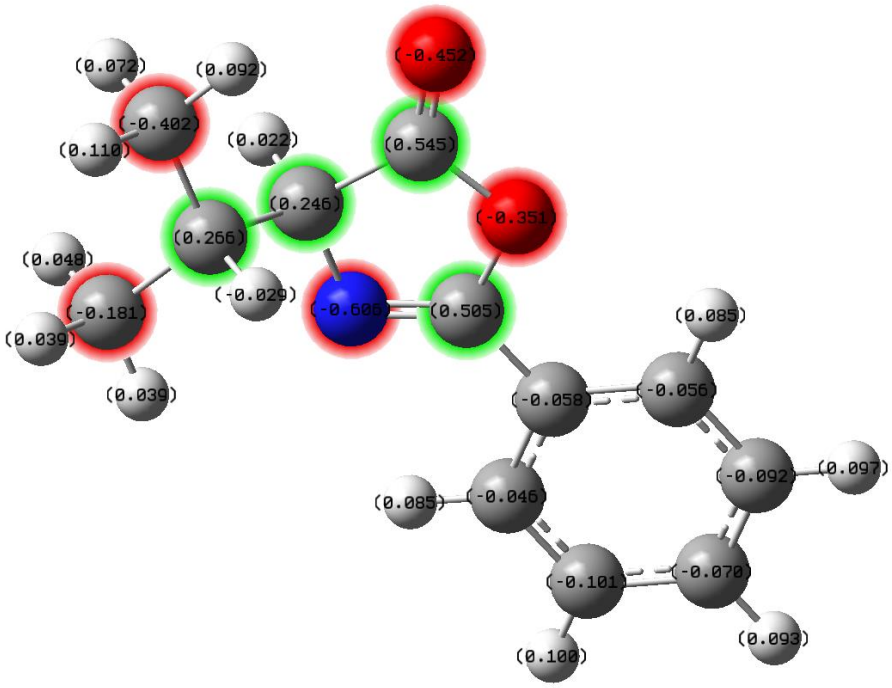


Figure S19. Eletrostatic potential for azlactone (keto).

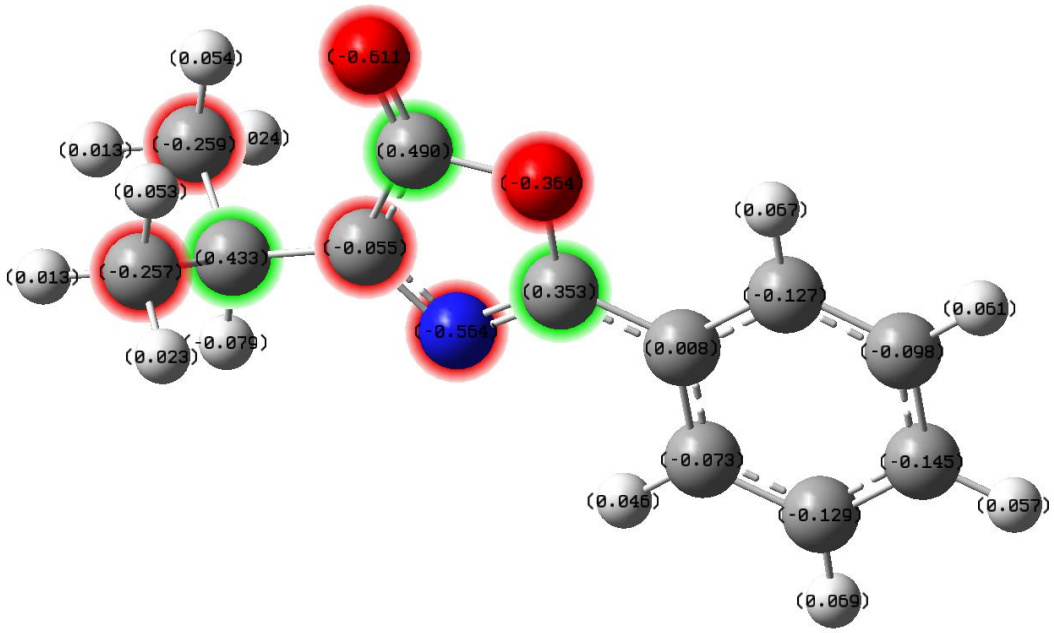


Figure S20. Eletrostatic potential for azlactone (enolate).

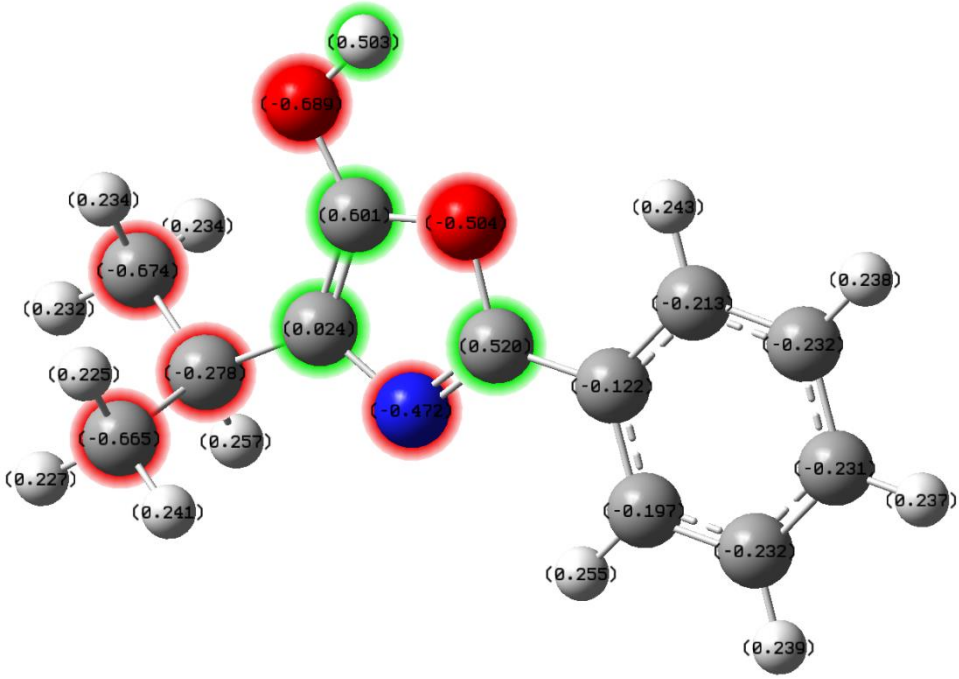
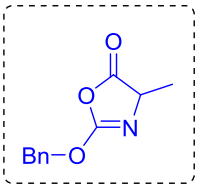


Figure S21. Eletrostatic potential for azlactone (enol).

4) 2-alcoxy azlactone pathway data



2-alcoxy azlactone tautomerism pathway (kcal/mol)			
	Gas phase	CH_2Cl_2	H_2O
Keto	0.0	0.0	0.0
TS Keto-Enol	77.9	78.3	78.4
Enol	13.5	14.6	14.8

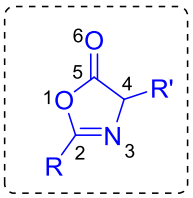
Table S7. Results for the tautomerism pathway for a 2-alcoxy azlactone at B3LYP-D3/6-31++G(d,p)//B3LYP/6-31G(d) level of theory.

2-alcoxy azlactone base-mediated pathway*						
	Gas phase			Dichloromethane		
	ΔE	ΔH	ΔG	ΔE	ΔH	ΔG
B + Keto	0.0	0.0	0.0	0.0	0.0	0.0
MC 1	-6.9	-5.4	3.1	-5.6	-4.2	4.4
BH^+ + Enolate	107.9	108.5	109.2	23.4	24.0	24.7
MC 3	-4.5	-3.0	8.0	-2.8	-1.3	9.8
B + Enol	13.6	13.4	13.5	14.7	14.5	14.6

* Unlike other azlactones, at gas phase and B3LYP/6-31G(d) level of theory no transition state exists for 2-alcoxy azlactone Keto→ Enolate conversion.

Table S8. Results for the base-mediated pathway for a 2-alcoxy azlactone at B3LYP-D3/6-31++G(d,p)//B3LYP/6-31G(d) level of theory.

5) %Keto and %Enol tautomers data for a wide scope of azlactones using B3LYP/6-31G(d) level of theory



Azlactone		Gas phase				Dichloromethane			
C2	C4	$\Delta G_{Keto \rightarrow Enol}$	K	$\%_{Enol}$	$\%_{Keto}$	$\Delta G_{Keto \rightarrow Enol}$	K	$\%_{Enol}$	$\%_{Keto}$
Me	Me	15.7	3.20×10^{-12}	3.20×10^{-10}	>99.999	15.8	2.66×10^{-12}	2.66×10^{-10}	>99.999
	H	18.3	3.73×10^{-14}	3.73×10^{-12}	>99.999	18.4	3.04×10^{-14}	3.04×10^{-12}	>99.999
	Ph	15.1	8.98×10^{-12}	8.98×10^{-10}	>99.999	15.4	5.35×10^{-12}	5.35×10^{-10}	>99.999
	*i*Pr	16.4	9.23×10^{-13}	9.23×10^{-11}	>99.999	16.4	9.44×10^{-13}	9.44×10^{-11}	>99.999
Ph	Me	14.0	5.12×10^{-11}	5.11×10^{-9}	>99.999	13.9	7.01×10^{-11}	7.01×10^{-9}	>99.999
	H	17.1	3.17×10^{-13}	3.17×10^{-11}	>99.999	16.8	4.62×10^{-13}	4.62×10^{-11}	>99.999
	Ph	14.4	2.88×10^{-11}	2.88×10^{-9}	>99.999	14.1	4.92×10^{-11}	4.92×10^{-9}	>99.999
	*i*Pr	15.1	8.71×10^{-12}	8.71×10^{-10}	>99.999	14.7	1.70×10^{-11}	1.70×10^{-9}	>99.999
OBn	Me	16.5	7.50×10^{-13}	7.50×10^{-11}	>99.999	17.1	3.17×10^{-13}	3.17×10^{-11}	>99.999
	H	22.6	2.57×10^{-17}	2.57×10^{-15}	>99.999	22.7	2.35×10^{-17}	2.35×10^{-15}	>99.999
	Ph	19.8	3.11×10^{-15}	3.11×10^{-13}	>99.999	20.1	1.92×10^{-15}	1.92×10^{-13}	>99.999
	*i*Pr	20.4	1.17×10^{-15}	1.17×10^{-13}	>99.999	20.3	1.39×10^{-15}	1.39×10^{-13}	>99.999

Table S9. Calculated percentage of tautomers for a wide scope of azlactones using B3LYP/6-31G(d) level of theory.

6) Intrinsic reaction pathway (for transition states) and rigid scan data

6.1) Alanine azlactone pathway

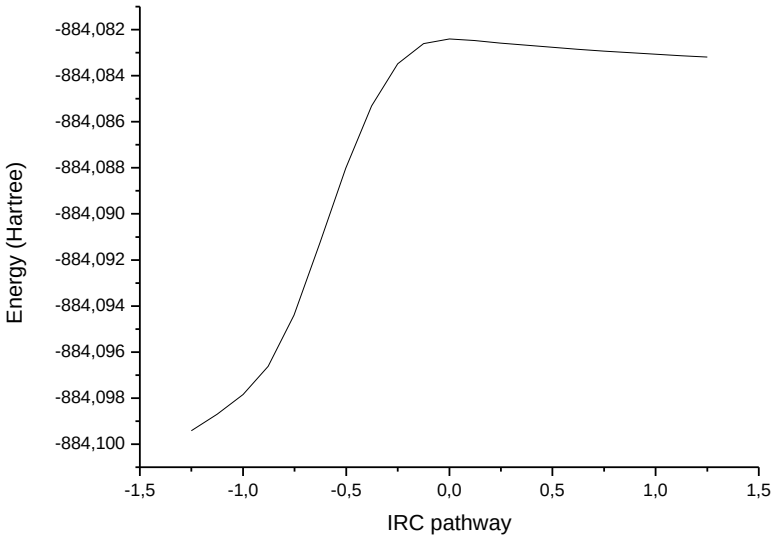


Figure S22. Intrinsic reaction coordinate for $TS_{Keto\text{-}Enolate}$.

