Electronic Supporting Information for

Catalytic Mechanism of C-F bond Cleavage: Insights from QM/MM Analysis of Fluoroacetate Dehalogenase

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Keywords

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Ten Pages

Contains two Tables, one Scheme and five Figures

Table S1 Hydrogen bond distances between FAcD and the substrates (FAc and ClAc). The unit is in Å. The definition of the hydrogen bonds is indicated in Figure S1.

Table S2 NPA (Natural Population Analysis) charge variations of key atoms/residues/substrates along the dehalogenation processes of systems $FAcD_{Hse155}$-FAc and $FAcD_{Hse155}$-ClAc. The atom labels are indicated in Scheme 1. The NPA charge of a residue is determined by summing the NPA charges of all the QM atoms of that residue. The unit is in e.

Scheme S1 Gas phase calculations of defluorination and dechlorination reactions performed at RIMP2/cc-pVTZ//B3LYP/6-31G(d,p) level.

Figure S1 a~b,binding of substrate FAc with FAcD in the present study; c~d, binding of substrate FAc with FAcD in a previous study (T. Kamachi, et. al., *Chem. Eur. J.*, 2009, 15, 7394); e, locations of a water molecule and the F atom. H1~H8 represents for eight hydrogen bonds, the corresponding distances are provided in Table S1.

Figure S2 Root-mean-square deviation during 10 ns molecular dynamics simulation.

Figure S3 Structures of reactant (R), transition state (TS), and product (P) involved in dechlorination process of system $FAcD_{Hse155}$-ClAc at snapshot 4.5 ns. The unit for bond distances and imaginary frequency are in Å and cm^{-1}.

Figure S4 a, potential energy barriers versus dihedral $O_\omega C_\gamma C_\delta O_\varepsilon$ variations for $FAcD_{Hse155}$-FAc and $FAcD_{Hse155}$-ClAc, b, potential energy barriers versus values of dihedral $O_\omega C_\gamma C_\delta O_\varepsilon$ in reactants, c, potential energy barriers versus values of dihedral $O_\omega C_\gamma C_\delta O_\varepsilon$ in transition states.

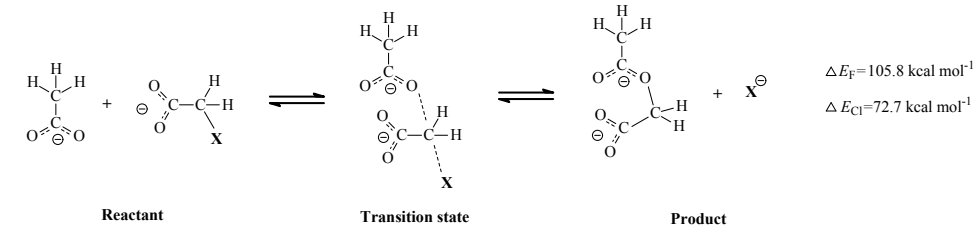
Figure S5 a, potential energy barriers versus bond $O_\varepsilon C_\delta$ variations for $FAcD_{Hse155}$-FAc and $FAcD_{Hse155}$-ClAc, b, potential energy barriers versus lengths of bond $O_\varepsilon C_\delta$ in reactants, c, potential energy barriers versus lengths of bond $O_\varepsilon C_\delta$ in transition states.

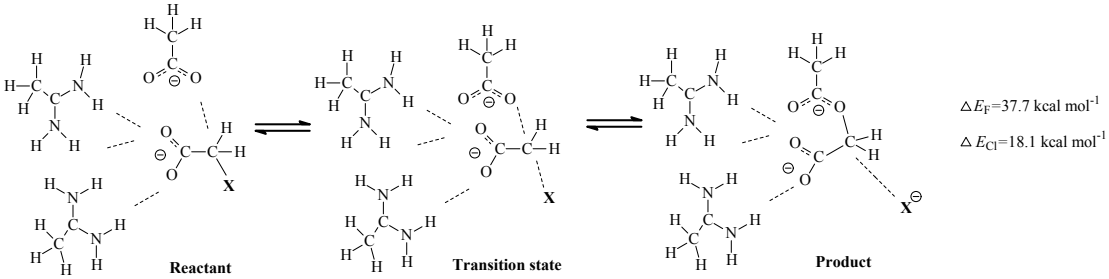
Table S1 Hydrogen bond distances between FAcD and the substrates (FAc and ClAc). The unit is in Å. The definition of the hydrogen bonds (H1~H8) is indicated in Figure S1.

