Origin of Asymmetric Induction in Bicyclic Guanidine-Catalyzed Thio-Michael Reaction: A Bifunctional Mode of Lewis Acid-Brønsted Acid Activation

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Supporting Information

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Cartesian coordinates of the M06-2X/6-31G* optimized geometries of all calculated structures are given as .xyz files (in zip format).

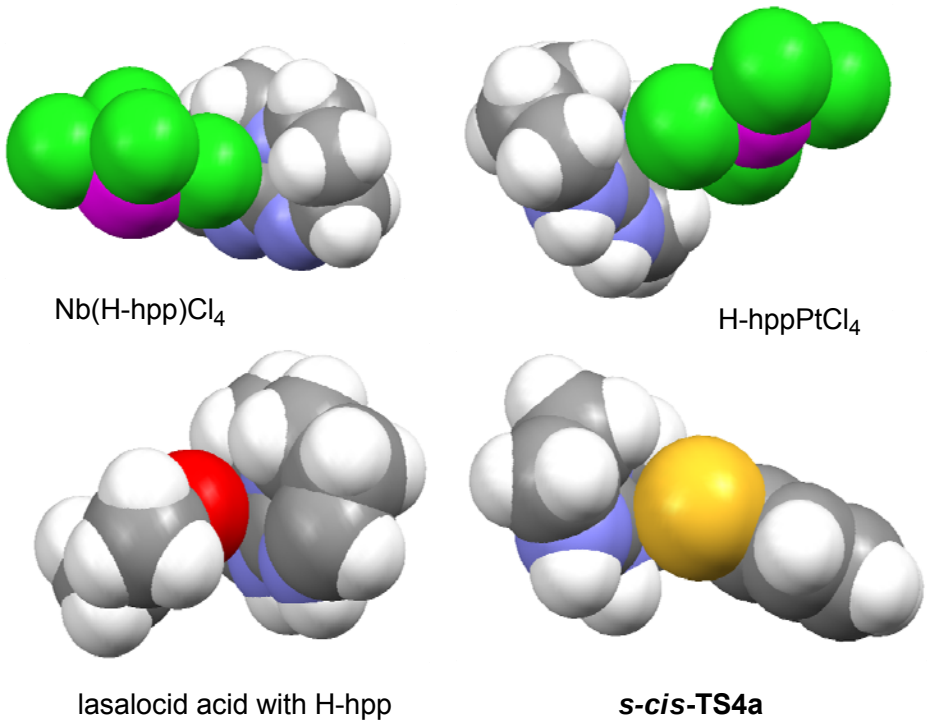

Figure S1. Space filling model (based on van der Waals radii) of interaction between Lewis base and the positively charged carbon of bicyclic guanidinium in various X-ray structures and **TS4a**. Selected functional group were removed for clarity.

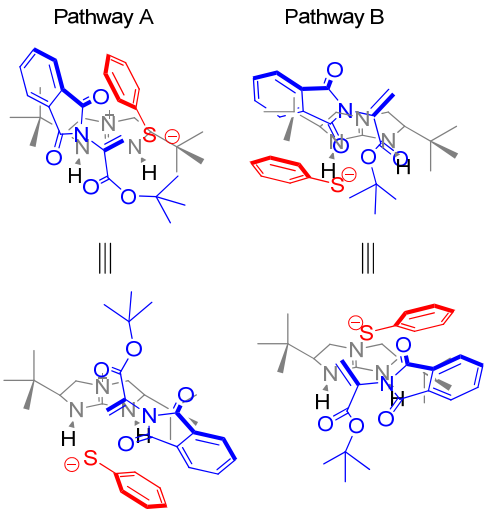

Figure S2. Lack of facial selectivity in both pathways (A and B) due to the symmetry of reactants and catalyst.

