ORIGIN OF ENANTIOSELECTIVITY IN CF_3-PIP-CATALYZED KINETIC RESOLUTION OF SECONDARY BENZYLIC ALCOHOLS

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SUPPORTING INFORMATION

I. General.

All reagents were obtained from Sigma-Aldrich and were used as received unless specified otherwise. Chloroform-d was distilled from anhydrous K_2CO_3. N,N-Diisopropylethylamine and dichloromethane were distilled from CaH_2. Preparation of (R)-CF_3-PIP and other experimental details have been previously described.[4a]

II. Kinetic resolution of 1-phenylethanol catalyzed by (R)-CF_3-PIP 1

Both experiments described below were performed in duplicate. A one-dram vial was charged with 0.25 mmol of racemic 1-phenylethanol, 100 mg of Na_2SO_4, 1.00 mL of the stock solution of the catalyst (0.010 M of **1** and 0.188 M of *i*-Pr_2NEt in $CDCl_3$) and a stir bar, closed with a rubber septum and stirred at room temperature for 15 minutes. Acetic or propionic anhydride (0.188 mmol) was added via syringe through the septum. The

reaction were monitored by periodically withdrawing aliquots and checking them by ^{1}H NMR. The reactions were stopped by quenching with methanol after reaching ca.50% conversion by NMR. The workup and HPLC analysis followed the previously described standard procedure.[4a]

Table S-1. Enantioselectivity data

Entry	Anhydride	t(h)	#	ee_{PR} %	ee_{SM} %	C_{HPLC} %	s	C_{AVG} %	s_{AVG}
1	$(MeCO)_2O$	4.0	1	71.8	66.1	47.9	12.0	48	12
			2	72.9	67.6	48.1	12.8		
2	$(EtCO)_2O$	2.3	1	85.8	66.8	43.8	26.1	44	26
			2	86.0	66.4	43.5	26.5		

III. (a) Preparation of N-acetyl-(R)-CF_3PIP hexafluoroantimonate 5a

Acetyl chloride (10 µL, 0.14 mmol) was added via syringe to a bright-yellow solution of (R)-CF_3-PIP **1** (28.2 mg, 0.107 mmol) in CH_2Cl_2 (1 mL). The solution immediately became colorless. After 5 minutes, the solvent and the excess acetyl chloride were rotary evaporated. A solution of $AgSbF_6$ (37 mg) in CH_3CN (~ 0.5 mL) was then added to the residue, resulting in the formation of a grainy white precipitate. After 35 minutes, the precipitated AgCl was filtered off. The filtrate was left at room temperature for several days to allow slow crystallization. One of the colorless crystals of **5a** thus obtained was used in the X-ray crystallography analysis producing the structure presented below. Additional details may be found in the accompanying .cif file.

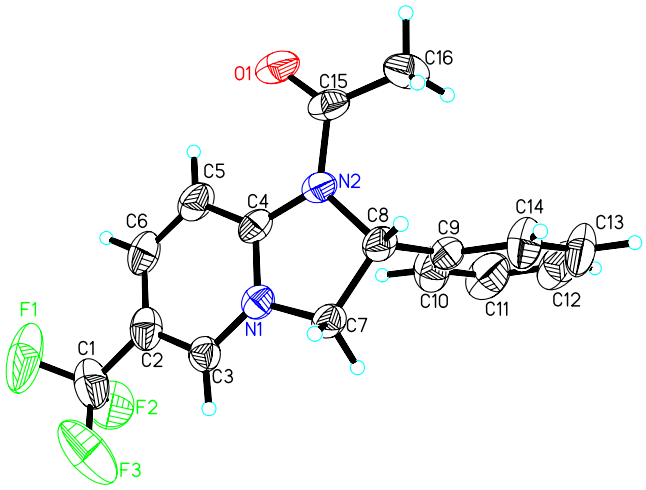

Figure S-1. Projection view of **5a** with 50% thermal ellipsoids. Anion not shown

IV. Details of the computational study.

All geometry optimizations and frequency calculations were performed in Gaussian 03.[1] Figures for the transition state structures are prepared with CYLview.[2] The Cartesian coordinates (Å), total SCF energies, enthalpies at 298K, and Gibbs free energies at 298K for the optimized structures are given below.

(a) Geometry of N-acetyl-(R)-CF_3-PIP^+ (5) optimized at the B3LYP/6-31G* level

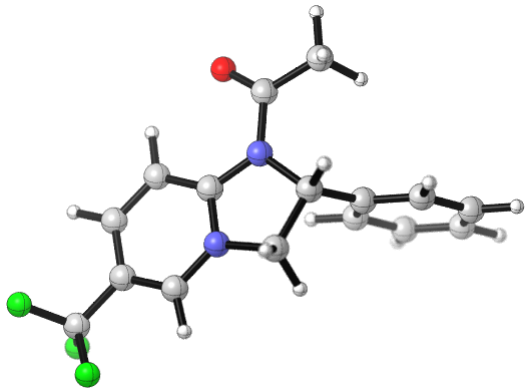

Figure S-2. Geometry of N-Acetyl-(R)-CF_3-PIP^+ (**5**)

C	-1.63316000	2.44286200	0.11307100
O	-1.00481700	3.23007000	0.83179400
C	-3.04624100	2.66820500	-0.33754500
H	-3.10706800	2.75562600	-1.42920200
H	-3.70763300	1.85421300	-0.02589800
H	-3.39204900	3.60180500	0.10570600
N	-0.98547400	1.25417100	-0.35283300
C	0.33619300	0.96312200	-0.11852300
C	-1.66483000	0.15014600	-1.12931400
C	1.30774500	1.62906100	0.65497700
N	0.68665200	-0.18152400	-0.79220400
C	-0.45118300	-0.71245800	-1.59918500
C	2.58487300	1.09024600	0.70982300
H	1.03283500	2.53095000	1.17851100
C	1.93203200	-0.72185900	-0.74120500
H	-0.22368800	-0.57709900	-2.65986800
H	-0.59890800	-1.77088400	-1.38227700
C	2.90464300	-0.09638900	0.01041700
H	3.34979000	1.58825500	1.29484500
H	2.10928200	-1.62594300	-1.30765500
C	4.27630500	-0.69100300	0.11307800
F	4.49254300	-1.24081900	1.36775700
F	4.45614800	-1.69570700	-0.82657800
F	5.24962000	0.27373900	-0.08461800
H	-2.15406700	0.59348000	-1.99937400
C	-2.68405000	-0.62686700	-0.31336500
C	-3.88860500	-1.01202000	-0.92458500
C	-2.42524800	-1.01660800	1.01220000
C	-4.82123400	-1.78324300	-0.22213400
H	-4.10168500	-0.71020000	-1.94675300
C	-3.36176800	-1.78169900	1.71379700
H	-1.50754500	-0.71497600	1.50918700
C	-4.55894600	-2.16830900	1.09727700
H	-5.74926700	-2.07472700	-0.70117800
H	-3.16000600	-2.07275800	2.73877200
H	-5.28364400	-2.76088200	1.64435700

(b) Conformational search on the transition state of a model system, N- Acetyl-DHIP$^+$ AcO$^-$, with (R)- and (S)-1-phenylethanol, at HF/3-21G level of theory

To locate the most stable conformations of the transition states, a conformational search was performed at HF/3-21G level on a model system. The unsubstituted heterocyclic core—2,3-dihydroimidazo[1,2-a]pyridine (DHIP)— was used as a simplified model of CF_3-PIP in these calculations (Figure S3). Diastereomeric transition state structures (R)-TS_{HF} and (S)-TS_{HF} were obtained by complexing the (R)- and (S)-enantiomers of 1-phenylethanol hydrogen-bound to the acetate anion on the *Si*-face of the carbonyl carbon C^2.

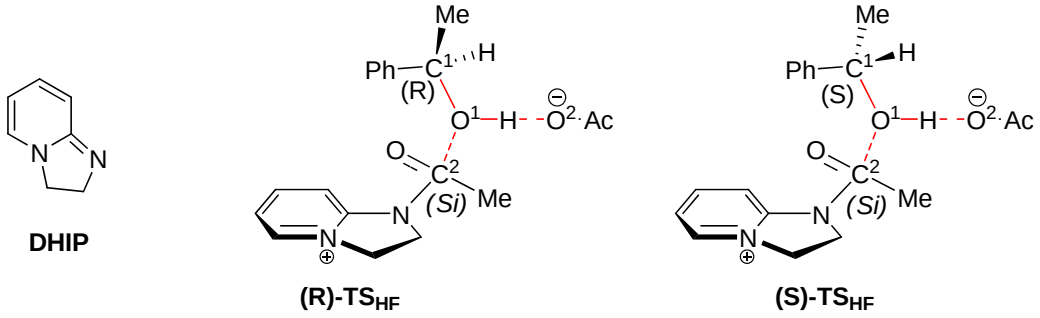

Figure S-3. Structures of DHIP-based diastereomeric transition states

For each of these structures, the starting geometries were generated by manually rotating each of the three highlighted bonds—C^1-O^1, O^1-C^2, and O^1-H-O^2—by 120°. Out of 27 structures thus generated for (R)-TS_{HF}, 8 transition state conformers were produced (Figure S4). The analogous operation performed with (S)-TS_{HF} resulted in 6 TS structures (Figure S5).

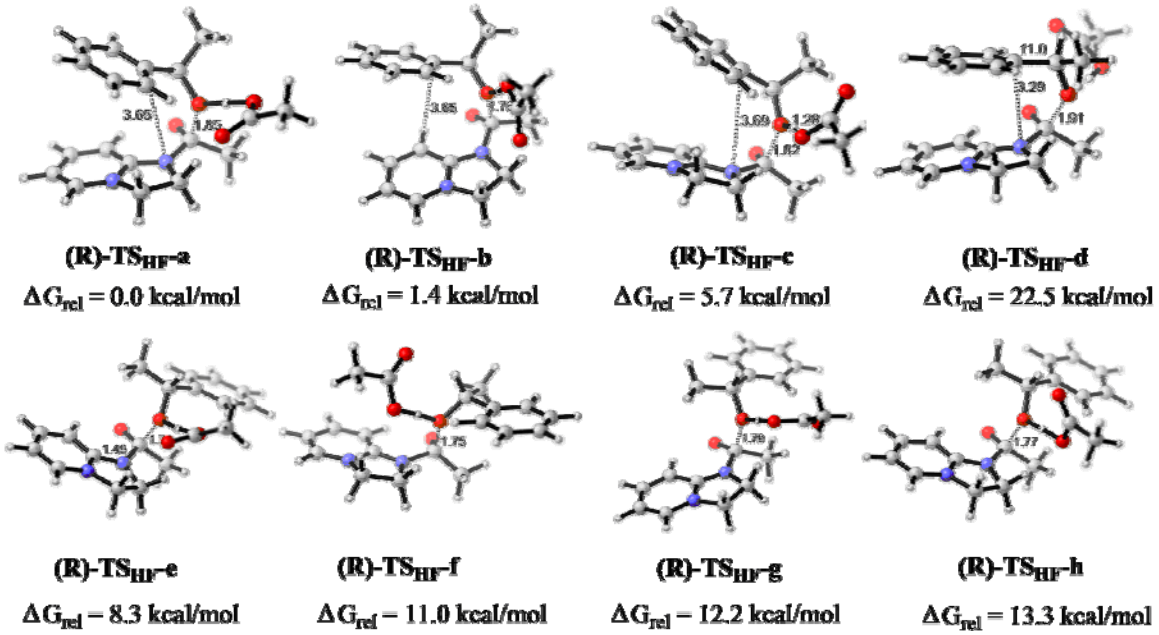

Figure S-4. TS of N-Acetyl-DHIP+ AcO$^-$ and (R)-1-phenylethanol

(R)-TS_{HF}-a

C	0.26654600	-1.71200400	-1.46664700
O	1.24944300	-0.20003300	-1.05987600
C	0.78052500	1.00125000	-1.67163900
O	-0.39914200	-1.47241000	-2.48367600
C	1.45688000	-2.64406700	-1.47652100
O	3.48042200	-0.23482100	-0.18321100
C	3.59264700	-0.18081400	1.10112200
O	2.64304600	-0.24594400	1.89493800
C	5.01575300	-0.03139900	1.59896200
H	1.96926400	-2.49165600	-2.41392100
H	1.10113300	-3.66821000	-1.43423500
H	2.14547800	-2.45356000	-0.67238600
H	5.61630200	-0.84361900	1.20838900
H	5.03540000	-0.02929800	2.67706200
H	5.42911500	0.89282500	1.21316500
H	2.35008400	-0.21382100	-0.65768600
N	-0.46129500	-1.74370800	-0.19937500
C	-1.72351500	-1.36209300	-0.05668000
C	0.19992000	-1.96585700	1.11038500
C	-2.71479200	-1.08051200	-1.02775800
N	-2.05842900	-1.26783900	1.24562600
C	-0.87567900	-1.49777800	2.12573000
H	0.42212600	-3.01586800	1.22973100
H	1.08709500	-1.36401700	1.20188100
C	-3.95463100	-0.74162600	-0.59981200
H	-2.42273600	-1.13788700	-2.04775400
C	-3.29865500	-0.91706200	1.67277800
H	-1.11246500	-2.24450800	2.86653100
H	-0.60082600	-0.56386400	2.58906400
C	-4.27321300	-0.65689300	0.78045700