Hydrogen	$FAcD_{Hse155}$-FAc			$FAcD_{Hse155}$-ClAc		
bonds	R	TS	P	R	TS	P
H1	1.90±0.03	1.89±0.03	2.01±0.05	1.92±0.03	1.95±0.08	2.03±0.06
H2	1.88±0.03	1.91±0.07	1.89±0.06	1.88±0.05	1.88±0.06	1.88±0.06
H3	1.79±0.03	1.77±0.03	1.79±0.03	1.86±0.02	1.82±0.03	1.83±0.04
H4	1.66±0.03	1.69±0.05	1.87±0.10	1.77±0.06	1.70±0.08	1.81±0.09
H5	2.69±0.16	2.71±0.15	2.83+0.16	2.94±0.15	3.01±0.17	3.48±0.33
H6	2.46±0.27	1.98±0.25	1.54±0.05	2.78±0.18	2.84±0.30	2.42±0.41
H7	2.13±0.19	1.78±0.10	1.65±0.07	2.70±0.17	2.45±0.22	2.38±0.20
H8	1.94±0.07	1.68±0.09	1.59±0.06	2.29±0.08	2.01±0.09	1.93±0.06

Table S2 NPA (Natural Population Analysis) charge variations of key atoms/residues/substrates along the dehalogenation processes of systems $FAcD_{Hse155}$-FAc and $FAcD_{Hse155}$-ClAc. The atom labels are indicated in Scheme 1. The NPA charge of a residue is determined by summing the NPA charges of all the QM atoms of that residue. The unit is in e.

Atoms/Residues/	$FAcD_{Hse155}$-FAc			$FAcD_{Hse155}$-ClA		
Substrates	R	TS	P	R	TS	P
O_β	-0.76±0.01	-0.76±0.01	-0.79±0.01	-0.76±0.01	-0.75±0.01	-0.79±0.01
O_ω	-0.77±0.01	-0.75±0.01	-0.74±0.01	-0.78±0.01	-0.75±0.01	-0.75±0.01
C_γ	0.82±0.01	0.82±0.00	0.82±0.01	0.84±0.00	0.82±0.00	0.82±0.00
O_ε	-0.82±0.02	-0.72±0.02	-0.57±0.01	-0.82±0.02	-0.74±0.01	-0.57±0.01
C_δ	-0.12±0.01	-0.16±0.01	-0.24±0.01	-0.52±0.01	-0.32±0.01	-0.24±0.01
F/Cl	-0.43±0.02	-0.59±0.03	-0.73±0.04	-0.18±0.02	-0.52±0.03	-0.89±0.02
FAc/ClAc	-0.78±0.01	-0.93±0.03	-1.17±0.03	-0.82±0.01	-0.96±0.03	-1.32±0.02
Asp110	-0.96±0.01	-0.73±0.01	-0.41±0.01	-0.95±0.01	-0.79±0.01	-0.40±0.01
Arg111	0.94±0.01	0.93±0.01	0.94±0.01	0.94±0.00	0.93±0.01	0.94±0.01
Arg114	0.92±0.01	0.92±0.01	0.92±0.01	0.91±0.02	0.91±0.02	0.90±0.02
Hse155	-0.04±0.02	-0.05±0.02	-0.11±0.02	-0.03±0.01	-0.04±0.01	-0.06±0.02
Trp156	-0.04±0.01	-0.06±0.01	-0.08±0.02	-0.03±0.01	-0.03±0.01	-0.05±0.02
Tyr219	-0.04±0.01	-0.06±0.00	-0.05±0.02	-0.03±0.01	-0.04±0.02	-0.04±0.01
Wat	-0.01±0.01	-0.05±0.01	-0.09±0.01	-0.01±0.01	-0.04±0.01	-0.04±0.01


Reactant
Transition state
Product
△E_F=105.8 kcal mol^{-1}
△E_{Cl}=72.7 kcal mol^{-1}