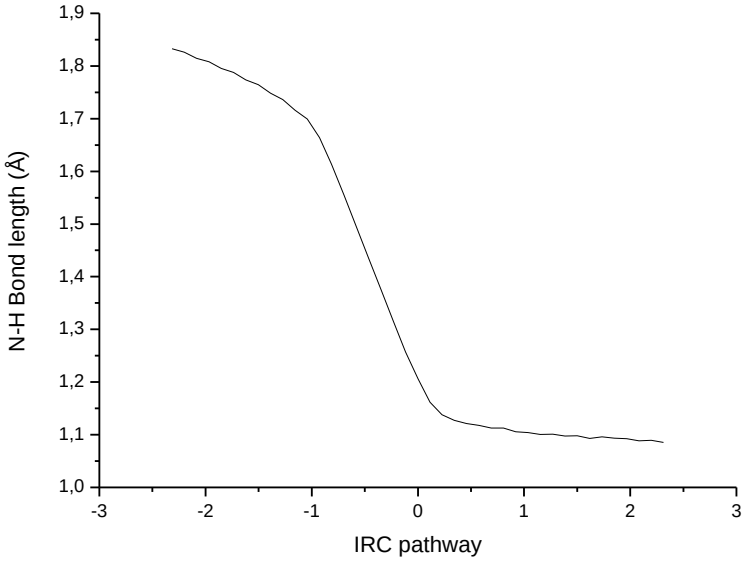


Figure S23. N-H bond length variation during intrinsic reaction coordinate for $TS_{Keto\text{-}Enolate}$.

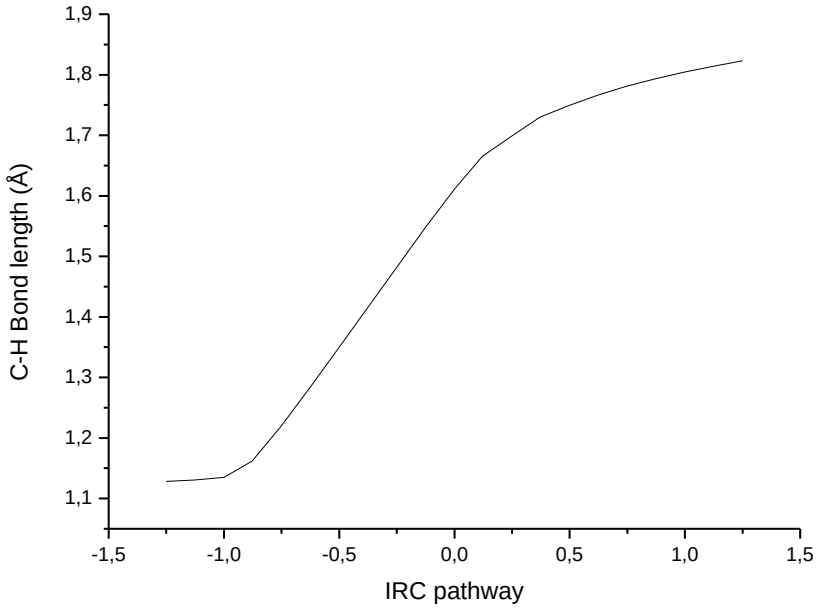


Figure S24. C-H bond length variation during intrinsic reaction coordinate for $TS_{Keto\text{-}Enolate}$.

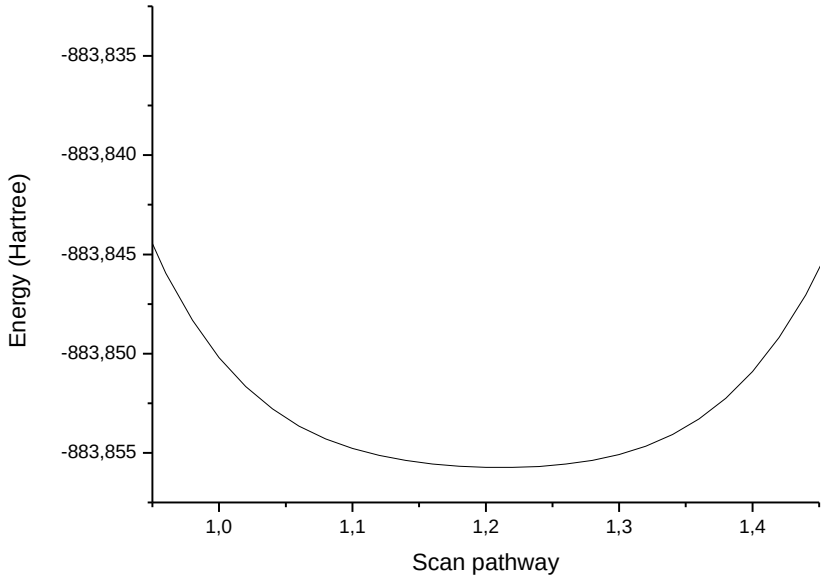


Figure S25. Rigid scan of Enolate$_{\rightarrow}$Enol.

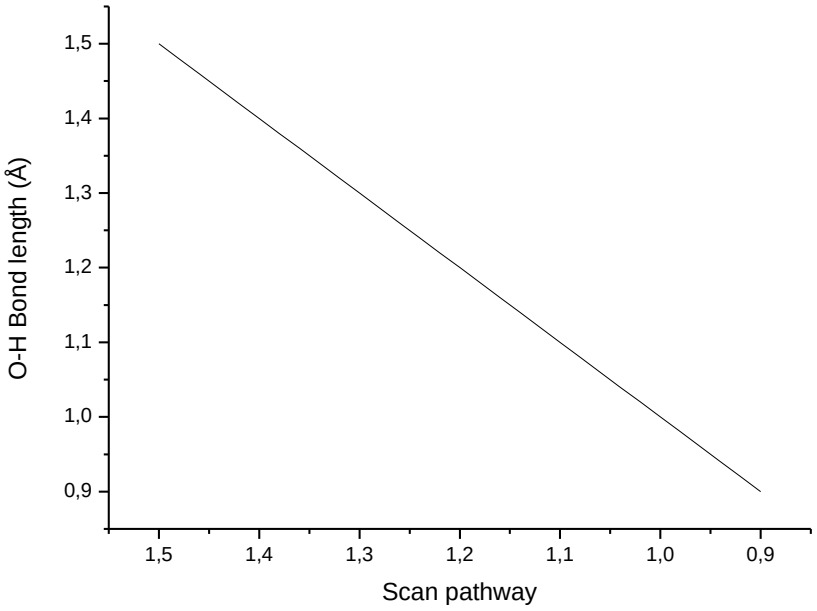


Figure S26. O-H bond length variation during Rigid scan for Enolate$_{\rightarrow}$Enol.

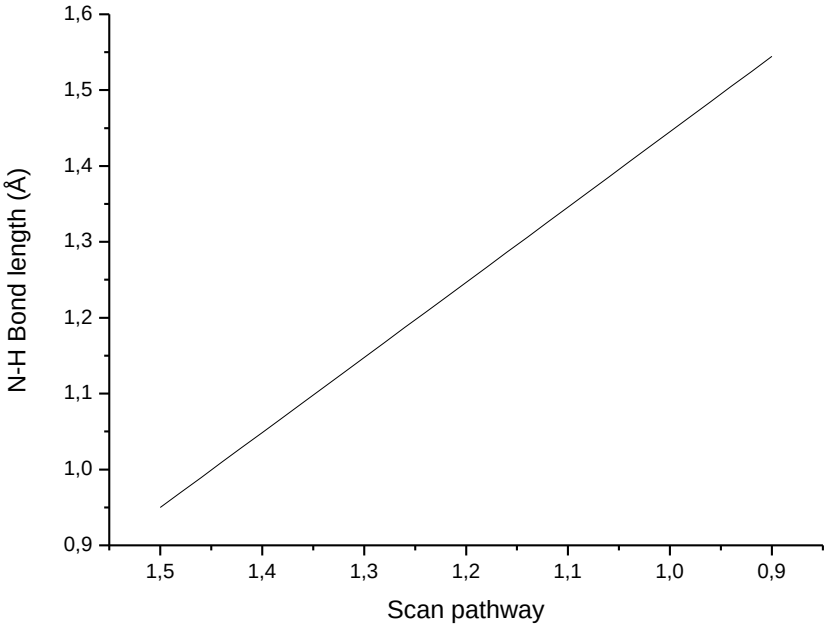


Figure S27. N-H bond length variation during Rigid scan for Enolate$_{\rightarrow}$Enol.

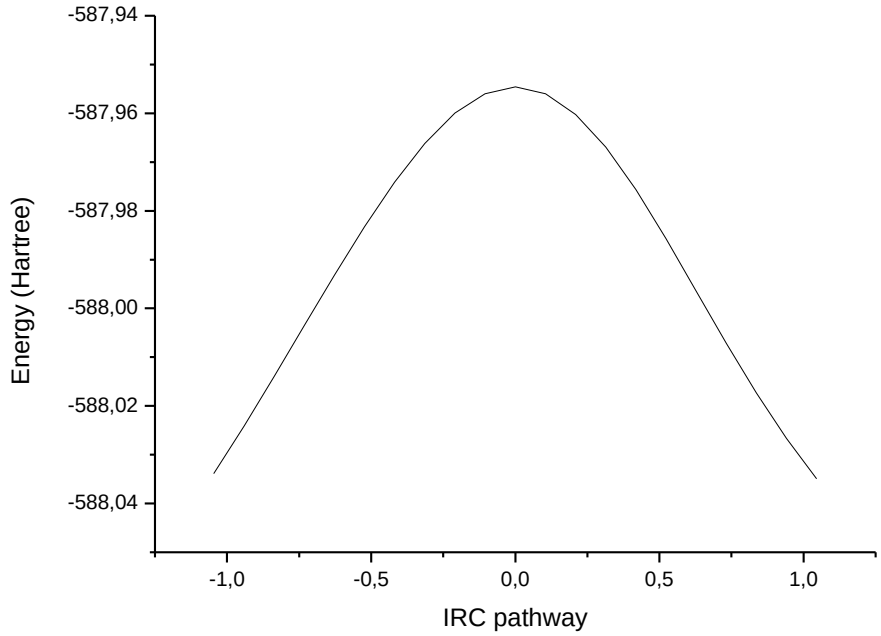


Figure S28. Intrinsic reaction coordinate for $TS_{Keto\text{-}Enol}$.

