

Supporting Information for

Steps Towards Rationalization of the Enantiomeric Excess of the Sakurai-Hosomi-Denmark Allylation Catalyzed by Biisoquinoline *N,N'*-Dioxides Using Computations.

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Summary

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Section S1: Additional calculations on the *Trans*-1-Chair-Re/Si structures.

The transition structures presented in **Table 1** of the main text show that the lowest energy structure is *Trans*-1-Chair-Si, the arrangement leading to the S enantiomer. This finding is in stark contrast with the experimental evidence, where the R enantiomer is obtained with an excess of 79%. This discrepancy could be due to an inherent limitation of the level of theory we chose for this study, which would invalidate its applicability altogether. To exclude this possibility, we tested thirty-two additional approximations (eight generalized gradient approximation (GGA) functionals, namely PBE,¹ PBE-D3(BJ),^{1,2} BLYP,^{3,4} BLYP-D3(BJ),²⁻⁴ B97-D,⁵ B97-D3(BJ),^{2,5} HCTH/407,⁶ HCTH/407-D3(BJ);^{2,6} nine meta-GGA functionals, *i.e.* B97M-V,⁷ M06-L,⁸ M11-L,⁹ MN15-L,¹⁰ SCAN,¹¹ TPSS,¹² TPSS-D3(BJ),^{2,12} τ -HCTH,¹³ τ -HCTH-D3(BJ);^{2,13} thirteen hybrid functionals: B3LYP,^{3,4,14} B3LYP-D3(BJ),^{2-4,14} PBE0,^{15,16} PBE0-D3(BJ),^{15,16} ω B97X-D,¹⁷ M06-2X,¹⁸ MN15,¹⁹ PW6B95-D3(BJ),^{2,20} τ -HCTH-hyb,¹³ τ -HCTH-hyb-D3(BJ),^{2,13} TPSSh,²¹ TPSSh-D3(BJ),^{2,21} ω B97M-V;²² two double-hybrid functionals, B2PLYP-D3(BJ)^{2,23} and DSD-PBEP86-D3(BJ))²⁴ with the def2-SVP basis set on the lowest-energy structures, *i.e.* *Trans*-1-Chair-Re and *Trans*-1-Chair-Si. We chose these approximations based on their optimal performance in recent benchmark studies,^{19,25-28} with MN15,¹⁹ ω B97M-V,²² B2PLYP-D3(BJ)^{2,23} and DSD-PBEP86-D3(BJ)²⁴ being among the most accurate functionals developed so far. The results of this step are collected in **Table S1**.

Table S1. Electronic energy differences (in kcal mol⁻¹ and in the gas phase) between the *Trans*-1-Chair-Si and *Trans*-1-Chair-Re structures calculated with twenty-nine different functionals and the def2-SVP basis set (unless noted otherwise). The values in bold are for functionals that predict the R enantiomer to be more stable.

Functional	$\Delta\Delta E$ (S–R), kcal mol ⁻¹	Functional	$\Delta\Delta E$ (S–R), kcal mol ⁻¹
PBE	-0.02	TPSS-D3(BJ) ^b	1.14
PBE-D3(BJ)	0.84	B3LYP	0.08
BLYP	-0.21	B3LYP-D3(BJ)	1.31
BLYP-D3(BJ)	1.24	PBE0	0.35

B97-D	0.97	PBE0-D3(BJ)	1.17
B97-D/TZV(2p,2d) ^a	0.84	ω B97X-D	1.40
B97-D3(BJ)	1.31	M06-2X	1.72
HCTH/407	-0.21	M11	1.76
HCTH/407-D3(BJ) ^b	0.81	MN15	1.51
B97M-V	1.63	PW6B95-D3(BJ)	1.48
M06-L	1.61	τ -HCTHhyb	0.35
M11-L	2.28	τ -HCTHhyb-D3(BJ) ^b	1.44
MN15-L	3.12	TPSSh	0.18
SCAN	1.28	TPSSh-D3(BJ)	1.26
τ -HCTH	-0.25	ω B97M-V	1.67
τ -HCTH-D3(BJ) ^b	1.13	B2PLYP-D3(BJ)	1.15
TPSS	0.07	DSD-PBEP86-D3(BJ)	1.22