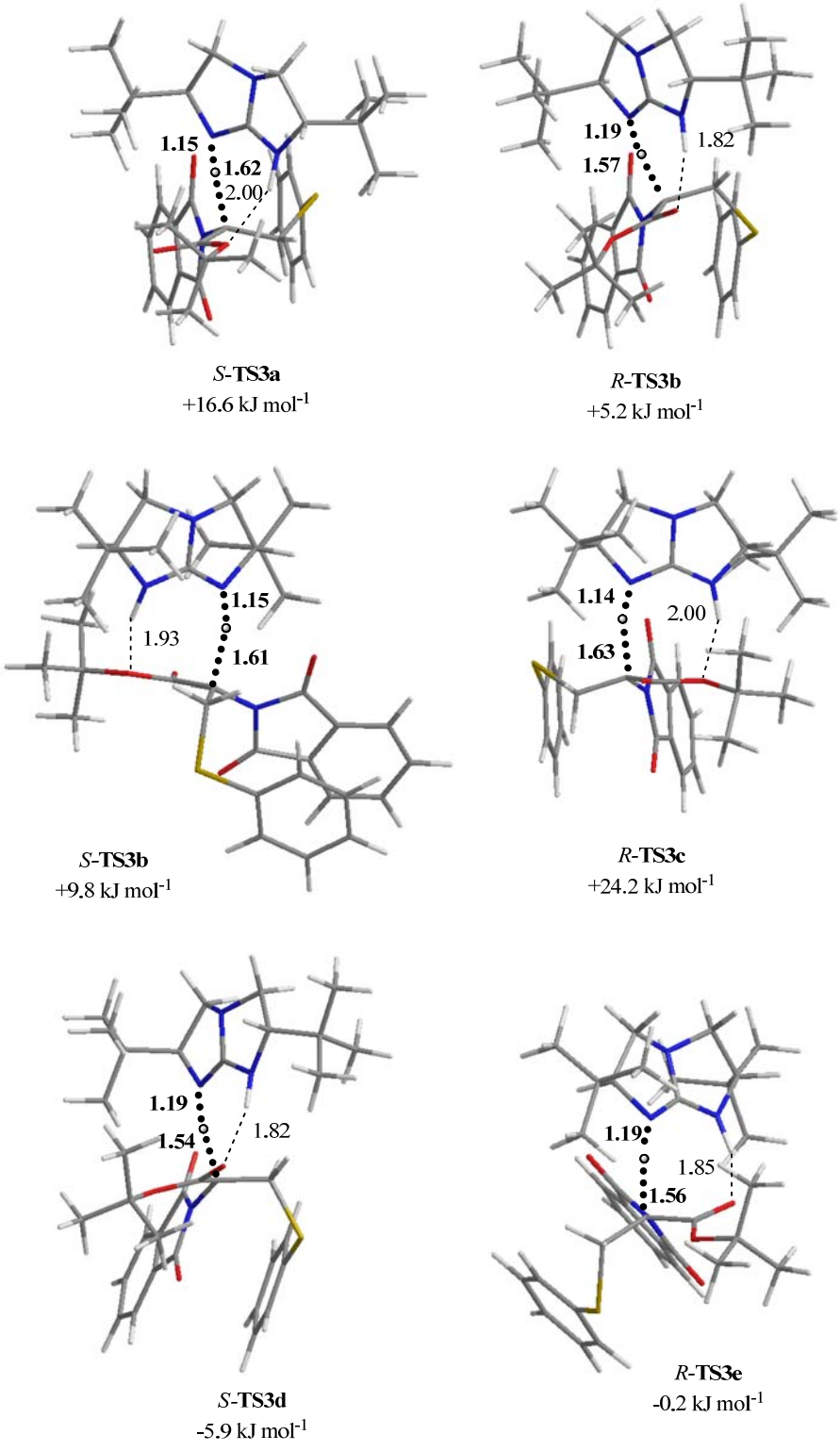

Figure S3. Protonation TS structures for pathway A. All bond distances are given in Å and the relative solvated free energies are taken with respect to *S*-**TS5a**.