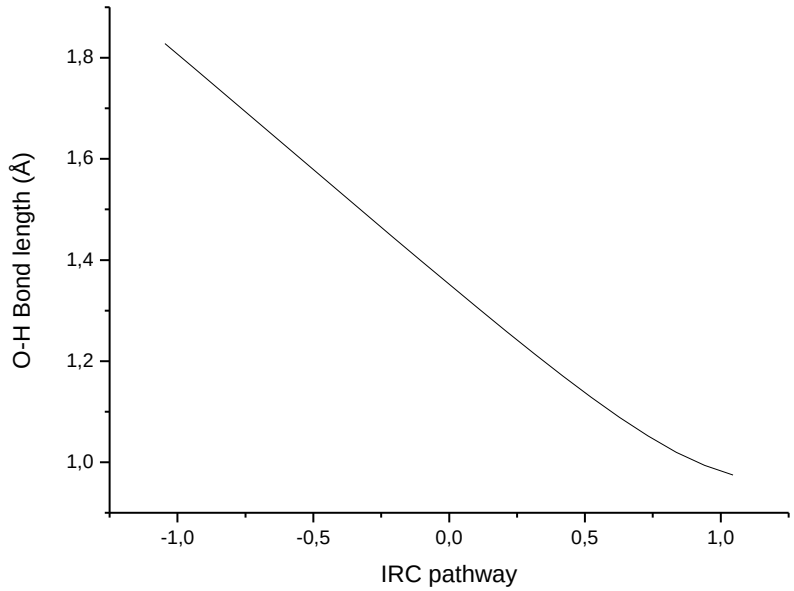


Figure S29. O-H bond length variation during intrinsic reaction coordinate for $TS_{Keto\text{-}Enol}$.

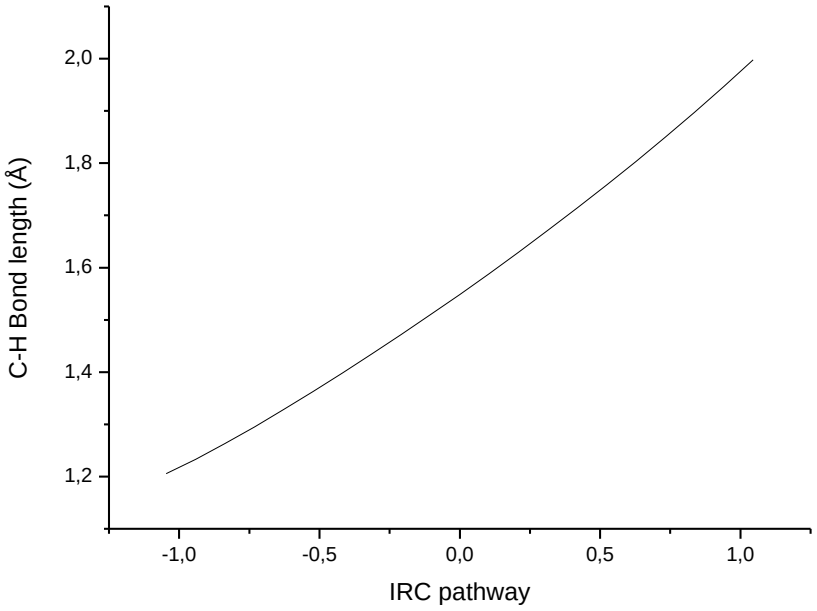


Figure S30. C-H bond length variation during intrinsic reaction coordinate for $TS_{Keto\text{-}Enol}$.

6.2) Valine azlactone pathway

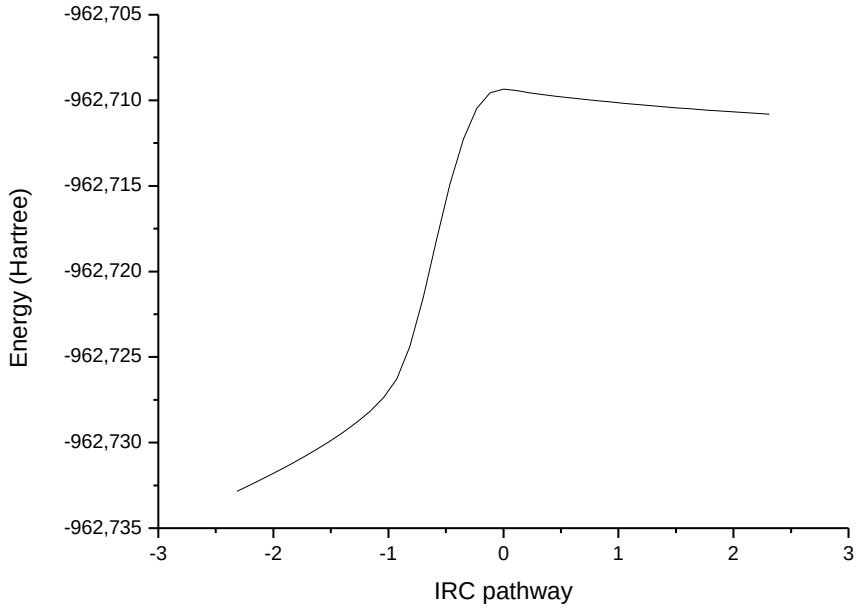


Figure S31. Intrinsic reaction coordinate for $TS_{Keto\text{-}Enolate}$.

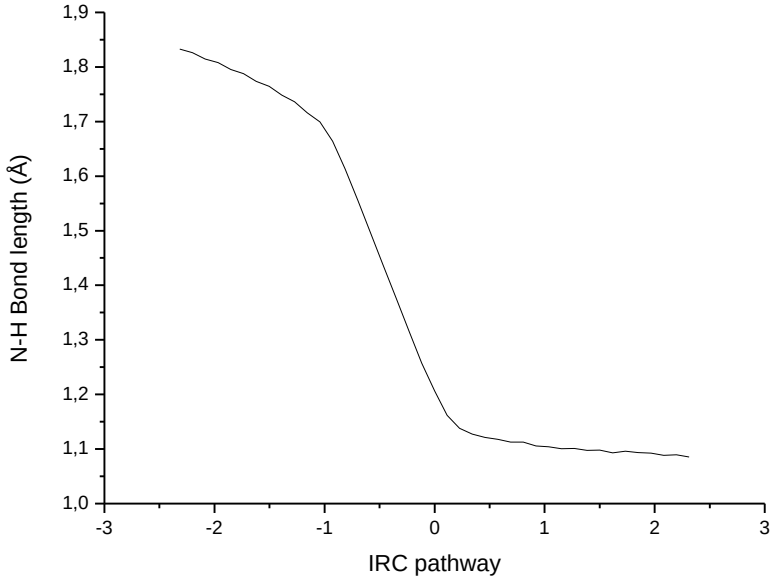


Figure S32. N-H bond length variation during intrinsic reaction coordinate for $TS_{Keto\text{-}Enolate}$.

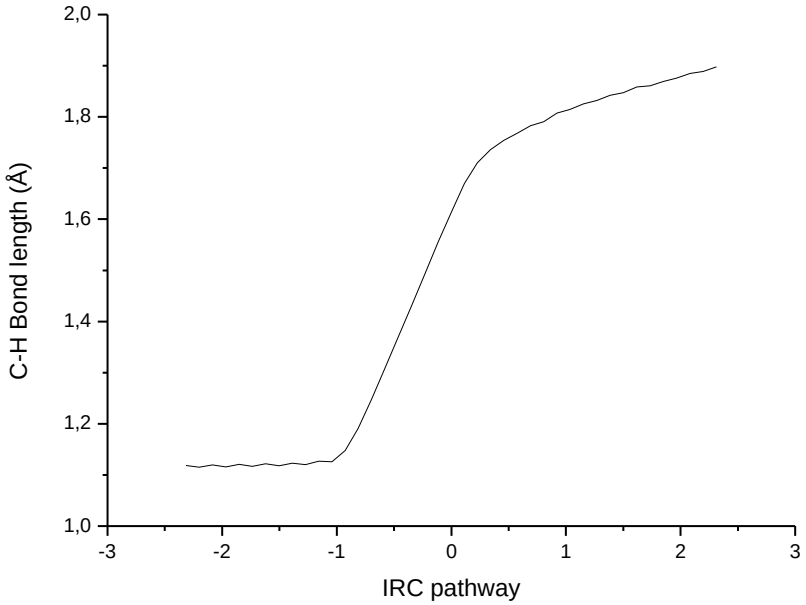


Figure S33. C-H bond length variation during intrinsic reaction coordinate for $TS_{Keto\text{-}Enolate}$.

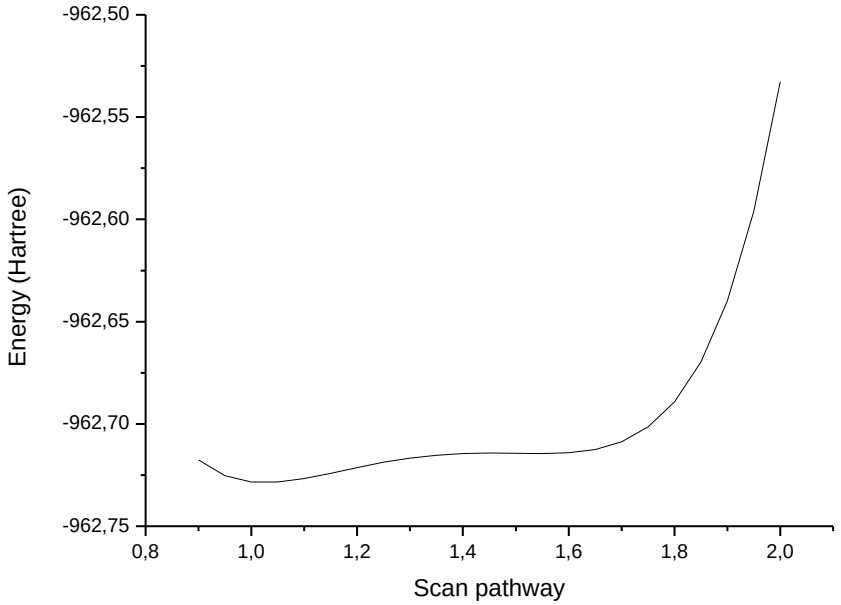


Figure S34. Rigid scan of Enolate$_{\rightarrow}$Enol.

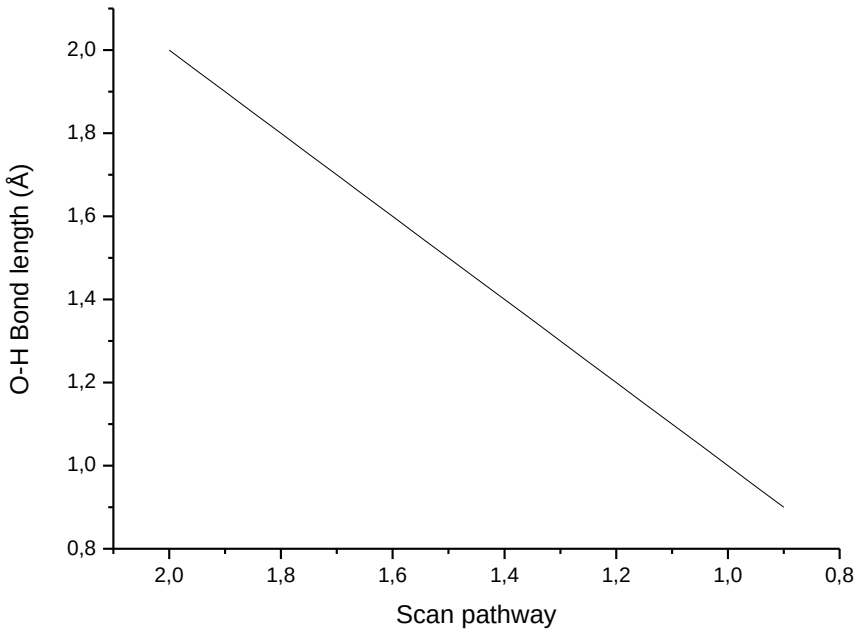


Figure S35. O-H bond length variation during Rigid scan for Enolate$_{\rightarrow}$Enol.