Reactant
Transition state
Product
△E_F=37.7 kcal mol^{-1}
△E_{Cl}=18.1 kcal mol^{-1}

Scheme S1

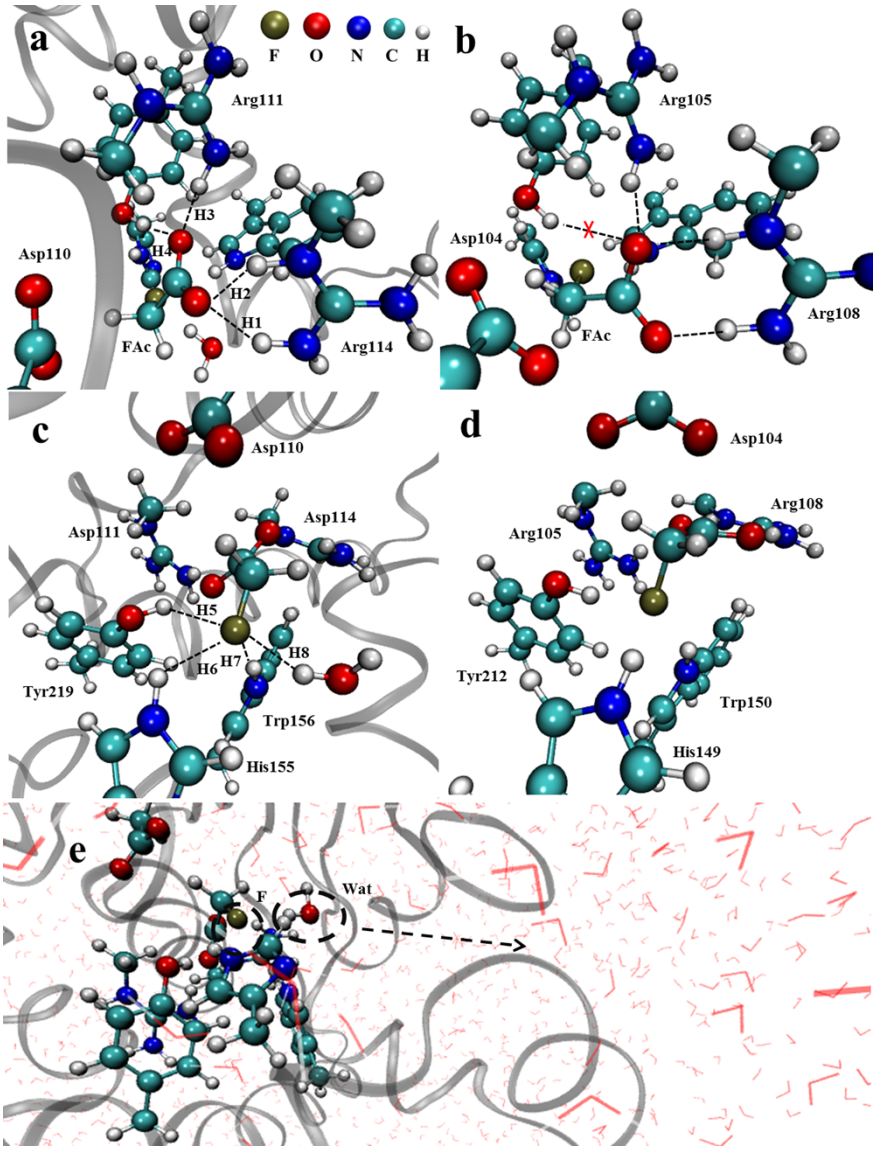

a
F O N C H
Arg111
H3
H4
Asp110
H2
H1
FAc
Arg114
b
Arg105
Asp104
Arg108
FAc
c
Asp110
Asp111
Asp114
H5
H8
H7
H6
Tyr219
Trp156
His155
d
Asp104
Arg108
Arg105
Tyr212
Trp150
His149
e
F
Wat