(R)-TS_{HF}-b

C	0.74335900	-0.25123300	-2.14646300
O	0.37636900	1.07418800	-1.05539900
C	-0.88683700	1.71865900	-1.30308800
O	-0.29937200	-0.53213000	-2.77827300
C	1.93557400	0.37061800	-2.84807900
O	1.53178700	2.21960200	0.70469200
C	2.48642500	1.83554800	1.49510500
O	3.06635600	0.75141700	1.43756900
C	2.85017000	2.87188900	2.53739900
H	1.54960200	1.13640300	-3.50363900
H	2.42780700	-0.38246200	-3.45330400
H	2.63845000	0.81431100	-2.16331900
H	3.15900500	3.78158500	2.03718200
H	3.64249000	2.50345400	3.16912800
H	1.97349800	3.10844200	3.12774000
H	1.04326100	1.59663800	-0.17358400
N	1.16499100	-1.21431000	-1.11463600
C	0.30769500	-1.96559200	-0.43889200
C	2.54448700	-1.34844500	-0.58356500
C	-1.07358100	-2.18322400	-0.65031700
N	0.90872500	-2.58431700	0.59634800
C	2.33416400	-2.15544400	0.72143600
H	3.16139200	-1.87210400	-1.29844400
H	2.95071900	-0.39253800	-0.31884600
C	-1.73167200	-2.99717400	0.20908900
H	-1.51703700	-1.68414600	-1.47742400
C	0.24936600	-3.40567800	1.45429500
H	2.97154700	-3.02116300	0.80076900
H	2.43892500	-1.49379600	1.56552800

(R)-TS_{HF}-c

C	-0.08736700	1.71625700	-1.51021000
O	-1.16301100	0.31137100	-1.09612500
C	-0.83968600	-0.96488600	-1.65749300
O	0.57642000	1.40741100	-2.51015900
C	-1.20820000	2.73168100	-1.54487100
O	-2.64841400	0.66427700	0.74699600
H	-4.71477400	-0.52753900	-1.32343300
H	-3.43485000	-0.86464700	2.73132100
H	-5.25241700	-0.38299000	1.10669200
C	-0.01655700	1.84837300	-0.68934400
C	-1.02382200	2.68107200	-1.15366500
C	0.26487600	1.82670200	0.66984400
C	-1.73647100	3.48853400	-0.28381100
H	-1.25329100	2.69732700	-2.20276000
C	-0.44583400	2.63800400	1.53955400
H	1.03723900	1.18930400	1.04980700
C	-1.44818100	3.46984900	1.06939800
H	-2.51028600	4.12881200	-0.66072500
H	-0.20636600	2.62799900	2.58586100
H	-1.99253200	4.09882700	1.74649100
C	1.97250500	1.80309700	-2.22581300
H	2.50708600	1.20368900	-2.95332700
H	2.65398600	2.05212300	-1.42367600
H	1.62999000	2.71536500	-2.69896500
H	0.13435000	0.70103200	-2.48551400

SCF: E(RHF) = -1135.40795892
Sum of electronic and zero-point Energies=-1135.044929
Sum of electronic and thermal Energies=-1135.022435
Sum of electronic and thermal Enthalpies=-1135.021491
Sum of electronic and thermal Free Energies=-1135.098177

C	-1.06727200	-3.63716600	1.28906700
H	-2.78057000	-3.16187600	0.07071200
H	0.83335900	-3.83293000	2.24065900
H	-1.59508200	-4.28033000	1.95869400
H	-1.22537700	1.34876700	-2.25800700
C	-1.91958600	1.34231700	-0.25162800
C	-3.22391200	1.06160900	-0.62674800
C	-1.58192900	1.28818700	1.09378200
C	-4.18009200	0.73527300	0.32154200
H	-3.49255400	1.09208300	-1.66564300
C	-2.53414700	0.96206100	2.04157600
H	-0.57985300	1.52201900	1.38568500
C	-3.83674200	0.68240400	1.66007500
H	-5.18620000	0.52404000	0.01497600
H	-2.26300400	0.93024900	3.07919800
H	-4.57421600	0.43272000	2.39770600
C	-0.68348900	3.24128100	-1.35315200
H	-1.62601200	3.74141800	-1.54130600
H	0.01193900	3.48986300	-2.14729600
H	-0.27110600	3.58979500	-0.41646200

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Sum of electronic and thermal Energies= -1135.019033
Sum of electronic and thermal Enthalpies= -1135.018089
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O	-4.35732700	-0.69396100	0.22585500
C	-4.60749400	0.82452300	2.06641100
H	-1.74149800	2.58104300	-2.47064500
H	-0.78056600	3.72881700	-1.54401300
H	-1.89361300	2.61520300	-0.72269500
H	-4.04503600	0.67926900	2.98144400
H	-5.58939700	0.38860000	2.15956400

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C  1.86643600   1.27276100  -0.06334700
C  0.00581200   2.09601500   1.06877400
C  2.83996100   0.88546200  -1.01608700
N  2.18489800   1.19676300   1.24513900
C  1.00811800   1.51934400   2.10224800
H -0.06011800   3.17143600   1.14969500
H -0.96894400   1.64403700   1.14910300
C  4.04854200   0.47170700  -0.56598000
H  2.55780100   0.93076400  -2.03968300
C  3.39456200   0.77134300   1.69509300
H  1.28878800   2.23216900   2.86072000
H  0.64894800   0.60335500   2.54441000
C  4.35207100   0.41169100   0.81981000
H  4.79577300   0.17850300  -1.27511900
H  3.52068100   0.74510400   2.75586700
H  5.30739000   0.07989500   1.16273600
C -0.11162600  -1.84648100  -0.65098600
C  0.84273600  -2.75283100  -1.08639400
C -0.40382900  -1.78069500   0.70499100
C  1.49267000  -3.58555500  -0.19097700
```

(R)-$\mathbf{TS_{HF}}$-**d**

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C  0.82085400   1.46216800  -0.57279300
O  1.52006600  -0.21516900  -1.15030700
C  1.36880300  -1.59634600  -0.75751500
O  1.04187300   1.66025700   0.62148600
C  1.56980100   2.18004000  -1.67434500
O  3.74442500   0.44810300  -0.33450200
C  3.93112900   0.20968100   0.95100300
O  3.27396400  -0.57302500   1.61256900
C  5.08369400   1.00601800   1.51278600
H  2.61005600   2.20399100  -1.39795800
H  1.18699000   3.19492000  -1.73157800
H  1.46681800   1.68897900  -2.62506000
H  5.96116200   0.84972300   0.89872000
H  5.27457800   0.71208600   2.53262500
H  4.83243400   2.05930400   1.46976700
H  2.81786400   0.12149200  -0.73851500
N -0.57473900   1.20134400  -0.93956000
C -1.59901900   1.29480900  -0.10711200
C -0.97432800   0.65301200  -2.24946400
C -1.67220000   1.82708500   1.20361900
N -2.73122100   0.84075700  -0.68039200
C -2.45387100   0.24189400  -2.01781000
H -0.89471900   1.41518000  -3.01012600
H -0.32512600  -0.17115500  -2.46790900
C -2.88176000   1.87388700   1.80861400
H -0.76023600   2.13813100   1.65280500
C -3.94096600   0.86391100  -0.06061500
H -3.12465300   0.66074300  -2.75074800
H -2.57156200  -0.82599000  -1.94265700
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(R)-$\mathbf{TS_{HF}}$-**e**

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C -0.03844200   1.12834300  -0.91432600
O  0.49104600   0.00619700   0.25848500
C  1.48760100   0.33007900   1.26249700
O -0.01684000   2.29980400  -0.46671900
C  0.83857700   0.74296500  -2.09302900
O  0.60916000  -2.36671800   0.04748800
C -0.21648600  -3.25948700   0.53125900
O -1.42061200  -3.09214200   0.68145000
C  0.45998700  -4.56944300   0.87237900
H  1.82290100   1.13930900  -1.90388600
H  0.43782000   1.21300600  -2.98397000
H  0.91444800  -0.32216400  -2.23621700
H  0.96752700  -4.94575300  -0.00730000
H  1.07904700  -2.80843100  -2.13229100
C  0.24326700  -2.61459500   1.60068500
H -1.14614200  -1.09020500   1.04788800
C  1.19478800  -3.51867400   1.15822200
H  2.22539100  -4.28387100  -0.54598400
H -0.00694200  -2.57061400   2.64362200
H  1.69004400  -4.16744300   1.85384400
C -2.13075500  -1.63654800  -2.15602300
H -2.54226200  -1.05396100  -2.97277700
H -2.86550500  -1.66611700  -1.36300500
H -1.92665000  -2.64043500  -2.50898800
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 Sum of electronic and thermal Energies=
-1135.013333
 Sum of electronic and thermal
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 Sum of electronic and thermal Free
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C -4.05613400   1.38577300   1.17443900
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C  0.08824800  -1.86969200   0.03245700
C -0.96513200  -2.63743900  -0.43896200
C  0.00768500  -1.34417100   1.32105200
C -2.08582300  -2.87142300   0.34975600
H -0.91113400  -3.08606300  -1.41097900
C -1.10362600  -1.57957100   2.10593700
H  0.83474500  -0.76832600   1.68476500
C -2.15914000  -2.34105200   1.62252400
H -2.88236700  -3.48607500  -0.02488300
H -1.14403800  -1.17969500   3.10024000
H -3.01511600  -2.53252100   2.24011700
C  1.51886700  -2.45626100  -2.01934000
H  2.47059800  -2.22030400  -2.47803500
H  0.74141800  -2.23480700  -2.74305300
H  1.49482200  -3.51534800  -1.78814200
H  2.17363000  -1.84897400  -0.08118300
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 Sum of electronic and zero-point
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 Sum of electronic and thermal
Enthalpies= -1134.986615
 Sum of electronic and thermal Free
Energies= -1135.062353
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H -0.26666600  -5.28408700   1.22420800
H  1.21284800  -4.39416400   1.63146300
H  0.45105600  -1.20023400   0.11744500
N -1.39159400   0.51811000  -1.05622700
C -2.44950200   0.93350400  -0.37606600
C -1.66492300  -0.76510200  -1.74745700
C -2.65649400   2.13071000   0.35095400
N -3.45338100   0.03498100  -0.43400000
C -3.00537700  -1.21879500  -1.11695700
H -1.74672900  -0.59547200  -2.81111300
H -0.88866400  -1.47476000  -1.53355700
C -3.85992700   2.31902400   0.94460400
H -1.84062400   2.81197100   0.38582500
C -4.65431000   0.22100700   0.16837000
```

```
H -3.74018900  -1.52310200  -1.84436300
H -2.81029300  -1.97069500  -0.36933500
C -4.89679600   1.35342600   0.85826600
H -4.03447400   3.22195800   1.49403700
H -5.36370800  -0.57076300   0.06029700
H -5.84097300   1.51147500   1.33165400
C  2.86249100   0.49996200   0.62394100
C  3.57308200   1.68631000   0.64055600
C  3.41311400  -0.60531800  -0.02008400
C  4.82025500   1.76951500   0.03709400
H  3.16090100   2.55281900   1.11433100
C  4.65347100  -0.52415100  -0.61939500
H  2.84894500  -1.51728600  -0.05328000
C  5.36410400   0.66685800  -0.59100700
H  5.35890900   2.69657700   0.05821500
H  5.06689600  -1.38400200  -1.10929800
```