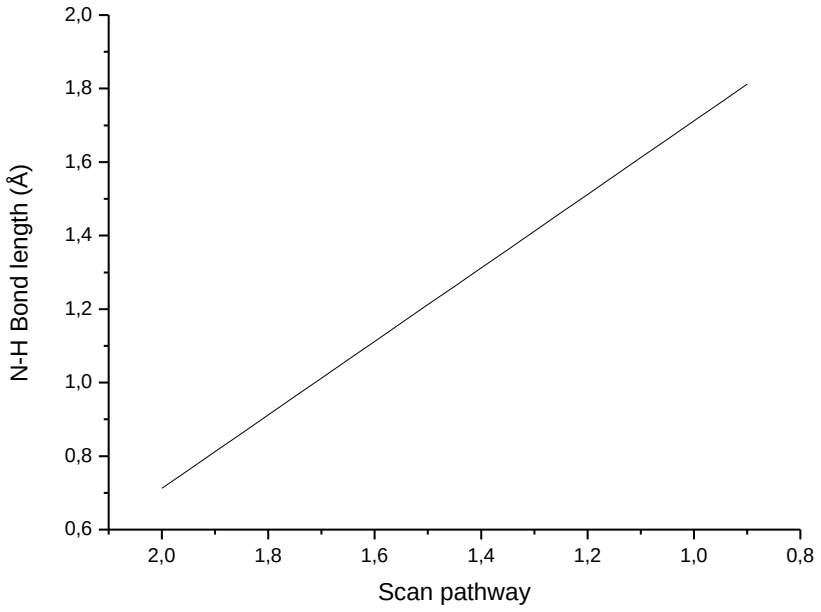


Figure S36. N-H bond length variation during Rigid scan for Enolate$_{\rightarrow}$Enol.

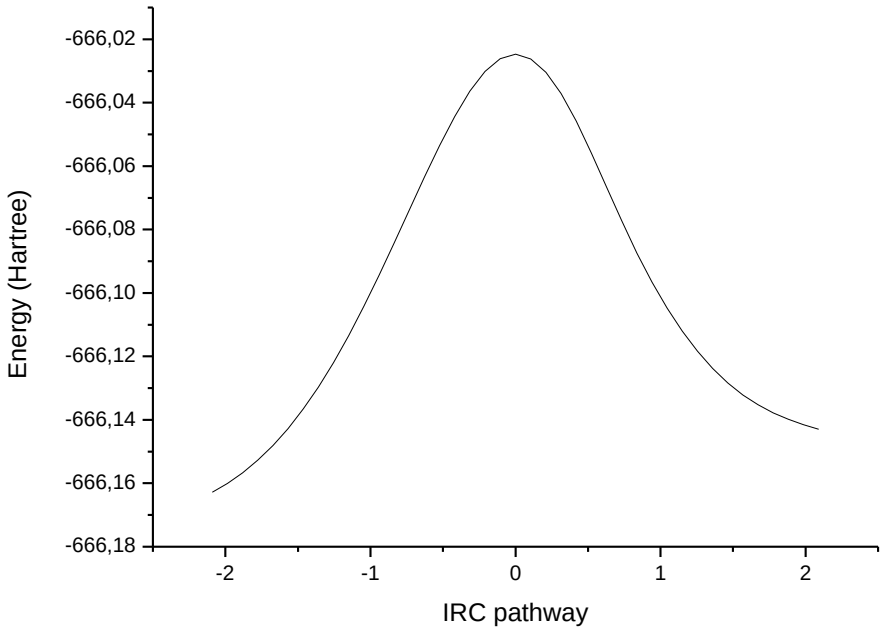


Figure S37. Intrinsic reaction coordinate for $TS_{Keto\text{-}Enol}$.

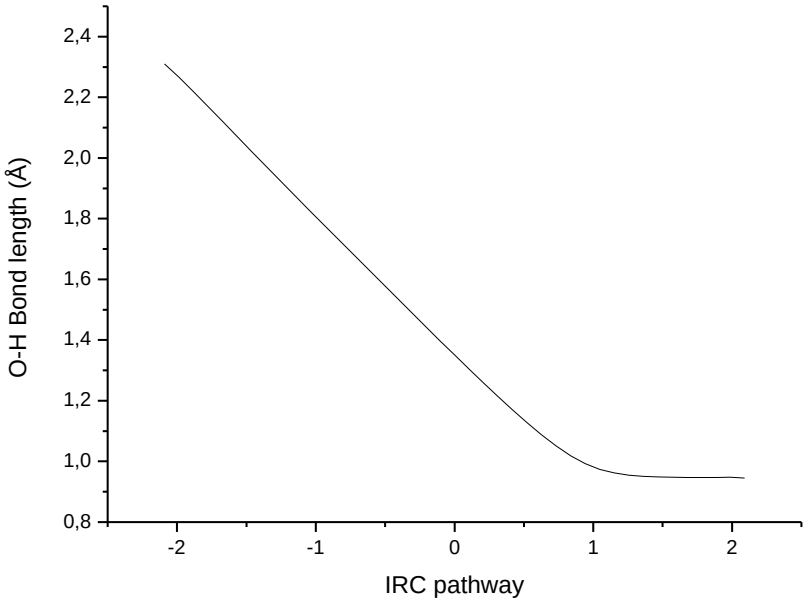


Figure S38. O-H bond length variation during intrinsic reaction coordinate for $TS_{Keto\text{-}Enol}$.

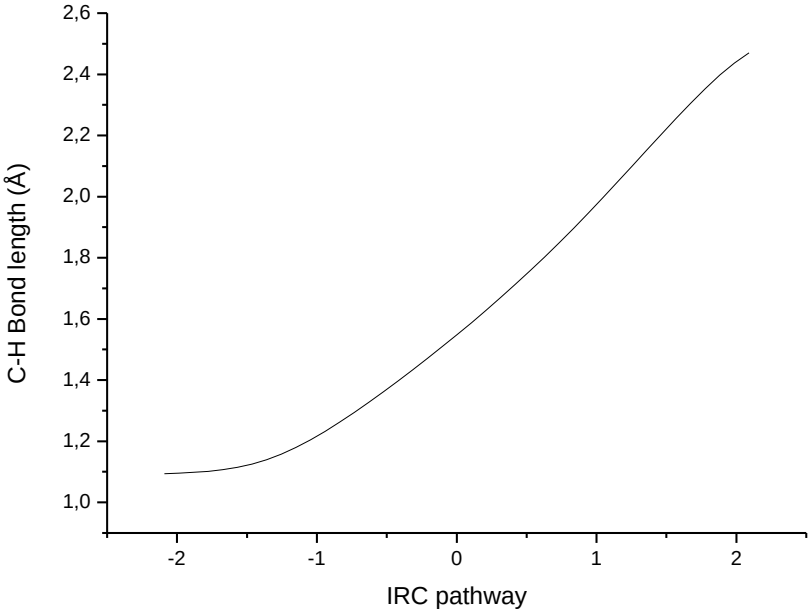


Figure S39. C-H bond length variation during intrinsic reaction coordinate for $TS_{Keto\text{-}Enol}$.

7) Z-matrix

7.1) Alanine pathway

- **Alanine azlactone (keto)**

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	0.00774	-0.17968	1.10242
C	-2.32423	-0.11946	1.1013
H	-2.93759	0.12361	2.00441
O	-0.4188	-1.56036	1.10242
N	-1.07122	0.65259	1.10212
C	-1.85076	-1.58487	1.10241
O	-2.60185	-2.59454	1.10319
C	-3.16638	0.21409	-0.14414
H	-4.13705	-0.22541	-0.04651
H	-3.26311	1.2758	-0.2354
H	-2.6841	-0.17635	-1.01584
C	1.48977	0.23889	1.10282
C	2.48943	-0.73432	1.10309
C	1.83271	1.5909	1.1028
C	3.83172	-0.35551	1.10402
H	2.21873	-1.80014	1.10388
C	3.17536	1.96999	1.10274
H	1.04495	2.35807	1.10241
C	4.17484	0.99707	1.10348
H	4.61972	-1.12255	1.10486

H	3.44546	3.03607	1.10231
H	5.23325	1.29551	1.10416

- **Triethylamine**

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

N	0.15158	-0.00741	0.31654
C	-0.22489	1.12519	-0.5353
H	0.66948	1.74152	-0.66459
H	-0.51576	0.78591	-1.54803
C	-1.33001	2.00377	0.05156
H	-1.07303	2.30658	1.07179
H	-1.44579	2.90498	-0.56065
H	-2.30113	1.49836	0.07511
C	-0.94841	-0.90062	0.69903
H	-0.53984	-1.60915	1.42894
H	-1.69153	-0.30685	1.23987
C	-1.63511	-1.6753	-0.4382
H	-0.93116	-2.31948	-0.97671
H	-2.42349	-2.31651	-0.02695
H	-2.10297	-1.00461	-1.16773
C	1.33986	-0.72291	-0.16187
H	1.42993	-1.6312	0.44477
H	1.21465	-1.0552	-1.20962
C	2.63989	0.07488	-0.03516
H	3.49053	-0.56491	-0.2969

H	2.66954	0.94198	-0.70301
H	2.76691	0.42885	0.99242

- Molecular complex 1

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-1.18782	0.79298	-0.09095
C	0.83014	1.44252	-0.60464
H	1.47666	0.52505	-0.49079
O	-0.64988	1.18218	1.13151
N	-0.43415	0.95615	-1.11265
C	0.61902	1.71657	0.84827
O	1.36403	2.10399	1.71223
C	1.63491	2.39533	-1.46678
H	2.49054	2.76755	-0.89507
H	2.00834	1.87036	-2.35192
H	1.04565	3.25364	-1.80567
C	-2.54331	0.22735	-0.07378
C	-3.26616	0.09981	1.12124
C	-3.12755	-0.19086	-1.28188
C	-4.55397	-0.43695	1.10604
H	-2.81756	0.42442	2.05415
C	-4.41193	-0.72616	-1.28924
H	-2.56163	-0.08429	-2.20159
C	-5.13	-0.85197	-0.09548
H	-5.10723	-0.5296	2.03658

H	-4.85633	-1.04519	-2.22812
H	-6.13318	-1.26974	-0.10399
N	2.41171	-0.79939	0.01201
C	2.47963	-1.69214	-1.15566
H	2.93787	-1.12237	-1.96976
H	3.14644	-2.55292	-0.96676
C	1.11598	-2.2001	-1.63922
H	0.42132	-1.37373	-1.8191
H	1.2527	-2.74421	-2.58042
H	0.65209	-2.89177	-0.92841
C	1.66136	-1.33863	1.16826
H	1.6813	-0.57123	1.94817
H	0.61352	-1.45722	0.87453
C	2.18359	-2.66385	1.73403
H	3.22312	-2.58679	2.06912
H	1.58046	-2.96256	2.59875
H	2.12631	-3.47151	0.99643
C	3.70459	-0.21974	0.43964
H	3.46305	0.59364	1.13259
H	4.29362	-0.96052	1.00687
C	4.59457	0.32387	-0.68093
H	5.44964	0.83931	-0.2299
H	4.99297	-0.47173	-1.31842
H	4.06996	1.04334	-1.31663