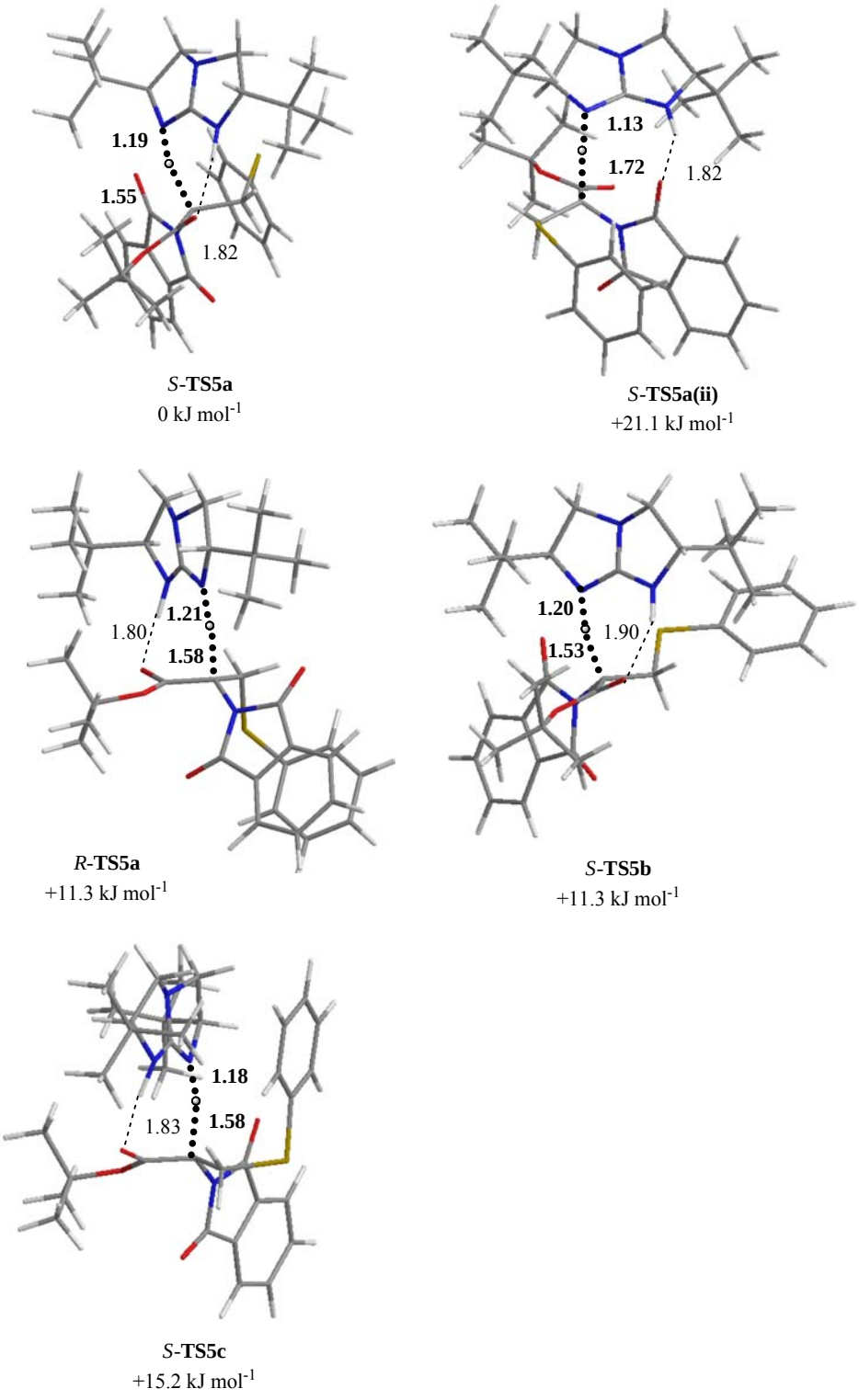

Figure S4. Protonation TS structures for pathway B. All bond distances are given in Å and the relative solvated free energies are taken with respect to *S*-**TS5a**.

Table S1. NBO hydrogen bonding analysis of C–S bond forming transition states.

E2pert is the donor and acceptor interactions of the NBO Lewis bonding molecular orbitals to the antibonding molecular orbitals.
SPh = thiophenolate, es = ester, C=O = carbonyl, C-O = ether, Pth = Pthalimide **5-2,** tBuGua = C-H interaction of *t*-butyl group in guanindine catalyst. H-CβGua = C-H interaction of hydrogen on β carbon w.r.t to N of guanidine.