(R)-TS_{HF}-f

```
C -0.16781700   1.87841000  -0.07518400
O  0.61065200   0.38793600   0.39745300
C  1.76266400   0.24060800   1.26660400
O -0.53994000   2.53643100   0.91375900
C  0.87430200   2.41974200  -1.03510800
O -0.55658200  -1.66624400   0.00259700
C -0.49604800  -2.60853000   0.91999900
O  0.14629800  -2.52681400   1.95157400
C -1.31490900  -3.83542100   0.56812900
H  1.68217100   2.83188300  -0.45136200
H  0.42447000   3.22304400  -1.60827600
H  1.27368100   1.66702200  -1.69138400
H -2.35420500  -3.55086600   0.44874600
H -1.22144600  -4.57710700   1.34510600
H -0.96902000  -4.23818600  -0.37651100
H  0.01307200  -0.63588100   0.24592000
N -1.23675900   1.15587100  -0.81538600
C -2.42945800   0.89172300  -0.30262400
C -1.00055500   0.39375000  -2.06111800
C -3.05978700   1.40840500   0.85576800
N -3.10059200   0.00128500  -1.05780600
C -2.23239100  -0.54436400  -2.14139100
H -0.94933200   1.06897300  -2.90185700
H -0.09478200  -0.17449700  -1.96903200
C -4.31420700   0.98654500   1.14276200
H -2.49344300   2.09253100   1.44101300
C -4.35590400  -0.42664500  -0.76457300
H -2.74805900  -0.49393800  -3.08642900
H -1.95142300  -1.54433700  -1.86569900
```

(R)-TS_{HF}-g

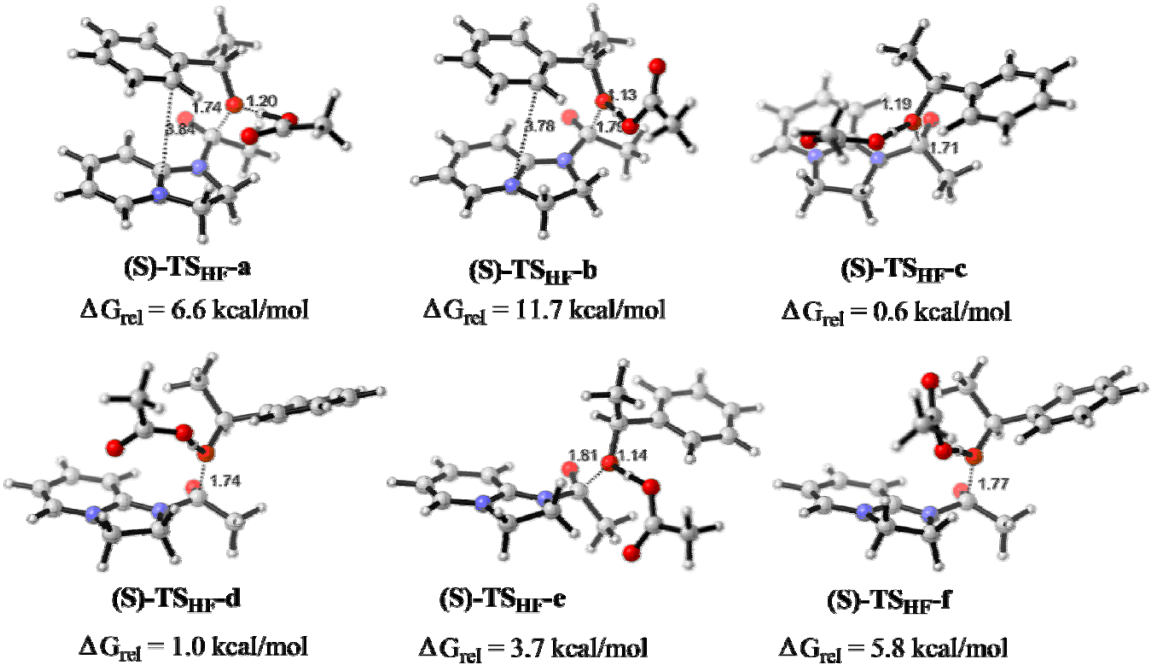
```
 C -0.29783900   0.55238200  -1.03264900
 O  0.49330800  -0.16858800   0.40309000
 C  1.33394800   0.59746200   1.29197500
 O -0.27650200   1.79047900  -0.95402100
 C  0.46948900  -0.20852200  -2.09281800
 O  0.43894700  -2.48932300   1.00761500
 C  1.26470100  -3.28776900   0.37925900
 O  1.91628300  -2.97201900  -0.60995500
 C  1.34129000  -4.67498000   0.98341800
 H  1.40601000   0.30878000  -2.22810100
 H -0.08959100  -0.16377600  -3.02226400
 H  0.68542500  -1.22690500  -1.81987100
 H  1.69488100  -4.59548900   2.00449700
 H  2.00628400  -5.29609900   0.40484500
 H  0.34926900  -5.10915400   1.01572800
 H  0.47476000  -1.31023300   0.68686900
 N -1.62841000  -0.08109300  -0.78272200
 C -2.69209700   0.57287200  -0.35849600
 C -1.87104500  -1.54437900  -0.85365800
 C -2.90107300   1.96356600  -0.15518300
 N -3.72166900  -0.26737900  -0.10835800
 H  6.32840400   0.73097200  -1.05565900
 C  1.02513900   1.48760200   2.15057200
 H  0.05241500   1.23787600   2.55753200
 H  0.92597000   2.38980600   1.57405800
 H  1.71957900   1.62565000   2.97146400
 H  1.54309900  -0.55977700   1.88039100

 SCF:  E(RHF) =  -1135.41503499
 Sum of electronic and zero-point
Energies= -1135.030860
 Sum of electronic and thermal Energies=
-1135.008413
 Sum of electronic and thermal
Enthalpies= -1135.007469
 Sum of electronic and thermal Free
Energies= -1135.084946

 C -4.99634200   0.05081000   0.31972800
 H -4.80510000   1.36631800   2.01574000
 H -4.77853500  -1.14382500  -1.43471900
 H -5.98555900  -0.27506700   0.55605100
 C  2.99880900   0.01088700   0.39976100
 C  4.22113400   0.61858500   0.62649100
 C  2.88633300  -0.88060900  -0.66439600
 C  5.31021600   0.34690800  -0.19063900
 H  4.33787100   1.30603800   1.43889500
 C  3.96784700  -1.15448200  -1.47556500
 H  1.94563100  -1.36455300  -0.83309400
 C  5.18824300  -0.53688900  -1.24334600
 H  6.24922900   0.82866700   0.00057100
 H  3.86595800  -1.85026200  -2.28574900
 H  6.02963200  -0.74795300  -1.87355700
 C  1.87985600   1.39338600   2.27057300
 H  0.91589800   1.56157700   2.72306600
 H  2.18270100   2.31715600   1.79761400
 H  2.60082000   1.13506300   3.03765000
 H  1.57588000  -0.66928800   1.82134900

 SCF:  E(RHF) =  -1135.36855976
 Sum of electronic and zero-point
Energies= -1135.026506
 Sum of electronic and thermal Energies=
-1135.004082
 Sum of electronic and thermal
Enthalpies= -1135.003138
 Sum of electronic and thermal Free
Energies= -1135.080582

 C -3.33103500  -1.68520000  -0.33640300
 H -1.77789800  -1.88139400  -1.87377200
 H -1.17541100  -2.05687600  -0.21449600
 C -4.11584300   2.37551800   0.27315500
 H -2.07706000   2.60407500  -0.35656000
 C -4.94228900   0.15108500   0.32519800
 H -3.99184700  -2.12992900  -1.06402700
 H -3.37922000  -2.22284100   0.59796200
 C -5.17572700   1.46012600   0.52519600
 H -4.28586100   3.42182900   0.42717100
 H -5.67107800  -0.61347900   0.48849200
 H -6.12977200   1.79893900   0.86503200
 C  2.61266000   1.04987500   0.59123500
 C  3.30420700   0.12253900  -0.18306100
 C  3.13690400   2.32351300   0.73151300
 C  4.49429100   0.46855000  -0.79334100
 H  2.90777900  -0.86427500  -0.31671800
 C  4.33161400   2.67019600   0.11828000
 H  2.61910500   3.05921600   1.31123700
 C  5.01473400   1.74465000  -0.64481500
 H  5.01482700  -0.25846900  -1.38559800
 H  4.71994900   3.66305800   0.23664000
```

```
H  5.93851200   2.01097300  -1.12005600
C  0.52812200   1.71687800   1.96148800
H -0.37784600   1.28378900   2.36975100
H  0.26071400   2.46438000   1.23367400
H  1.08797900   2.16254100   2.77518000
H  1.63428700  -0.10351100   2.06635300

SCF:  E(RHF) =  -1135.41751855
```

(R)-**TS_{HF}-h**

```
C -0.32806500   0.90024200  -1.12628200
O  0.45580700  -0.06947300   0.13558100
C  1.35321700   0.42815300   1.16317600
O -0.33313500   2.10325200  -0.81813200
C  0.46007900   0.37637900  -2.30927200
O  0.74029200  -2.41454100  -0.28575100
C  0.93930300  -3.19803400   0.75015100
O  1.01101400  -2.80849400   1.90528700
C  1.08576300  -4.66151700   0.37798500
H  1.43680400   0.83111500  -2.26711200
H -0.03658300   0.69463700  -3.21957500
H  0.57312300  -0.69473700  -2.29950400
H  0.21346200  -4.98407000  -0.17783700
H  1.20965700  -5.26086800   1.26601300
H  1.94536600  -4.77521000  -0.27200700
H  0.59549600  -1.18310900  -0.03801800
N -1.63521000   0.19315100  -1.00848600
C -2.67406800   0.67814500  -0.35357300
C -1.86339400  -1.21211100  -1.43678200
C -2.90112400   1.97235200   0.18259600
N -3.64599600  -0.25018900  -0.21371000
C -3.20859300  -1.57018700  -0.74714700
H -1.95372200  -1.24982000  -2.51198200
H -1.05696000  -1.84057000  -1.09904500
C -4.08200400   2.21448700   0.79723800
H -2.11638600   2.68041900   0.06807600
C -4.83145900  -0.00432800   0.40760100
H -3.94533400  -1.94951900  -1.43715300
H -3.07204000  -2.25276600   0.07796800
```

```
 Sum of electronic and zero-point
Energies= -1135.025119
 Sum of electronic and thermal Energies=
-1135.002693
 Sum of electronic and thermal
Enthalpies= -1135.001749
 Sum of electronic and thermal Free
Energies= -1135.078806

 C -5.08519700   1.21368500   0.91918700
 H -4.26752000   3.18802700   1.20359600
 H -5.51663000  -0.82308500   0.45659300
 H -6.01300100   1.41790300   1.40699300
 C  2.69564100   0.81380100   0.54803300
 C  3.31906400  -0.11153100  -0.28594300
 C  3.33284200   2.01651500   0.79617300
 C  4.54937300   0.16164600  -0.84811600
 H  2.82741600  -1.04178000  -0.48978900
 C  4.57009600   2.29283200   0.23167500
 H  2.87194200   2.74998500   1.42460400
 C  5.18226200   1.36848100  -0.59016300
 H  5.01680200  -0.56364300  -1.48523500
 H  5.04758400   3.23145700   0.43491300
 H  6.13858300   1.58116100  -1.02611100
 C  0.66783400   1.52916600   1.97513100
 H -0.28718200   1.15128500   2.31989400
 H  0.49571600   2.39896700   1.36367700
 H  1.26434700   1.78488900   2.84298800
 H  1.51626500  -0.42641500   1.80754700
 SCF:  E(RHF) =  -1135.41976004
 Sum of electronic and zero-point
Energies= -1135.022499
 Sum of electronic and thermal Energies=
-1135.000076
 Sum of electronic and thermal
Enthalpies= -1134.999132
 Sum of electronic and thermal Free
Energies= -1135.076972
```