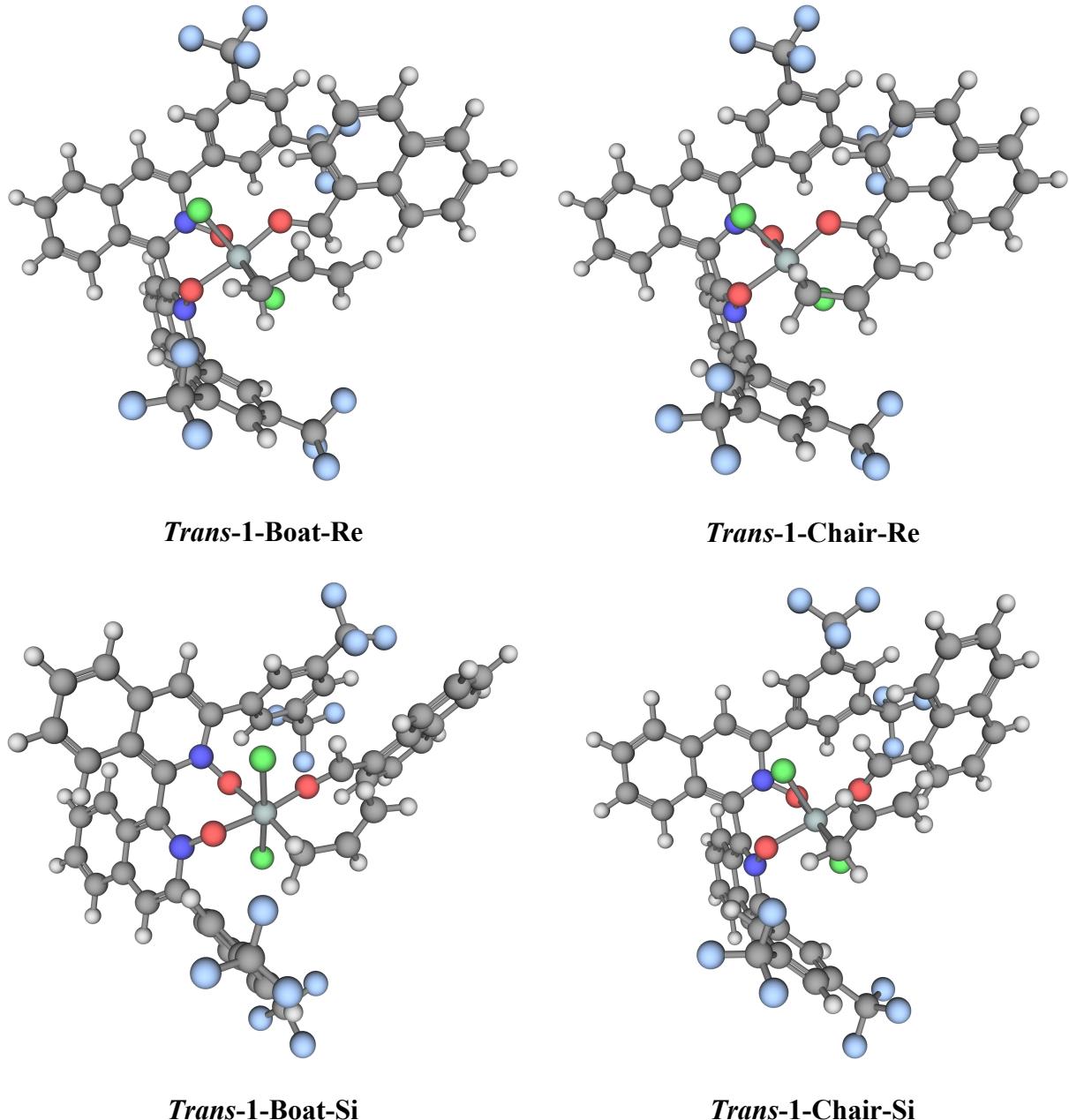
^aRecommended by Wheeler and co-workers;

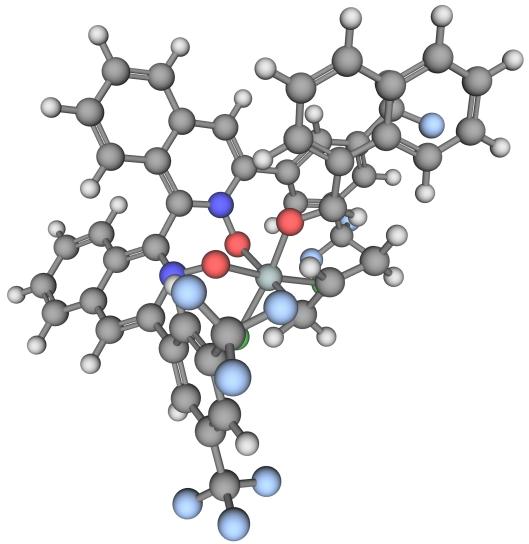
^bD3(BJ) corrections obtained with a locally-modified version of the dftd3 program

Analysis of **Table S1** shows that most of the functionals, including the most accurate and reliable, agree with the results obtained at the M11/def2-SVP level of theory. Given the size of the system under investigation, it is not surprising to see that dispersion corrections must be included for a better performance. This is most striking for functionals such as PBE, BLYP, HCTH/407 and τ -HCTH, since inclusion of dispersion corrections changes the outcome from favoring the R enantiomer to favoring the S one. The effect is also prominent for the TPSS, B3LYP, PBE0, TPSSh, and τ -HCTHhyb functionals, suggesting that dispersion corrections should always be included when using these approximations, as reported in the literature.^{25,26} Functionals that include dispersion interactions by construction, such as M11, MN15, and ω B97M-V, are the best option. Overall, all the functionals we tested—once they can correctly describe the system under investigation using dispersion corrections—agree with the M11/def2-SVP results. This is somewhat surprising, as many authors have reported the successful application of DFT to study the