Thio-Michael	Hydrogen bond Base ---Acid	Bond Length	Bond Angle X---H-Y	NBO e2pert/ kJ mol^{-1}
s-*trans*-**TS2a**	**PthC=O--H-N**	**1.8**	**145**	**39.4**
	esC-O--H-N	**2.72**	**104**	**3.6**
	Ph-S--H-N	**2.31**	**154**	**21.4**
	Pth SPh π-π	**3.3**		**1.3**
	Pth SPh π-π	**3.17**		**5.8**
	PhS--tBuGua	2.74	158	**2.1**
	esC=O--tBuGua	2.34	169	**3.7**
s-*trans*-**TS2b**	**esC=O--H-N**	**2.05**	**150**	**10.2**
	PthC=O--H-N	**2.09**	**118**	**11.3**
	PthC=O--H-N	**2.8**	**95**	**1.2**
	Ph-S--H-N	**2.24**	**168**	**20.1**
	Pth SPh π-π	**3.32**		**1.9**
	Pth SPh π-π	**3.55**		**1.0**
	PthC=O--tBuGua	2.6	148	**1.0**
	esC=O--tBugua	2.43	123	**1.0**
	Ph-S--tBu-Gua	2.66	158	**2.6**
	Ph-S--tBu-Gua	3.01	147	**1.1**
s-*cis*-**TS2c**	**PthC=O--H-N**	**1.78**	**163**	**46.8**
	Ph-S--H-N	**2.15**	**157**	**14.2**
	Pth SPh π-π	**3.27**		**1.3**
	Pth SPh π-π	3.44		**2.4**
	PthC=O--tBuGua	2.29	153	**4.6**
	esC=O--tBuGua	2.52	152	**1.5**
	esC=O--tBuGua	2.46	152	**2.9**
	estBu-N	2.78	110	**0.0**
s-*cis*-**TS2d**	**esC=O--H-N**	**1.79**	**176**	**33.8**
	PthC=O--H-N	**1.85**	**150**	**45.1**
	Pth SPh π-π	**3.36**		**1.8**
	Pth SPh π-π	**3.33**		**1.4**
	Pth SPh π-π	**3.36**		**1.6**
	Pth SPh π-π	**3.36**		**2.5**

s-*trans*-**TS4e**	**esC=O--H-N**	**1.71**	**170**	**42.3**
	PthC=O--H-N	**2.37**	**109**	**2.5**
	Pth SPh π-π	**3.24**		**3.1**
	Pth SPh π-π	**3.24**		**1.0**
	Pth SPh π-π	**3.32**		**1.7**
	Pth SPh π-π	**3.34**		**2.0**
	PthC=O--H-CαGua	2.41	119	**0.9**
s-*cis*-**TS4a**	**esC=O--H-N**	**1.78**	**159**	**40.2**
	PthC=O--H-N	**1.92**	**145**	**26.2**
	PhS-Cgua	**3.2**		**13.7**
	Pth SPh π-π	3.51		**2.4**
	Pth C=O-- SPh π-π	3.41		**0.9**
	es C=O--tBuGua	2.83	146	**0.5**
	PhS--H-CβGua	2.91	115	**2.0**
	PhS--tBuGua	2.74	137	**2.6**
s-*cis*-**TS4b**	**esC=O--H-N**	**1.78**	**166**	**42.7**
	PthC=O--H-N	**1.94**	**152**	**22.7**
	PhS-Cgua	**3.22**		**27.7**
	Gua SPh C-H-π	**2.85**		**2.6**
	Gua SPh C-H-π	**2.87**		**0.8**
	PhS--H-CβGua	2.99	130	**0.6**
s-*cis*-**TS4c**	**esC=O--H-N**	**1.78**	**176**	**41.3**
	PthC=O--H-N	**1.9**	**161**	**25.3**
	PhS-Cgua	**3.31**		**30.1**
	Gua SPh C-H-π	2.41		**1.4**
	Gua SPh C-H-π	2.6		**1.6**
	Gua SPh C-H-π	2.71		**1.7**
	esC=O--tBuGua	2.5	151	**2.1**
	esC=O--tBuGua	2.64	146	**2.3**
s-trans-**TS4d**	esC-O--H-N	**1.91**	**151**	**33.1**
	PthC=O--H-N	**1.98**	**135**	**23.1**
	PhS-Cgua	**3.12**		**16.4**
	Gua SPh C-H-π	3.4		1.9
	Gua SPh C-H-π	3.29		1.3

Table S2. NBO hydrogen bonding analysis of enolate complexes.