(S)-TS_{HF}-a ΔG_{rel} = 6.6 kcal/mol

(S)-TS_{HF}-b ΔG_{rel} = 11.7 kcal/mol

(S)-TS_{HF}-c ΔG_{rel} = 0.6 kcal/mol

(S)-TS_{HF}-d ΔG_{rel} = 1.0 kcal/mol

(S)-TS_{HF}-e ΔG_{rel} = 3.7 kcal/mol

(S)-TS_{HF}-f ΔG_{rel} = 5.8 kcal/mol

Figure S-5. TS of N-Acetyl-DHIP+ AcO^- and (S)-1-phenylethanol

(S)-$\mathbf{TS_{HF}}$-a

```
 C -0.42249600  -0.30447900  -2.08696300
 O -1.24769600  -1.02434800  -0.73111700
 C -0.75486500  -2.23942400  -0.12665500
 O  0.59206400  -0.97102300  -2.38476300
 C -1.61609500  -0.23447300  -3.02361000
 O -3.23149300  -0.19851800   0.32790500
 C -3.19815000   0.42733000   1.46768400
 O -2.19088200   0.93437700   1.96534700
 C -4.54550700   0.50473500   2.15333400
 H -1.80481700  -1.23718300  -3.37476100
 H -1.35329300   0.38688900  -3.87251000
 H -2.50719500   0.14270700  -2.54996800
 H -5.26820700   0.93727700   1.47294000
 H -4.47207200   1.09072700   3.05544400
 H -4.88002700  -0.49935800   2.38590700
 H -2.23604900  -0.58893200  -0.20189100
 N -0.16767900   1.00535100  -1.45471500
 C  0.99775800   1.35326200  -0.91859100
 C -1.22918100   1.97863300  -1.10967700
 C  2.28252700   0.78579500  -1.07476100
 N  0.86077900   2.43703800  -0.12968400
 C -0.58210600   2.79633100   0.03315800
 H -1.45401600   2.59216500  -1.97062200
 H -2.10611500   1.46380000  -0.76991100
 C  3.32113000   1.37087100  -0.43136500
 H  2.34934000  -0.09378300  -1.66747500
 C  1.90066800   3.01773100   0.52141500
 H -0.71088000   3.86088000  -0.07528700
 H -0.92973300   2.42849200   0.98502900
```

(S)-$\mathbf{TS_{HF}}$-b

```
 C -0.25201000   0.67979800  -2.02619600
 O -1.40367900  -0.24418200  -1.01243900
 C -1.34206000  -1.67124500  -0.77332300
 O  0.47568900  -0.09755400  -2.66463900
 C -1.32602800   1.51567200  -2.69287400
 O -2.64340500   0.90094100   0.68871200
 C -3.73009000   0.34089100   1.16625400
 O -4.09132400  -0.79427700   0.90130400
 C -4.51199300   1.24151700   2.10467100
 H -1.84057400   0.87355200  -3.39000900
 H -0.85069100   2.32185400  -3.24158700
 H -2.03957100   1.91294600  -1.99043900
 H -3.87632400   1.53490700   2.93196900
 H -5.38590400   0.72659900   2.47069800
 H -4.80110600   2.14249500   1.57653600
 H -2.03467100   0.28241300  -0.23173400
 N  0.40642800   1.42655700  -0.93269500
 C  1.62657100   1.16319200  -0.48672200
 C -0.25208300   2.49504900  -0.13395300
 C  2.61143100   0.26805400  -0.97344000
 N  1.92265900   1.91326700   0.59443200
 C  0.74995800   2.71934800   1.02998500
 H -0.35483600   3.38442600  -0.73768900
 H -1.20638200   2.15501800   0.23109300
 C  3.80126900   0.21330000  -0.33201300
 H  2.34507400  -0.32714200  -1.81204700
 C  3.11926300   1.85496200   1.23985800
 H  1.03636300   3.75245000   1.14639100
 H  0.37754800   2.31892500   1.96051400
```

(S)-$\mathbf{TS_{HF}}$-c

```
 C -0.24790100   1.41652600  -0.92350500
 O  0.58265800   0.23122600  -0.00645500
 C  1.51410700   0.75250300   0.96155500
 O -0.27760000   2.49258000  -0.27714200
 C  0.53542400   1.32148900  -2.21989400
 C  3.14510500   2.52023200   0.38256900
 H  4.30052200   0.95035900  -0.53374500
 H  1.66410700   3.86521400   1.12770700
 H  3.97131500   2.97281500   0.88582600
 C  0.54574900  -1.98119000   0.63130900
 C  1.70120300  -2.71680800   0.43195500
 C  0.54860700  -0.97871700   1.59736500
 C  2.83573900  -2.47290000   1.19191300
 H  1.72852500  -3.47986000   0.31749200
 C  1.67674000  -0.73993300   2.35854400
 H -0.33420400  -0.39030300   1.75585000
 C  2.82671300  -1.48816000   2.16058600
 H  3.71991800  -3.05756000   1.02660000
 H  1.65655800   0.02493500   3.11060800
 H  3.69954200  -1.30840500   2.75777700
 C -0.70472000  -3.37480400  -1.15408900
 H  0.01203500  -3.14227600  -1.92391100
 H -1.68565400  -3.46761100  -1.60553000
 H -0.46124500  -4.31538700  -0.67369600
 H -1.49890900  -2.50044000   0.62020300

 SCF: E(RHF) =  -1135.42545416
 Sum of electronic and zero-point
Energies= -1135.035616
 Sum of electronic and thermal Energies=
-1135.013383
 Sum of electronic and thermal
Enthalpies= -1135.012438
 Sum of electronic and thermal Free
Energies= -1135.087723
```

```
 C  4.08213100  1.02548700   0.80018900
 H  4.55188000 -0.46389800  -0.68509100
 H  3.22838500  2.49534100   2.08847100
 H  5.02593800  0.97341000   1.29729300
 C -0.15486800 -1.98652000   0.13345200
 C  0.77501800 -2.97656900  -0.12782600
 C -0.02875000 -1.24681600   1.30820500
 C  1.80748600 -3.23295600   0.76477100
 H  0.70322100 -3.55550800  -1.02521200
 C  0.99423100 -1.50293800   2.19807500
 H -0.75261300 -0.48274200   1.51239600
 C  1.92080300 -2.50039500   1.92893500
 H  2.51491400 -4.00958300   0.54740300
 H  1.06536100 -0.93881500   3.10843100
 H  2.71138600 -2.70618900   2.62385500
 C -1.38072700 -2.43076100  -2.10057500
 H -0.51068000 -2.20240700  -2.69344600
 H -2.26110700 -2.11042100  -2.64402600
 H -1.46037900 -3.49777200  -1.92733200
 H -2.24439700 -1.89246800  -0.21694900
 SCF:  E(RHF) = -1135.39898071
 Sum of electronic and zero-point
Energies= -1135.026097
 Sum of electronic and thermal Energies=
-1135.003723
 Sum of electronic and thermal
Enthalpies= -1135.002779
 Sum of electronic and thermal Free
Energies= -1135.079539
```

```
 O  0.62428100  -2.15092700  -0.16672700
 C -0.17379000  -3.06873300   0.30730800
 O -1.38348900  -2.93993500   0.46203700
 C  0.53709200  -4.36454700   0.63755000
 H  1.50645100   1.75649000  -2.03956100
 H  0.02659700   1.90468900  -2.97885900
```

```
H  0.66879400   0.30689300  -2.55740700
H  1.06805200  -4.71174800  -0.24014600
H -0.17232900  -5.10575800   0.96910600
H  1.27407500  -4.17900500   1.40995600
H  0.51279400  -0.95840800  -0.08158000
N -1.53088200   0.68516800  -1.02055000
C -2.57421200   0.92061300  -0.23677400
C -1.73070400  -0.52985200  -1.84633400
C -2.81900700   1.98266600   0.66633100
N -3.51546300  -0.03247600  -0.37841300
C -3.03471200  -1.13717900  -1.26572900
H -1.83444400  -0.25337700  -2.88485100
H -0.90459900  -1.20306600  -1.70901500
C -3.99608600   1.99253100   1.33847300
H -2.05058700   2.71123400   0.76390200
C -4.68751300  -0.02772500   0.30347200
H -3.77788000  -1.35090600  -2.01654800
H -2.79002100  -1.98320500  -0.64572300
C -4.96681100   0.97309500   1.16258900
H -4.19802700   2.79117300   2.02329700
H -5.34438000  -0.84951800   0.11683000
H -5.88911800   0.98780100   1.70072100
C  2.94880700   0.64140800   0.47531700
C  3.38820300  -0.48987400  -0.20036700
C  3.84611300   1.66548900   0.73107900
C  4.70724700  -0.58890200  -0.60342600
H  2.69934300  -1.28616600  -0.39556000
C  5.16799300   1.56495000   0.32930100
H  3.50991200   2.54929500   1.23940000
C  5.60188400   0.43590300  -0.34030100
H  5.03848500  -1.46660600  -1.12360300
H  5.85088000   2.36640800   0.53308000
H  6.62351100   0.35502000  -0.65597800
C  1.32638800  -0.00185700   2.28651200
H  1.55039100  -1.05096000   2.14604600
H  0.29993400   0.09540400   2.62150100
H  1.98749000   0.39998700   3.04459900
H  1.24716200   1.79090600   1.08048900
 SCF:  E(RHF) =  -1135.42162748
 Sum of electronic and zero-point
Energies= -1135.042386
 Sum of electronic and thermal Energies=
-1135.019816
 Sum of electronic and thermal
Enthalpies= -1135.018872
 Sum of electronic and thermal Free
Energies= -1135.097182
```

(S)-TS_{HF}-**d**

```
 C -0.13510400   1.62373100  -0.77456600
O  0.69289200   0.28871000  -0.02051400
C  1.67131200   0.65979000   0.96668500
O -0.16855600   2.57966100   0.03309100
C  0.69480600   1.71245400  -2.04132800
O  0.35752300  -2.07350800  -0.12613900
C -0.72460200  -2.70523900   0.22462200
O -1.84514000  -2.20141000   0.25547300
C -0.48869400  -4.15808700   0.58083600
H  1.65658300   2.11720100  -1.76588500
H  0.21407400   2.39780100  -2.73054300
H  0.84607100   0.75442800  -2.50964200
H  0.01762000  -4.64948000  -0.24061100
H -1.42480200  -4.64779800   0.79773000
H  0.16704200  -4.20886400   1.44207000
H  0.45380700  -0.87137400  -0.08835000
N -1.40436300   0.91593700  -1.00787800
C -2.42819400   0.94840700  -0.16266300
C -1.59582300  -0.11592600  -2.05278900
C -2.61173900   1.71034500   1.01353300
N -3.41326400   0.12631400  -0.55862400
C -3.03668500  -0.63172700  -1.78261300
H -1.51034300   0.32705300  -3.03159800
H -0.86866400  -0.89719100  -1.92146100
C -3.76396700   1.54404800   1.70860200
H -1.82440400   2.37270300   1.28189100
C -4.55316300  -0.05922900   0.14890700
H -3.72232800  -0.38259400  -2.57758500
H -3.03806600  -1.67699100  -1.54235300
C -4.76800000   0.63891200   1.28215500
H -3.91743300   2.10821700   2.60621800
H -5.24169700  -0.77466600  -0.24479000
H -5.66569800   0.50237100   1.84410200
C  3.08004400   0.38034300   0.47399100
C  4.10328400   1.27468100   0.74132700
C  3.36642900  -0.78529700  -0.22554900
C  5.39885400   1.01285700   0.32536700
H  3.88770100   2.18296200   1.27172200
C  4.65868400  -1.04605000  -0.64158300
H  2.57994600  -1.48407400  -0.42664500
C  5.67948100  -0.14916800  -0.36860000
H  6.18075500   1.71538600   0.53839000
H  4.87136800  -1.94971200  -1.17902100
H  6.68016200  -0.35478300  -0.69462600
C  1.38758000  -0.10223700   2.27122000
H  1.46412000  -1.16691600   2.09682700
H  0.38400200   0.12481200   2.61329100
H  2.09772000   0.18396700   3.03742800
H  1.53508700   1.71851400   1.12836400
 SCF:  E(RHF) = -1135.40982363
 Sum of electronic and zero-point
Energies= -1135.042719
 Sum of electronic and thermal Energies=
-1135.020304
 Sum of electronic and thermal
Enthalpies= -1135.019359
 Sum of electronic and thermal Free
Energies= -1135.096648
```