Figure S1

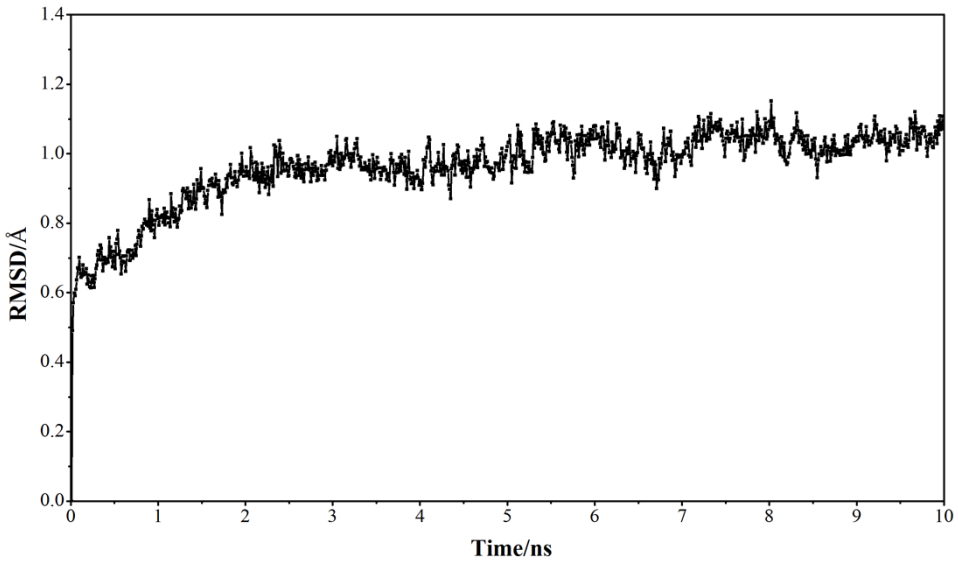


Figure S2

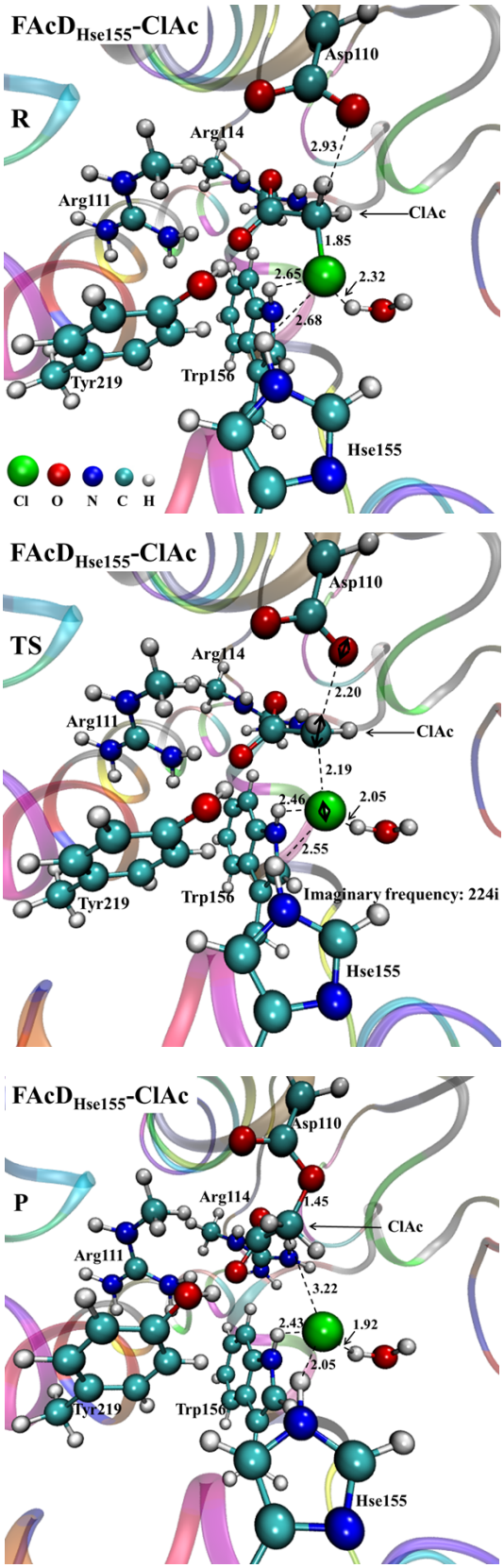

FAcD$_{Hse155}$-ClAc
R
Asp110
Arg114
2.93
Arg111
ClAc
1.85
2.65
2.32
2.68
Tyr219
Trp156
Hse155
Cl O N C H
FAcD$_{Hse155}$-ClAc
TS
Asp110
Arg114
2.20
Arg111
ClAc
2.19
2.46
2.05
2.55
Tyr219
Trp156
Imaginary frequency: 224i
Hse155
FAcD$_{Hse155}$-ClAc
P
Asp110
Arg114
1.45
ClAc
Arg111
3.22
2.43
1.92
2.05
Tyr219
Trp156
Hse155