- Transition state keto-enolate

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-1.77694	-0.71208	0.12928
C	0.23881	-1.44341	0.62376
H	1.28376	-0.67693	0.37278
O	-1.48581	-1.55633	-0.9393
N	-0.88241	-0.59844	1.03445
C	-0.21529	-2.07351	-0.68668
O	0.32111	-2.85054	-1.42536
C	0.62429	-2.48668	1.67802
H	1.42479	-3.12511	1.29159
H	0.97211	-1.98497	2.58516
H	-0.23167	-3.11798	1.93808
C	-3.08642	-0.05219	0.08669
C	-3.97394	-0.27403	-0.97596
C	-3.4501	0.81194	1.13184
C	-5.21366	0.36399	-0.99019
H	-3.68918	-0.94275	-1.78087
C	-4.68855	1.44481	1.11056
H	-2.75147	0.97202	1.94649
C	-5.57295	1.22259	0.04999
H	-5.89897	0.1895	-1.8149
H	-4.96712	2.11272	1.92093
H	-6.5398	1.71851	0.03599
N	2.24163	0.02569	0.14274
C	2.2371	1.19811	1.02988
H	2.54602	0.85255	2.02145

H	2.99109	1.9463	0.71859
C	0.87151	1.87466	1.16514
H	0.0949	1.14983	1.43249
H	0.91735	2.63449	1.95349
H	0.5641	2.38222	0.24469
C	1.80615	0.30887	-1.23625
H	1.75982	-0.6555	-1.75732
H	0.77632	0.68091	-1.19555
C	2.66277	1.28718	-2.05845
H	3.69319	0.93243	-2.17041
H	2.23867	1.3961	-3.06333
H	2.69735	2.28407	-1.60512
C	3.52467	-0.69169	0.18003
H	3.51929	-1.40455	-0.65282
H	4.3791	-0.01112	0.00433
C	3.76304	-1.46843	1.47757
H	4.68861	-2.04974	1.39544
H	3.86879	-0.8127	2.34792
H	2.93836	-2.162	1.67171

- Alanine azlactone (enolate)

Symbolic Z-matrix:

Charge = -1 Multiplicity = 1

C	0.34009	0.10574	-0.15607
C	2.44815	0.69418	-0.35712
O	1.0101	-1.11163	-0.04274

N	1.05965	1.14677	-0.33228
C	2.3659	-0.81867	-0.15406
O	3.21891	-1.6559	-0.08004
C	3.32458	1.37716	0.69957
H	4.33773	0.96562	0.66435
H	3.36485	2.45286	0.50872
H	2.91561	1.21883	1.70236
C	-1.1213	0.04454	-0.05716
C	-1.78332	-1.1765	0.13528
C	-1.86125	1.23371	-0.15753
C	-3.17424	-1.20442	0.22672
H	-1.20813	-2.0927	0.21199
C	-3.24853	1.19738	-0.06527
H	-1.33238	2.16935	-0.30661
C	-3.90786	-0.02112	0.12697
H	-3.68458	-2.15171	0.37596
H	-3.81872	2.11881	-0.14325
H	-4.99187	-0.04638	0.19851

- Protonated triethylamine

Symbolic Z-matrix:

Charge = 1 Multiplicity = 1

N	0.15867	0.00003	0.35668
C	-0.22121	1.14854	-0.47204
H	0.66696	1.77869	-0.5748
H	-0.49514	0.8307	-1.49638

C	-1.34445	1.99895	0.12187
H	-1.10405	2.27973	1.15239
H	-1.4638	2.91344	-0.46962
H	-2.30941	1.48135	0.12064
C	-0.9348	-0.9156	0.70316
H	-0.52659	-1.63681	1.42075
H	-1.69197	-0.34436	1.24875
C	-1.5975	-1.67043	-0.46133
H	-0.8789	-2.29259	-1.00633
H	-2.38291	-2.33108	-0.07597
H	-2.06454	-0.98778	-1.18022
C	1.36167	-0.68901	-0.12378
H	1.45546	-1.61075	0.46164
H	1.25373	-0.99699	-1.18083
C	2.64996	0.12118	0.039
H	3.51173	-0.5016	-0.22736
H	2.67715	1.0047	-0.60708
H	2.75969	0.45134	1.07644
H	0.41867	0.40846	1.23165

- Molecular complex 2

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-1.19766	0.78822	-0.08287
C	0.74889	1.5568	-0.61499
H	1.77452	0.08576	-0.28735

O	-0.629	1.13744	1.11779
N	-0.44455	1.01898	-1.11744
C	0.64826	1.70127	0.8012
O	1.41677	2.04585	1.70158
C	1.65369	2.38377	-1.48738
H	2.48864	2.77061	-0.89263
H	2.06137	1.82185	-2.34014
H	1.12827	3.25166	-1.91137
C	-2.53879	0.21724	-0.07331
C	-3.26681	0.08498	1.12238
C	-3.13341	-0.19598	-1.28083
C	-4.55538	-0.44687	1.10665
H	-2.81668	0.41027	2.05466
C	-4.41775	-0.72867	-1.2871
H	-2.57234	-0.08101	-2.20297
C	-5.13746	-0.85814	-0.09397
H	-5.10828	-0.53805	2.0384
H	-4.86463	-1.04158	-2.22771
H	-6.14236	-1.27203	-0.10263
N	2.38743	-0.77242	0.01699
C	2.4717	-1.69942	-1.16315
H	2.94857	-1.12802	-1.96109
H	3.13942	-2.52626	-0.89957
C	1.10615	-2.19162	-1.63606
H	0.42171	-1.35275	-1.80247
H	1.23807	-2.72238	-2.58452
H	0.64352	-2.88803	-0.93065

C	1.64043	-1.34183	1.20741
H	1.66672	-0.55386	1.96345
H	0.60018	-1.44737	0.89677
C	2.18654	-2.66176	1.7398
H	3.22419	-2.58802	2.07971
H	1.5831	-2.95355	2.60535
H	2.11811	-3.47144	1.00633
C	3.71472	-0.19184	0.45789
H	3.43969	0.62253	1.13399
H	4.23961	-0.96578	1.02472
C	4.59842	0.32572	-0.6718
H	5.44888	0.8471	-0.22042
H	5.00105	-0.47676	-1.29708
H	4.07247	1.04371	-1.30667

- Alanine azlactone (enol)

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-0.32113	-0.10343	-0.07905
O	-1.15088	0.98672	0.13035
N	-1.03867	-1.1342	-0.31307
C	-3.40309	-1.88877	-0.43849
H	-4.44241	-1.54601	-0.3896
H	-3.23195	-2.3591	-1.41166
H	-3.24685	-2.63854	0.34351
C	1.14565	-0.04559	-0.02659

C	1.81384	1.14659	0.28557
C	1.8856	-1.2073	-0.29743
C	3.20729	1.1744	0.3264
H	1.23971	2.04258	0.49498
C	3.27591	-1.17243	-0.25644
H	1.35285	-2.12177	-0.53646
C	3.94037	0.01781	0.05561
H	3.72044	2.10073	0.56964
H	3.84428	-2.07409	-0.46753
H	5.02639	0.04223	0.08723
C	-2.44536	-0.70748	-0.24964
C	-2.4546	0.63159	-0.04137
O	-3.59579	1.4927	-0.00867
H	-3.9167	1.56533	0.89319

- Molecular complex 3

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-1.99276	0.84681	0.00907
O	-0.61611	0.54605	0.15313
N	-2.20242	2.14433	-0.02032
C	-2.95039	-0.23421	-0.08399
C	-2.55439	-1.58593	-0.02997
C	-4.32174	0.06767	-0.23297
C	-3.50432	-2.60593	-0.12258
H	-1.50373	-1.82653	0.08641

C	-5.26308	-0.9562	-0.32453
H	-4.62063	1.10888	-0.27379
C	-4.86232	-2.29935	-0.27024
H	-3.18397	-3.64287	-0.07861
H	-6.31414	-0.70843	-0.43853
H	-5.59859	-3.09377	-0.34161
C	-0.95914	2.7778	0.10466
C	0.0332	1.823	0.21285
O	1.33344	1.85921	0.34836
N	3.16107	-0.49686	0.18491
C	4.47657	0.17447	-0.14338
H	4.71392	0.79311	0.72782
H	5.2548	-0.59334	-0.22976
C	4.40672	1.05609	-1.39132
H	3.56016	1.74525	-1.31801
H	5.32731	1.64458	-1.46676
H	4.31559	0.47269	-2.31303
C	2.64634	-1.41029	-0.90179
H	1.62888	-1.68376	-0.61544
H	2.55659	-0.79711	-1.8016
C	3.50556	-2.64663	-1.16908
H	3.58973	-3.29037	-0.28702
H	3.04227	-3.23985	-1.96482
H	4.51613	-2.38626	-1.50155
C	3.22942	-1.13183	1.55542
H	4.07177	-1.83466	1.57538
H	3.46364	-0.31103	2.24102

C	1.93026	-1.81202	1.98829
H	2.00117	-2.06859	3.05065
H	1.07004	-1.15092	1.85164
H	1.743	-2.74047	1.43917
C	-0.80503	4.31006	0.11134
H	-0.36016	4.61976	1.03387
H	-0.18018	4.60923	-0.70411
H	-1.76769	4.76579	0.00889
H	1.67592	0.96333	0.38977

- Tautomerism transition state (M06-2X/6-31G(d))

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	0.3125	0.0877	-0.02684
O	0.97098	-1.10783	0.07835
N	1.07694	1.08676	-0.13535
C	-1.15327	0.04957	-0.01041
C	-1.83735	-1.15251	0.12367
C	-1.86107	1.24321	-0.12846
C	-3.22231	-1.1594	0.14133
H	-1.29316	-2.0735	0.21213
C	-3.24176	1.22931	-0.11095
H	-1.32203	2.16572	-0.2323
C	-3.92443	0.02803	0.02433
H	-3.74905	-2.09052	0.24533
H	-3.78645	2.15146	-0.20229

H	-4.99953	0.02008	0.03763
C	2.38816	0.58125	-0.0674
C	2.26487	-0.79544	0.05757
O	3.19705	-1.61925	-0.22433
H	3.10668	-0.4766	-0.94102
C	3.54855	1.4626	0.29874
H	4.46197	0.88516	0.37537
H	3.69069	2.23914	-0.44331
H	3.36479	1.94249	1.25433

7.2) Valine pathway

- **Valine azlactone (keto)**

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	0.34009	0.10574	-0.15607
C	2.44815	0.69418	-0.35712
H	2.87452	0.88615	-1.3518
O	1.0101	-1.11163	-0.04274
N	1.05965	1.14677	-0.33228
C	2.3659	-0.81867	-0.15406
O	3.21891	-1.6559	-0.08004
C	3.32458	1.37716	0.69957
H	2.91561	1.21883	1.70236
C	-1.1213	0.04454	-0.05716
C	-1.78332	-1.1765	0.13528
C	-1.86125	1.23371	-0.15753

C	-3.17424	-1.20442	0.22672
H	-1.20813	-2.0927	0.21199
C	-3.24853	1.19738	-0.06527
H	-1.33238	2.16935	-0.30661
C	-3.90786	-0.02112	0.12697
H	-3.68458	-2.15171	0.37596
H	-3.81872	2.11881	-0.14325
H	-4.99187	-0.04638	0.19851
C	3.38131	2.89245	0.43073
H	2.55962	3.37248	0.91991
H	4.30127	3.28746	0.80826
H	3.32245	3.07023	-0.62275
C	4.75062	0.79791	0.65
H	4.80558	-0.06856	1.27539
H	4.99069	0.52685	-0.35687
H	5.44643	1.53297	0.99704

- Molecular complex 1

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	1.63876	-0.67368	-0.05928
C	-0.33695	-1.51753	-0.53278
H	-1.21703	-0.85207	-0.55525
O	1.24323	-1.23008	1.15534
N	0.82724	-0.7919	-1.039
C	-0.00738	-1.80177	0.92746