(S)-TS_{HF}-**e**

```
 C  0.53970800   0.56409100   1.02767100
O -0.60050200  -0.01916700  -0.25240100
C -1.29130600   1.01230000  -0.97772700
O  0.53931800   1.80339700   1.02639500
C -0.03654000  -0.25682400   2.15628400
O -1.48218700  -2.22741500  -0.61780200
C -1.19877000  -3.28679400   0.06620500
O -0.28095900  -3.37552000   0.89073500
C -2.10116700  -4.47218600  -0.21991000
H -1.01432900   0.14209300   2.38139400
H  0.60104100  -0.12398200   3.02435700
H -0.11719900  -1.30411200   1.92212500
H -3.11402700  -4.22439600   0.07609900
H -1.75928800  -5.33983400   0.32140200
H -2.11192000  -4.66437400  -1.28536800
H -0.98806900  -1.07944600  -0.39451600
N  1.75185800  -0.07099700   0.44680300
C  2.88417100   0.56936400   0.22146600
C  1.77971300  -1.42511900  -0.16730600
C  3.24369600   1.92623600   0.43079600
N  3.82387100  -0.27167200  -0.27278700
C  3.29444200  -1.66760400  -0.33332400
H  1.28075100  -2.15772900   0.44247100
H  1.27906100  -1.36504700  -1.11967400
C  4.50787800   2.30837700   0.13481600
H  2.48369500   2.57632500   0.79214200
```

```
C  5.09228400   0.11678000  -0.56782600
H  3.71363500  -2.23051600   0.48794000
H  3.54775400  -2.12179600  -1.27732600
C  5.46927900   1.39516300  -0.37928300
H  4.79079700   3.33086400   0.28321400
H  5.74151300  -0.64249100  -0.94777000
H  6.46180800   1.71194100  -0.61370800
C -2.68801800   1.26495500  -0.43216300
C -3.50865400   0.21633700  -0.03994800
C -3.16936800   2.56194300  -0.35410200
C -4.78998700   0.46931900   0.41603900
H -3.14567900  -0.78851300  -0.10450200
C -4.45280000   2.81522800   0.09907800
H -2.53450900   3.37979800  -0.63735300
C -5.26763200   1.76722800   0.48658600
H -5.41659600  -0.34783200   0.71642100
```

(S)-**TS_{HF}-f**

```
C -0.43331000   1.73760600  -0.88557500
O  0.50673400   0.49827900  -0.03350100
C  1.50207800   0.99951000   0.87501100
O -0.57710800   2.71530500  -0.12727400
C  0.41119400   1.84034800  -2.13877600
O -0.05127100  -1.82070500  -0.30072200
C  0.19674000  -2.81632700   0.51954200
O  0.55161200  -2.70226200   1.67921800
C -0.00997200  -4.17927700  -0.12137600
H  1.32485900   2.34882300  -1.87126000
H -0.11875400   2.44489200  -2.86659200
H  0.66079500   0.88244000  -2.56023700
H -1.03929900  -4.28072500  -0.44747800
H  0.22958100  -4.95781800   0.58511500
H  0.62120900  -4.25982700  -0.99796400
H  0.24287000  -0.64317700  -0.05187600
N -1.60555500   0.86935700  -1.08201800
C -2.60878300   0.80354400  -0.21640600
C -1.67160200  -0.22745100  -2.07827400
C -2.94739800   1.66475000   0.85334700
N -3.38955000  -0.26772100  -0.45524800
C -2.79776300  -1.13114800  -1.51996600
H -1.91056600   0.17558300  -3.05070300
H -0.75004000  -0.77610300  -2.08230300
C -4.05383400   1.37538300   1.58074300
H -2.29834100   2.48949200   1.02652000
C -4.49645200  -0.55877300   0.27633300
H -3.54951900  -1.38911800  -2.24755800
H -2.35902600  -1.99413400  -1.05025400
H -4.80989300   3.82492600   0.15621800
H -6.26106900   1.95871300   0.84205000
C -1.35181900   0.61505100  -2.46137300
H -1.88041100  -0.32402900  -2.56383200
H -0.34721300   0.49200200  -2.85240500
H -1.86340400   1.37635000  -3.03751200
H -0.70257000   1.90635000  -0.84126700
 SCF:  E(RHF) =  -1135.40523051
 Sum of electronic and zero-point
Energies= -1135.038056
 Sum of electronic and thermal Energies=
-1135.015641
 Sum of electronic and thermal
Enthalpies= -1135.014697
 Sum of electronic and thermal Free
Energies= -1135.092233
```

```
C -4.86259900   0.24441100   1.29419400
H -4.32536300   2.01657100   2.39457600
H -5.03040100  -1.44066300  -0.00477800
H -5.73243800   0.02607600   1.87400400
C  2.89875600   0.62672000   0.40445700
C  3.99291400   1.36044800   0.83950400
C  3.10634200  -0.44748200  -0.44600100
C  5.27392600   1.02365600   0.44123400
H  3.84204700   2.20139100   1.49009300
C  4.38796300  -0.78690600  -0.84388000
H  2.26581900  -1.01473100  -0.78443100
C  5.47584200  -0.05443300  -0.40340700
H  6.10969400   1.60123100   0.78506400
H  4.53671200  -1.62439100  -1.49749900
H  6.46754000  -0.31837400  -0.71413500
C  1.22192300   0.46860200   2.29071200
H  1.18886000  -0.61104700   2.28766400
H  0.26044500   0.84512400   2.62436200
H  1.98602500   0.80870900   2.97956100
H  1.38749400   2.07430300   0.87071700
 SCF:  E(RHF) =  -1135.42244652
 Sum of electronic and zero-point
Energies= -1135.034122
 Sum of electronic and thermal Energies=
-1135.011607
 Sum of electronic and thermal
Enthalpies= -1135.010663
 Sum of electronic and thermal Free
Energies= -1135.088984
```

(c) Transition state geometries of N-Acetyl-(R)-CF_3-PIP^+ AcO^- and N-Propionyl-(R)-CF_3-PIP^+ $EtCO_2^-$ with (R)- and (S)-1-phenylethanol at B3LYP/6-31G* level of theory

C1. The lowest-energy stacked and splayed conformers of (R)-**TS_{HF}** (structures (R)-**TS_{HF}-a** and (R)-**TS_{HF}–h**, respectively) and the lowest-energy stacked and splayed conformers of (S)-**TS_{HF}** (structures (S)-**TS_{HF}-a** and (S)-**TS_{HF}–c**, respectively), obtained as described in the preceeding section, were transformed into (R)-CF_3-PIP derivatives by attaching a trifluoromethyl group at C6 and a phenyl group to the α–face of C2. The resulting structures **7a**, **7b**, **8a**, and **8b** were optimized at B3LYP/6-31G* level of theory.

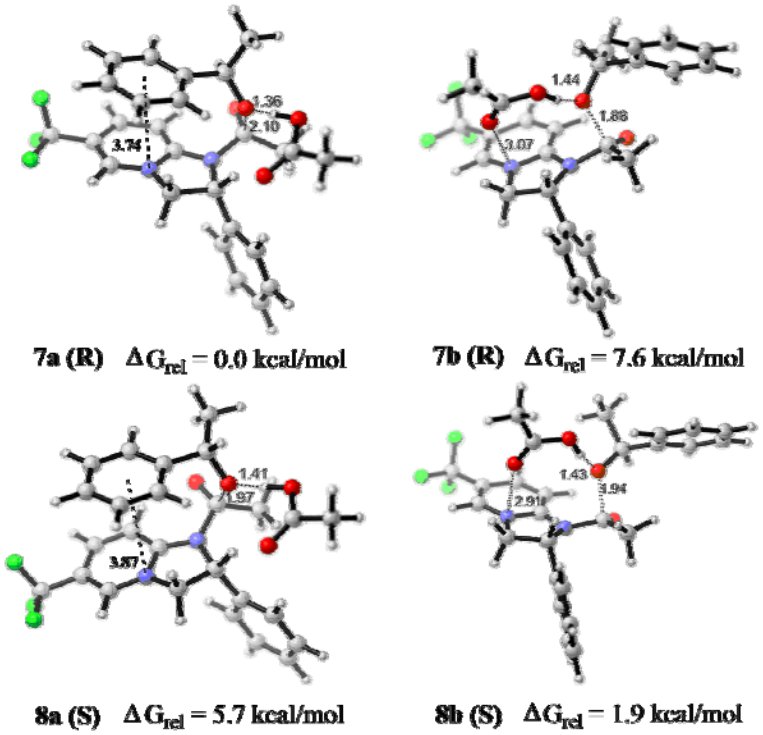


Figure S-6. TS of Ac-CF_3-PIP acetate and 1-phenylethanol

7a

```
C 1.22172300  -0.08562300  -2.16872300
 O  1.40547200   1.66425700  -1.02803700
 C  0.36668800   2.55304800  -1.30250200
 O  0.50007500   0.16743400  -3.12131200
 C  2.71584700  -0.26472000  -2.28734100
 O  3.51382000   2.56000400  -0.11778500
 C  3.86119000   2.01956200   1.02159500
 O  3.24256600   1.12161800   1.60372500
 C  5.13900100   2.60688200   1.59580400
 H  3.07383500   0.48996500  -2.98831800
 H  2.92236500  -1.26054700  -2.69991200
 H  3.24852200  -0.15612000  -1.34369400
 H  5.95957600   2.48225400   0.88103400
 H  5.39078800   2.11974000   2.53933600
 H  5.01362900   3.68326400   1.75502500
 H  2.56792400   2.16060800  -0.51399100
 N  0.59882900  -0.79730700  -1.02005000
 C -0.73081900  -0.88541600  -0.88146800
 C  1.29179000  -0.98975800   0.28268300
 C -1.76898400  -0.83901600  -1.84974500
 N -1.07894100  -1.07023200   0.43156900
 C  0.11761100  -1.03778700   1.29978200
 H  1.89036500  -0.09990900   0.48880000
 C -3.06870500  -0.95643300  -1.42331600
 H -1.49512800  -0.69173000  -2.88285700
 C -2.35703400  -1.17780500   0.85679300
 H  0.14253700  -1.93198900   1.92597200
 H  0.07300900  -0.13953900   1.91955700
 C -3.38342400  -1.12266600  -0.04995400
 H -3.87489800  -0.92618700  -2.14975000
 H -2.50599400  -1.29786100   1.92204100
 C -0.67356700   2.58109400  -0.17459900
 C -2.04379400   2.66713200  -0.45268600
 C -0.27246500   2.51762700   1.16889900
 C -2.99260000   2.68855700   0.57378600
 H -2.37213700   2.71241800  -1.48975600
 C -1.21514500   2.55083600   2.19928900
 H  0.78524100   2.42249900   1.39863000
 C -2.58051800   2.63166400   1.90648900
 H -4.05176100   2.73933200   0.33271100
 H -0.88310300   2.51723200   3.23502500
 H -3.31399100   2.65488200   2.70879500
 C  0.89361000   3.97390300  -1.58964000
 H  1.60151200   3.93764300  -2.42467200
 H  1.41643100   4.37782100  -0.71578300
 H  0.07643600   4.65743200  -1.84983800
 H -0.15205400   2.21029300  -2.21780600
 C  2.16081100  -2.23538300   0.32696500
 C  3.33800200  -2.20089100   1.08704700
 C  1.79778400  -3.42279100  -0.32093500
 C  4.13158200  -3.34357500   1.20243500
 H  3.62755300  -1.27262300   1.57374500
 C  2.59647700  -4.56144700  -0.20883500
 H  0.89909000  -3.45536600  -0.93188500
 C  3.76405400  -4.52513000   0.55625200
 H  5.04432200  -3.30623600   1.79117000
 H  2.30866700  -5.47522500  -0.72206100
 H  4.38684400  -5.41151600   0.64220900
 C -4.81269200  -1.18544600   0.40105300
 F -4.91140100  -1.52347800   1.70405700
 F -5.51046200  -2.09181100  -0.31735400
 F -5.43289400   0.00275900   0.23864400
 SCF:  E(RB+HF-LYP) =  -1716.95136698
 Sum of electronic and zero-point
Energies= -1716.465171
 Sum of electronic and thermal Energies=
-1716.432162
 Sum of electronic and thermal
Enthalpies= -1716.431218
 Sum of electronic and thermal Free
Energies= -1716.533805
```