Figure S3

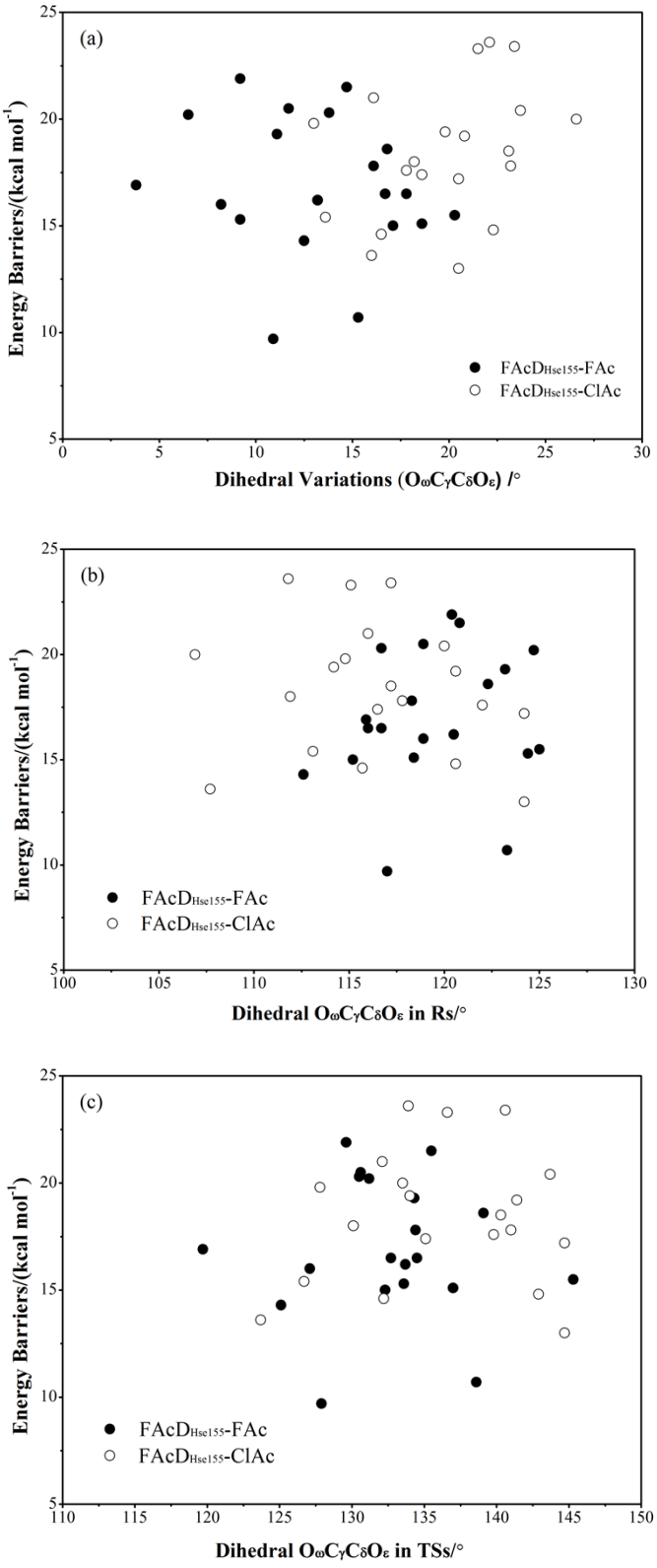

(a)
Energy Barriers/(kcal mol-1)
Dihedral Variations (OωCγCδOε) /°
FAcDHse155-FAc
FAcDHse155-ClAc
(b)
Energy Barriers/(kcal mol-1)
Dihedral OωCγCδOε in Rs/°
FAcDHse155-FAc
FAcDHse155-ClAc
(c)
Energy Barriers/(kcal mol-1)
Dihedral OωCγCδOε in TSs/°
FAcDHse155-FAc
FAcDHse155-ClAc