O	-0.61879	-2.37507	1.78509
C	-0.64637	-2.79095	-1.32816
H	-1.49105	-3.31632	-0.87196
C	2.95018	-0.01662	-0.06722
C	3.73533	0.04774	1.09275
C	3.42011	0.5529	-1.26148
C	4.97916	0.67686	1.05515
H	3.36912	-0.39341	2.01336
C	4.66198	1.17855	-1.2911
H	2.79947	0.49347	-2.14953
C	5.44424	1.24208	-0.13329
H	5.58505	0.72487	1.95562
H	5.02288	1.6178	-2.21695
H	6.41418	1.73144	-0.15921
N	-3.00764	0.6708	-0.06654
C	-2.82489	1.92819	-0.80556
H	-3.08132	1.72744	-1.85059
H	-3.53024	2.70926	-0.46345
C	-1.3962	2.4741	-0.76371
H	-0.6763	1.71547	-1.08936
H	-1.31311	3.33571	-1.43592
H	-1.10683	2.81565	0.23582
C	-2.74003	0.77395	1.37844
H	-2.78282	-0.24381	1.78406
H	-1.70314	1.10369	1.50674
C	-3.66336	1.68972	2.20025
H	-4.71005	1.37129	2.14125

H	-3.36747	1.66195	3.25528
H	-3.60983	2.73306	1.86998
C	-4.30858	0.04712	-0.35116
H	-4.47849	-0.71654	0.41693
H	-5.1396	0.77142	-0.25912
C	-4.37708	-0.62612	-1.72454
H	-5.35032	-1.11409	-1.85256
H	-4.25993	0.08691	-2.54738
H	-3.59557	-1.38703	-1.82256
C	0.56767	-3.73812	-1.35226
H	0.29316	-4.65784	-1.8252
H	1.36612	-3.28071	-1.89828
H	0.88723	-3.93393	-0.35004
C	-1.00444	-2.42367	-2.78022
H	-1.57561	-3.21555	-3.21793
H	-1.58028	-1.52187	-2.78839
H	-0.10622	-2.2784	-3.34324

- Transition state keto-enolate

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-1.27574	0.83606	-0.06185
C	0.7178	1.51922	-0.57129
H	1.63394	0.22255	-0.29527
O	-0.73497	1.22271	1.14404
N	-0.49974	1.00559	-1.08352

C	0.55179	1.75772	0.84213
O	1.29089	2.14725	1.73699
C	1.56019	2.42162	-1.44325
H	2.40682	2.81087	-0.86743
C	-2.62482	0.2749	-0.05398
C	-3.35256	0.14819	1.14097
C	-3.21409	-0.14241	-1.26125
C	-4.63991	-0.38727	1.12568
H	-2.90317	0.4756	2.07268
C	-4.49802	-0.67682	-1.26804
H	-2.64942	-0.0329	-2.18174
C	-5.2178	-0.80362	-0.07492
H	-5.19387	-0.47794	2.05662
H	-4.94324	-0.99417	-2.20772
H	-6.22139	-1.22064	-0.08362
N	2.30083	-0.71582	0.02378
C	2.38727	-1.6402	-1.14955
H	2.85291	-1.06799	-1.95429
H	3.06389	-2.46642	-0.89914
C	1.02694	-2.15115	-1.62033
H	0.3341	-1.32184	-1.79602
H	1.16495	-2.69176	-2.56257
H	0.56983	-2.84486	-0.9083
C	1.56023	-1.288	1.20674
H	1.58411	-0.50873	1.97191
H	0.51844	-1.39815	0.9011
C	2.10149	-2.60927	1.74795

H	3.13789	-2.53452	2.09155
H	1.49438	-2.90114	2.6112
H	2.03848	-3.41946	1.0145
C	3.62638	-0.15135	0.46351
H	3.36936	0.65896	1.15133
H	4.15998	-0.9274	1.02241
C	4.51215	0.37532	-0.66168
H	5.36592	0.89014	-0.20883
H	4.91015	-0.42356	-1.29458
H	3.98745	1.09834	-1.29188
C	0.75669	3.6325	-1.95293
H	1.42109	4.3325	-2.41496
H	0.03137	3.30396	-2.66768
H	0.25935	4.10236	-1.13026
C	2.10508	1.69507	-2.68696
H	2.90542	2.26489	-3.11083
H	2.46593	0.72788	-2.40549
H	1.32249	1.58763	-3.4087

- Valine azlactone (enolate)

Symbolic Z-matrix:

Charge = -1 Multiplicity = 1

C	0.3275	0.04922	-0.00005
C	2.39418	0.61887	-0.00005
O	1.01308	-1.14441	0.00002
N	1.12217	1.10324	-0.00003

C	2.39986	-0.80311	0.00001
O	3.26943	-1.67797	-0.00006
C	3.61787	1.47642	0.00012
H	3.67887	2.13374	-0.88232
C	-1.1068	0.03827	-0.00004
C	-1.84501	-1.17165	0.00001
C	-1.84149	1.25206	-0.00008
C	-3.2364	-1.16044	0.00006
H	-1.3014	-2.11123	-0.00001
C	-3.22926	1.24813	-0.00002
H	-1.28516	2.18463	-0.00015
C	-3.9495	0.04376	0.00006
H	-3.77464	-2.10786	0.00011
H	-3.76394	2.19761	-0.00004
H	-5.03736	0.04653	0.00011
C	3.70346	2.39397	1.23396
H	4.69344	2.79189	1.31454
H	3.00368	3.1968	1.13065
H	3.47273	1.83074	2.11398
C	4.86231	0.56925	-0.0005
H	4.85708	-0.04399	0.87632
H	4.84973	-0.0529	-0.87095
H	5.74477	1.17433	-0.0073

- Molecular complex 2

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C

C 1 B1

H 2 B2 1 A1

O 1 B3 2 A2 3 D1 0

N 1 B4 4 A3 2 D2 0

C 2 B5 1 A4 5 D3 0

O 6 B6 2 A5 1 D4 0

C 2 B7 1 A6 5 D5 0

H 8 B8 2 A7 1 D6 0

C 1 B9 5 A8 2 D7 0

C 10 B10 1 A9 5 D8 0

C 10 B11 1 A10 5 D9 0

C 11 B12 10 A11 1 D10 0

H 11 B13 10 A12 1 D11 0

C 12 B14 10 A13 1 D12 0

H 12 B15 10 A14 1 D13 0

C 13 B16 11 A15 10 D14 0

H 13 B17 11 A16 10 D15 0

H 15 B18 12 A17 10 D16 0

H 17 B19 13 A18 11 D17 0

N 2 B20 1 A19 5 D18 0

C 21 B21 2 A20 1 D19 0

H 22 B22 21 A21 2 D20 0

H 22 B23 21 A22 2 D21 0

C 22 B24 21 A23 2 D22 0

H 25 B25 22 A24 21 D23 0

H 25 B26 22 A25 21 D24 0

H 25 B27 22 A26 21 D25 0

C 21 B28 2 A27 1 D26 0

H 29 B29 21 A28 2 D27 0

H 29 B30 21 A29 2 D28 0

C 29 B31 21 A30 2 D29 0

H 32 B32 29 A31 21 D30 0

H 32 B33 29 A32 21 D31 0

H 32 B34 29 A33 21 D32 0

C 21 B35 2 A34 1 D33 0

H 36 B36 21 A35 2 D34 0

H 36 B37 21 A36 2 D35 0

C 36 B38 21 A37 2 D36 0

H 39 B39 36 A38 21 D37 0

H 39 B40 36 A39 21 D38 0

H 39 B41 36 A40 21 D39 0

C 8 B42 2 A41 1 D40 0

H 43 B43 8 A42 2 D41 0

H 43 B44 8 A43 2 D42 0

H 43 B45 8 A44 2 D43 0

C 8 B46 2 A45 1 D44 0

H 47 B47 8 A46 2 D45 0

H 47 B48 8 A47 2 D46 0

H 47 B49 8 A48 2 D47 0

Variables:

B1 2.16251

B2 1.89803

B3	1.37403
B4	1.30057
B5	1.42685
B6	1.23435
B7	1.51464
B8	1.10004
B9	1.45697
B10	1.40657
B11	1.40816
B12	1.39396
B13	1.08519
B14	1.39044
B15	1.08552
B16	1.39634
B17	1.08731
B18	1.08739
B19	1.0868
B20	2.97737
B21	1.50351
B22	1.0909
B23	1.09452
B24	1.52682
B25	1.0953
B26	1.09477
B27	1.09395
B28	1.51761
B29	1.09179

B30	1.09038
B31	1.52422
B32	1.09428
B33	1.09472
B34	1.09456
B35	1.51619
B36	1.09324
B37	1.09345
B38	1.5244
B39	1.09484
B40	1.09417
B41	1.09332
B42	1.54362
B43	1.09822
B44	1.09633
B45	1.0951
B46	1.53714
B47	1.09661
B48	1.09842
B49	1.09486
A1	98.02292
A2	75.60248
A3	114.07555
A4	74.10943
A5	135.26757
A6	150.81041
A7	107.33611

A8	127.56424
A9	121.23201
A10	119.92061
A11	120.33526
A12	119.17684
A13	120.44213
A14	118.60755
A15	120.50719
A16	119.48836
A17	119.575
A18	120.30789
A19	96.86135
A20	111.42194
A21	105.9892
A22	107.99306
A23	112.93762
A24	111.12505
A25	108.53779
A26	112.5796
A27	100.219
A28	105.1472
A29	106.38334
A30	114.97378
A31	112.95237
A32	107.91619
A33	112.65298
A34	104.92178

A35	104.1309
A36	107.3653
A37	114.87855
A38	107.74954
A39	113.01451
A40	111.90663
A41	110.80638
A42	111.517
A43	110.25152
A44	110.54222
A45	112.40163
A46	111.17493
A47	112.11224
A48	110.11139
D1	78.92766
D2	-0.53484
D3	176.94374
D4	173.9334
D5	43.92139
D6	162.50054
D7	-178.93449
D8	-175.20327
D9	3.95667
D10	179.02235
D11	-0.36756
D12	-179.23998
D13	0.23625

D14	0.27451
D15	-179.59548
D16	179.89697
D17	179.98173
D18	-104.34746
D19	92.13239
D20	62.97529
D21	178.33725
D22	-56.96664
D23	50.68099
D24	169.67435
D25	-71.41213
D26	-28.98701
D27	-60.34981
D28	52.97135
D29	176.18188
D30	60.08369
D31	178.36527
D32	-63.35426
D33	-143.43338
D34	45.95807
D35	162.01622
D36	-74.79378
D37	171.84119
D38	-69.64039
D39	53.96134
D40	46.1826

D41	178.34303
D42	-61.41624
D43	57.95319
D44	-77.51185
D45	177.33346
D46	-62.08422
D47	57.30688

- Valine azlactone (enol)

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	0.29782	0.11097	-0.00964
O	0.9994	-1.0822	-0.00733
N	1.07693	1.15056	-0.01007
C	3.584	1.54753	0.00917
H	3.63997	2.15017	-0.90549
C	-1.15753	0.05423	-0.00411
C	-1.84659	-1.16943	-0.00509
C	-1.88786	1.25547	0.00131
C	-3.2399	-1.18805	0.0002
H	-1.28857	-2.1002	-0.01084
C	-3.27863	1.22759	0.006
H	-1.34697	2.19616	0.00168
C	-3.9613	0.00731	0.00572
H	-3.76335	-2.14041	-0.00067
H	-3.83391	2.16171	0.01012