7b

```
C -1.17952000  -0.34495300   1.17291700
 O -1.23260900   1.04727700  -0.08619600
 C -1.94405900   2.25787700   0.16862900
 O -1.09808100   0.10428300   2.31338800
 C -2.36296000  -1.17459000   0.70867900
 O -1.38259900   0.90570300  -2.57462500
 C -0.25276100   0.73386900  -3.22731300
 O  0.80574900   0.37018900  -2.71742600
 C -0.37966400   1.03587600  -4.70894700
 H -3.26676400  -0.64775800   1.01287000
 H -2.33952600  -2.14700400   1.21303500
 H -2.39565500  -1.32525100  -0.37144600
 H -1.25329200   0.52679300  -5.12787700
 H  0.52562600   0.73121800  -5.23671100
 H -0.53607000   2.11158200  -4.84903200
 H -1.26270500   0.86405300  -1.50916500
 N  0.14850200  -0.87607500   0.58557900
 C  1.26229700  -0.15124700   0.69513900
 C  0.27204100  -1.86837300  -0.50789600
 C  1.56244700   0.93554700   1.55993300
 N  2.23366900  -0.57753800  -0.16918700
 C  1.75802400  -1.72878000  -0.95569200
 H -0.37162800  -1.55546900  -1.33330400
 C  2.79463000   1.52781500   1.46137300
 H  0.80014000   1.23854500   2.26168000
 C  3.44818600   0.00607600  -0.27710600
 H  2.34817500  -2.61108900  -0.69231700
 H  1.84180700  -1.49671800  -2.01635700
 C  3.76312200   1.06994300   0.52658700
 H  3.04003900   2.36509000   2.10759100
 H  4.12194400  -0.40708700  -1.01651900
 C -3.44879900   2.06016700   0.36987800
 C -4.29947200   2.13894900  -0.74138600
 C -4.01947500   1.79907800   1.62434000
 C -5.67897600   1.97195900  -0.60967800
 H -3.86871600   2.32727900  -1.72255100
 C -5.39894200   1.63023400   1.76077900
 H -3.37881000   1.70342000   2.49548100
 C -6.23485300   1.72040100   0.64557900
 H -6.31898400   2.04306700  -1.48599900
 H -5.82210600   1.42943700   2.74224900
 H -7.30939200   1.59590600   0.75470000
 C -1.29296700   3.09623500   1.27835400
 H -0.24380300   3.27985700   1.02228000
 H -1.32684800   2.59009100   2.24518800
 H -1.79773800   4.06544500   1.37184400
 H -1.84584200   2.84216200  -0.76057100
 C -0.06132800  -3.29127900  -0.09183800
 C -0.62188300  -4.16672500  -1.02824700
 C  0.24194700  -3.76703400   1.19004100
 C -0.86796700  -5.49965200  -0.69452300
 H -0.87302100  -3.80269900  -2.02215600
 C -0.01081100  -5.09698200   1.52634800
 H  0.65172500  -3.08742900   1.93221000
 C -0.56213400  -5.96791400   0.58395000
 H -1.30673700  -6.16781300  -1.43048500
 H  0.21868800  -5.45164400   2.52752700
 H -0.75961600  -7.00322800   0.84785300
 C  5.10507100   1.73288300   0.44213100
 F  5.78466500   1.61258300   1.60494600
 F  4.98671200   3.05461500   0.19725200
 F  5.86941000   1.19820800  -0.53420600
 SCF:  E(RB+HF-LYP) =  -1716.93686151
 Sum of electronic and zero-point
Energies= -1716.451349
 Sum of electronic and thermal Energies=
-1716.418392
 Sum of electronic and thermal
Enthalpies= -1716.417448
 Sum of electronic and thermal Free
Energies= -1716.521745
```

8a

```
C  1.09911100   0.31842000  -2.00114400
 O  1.90713200   1.62241100  -0.75796000
 C  1.40158400   2.93932300  -0.66978600
 O  0.35396400   0.85776500  -2.81028700
 C  2.44093500  -0.26639800  -2.39059900
 O  4.19361100   1.66188100   0.20962900
 C  4.27779800   1.09663800   1.39176500
 O  3.36980600   0.47648000   1.94994800
 C  5.64267500   1.27277600   2.03195000
 H  2.93953800   0.46198800  -3.03125100
 H  2.26932300  -1.18564000  -2.96454500
 H  3.08471700  -0.49453000  -1.54145200
 H  6.41682500   0.85886900   1.37688500
 H  5.67214600   0.77606200   3.00304600
 H  5.86146800   2.33910700   2.15295800
 H  3.20443100   1.58798700  -0.21343300
 N  0.41324200  -0.45050100  -0.89807300
 C -0.91294100  -0.48051400  -0.75114400
 C  1.09697300  -0.99952500   0.30164900
 C -1.96344000  -0.19292200  -1.66753900
 N -1.25818500  -0.90689800   0.50937900
 C -0.04775100  -1.03926800   1.34831600
 H  1.85096100  -0.28347000   0.63274200
 C -3.25888900  -0.38162200  -1.26000400
 H -1.69446500   0.16786700  -2.64824900
 C -2.53475100  -1.08852600   0.91573500
 H -0.07644200  -1.97526600   1.90830400
 H -0.00736400  -0.18736200   2.03165700
 C -3.56649900  -0.84134900   0.04930900
 H -4.07097500  -0.17931300  -1.95161700
 H -2.67687500  -1.42780600   1.93387800
 C  0.04033600   2.95681100   0.03477800
 C -1.16036000   3.30534700  -0.59237600
 C -0.00238800   2.60218800   1.39420400
 C -2.36897800   3.30129000   0.11294700
 H -1.15716900   3.58552600  -1.64104400
 C -1.20313600   2.60122800   2.10373600
 H  0.92679100   2.32942400   1.89131300
 C -2.39711900   2.95022100   1.46223300
 H -3.28902200   3.58163700  -0.39489300
 H -1.20770500   2.34749500   3.16201300
 H -3.33439700   2.96121900   2.01316300
 C  1.44643300   3.68329100  -2.01198500
 H  0.82072700   3.20107700  -2.76533400
 H  2.47816200   3.67390900  -2.37885600
 H  1.13514300   4.72918200  -1.89662400
 H  2.08424600   3.48160300   0.00960800
 C  1.72354300  -2.36755700   0.07609200
 C  2.87243700  -2.69909800   0.80760700
 C  1.16114300  -3.32075000  -0.78169200
 C  3.44145900  -3.96778600   0.68641500
 H  3.31627000  -1.95352900   1.46270900
 C  1.73510100  -4.58691100  -0.90527500
 H  0.28308800  -3.07121200  -1.37189000
 C  2.87513800  -4.91461800  -0.16903600
 H  4.33465800  -4.21265400   1.25505800
 H  1.29307700  -5.31566700  -1.57961500
 H  3.32281200  -5.89993000  -0.26701800
 C -4.99214000  -1.05310400   0.46230600
 F -5.58907000  -1.99251700  -0.30427600
 F -5.08768700  -1.45264700   1.74853100
 F -5.71647700   0.07754100   0.32596000
```

```
 SCF:  E(RB+HF-LYP) =  -1716.94617282
 Sum of electronic and zero-point
Energies= -1716.455704
 Sum of electronic and thermal Energies=
-1716.422755
```

```
 Sum of electronic and thermal
Enthalpies= -1716.421811
 Sum of electronic and thermal Free
Energies= -1716.524792
```

8b

```
 C -1.09469100  -0.60372600   1.32372900
 O -1.33955400   0.89567300   0.11870500
 C -2.02215800   1.95099000   0.75258200
 O -0.99138400  -0.16073000   2.46395900
 C -2.28818700  -1.42550800   0.88110200
 O -1.22502800   1.22765600  -2.35349500
 C -0.08657900   1.00776000  -2.97017000
 O  0.89939700   0.47621800  -2.46021000
 C -0.09775900   1.48193200  -4.41143900
 H -3.17877200  -0.89483500   1.22014600
 H -2.25927700  -2.40771700   1.36690700
 H -2.35273600  -1.55551000  -0.19988300
 H -0.96908900   1.07684000  -4.93594000
 H  0.82046300   1.17912300  -4.91742000
 H -0.18644000   2.57373400  -4.43716300
 H -1.20628800   1.02697700  -1.29527000
 N  0.20729500  -1.01241500   0.66046700
 C  1.28404700  -0.22697200   0.76350500
 C  0.33409900  -1.92668200  -0.50040700
 C  1.53600800   0.87241500   1.62616200
 N  2.25773800  -0.59264400  -0.12276900
 C  1.82256800  -1.75281700  -0.91869200
 H -0.30270200  -1.54849600  -1.30430900
 C  2.73542100   1.52827100   1.51197800
 H  0.76941900   1.13555800   2.33990400
 C  3.43654900   0.05448400  -0.24848700
 H  2.42716500  -2.62205300  -0.64314800
 H  1.92399900  -1.52096700  -1.97752300
 C  3.71161900   1.12502500   0.56175400
 H  2.94475900   2.37734400   2.15542200
 H  4.11536600  -0.31374100  -1.00658400
 H -1.82349400   1.86900200   1.83345200
 C -1.46389100   3.30492700   0.27420100
 H -0.38203300   3.34293900   0.44768700
 H -1.93477600   4.13720700   0.81071300
 H -1.64372900   3.44411300  -0.79726600
 C -3.54258300   1.89561600   0.57546000
 C -4.38581900   2.12000700   1.67109600
 C -4.12871500   1.64752800  -0.67462900
 C -5.77537100   2.10752200   1.52866600
 H -3.94648800   2.30068500   2.65028800
 C -5.51609100   1.63251800  -0.82076000
 H -3.49375600   1.46396200  -1.53607600
 C -6.34614000   1.86340100   0.27928800
 H -6.40984500   2.28094600   2.39476400
 H -5.95246000   1.43898600  -1.79819500
 H -7.42709800   1.84903100   0.16334300
 C -0.00308200  -3.37575600  -0.19922000
 C -0.63533400  -4.15082900  -1.17701600
 C  0.36301500  -3.97325400   1.01365200
 C -0.89290500  -5.50428200  -0.95213200
 H -0.93377900  -3.69207100  -2.11710800
 C  0.09893000  -5.32342100   1.24205300
 H  0.83300400  -3.37341000   1.78862800
 C -0.52632600  -6.09339900   0.25832300
 H -1.38767600  -6.09375000  -1.71909200
 H  0.37714600  -5.77327600   2.19120300
 H -0.73294700  -7.14475800   0.43821300
 C  5.01816800   1.85416700   0.46287100
 F  5.78996300   1.36848300  -0.53296400
 F  4.83168600   3.17110500   0.23706600
 F  5.72286500   1.75258000   1.61233600
 SCF:  E(RB+HF-LYP) =  -1716.94706510
 Sum of electronic and zero-point
Energies= -1716.460356
 Sum of electronic and thermal Energies=
-1716.427306
 Sum of electronic and thermal
Enthalpies= -1716.426362
 Sum of electronic and thermal Free
Energies= -1716.530767
```

C2. The optimized TS structures of N-Acetyl-(R)-CF_3-PIP Acetate with (R)- and (S)-1-phenylethanol**, 7a** and **8b**, respectively, obtained as described above, were transformed into the analogous TS structures of N-Propionyl-(R)-CF_3-PIP Propionate, **9a** and **10b**, respectively, and re-optimized at B3LYP/6-31G* level of theory.