Figure S4

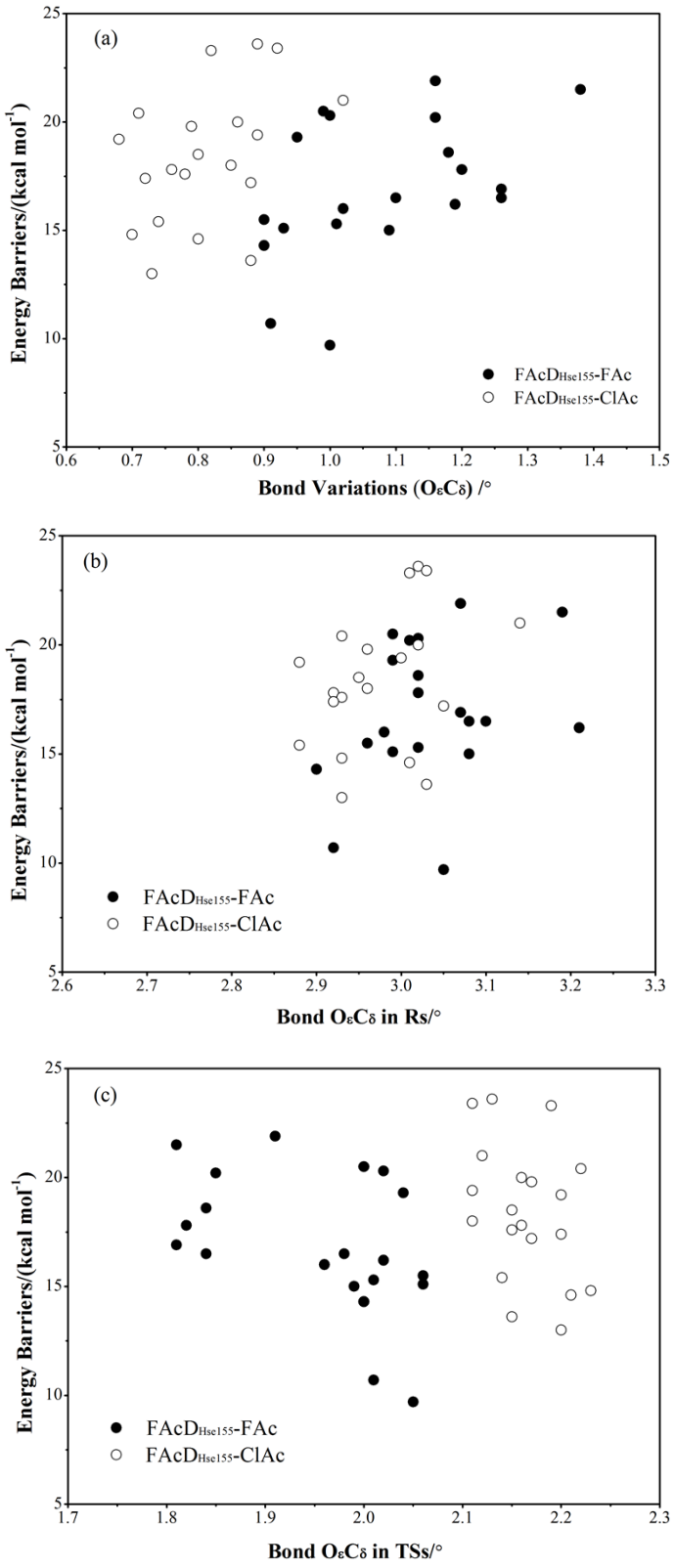

(a)
Energy Barriers/(kcal mol-1)
Bond Variations (OεCδ) /°
FAcDHse155-FAc
FAcDHse155-ClAc
(b)
Energy Barriers/(kcal mol-1)
Bond OεCδ in Rs/°
FAcDHse155-FAc
FAcDHse155-ClAc
(c)
Energy Barriers/(kcal mol-1)
Bond OεCδ in TSs/°
FAcDHse155-FAc
FAcDHse155-ClAc

Figure S5