H	-5.0477	-0.01079	0.00946
C	2.38128	0.66317	0.00203
C	2.30685	-0.69583	0.00256
O	3.25226	-1.65322	-0.02291
H	2.84582	-2.50083	0.22021
C	3.54235	2.52391	1.19935
H	4.50644	2.96959	1.32897
H	2.81871	3.28858	1.00822
H	3.27296	1.99197	2.08781
C	4.873	0.71124	0.11259
H	4.84119	0.11523	1.00066
H	4.95373	0.07312	-0.74251
H	5.7197	1.3643	0.15148

- Molecular complex 3

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-1.75257	0.908	0.10919
O	-0.48226	0.50315	0.46517
N	-1.84105	2.19208	-0.07668
C	-2.79267	-0.10261	-0.02432
C	-2.54923	-1.45686	0.25913
C	-4.07654	0.28741	-0.44622
C	-3.5671	-2.39841	0.11864
H	-1.56425	-1.76471	0.59537
C	-5.08729	-0.65837	-0.58261

H	-4.25771	1.33538	-0.66167
C	-4.83893	-2.00588	-0.30272
H	-3.3659	-3.44303	0.34212
H	-6.07494	-0.34409	-0.90997
H	-5.63077	-2.74215	-0.41096
C	-0.56861	2.70297	0.14969
C	0.25619	1.66455	0.48004
O	1.53406	1.60484	0.8304
N	2.9045	-0.58478	0.08024
C	4.11843	0.0069	-0.5283
H	4.59142	0.60833	0.25646
H	4.84424	-0.77709	-0.80021
C	3.83685	0.90665	-1.73149
H	3.09185	1.66801	-1.47942
H	4.76025	1.41763	-2.0247
H	3.48355	0.34761	-2.60378
C	2.12322	-1.43787	-0.84655
H	1.18873	-1.69269	-0.34033
H	1.83593	-0.81292	-1.69707
C	2.80954	-2.71366	-1.35195
H	3.07043	-3.39428	-0.53425
H	2.1288	-3.25002	-2.02222
H	3.72348	-2.49773	-1.91573
C	3.25198	-1.24743	1.35888
H	3.97103	-2.06708	1.19427
H	3.77292	-0.4939	1.96085
C	2.04529	-1.75816	2.14556

H	2.37187	-2.07431	3.14207
H	1.29377	-0.9716	2.26604
H	1.56821	-2.62149	1.67024
C	-0.2388	4.15478	0.03436
H	-0.50186	4.54399	-0.95676
H	1.97847	0.73196	0.52295
C	-1.00961	4.99239	1.0716
H	-0.57369	5.96732	1.13779
H	-2.03284	5.07887	0.7709
H	-0.95785	4.51294	2.02677
C	1.26746	4.38083	0.26173
H	1.52608	4.086	1.25727
H	1.82567	3.79657	-0.43965
H	1.49717	5.41697	0.12556

- Tautomerism transition state (M06-2X/6-31G(d))

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	0.26762	0.229	-0.08264
O	-0.15312	1.52205	0.07447
N	-0.66996	-0.59794	-0.25726
C	1.71305	-0.0152	-0.03923
C	2.6094	1.02547	0.17177
C	2.18422	-1.31461	-0.21006
C	3.96943	0.76644	0.21354
H	2.24801	2.02792	0.30084

C	3.54136	-1.56603	-0.1682
H	1.48286	-2.11068	-0.3735
C	4.43605	-0.52589	0.04407
H	4.66049	1.57326	0.37711
H	3.90307	-2.56956	-0.30045
H	5.49229	-0.72439	0.07617
C	-1.86451	0.14454	-0.18475
C	-1.48177	1.46433	0.01367
O	-2.2304	2.46456	-0.2434
H	-2.34931	1.35991	-1.01134
C	-3.19061	-0.51581	0.12259
H	-3.9358	0.27248	0.1806
C	-3.13728	-1.2235	1.48313
H	-4.0974	-1.67529	1.71346
H	-2.38692	-2.00643	1.48008
H	-2.89573	-0.52509	2.27763
C	-3.59314	-1.48904	-0.99057
H	-4.54036	-1.96427	-0.75586
H	-3.70046	-0.97769	-1.94207
H	-2.84584	-2.2658	-1.11034

7.3) 2-alcoxy azlactone pathway

- **2-alcoxy azlactone (keto)**

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-0.4033	-0.91081	0.13168

C	1.63668	-1.53666	0.42258
O	0.03454	-1.12083	-1.14384
N	0.41532	-1.15265	1.08442
C	1.38454	-1.6366	-0.98734
O	2.04874	-1.90059	-1.97722
C	2.55767	-2.50751	1.12429
H	3.34392	-2.83445	0.43484
H	3.0343	-2.07194	2.01314
H	2.02185	-3.40587	1.46289
O	-1.63431	-0.38526	0.27816
C	-2.61856	-0.79108	-0.70183
H	-2.65641	-1.8881	-0.7235
H	-2.31865	-0.44527	-1.6956
C	-3.94832	-0.20938	-0.29967
C	-4.5384	-0.57777	0.91722
C	-4.61621	0.69459	-1.1306
C	-5.7727	-0.05229	1.29262
H	-4.01737	-1.27096	1.57252
C	-5.85776	1.21778	-0.76072
H	-4.16329	0.98946	-2.07451
C	-6.43732	0.84571	0.45175
H	-6.21982	-0.34436	2.23918
H	-6.36766	1.91716	-1.41808
H	-7.40249	1.25211	0.74258
H	2.21132	-0.6357	0.47691

- **Molecular complex 1**

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-0.76542	0.82116	-0.35911
C	1.29363	1.42803	-0.74149
O	-0.50845	1.64534	0.73057
N	0.15128	0.6466	-1.22072
C	0.81085	2.08535	0.54645
O	1.34664	2.82497	1.32132
C	1.78998	2.45605	-1.76453
H	2.14336	1.93855	-2.66083
H	0.98582	3.13894	-2.05791
H	2.61231	3.0405	-1.34064
O	-1.96969	0.26304	-0.39458
C	-2.96353	0.68942	0.5743
H	-3.08615	1.77537	0.48875
H	-2.60677	0.46856	1.58434
C	-4.25002	-0.03638	0.28007
C	-4.94931	-0.66824	1.31271
C	-4.7821	-0.05324	-1.01595
C	-6.16933	-1.29937	1.06095
H	-4.53859	-0.66744	2.31985
C	-5.99386	-0.69252	-1.27047
H	-4.23543	0.42246	-1.8252
C	-6.69282	-1.31356	-0.23161
H	-6.70335	-1.78583	1.87267
H	-6.39507	-0.70548	-2.28027

H	-7.6391	-1.809	-0.43146
H	2.12494	0.75181	-0.4783
N	3.703	-0.90711	0.19214
C	4.87166	-0.97095	-0.69654
H	5.48835	-0.09244	-0.48227
H	5.50595	-1.84982	-0.47286
C	4.52473	-0.96118	-2.18602
H	3.88405	-0.10754	-2.43235
H	5.44332	-0.8816	-2.77822
H	4.00993	-1.87364	-2.50363
C	2.76687	-2.03384	0.03645
H	1.90735	-1.82252	0.68442
H	2.37788	-2.01282	-0.9868
C	3.30122	-3.4412	0.35356
H	3.66327	-3.51732	1.38495
H	2.4998	-4.17833	0.22722
H	4.12174	-3.73045	-0.3125
C	4.09506	-0.68909	1.59418
H	3.22392	-0.92667	2.21649
H	4.89673	-1.385	1.90518
C	4.52535	0.74921	1.89684
H	4.77437	0.84352	2.96037
H	5.41388	1.04734	1.32994
H	3.72169	1.45763	1.67191

- **2-alcoxy azlactone (enolate)**

Symbolic Z-matrix:

Charge = -1 Multiplicity = 1

C	0.34009	0.10574	-0.15607
C	2.44815	0.69418	-0.35712
O	1.0101	-1.11163	-0.04274
N	1.05965	1.14677	-0.33228
C	2.3659	-0.81867	-0.15406
O	3.21891	-1.6559	-0.08004
C	3.89449	1.18732	-0.48392
H	4.38182	0.69539	-1.33104
H	3.90484	2.26934	-0.63983
H	4.46061	0.96347	0.42565
O	-1.0854	0.04605	-0.05959
C	-1.66803	0.67184	-1.20582
H	-1.50385	1.72807	-1.15758
H	-1.21662	0.2809	-2.09368
C	-3.18147	0.38824	-1.23178
C	-4.04349	1.12646	-0.42035
C	-3.69049	-0.60654	-2.06656
C	-5.41412	0.86944	-0.44326
H	-3.64179	1.91014	0.23824
C	-5.06162	-0.8631	-2.09033
H	-3.01124	-1.18835	-2.7063
C	-5.92344	-0.12542	-1.27876
H	-6.09356	1.45084	0.19676
H	-5.46272	-1.64722	-2.74892
H	-7.00418	-0.32785	-1.2967

- **2-alcoxy azlactone (enol)**

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	0.29782	0.11097	-0.00964
O	0.9994	-1.0822	-0.00733
N	1.07693	1.15056	-0.01007
C	3.584	1.54753	0.00917
H	4.49969	0.95344	0.08264
H	3.63997	2.15017	-0.90549
H	3.55435	2.24255	0.85638
C	2.38128	0.66317	0.00203
C	2.30685	-0.69583	0.00256
O	3.25226	-1.65322	-0.02291
H	2.84582	-2.50083	0.22021
O	-1.13109	0.05526	-0.00421
C	-1.65038	1.03369	-0.90859
H	-1.45756	2.01321	-0.52355
H	-1.17643	0.92547	-1.86177
C	-3.16928	0.83336	-1.06485
C	-4.04224	1.33788	-0.10056
C	-3.6723	0.14764	-2.17044
C	-5.41785	1.1561	-0.24155
H	-3.64531	1.87777	0.77134
C	-5.04836	-0.03342	-2.31212
H	-2.98442	-0.24991	-2.93064

C	-5.92114	0.47054	-1.34786
H	-6.10594	1.5532	0.5188
H	-5.4447	-0.57376	-3.18414
H	-7.0058	0.32738	-1.45884

- **Molecular complex 3**

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	-1.75257	0.908	0.10919
O	-0.48226	0.50315	0.46517
N	-1.84105	2.19208	-0.07668
C	-0.56861	2.70297	0.14969
C	0.25619	1.66455	0.48004
O	1.53406	1.60484	0.8304
N	2.9045	-0.58478	0.08024
C	4.11843	0.0069	-0.5283
H	4.59142	0.60833	0.25646
H	4.84424	-0.77709	-0.80021
C	3.83685	0.90665	-1.73149
H	3.09185	1.66801	-1.47942
H	4.76025	1.41763	-2.0247
H	3.48355	0.34761	-2.60378
C	2.12322	-1.43787	-0.84655
H	1.18873	-1.69269	-0.34033
H	1.83593	-0.81292	-1.69707
C	2.80954	-2.71366	-1.35195

H	3.07043	-3.39428	-0.53425
H	2.1288	-3.25002	-2.02222
H	3.72348	-2.49773	-1.91573
C	3.25198	-1.24743	1.35888
H	3.97103	-2.06708	1.19427
H	3.77292	-0.4939	1.96085
C	2.04529	-1.75816	2.14556
H	2.37187	-2.07431	3.14207
H	1.29377	-0.9716	2.26604
H	1.56821	-2.62149	1.67024
C	-0.2388	4.15478	0.03436
H	-0.78802	4.75159	0.77341
H	0.83139	4.31539	0.1959
H	-0.50186	4.54399	-0.95676
H	1.97847	0.73196	0.52295
O	-2.77384	-0.08432	-0.0219
C	-3.92638	0.31539	0.72428
H	-4.38173	1.16054	0.25176
H	-3.6336	0.57794	1.71939
C	-4.9336	-0.84842	0.77573
C	-5.77013	-1.09557	-0.31313
C	-5.00953	-1.6555	1.91081
C	-6.68281	-2.14917	-0.26657
H	-5.71056	-0.45862	-1.20755
C	-5.92175	-2.71007	1.95715
H	-4.35017	-1.46096	2.76902
C	-6.75843	-2.95693	0.86878