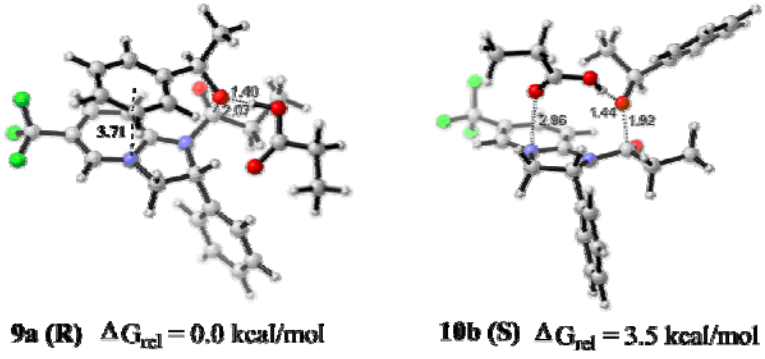


Figure S-7. TS of EtCO-CF_3-PIP propionate and 1-phenylethanol

9a (R)

C	0.88380300	-0.30262000	-2.16432000
O	1.23932400	1.44568700	-1.10704200
C	0.24892200	2.39459000	-1.35789400
O	0.16164200	-0.02011100	-3.10916500
C	2.35215000	-0.65846800	-2.30811900
O	3.45626800	2.21616200	-0.30443500
C	3.83015600	1.67002600	0.82748500
O	3.17662300	0.83690700	1.46241500
C	5.18438900	2.17672600	1.30909800
H	2.87953700	-0.53784900	-1.36027400
H	2.38641300	-1.72993700	-2.55695000
H	5.10018400	3.26508400	1.42756400
H	5.90085100	2.03087700	0.49059700
H	2.47939400	1.87917300	-0.63234500
N	0.21977800	-0.92741700	-0.97771100
C	-1.10960300	-0.89971300	-0.82076500
C	0.91168300	-1.13338400	0.32431300
C	-2.15456500	-0.80501400	-1.77931400
N	-1.45514300	-1.00529700	0.50229000
C	-0.24894100	-1.04824800	1.35558800
H	1.58892500	-0.29291300	0.48791000
C	-3.45325600	-0.79184800	-1.33517200
H	-1.88419200	-0.72635900	-2.82082400
C	-2.73174400	-0.98314900	0.94475900
H	-0.29105600	-1.92239500	2.00864700
H	-0.21051400	-0.13164700	1.94796400
C	-3.76202900	-0.87281300	0.04763200
H	-4.26395700	-0.72281600	-2.05386600
H	-2.87570700	-1.04800300	2.01548900
C	-0.71975200	2.53891600	-0.17693300
C	-2.09301100	2.72497500	-0.38387800
C	-0.24895100	2.49387100	1.14435400
C	-2.97731400	2.85815200	0.69050500
H	-2.47524000	2.76001800	-1.40270100
C	-1.12591200	2.63863400	2.22211800
H	0.81006900	2.32731900	1.32096400
C	-2.49545000	2.81560200	2.00038700
H	-4.04147900	2.98295600	0.50503900
H	-0.73889400	2.61695700	3.23886100
H	-3.17793500	2.92589800	2.83959200
C	0.85367500	3.76422200	-1.72973900
H	1.49876300	3.65264300	-2.60795400
H	1.46050600	4.15767800	-0.90678100
H	0.07062100	4.49645500	-1.96113800
H	-0.34350100	2.05775100	-2.22918500
C	1.66823000	-2.44907000	0.40736700
C	2.87006700	-2.48582100	1.12695300
C	1.17282600	-3.63003100	-0.16028800
C	3.55776400	-3.69094300	1.28211000
H	3.26255300	-1.56470200	1.55060000
C	1.86556300	-4.83163000	-0.00870900
H	0.25270100	-3.61077200	-0.73924900
C	3.05853500	-4.86525600	0.71644700
H	4.49074000	-3.70892600	1.83917900
H	1.47541800	-5.74021000	-0.45980000
H	3.59864400	-5.80094500	0.83350400
C	-5.18334500	-0.78153200	0.51793800
F	-5.29650200	-1.08385500	1.82858000
F	-5.98116400	-1.62381900	-0.17345200
F	-5.68203200	0.46130900	0.34164200
C	5.66963900	1.51827300	2.59846600
H	4.95042400	1.66742600	3.40955200
H	6.63316400	1.93766900	2.90852000
H	5.79309400	0.43836800	2.46742600
C	3.02617200	0.16158300	-3.40743700
H	2.48135600	0.06852700	-4.35099100
H	4.05452800	-0.18299500	-3.55970300
H	3.05036000	1.21659500	-3.12452300

SCF: E(RB+HF-LYP) = -1795.58450359
Sum of electronic and zero-point Energies= -1795.036948
Sum of electronic and thermal Energies= -1795.001259
Sum of electronic and thermal Enthalpies= -1795.000315
Sum of electronic and thermal Free Energies= -1795.109207

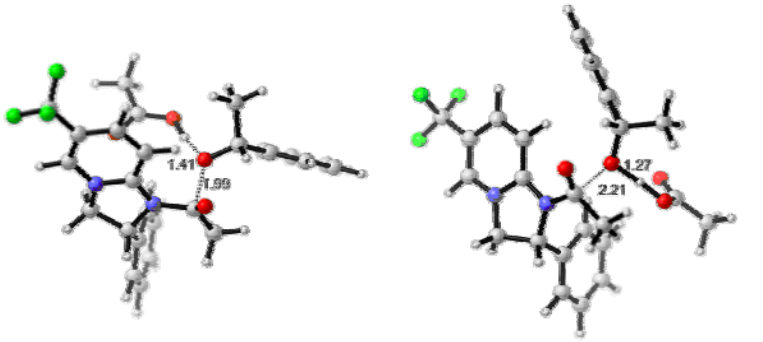
10b (S)

C	-1.01837700	-0.84723800	1.48109400
O	-1.60100200	0.41493500	0.16229300
C	-2.09813100	1.60129500	0.73093500
O	-0.98726700	-0.29062200	2.57599600
C	-2.00093800	-1.96954600	1.16871700
O	-1.39766600	0.52383000	-2.32700300
C	-0.22708100	0.80327200	-2.86311000
O	0.84230100	0.79373900	-2.25495500
C	-0.32809100	1.14814100	-4.34284500
H	-2.10651200	-2.10363700	0.08938800
H	-1.56873600	-2.89477100	1.57322500
H	-0.97865100	0.40455600	-4.81924000
H	-0.87552300	2.09802200	-4.41258700
H	-1.38536400	0.46737600	-1.25594800
N	0.34999100	-1.07360800	0.82629100
C	1.33288200	-0.17870200	0.98097700
C	0.57190000	-1.88530300	-0.39963100
C	1.49442700	0.85738100	1.94086300
N	2.31632500	-0.34147800	0.04307000
C	1.99918300	-1.46342800	-0.85438100
H	-0.15622900	-1.56809200	-1.15007500
C	2.60908000	1.65442000	1.86506700
H	0.72209000	0.97194700	2.68665500
C	3.41120000	0.44388300	-0.04253600
H	2.72790300	-2.26383000	-0.69736600
H	2.01742000	-1.11144000	-1.88446600
C	3.59299100	1.45835300	0.86082800
H	2.74297800	2.45417500	2.58717900
H	4.10276400	0.22635700	-0.84595400
H	-1.89521500	1.55646700	1.81323300
C	-1.36665200	2.83559700	0.16358300
H	-0.28399500	2.72496200	0.29082100
H	-1.68921600	3.75290400	0.67040300
H	-1.57582300	2.95217400	-0.90556800
C	-3.61049100	1.76701000	0.56154600
C	-4.36615600	2.37793300	1.57082600
C	-4.26778600	1.36110600	-0.60810500
C	-5.73799000	2.58754100	1.41953400
H	-3.87260700	2.68762700	2.49036300
C	-5.63984300	1.56659300	-0.76224700
H	-3.69998700	0.88055200	-1.39861500
C	-6.38101700	2.18170700	0.24907000
H	-6.30491100	3.05958800	2.21862400
H	-6.13282600	1.24376600	-1.67652300
H	-7.45002600	2.33861400	0.12804100
C	0.48176400	-3.38778800	-0.19463500
C	-0.12256400	-4.17935800	-1.17633400
C	1.05437200	-4.00798100	0.92348600
C	-0.15293900	-5.56934400	-1.04786000
H	-0.57892700	-3.70587300	-2.04270900
C	1.01803800	-5.39551100	1.05656900
H	1.50898700	-3.40154000	1.70286000
C	0.41683100	-6.18039500	0.06927700
H	-0.62924400	-6.17137300	-1.81673100
H	1.45538800	-5.86415700	1.93395200
H	0.38791000	-7.26132700	0.17466500
C	4.79891400	2.34742200	0.79396200
F	5.63451600	1.98417400	-0.20248300
F	4.45248500	3.63541400	0.59304300

```
F  5.49749100   2.30758900   1.95061300
C  1.02459000   1.24778100  -5.04458000
H  1.66310200   1.98946000  -4.55604800
H  0.89706400   1.53596200  -6.09354000
H  1.55577200   0.28997700  -5.01842900
C -3.36411000  -1.72106600   1.81364900
H -3.25453500  -1.55677100   2.88921100
H -4.01707500  -2.58661100   1.65592300
H -3.84556700  -0.84174800   1.38021300
```

```
 SCF:  E(RB+HF-LYP) =  -1795.57744074
 Sum of electronic and zero-point
Energies= -1795.029728
 Sum of electronic and thermal Energies=
-1794.993985
 Sum of electronic and thermal
Enthalpies= -1794.993041
 Sum of electronic and thermal Free
Energies= -1795.103606
```

C3. The geometries of the transition states of (R)- and (S)-1-phenylethanol approaching N-acetyl-(R)-CF_3-PIP acetate from the α-face were optimized at B3LYP/6-31G* level.



11 (R) $\Delta G_{rel} = 6.6$ kcal/mol **12 (S)** $\Delta G_{rel} = 10.1$ kcal/mol