E2pert is the donor and acceptor interactions of the NBO Lewis bonding molecular orbitals to the antibonding molecular orbitals.
SPh = thiophenolate, es = ester, C=O = carbonyl, C-O = ether, Pth = Pthalimide **5-2,** tBuGua = C-H interaction of *t*-butyl group in guanindine catalyst. H-CβGua = C-H interaction of hydrogen on β carbon w.r.t to N of guanidine.

Enolate complex	Hydrogen bond Base ---Acid	Bond Length	Bond Angle X---H-Y	NBO e2pert/ kJ mol^{-1}
***Z*-5a**	**esC=O--H-N**	2.26	127	**6.4**
	esC-O--H-N	1.83	140	**48.7**
	PthC=O--H-N	1.82	153	**36.8**
	esC=O--tBuGua	2.33	168	**2.9**
	PhS--tBuGua	2.87	152	**3.6**
***Z*-5b**	**esC=O--H-N**	**1.6**	**168**	**109.5**
	PthC=O--H-N	**2.72**	**92**	**0.8**
	PthC=O--H-N	**2.7**	**97**	**1.0**
	GuaN-H--S	2.65	**140**	**13.6**
	PthC=O--tBuGua	2.37	159	**4.2**
	esC-O--tBuGua	2.48	159	**4.6**
	esC-O--tBuGua	2.79	145	**1.3**
***E*-5c**	**esC-O--H-N**	**1.97**	**149**	**35.4**
	PthC=O--H-N	**2.21**	**116**	**7.9**
	Ph-S--H-N	**2.56**	**139**	**17.9**
	PthC=O--tBuGua	2.41	157	**3.8**
	esC=O--tBuGua	2.38	155	**6.0**
	esC=O--tBuGua	2.53	147	**2.0**
	PhS--tBuGua	2.94	115	**1.0**
***E*-5d**	esC=O--H-N	1.5	174	**155.6**
	PthC=O--H-N	2.08	132	**15.2**
	esC=O---tBuGua	2.47	145	**2.2**
***Z*-5e**	**esC=O--H-N**	**1.66**	**150**	**83.0**
	PthC=O--H-N	**2.6**	**100**	**1.1**
	PthC=O--HCαGua	2.42	122	**1.2**
***E*-7a**	esC=O--H-N	1.48	172	**142.4**
	PthC=O--H-N	1.91	147	**33.0**
	esC=O---tBuGua	2.45	144	**2.9**
	PhS--tBuGua	2.8	153	**1.5**

E-**7b**	esC=O--H-N	1.5	168	**137.0**
	esC-O--H-N	2	137	**18.3**
	PthC=O--H-N	2.12	133	**11.7**
	esC=O---tBuGua	2.29	153	**5.2**
E-**7c**	esC=O--H-N	1.57	176	**116.3**
	PthC=O--H-N	1.93	156	**31.6**
	PthC=O--tBuGua	2.45	120	**0.9**
	esC=O---tBuGua	2.41	148	**3.1**

Table S3. NBO hydrogen bonding analysis of protonation transition states.

E2pert is the donor and acceptor interactions of the NBO Lewis bonding molecular orbitals to the antibonding molecular orbitals.
SPh = thiophenolate, es = ester, C=O = carbonyl, C-O = ether, Pth = Pthalimide **5-2,** tBuGua = C-H interaction of *t*-butyl group in guanindine catalyst. H-CβGua = C-H interaction of hydrogen on β carbon w.r.t to N of guanidine.

Protonation TS	Hydrogen bond Base ---Acid	Bond Length	Bond Angle X---H-Y	**NBO e2pert/ kJmol-1**
S-**TS3a**	C=C--H-N	1.62	164	
	esC-O--H-N	2	151	**21.3**
	PthC=O--H-N	2.45	106	**3.2**
	GuaN-H--S	3.18	115	**1.6**
	PhS--tBuGua	2.94	160	**3.5**
R-**TS3b**	C=C--H-N	1.57	166	
	esC=O--H-N	1.82	150	**31.0**
	PthC=O--H-CαGua	2.66	114	**0.5**
	PthC=O--tBuGua	2.33	180	**1.7**
	GuaN-H--S	3.4	137	**2.3**
S-**TS3b**	C=C--H-N	1.61	167	
	esC-O--H-N	1.93	156	**24.4**
	esC=O--tBuGua	2.67	151	**1.9**
	esC=O--tBuGua	2.63	154	**1.6**
R-**TS3c**	C=C--H-N	1.63	168	
	esC-O--H-N	2.07	150	**14.4**
	PthC=O--H-N	2.61	99	**2.0**
	GuaN-H--S	3.03	125	**2.2**
	PthC=O--tBuGua	2.35	171	**2.7**