H	-7.34263	-2.34365	-1.12453
H	-5.9811	-3.34651	2.85208
H	-7.47808	-3.78763	0.90524

- **Tautomerism transition state (M06-2X/6-31G(d))**

Symbolic Z-matrix:

Charge = 0 Multiplicity = 1

C	1.28939	0.1063	-0.06514
O	2.01454	1.10827	-0.59111
N	1.94415	-0.83988	0.45486
C	3.29489	-0.48673	0.24238
C	3.29695	0.73022	-0.40655
O	4.28533	1.54154	-0.47934
H	4.06496	0.83034	0.65321
C	4.39736	-1.49465	0.36792
H	5.35302	-1.05499	0.10999
H	4.45245	-1.88407	1.37772
H	4.21008	-2.32814	-0.30104
O	0.00508	0.27773	-0.16548
C	-0.82189	-0.75065	0.39443
H	-0.58935	-1.68412	-0.09664
H	-0.57301	-0.84712	1.44206
C	-2.25949	-0.35892	0.19288
C	-2.80159	0.70616	0.9048
C	-3.06295	-1.05555	-0.69573
C	-4.12365	1.06767	0.72681

H	-2.18443	1.25457	1.59472
C	-4.39228	-0.69911	-0.87243
H	-2.65413	-1.87936	-1.2543
C	-4.92291	0.36267	-0.16275
H	-4.53268	1.89372	1.28026
H	-5.00615	-1.24824	-1.5635
H	-5.95235	0.64184	-0.29884

8) Total energy for all calculations

- Alanine azlactone - B3LYP-D3/6-31++G(d,p)//B3LYP/6-31G(d)

Gas phase - Hartree			
	Eletronic energy	Enthalpy	Gibbs Free Energy
Triethylamine	-292.4609083	-292.2435125	-292.2881285
4-Methyl-2-phenyl-oxazol-5(4H)-one	-591.748019	-591.563886	-591.612531
Molecular complex 1	-884.2209618	-883.8170699	-883.8956549
Transition state keto-enolate	-884.1984839	-883.7982313	-883.8701433
Molecular complex 2	-884.2014694	-883.79645	-883.869632
Triethylammonium	-292.8506674	-292.6176182	-292.6621312
4-Methyl-2-phenyl-oxazol-5-olate	-591.1999594	-591.0303325	-591.0790145
Molecular complex 3	-884.219072	-883.815569	-883.891674
4-Methyl-2-phenyl-oxazol-5-ol	-591.727649	-591.5440288	-591.5946478
Transition state keto-enol	-591.621805	-591.4457466	-591.4916526

Table S10. Total energy calculations for alanine azlactone in gas phase.

Dichloromethane - Hartree			
	Eletronic energy	Enthalpy	Gibbs Free Energy
Triethylamine	-292.4626694	-292.2452736	-292.2898896
4-Methyl-2-phenyl-oxazol-5(4H)-one	-591.7557138	-591.5715808	-591.6202258
Molecular complex 1	-884.2284573	-883.8245654	-883.9031504
Transition state keto-enolate	-884.2156956	-883.815443	-883.887355
Molecular complex 2	-884.2227625	-883.8177431	-883.8909251
Triethylammonium	-292.9206598	-292.6876106	-292.7321236
4-Methyl-2-phenyl-oxazol-5-olate	-591.2705516	-591.1009247	-591.1496067
Molecular complex 3	-884.2271491	-883.8236461	-883.8997511
4-Methyl-2-phenyl-oxazol-5-ol	-591.7348399	-591.5512197	-591.6018387
Transition state keto-enol	-591.6299927	-591.4539343	-591.4998403

Table S11. Total energy calculations for alanine azlactone in dichloromethane.

Water - Hartree			
	Eletronic energy	Enthalpy	Gibbs Free Energy
Triethylamine	-292.4631215	-292.2457257	-292.2903417
4-Methyl-2-phenyl-oxazol-5(4H)-one	-591.7571568	-591.5730238	-591.6216688
Molecular complex 1	-884.2299106	-883.8260187	-883.9046037
Transition state keto-enolate	-884.2190362	-883.8187836	-883.8906956
Molecular complex 2	-884.226991	-883.8219716	-883.8951536
Triethylammonium	-292.9288354	-292.6957862	-292.7402992
4-Methyl-2-phenyl-oxazol-5-olate	-591.2798031	-591.1101762	-591.1588582
Molecular complex 3	-884.2287494	-883.8252464	-883.9013514
4-Methyl-2-phenyl-oxazol-5-ol	-591.7362613	-591.5526411	-591.6032601
Transition state keto-enol	-591.6315474	-591.455489	-591.501395

Table S12. Total energy calculations for alanine azlactone in water.

- Valine azlactone - B3LYP-D3/6-31++G(d,p)//B3LYP/6-31G(d)

Gas phase - Hartree			
	Eletronic energy	Enthalpy	Gibbs Free Energy
Triethylamine	-292.4609083	-292.2435125	-292.2881285
4-Isopropyl-2-phenyl-oxazol-5(4H)-one	-670.3898653	-670.1461864	-670.2011584
Molecular complex 1	-962.8648363	-962.40159	-962.487415
Transition state keto-enolate	-962.8420984	-962.382324	-962.459982
Molecular complex 2	-962.8445233	-962.3799122	-962.4600282
Triethylammonium	-292.8506674	-292.6176182	-292.6621312
4-Isopropyl-2-phenyl-oxazol-5-olate	-669.8425132	-669.6131153	-669.6675933
Molecular complex 3	-962.8598549	-962.3966602	-962.4798392
4-Isopropyl-2-phenyl-oxazol-5-ol	-670.3682545	-670.1249059	-670.1818359
Transition state keto-enol	-670.2633645	-670.0275662	-670.0803112

Table S13. Total energy calculations for valine azlactone in gas phase.

Dichloromethane - Hartree			
	Eletronic energy	Enthalpy	Gibbs Free Energy
Triethylamine	-292.4626694	-292.2452736	-292.2898896
4-Isopropyl-2-phenyl-oxazol-5(4H)-one	-670.3968095	-670.1531306	-670.2081026
Molecular complex 1	-962.8716971	-962.4084508	-962.4942758
Transition state keto-enolate	-962.8579161	-962.3981417	-962.4757997
Molecular complex 2	-962.8649154	-962.4003043	-962.4804203
Triethylammonium	-292.9206598	-292.6876106	-292.7321236
4-Isopropyl-2-phenyl-oxazol-5-olate	-669.9104781	-669.6810802	-669.7355582
Molecular complex 3	-962.8675202	-962.4043255	-962.4875045
4-Isopropyl-2-phenyl-oxazol-5-ol	-670.3750499	-670.1317013	-670.1886313
Transition state keto-enol	-670.2707952	-670.0271163	-670.0820883

Table S14. Total energy calculations for valine azlactone in dichloromethane.

Water - Hartree			
	Eletronic energy	Enthalpy	Gibbs Free Energy
Triethylamine	-292.4631215	-292.2457257	-292.2903417
4-Isopropyl-2-phenyl-oxazol-5(4H)-one	-670.3981758	-670.1544969	-670.2094689
Molecular complex 1	-962.8730417	-962.4097954	-962.4956204
Transition state keto-enolate	-962.861065	-962.4012906	-962.4789486
Molecular complex 2	-962.8690184	-962.4044073	-962.4845233
Triethylammonium	-292.9288354	-292.6957862	-292.7402992
4-Isopropyl-2-phenyl-oxazol-5-olate	-669.919523	-669.6901251	-669.7446031
Molecular complex 3	-962.8690741	-962.4058794	-962.4890584
4-Isopropyl-2-phenyl-oxazol-5-ol	-670.3764226	-670.133074	-670.190004
Transition state keto-enol	-670.2722524	-670.0285735	-670.0835455

Table S15. Total energy calculations for valine azlactone in water.

- <u>2-alcoxy azlactone - B3LYP-D3/6-31++G(d,p)//B3LYP/6-31G(d)</u>

Gas phase - Hartree			
	Eletronic energy	Enthalpy	Gibbs Free Energy
Triethylamine	-292.4609083	-292.2435125	-292.2881285
2-(benzyloxy)-4-methyloxazol-5(4H)-one	-706.2752003	-706.0556864	-706.1129634
Molecular complex 1	-998.747028	-998.3078123	-998.3960953
Transition state keto-enolate	-998.7246908	-998.2894881	-998.3693881
Molecular complex 2	-998.71966	-998.2805927	-998.3604107
Triethylammonium	-292.8506674	-292.6176182	-292.6621312
2-(benzyloxy)-4-methyloxazol-5-olate	-705.7134376	-705.50865	-705.564983
Molecular complex 3	-998.743358	-998.3040415	-998.3882825
2-(benzyloxy)-4-methyloxazol-5-ol	-706.253484	-706.0342676	-706.0913886
Transition state keto-enol	-706.149854	-705.9388646	-705.9888036

Table S16. Total energy calculations for a 2-alcoxy azlactone in gas phase.

Dichloromethane - Hartree			
	Eletronic energy	Enthalpy	Gibbs Free Energy
Triethylamine	-292.4626694	-292.2452736	-292.2898896
2-(benzyloxy)-4-methyloxazol-5(4H)-one	-706.2859313	-706.0664174	-706.1236944
Molecular complex 1	-998.757538	-998.3183223	-998.4066053
Transition state keto-enolate	-998.7450422	-998.3098395	-998.3897395
Molecular complex 2	-998.7495419	-998.3104746	-998.3902926
Triethylammonium	-292.9206598	-292.6876106	-292.7321236
2-(benzyloxy)-4-methyloxazol-5-olate	-705.7905726	-705.585785	-705.642118
Molecular complex 3	-998.7531188	-998.3138023	-998.3980433
2-(benzyloxy)-4-methyloxazol-5-ol	-706.2625552	-706.0433388	-706.1004598
Transition state keto-enol	-706.1600339	-705.9490445	-705.9989835

Table S17. Total energy calculations for a 2-alcoxy azlactone in dichloromethane.

Water - Hartree			
	Eletronic energy	Enthalpy	Gibbs Free Energy
Triethylamine	-292.4631215	-292.2457257	-292.2903417
2-(benzyloxy)-4-methyloxazol-5(4H)-one	-706.2881119	-706.068598	-706.125875
Molecular complex 1	-998.7597636	-998.3205479	-998.4088309
Transition state keto-enolate	-998.749174	-998.314083	-998.394294
Molecular complex 2	-998.7554888	-998.3151194	-998.3971874
Triethylammonium	-292.9288354	-292.6957862	-292.7402992
2-(benzyloxy)-4-methyloxazol-5-olate	-705.8006646	-705.595877	-705.65221
Molecular complex 3	-998.7550614	-998.3157449	-998.3999859
2-(benzyloxy)-4-methyloxazol-5-ol	-706.2643214	-706.045105	-706.102226
Transition state keto-enol	-706.1620387	-705.9510493	-706.0009883

Table S18. Total energy calculations for a 2-alcoxy azlactone in water.