Figure S-8. Substrate approaching N-acetyl-(R)-CF_3-PIP acetate from the α-face

11 (R)

```
C  0.88845700  -0.01791200   -1.87078400
O  1.21415200  -1.01694800   -0.18264600
C  1.87615700  -2.23042900   -0.43026800
O  0.56487800  -0.84048200   -2.71802800
C  2.20110300   0.72968200   -1.93279200
O  0.71526600  -0.70724700    2.23603800
C -0.41824700  -0.17232800    2.63029200
O -1.23167900   0.38796100    1.89549600
C -0.64214800  -0.30914900    4.12550700
H  2.95430700   0.01416000   -2.26662000
H  2.13715300   1.52954800   -2.68327700
H  2.50392000   1.14993500   -0.97747100
H  0.24603800   0.01988700    4.67399900
H -1.51302900   0.27208000    4.43332600
H -0.80142300  -1.36418000    4.37564800
H  0.85619100  -0.77824900    1.16097500
N -0.24280800   0.74667600   -1.21434800
C -1.40949900   0.13377700   -0.99829700
C -0.42048000   2.22514000   -1.15578300
C -1.75650300  -1.23885400   -1.10964600
N -2.38277700   1.02173700   -0.63116000
C -1.78162200   2.34738700   -0.42274900
C -3.03747800  -1.61207300   -0.79618500
H -1.00534100  -1.93158600   -1.45174300
C -3.63347800   0.65281600   -0.27155100
H -2.41626000   3.13532200   -0.83325700
H -1.63907900   2.48408700    0.65179800
C -4.00174000  -0.66219400   -0.36122600
H -3.32463000  -2.65619800   -0.87387600
H -4.29587000   1.43958400    0.06524900
H  1.71564700  -2.48901800   -1.49141100
C -5.39391200  -1.09947300   -0.01798700
F -6.02389800  -1.62382800   -1.09332900
F -5.38844100  -2.05641000    0.93309400
F -6.14607700  -0.07225600    0.43354700
H -0.52562000   2.58822700   -2.18789100
C  0.65377700   3.04485200   -0.46800200
C  1.05569800   4.25145900   -1.05010800
C  1.19826100   2.66124700    0.76487900
C  1.98582700   5.07303700   -0.41021000
H  0.64301000   4.55099000   -2.01141800
C  2.13579900   3.47704600    1.39626800
H  0.91332200   1.71293200    1.20589200
C  2.52816000   4.68582600    0.81488100
H  2.29049800   6.00715100   -0.87396800
H  2.56513900   3.16409200    2.34391700
H  3.25891000   5.31801800    1.31179900
C  3.38789100  -2.14379500   -0.20443900
C  4.27439800  -2.81421200   -1.05631900
C  3.91798800  -1.41840900    0.87132900
C  5.65369800  -2.77144000   -0.84045700
H  3.87879100  -3.37346300   -1.90254700
C  5.29493400  -1.37366900    1.09147400
H  3.24226200  -0.88687800    1.53488400
C  6.16943300  -2.04980000    0.23682100
H  6.32419000  -3.29603100   -1.51727300
H  5.68854400  -0.80708400    1.93252200
H  7.24251000  -2.01093700    0.40726700
C  1.27443500  -3.37166800    0.41582300
H  0.19940000  -3.46089300    0.21781800
H  1.75167600  -4.33010800    0.18000600
H  1.40818200  -3.17529600    1.48469000
 SCF:  E(RB+HF-LYP) =  -1716.94405748
 Sum of electronic and zero-point
Energies= -1716.454481
 Sum of electronic and thermal Energies=
-1716.421393
 Sum of electronic and thermal
Enthalpies= -1716.420449
 Sum of electronic and thermal Free
Energies= -1716.523277
```

12 (S)

```
 C  0.97758200  -0.19313800   2.49901400
 O  1.38021000   1.19955100   0.83692700
 C  0.98671700   2.50328300   1.18075600
 O  0.27738500   0.47427700   3.23646400
 C  2.43381400  -0.50798200   2.72631800
 O  3.68448700   1.01737900   0.08547400
 C  3.90273200   1.15299200  -1.19638300
 O  3.03924900   1.34274900  -2.05703200
 C  5.37473500   1.02600800  -1.57014300
 H  2.89076400   0.37063900   3.18211500
 H  2.52147500  -1.34322300   3.43647000
 H  2.96782100  -0.74554500   1.80622100
 H  5.71237000   0.00015600  -1.37998900
 H  5.52202000   1.26659600  -2.62495800
 H  5.98403000   1.68696400  -0.94519100
 H  2.56848300   1.13552400   0.38480000
 N  0.27802800  -1.16429100   1.61619300
 C -0.95533900  -0.93769500   1.14525200
 C  0.72798700  -2.53398800   1.25864000
 C -1.70353700   0.25955500   1.06670900
 N -1.50773400  -2.09027200   0.65178600
 C -0.63045000  -3.23395800   0.96765700
 C -2.92578700   0.22265500   0.44199100
 H -1.28916300   1.16985100   1.46499100
 C -2.71690300  -2.13835500   0.04142100
 H -1.03728700  -3.75065800   1.84410500
 H -0.57076100  -3.92057400   0.12314900
 C -3.45037500  -0.98797000  -0.08528400
 H -3.48750700   1.14481300   0.33002700
 H -3.04337600  -3.10380600  -0.32310100
 C -0.06029500   3.04892000   0.20566100
 C  0.05014300   2.80038200  -1.17076700
 C -1.14554700   3.80530500   0.66856000
 C -0.90864100   3.29839000  -2.05457900
 H  0.89593700   2.22322300  -1.53853100
 C -2.10920500   4.29999200  -0.21583000
 H -1.23754700   4.00973300   1.73480100
 C -1.99386100   4.04386000  -1.58347800
 H -0.80786000   3.10384500  -3.12001100
 H -2.94382600   4.88615700   0.16284300
 H -2.73909100   4.42656900  -2.27679300
 C  2.17366600   3.48185000   1.29329200
 H  2.91988200   3.09406000   1.99520400
 H  2.65859100   3.62344900   0.32245400
 H  1.83103200   4.45985700   1.65143900
 H  0.51253700   2.46177900   2.18045300
 C -4.79206400  -1.00291600  -0.76178100
 F -5.76760100  -0.62089000   0.08862700
 F -4.82254000  -0.15415600  -1.80635900
 F -5.10398200  -2.23564400  -1.21821500
 H  1.19293000  -2.99417700   2.13422400
 C  1.66594400  -2.62781200   0.06306600
 C  2.36089400  -3.83350100  -0.11817300
 C  1.78084500  -1.61210900  -0.88909600
 C  3.14274900  -4.03150500  -1.25373700
 H  2.29232300  -4.61996100   0.63237800
 C  2.56896000  -1.81374200  -2.02714400
 H  1.30492600  -0.64851400  -0.73173100
 C  3.24123000  -3.02090100  -2.21452100
 H  3.68083800  -4.96676500  -1.38333200
 H  2.67354400  -0.99853100  -2.73510700
 H  3.85533900  -3.17068200  -3.09845700
 SCF:  E(RB+HF-LYP) =  -1716.93647035
 Sum of electronic and zero-point
Energies= -1716.448851
 Sum of electronic and thermal Energies=
-1716.415718
 Sum of electronic and thermal
Enthalpies= -1716.414774
 Sum of electronic and thermal Free
Energies= -1716.517683
```

(d) Single-point calculations using other computational methods and solvation correction

TS structures **7a**, **8b**, **9a**, and **10b** optimized at B3LYP/6-31G* level of theory as described above were subjected to single-point energy calculations using other computational methods in gas phase (Table S-2). Subsequently, these results were subjected to solvent correction using the CPCM[3] polarizable conductor calculation model as implemented in Gaussian 03 (Table S-3). Chloroform was specified as the solvent. The UFF atomic radii were used. Hydrogens have individual spheres.

Table S-2. Free energies of **7a**, **8b**, **9a**, and **10b** in gas phase

Method	G_{298} of **7a** (a.u.)	G_{298} of **8b** (a.u.)	ΔG_{rel} (**8b -7a**) (kcal/mol)	G_{298} of **9a** (a.u.)	G_{298} of **10b** (a.u.)	ΔG_{rel} (**10b -9a**) (kcal/mol)
B3LYP/6-31G*	-1716.533805	-1716.530767	1.9	-1795.109244	-1795.103606	3.5
MP2/6-31G*// B3LYP/6-31G* [a]	-1711.434669	-1711.427432	4.5	-1789.716955	-1789.707359	6.0
SCS-MP2/6-31G*// B3LYP/6-31G* [a]	-1711.254999	-1711.249121	3.7	-1789.534322	-1789.525727	5.4
M05-2X/6-31G*// B3LYP/6-31G* [a]	-1716.368694	-1716.364145	2.9	-1794.932492	-1794.924754	4.9

[a] Thermal correction was calculated at B3LYP/6-31G* level.

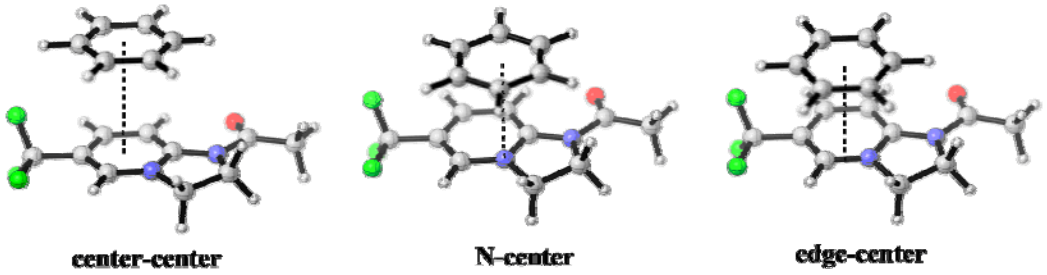
Table S-3. Free energies of **7a**, **8b**, **9a**, and **10b** in chloroform

Method	G_{298} of **7a** (a.u.)	G_{298} of **8b** (a.u.)	ΔG_{rel} (**8b -7a**) (kcal/mol)	G_{298} of **9a** (a.u.)	G_{298} of **10b** (a.u.)	ΔG_{rel} (**10b -9a**) (kcal/mol)
B3LYP/6-31G*	-1716.511641	-1716.509035	1.6	-1795.081571	-1795.077051	2.8
MP2/6-31G*// B3LYP/6-31G* [a]	-1711.451895	-1711.443409	5.3	-1789.732726	-1789.722749	6.3
SCS-MP2/6-31G*// B3LYP/6-31G* [a]	-1711.272472	-1711.265275	4.5	-1789.550318	-1789.541284	5.7
M05-2X/6-31G*// B3LYP/6-31G* [a]	-1716.348901	-1716.344598	2.7	-1794.907011	-1794.900313	4.2

[a] Thermal correction was calculated at B3LYP/6-31G* level.

(e) Interaction energies of benzene and N-acetyl-6-CF_3-DHIP$^+$

N-acetyl-6-trifluoromethyl-DHIP cation lacking the phenyl group at C2 was used instead of the analogous CF_3-PIP derivative to simplify the calculation. Geometries of the complexes of benzene and this cation are shown in Figure S-9. Intermolecular distances are the distance between the centers of benzene and pyridinium ring (center-center), between the pyridinium nitrogen and the center of benzene (N-center), and between the midpoint of the N-C bond and the center of benzene (edge-center).



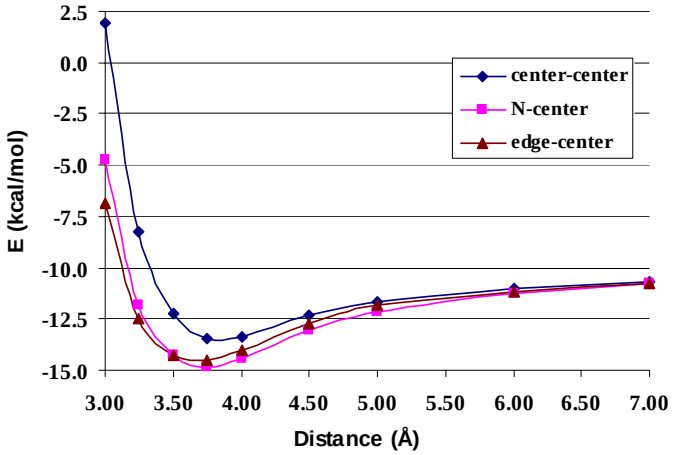


Figure S-9. Interaction energies of benzene and **N-acetyl-6-CF_3-DHIP$^+$**

(f) Electrostatic potential of 7a

The electrostatic potential of **7a** was calculated in Gaussian 03.

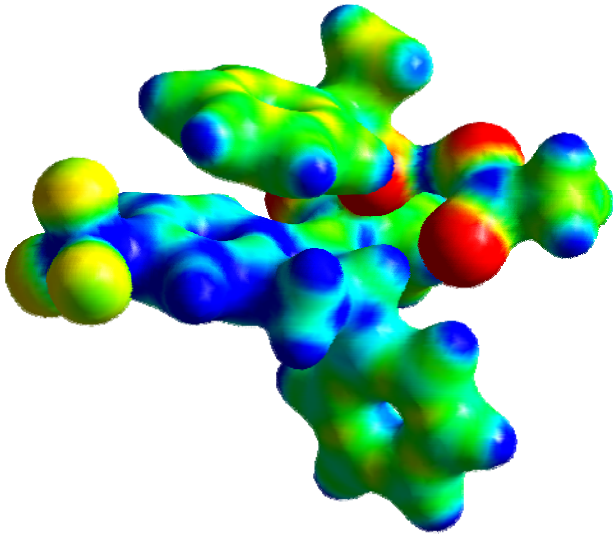


Figure S-10. Electrostatic potential of **7a** (R)

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