	esC=O---tBuGua	2.49	179	**2.1**
	PhS--tBuGua	3.09	130	**1.0**
S-**TS3d**	C=C--H-N	1.54	167	
	esC=O--H-N	1.82	157	**31.0**
	PthC=O--H-N	2.56	107	**2.1**
	esC-O--tBuGua	2.84	177	**0.8**
	PthC=O--H-CαGua	2.58	120	**1.0**
R-**TS3e**	C=C--H-N	1.56	165	
	esC=O--H-N	1.85	148	**32.6**
	PthC=O--H-CαGua	2.7	117	**0.6**
S-**TS5a**	C=C--H-N	1.55	163	
	esC=O--H-N	1.82	156	**31.6**
	PthC=O--H-N	2.52	107	**4.1**
	GuaN-H--S	2.98	106	**2.2**
	GuaαC-H--O=CPth	2.4	122	**1.5**
	PthC=O--tBuGua	2.39	121	**1.2**
	PhS--tBuGua	3	1.44	**0.8**
S-**TS5a(ii)**	C=C--H-N	1.72	163	
	PthC=O--H-N	1.82	148	**41.5**
	GuaN-H--S	3.29	136	**1.2**
	esC=O--H-CαGua	2.34	12.6	**1.6**
	esC=O--tBuGua	2.46	139	**1.5**
	PthC=O--tBuGua	2.57	157	**0.8**
	PhS--tBuGua	3.01	150	**1.1**
R-**TS5a**	C=C--H-N	1.58	163	
	esC=O--H-N	1.8	150	**32.8**
	esC=O---tBuGua	2.5	157	**2.7**
	PthC=O--tBuGua	2.36	125	**2.2**
S-**TS5b**	C=C--H-N	1.53	163	
	esC=O--H-N	1.9	150	**21.2**
	PthC=O--H-N	2.6	110	**2.4**
	GuaN-H--S	2.9	109	**2.8**
	PthC=O--H-CαGua	2.61	120	**0.8**
	esC-O--tBuGua	2.79	176	**1.0**
S-**TS5c**	C=C--H-N	1.58	164	
	esC=O--H-N	1.83	156	**28.6**
	PthC=O--H-N	2.58	110	**4.4**
	Gua SPh C-H-π	2.57		**3.1**
	esC-O---tBuGua	2.59	173	**1.9**

Table S4. AUTOF inputs for pathways A and B for *R*- and *S*-products.

All energies expressed in kcal mol^{-1}. The first 2 rows indicate the pathway calculated and the TOF obtained. 223.15 show the temperature of the calculation while 5 indicate the number of steps in the reaction. First columns show the energy of the intermediate while the second is the energy of the transition state.

Pathway B (*S* product) TOF=1.02 x 10^5 cycles h^{-1} 223.15 5 0.0 1.7 1.0 x 1.7 2.2 x x -1.9 3.5 1.0 x 3.5 7.5 x x -0.3 4.8 x 0.5 -16.0	Pathway B (*R* product) TOF=44400 cycles h^{-1} 223.15 5 0.0 1.7 1.0 x 1.7 2.2 x x -1.9 3.5 1.0 x 3.5 7.5 x x -0.3 9.9 x 0.5 -16.0
Pathway A (*S* product) TOF=320 cycles h^{-1} 223.15 5 0.0 1.7 1.0 x 1.7 2.2 x x -1.9 1.9 1.0 x 1.9 9.8 x x 0.9 3.4 x 0.5 -16.0	Pathway A (*R* product) TOF=57400 cycles h^{-1} 223.15 5 0.0 1.7 1.0 x 1.7 2.2 x x -1.9 1.9 1.0 x 1.9 9.8 x x 5.4 6.0 x 0.5 -16.0