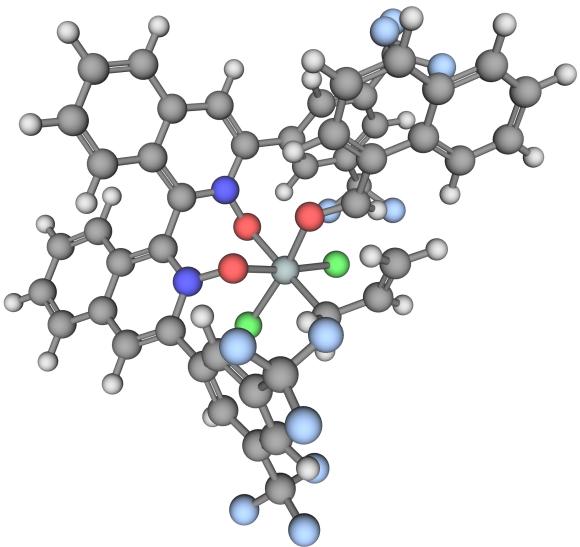
stereochemistry of organic reactions.^{29–31} The reason behind such apparent failure of all the approximations we tested is not clear, and it requires further investigation.

Section S2: Pictures of all the transition structures optimized with M11/def2-SVP.

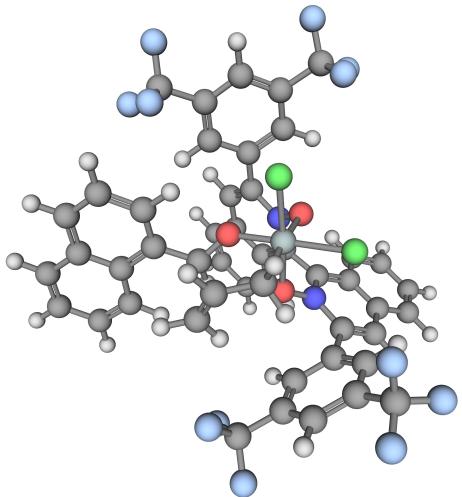




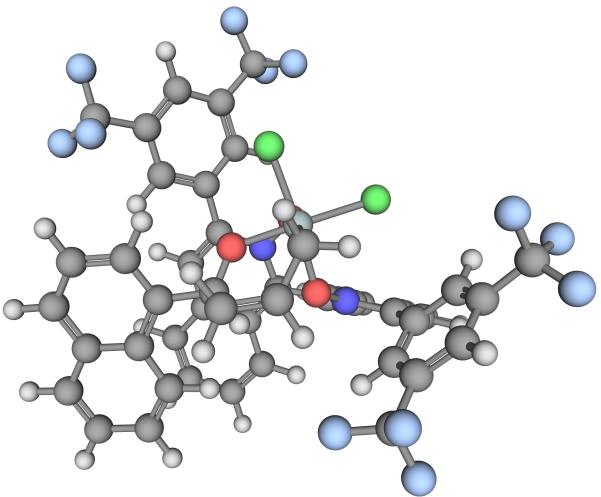
Cis-2-Boat-Re



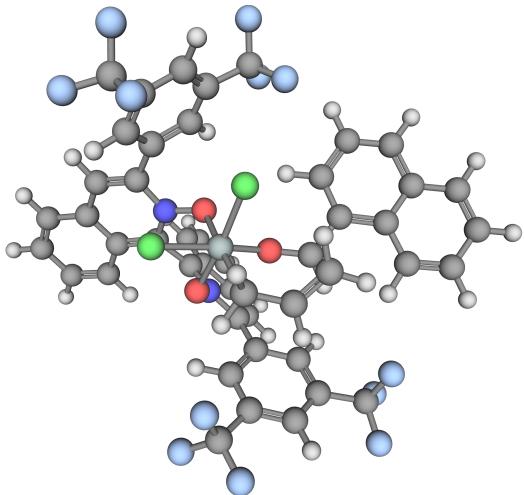
Cis-2-Chair-Re



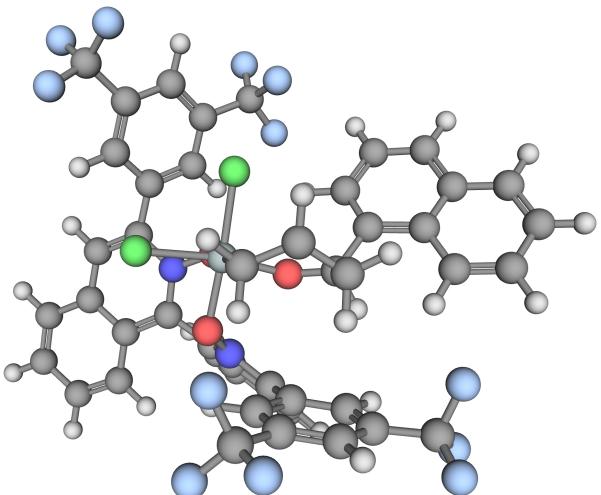
Cis-2-Boat-Si



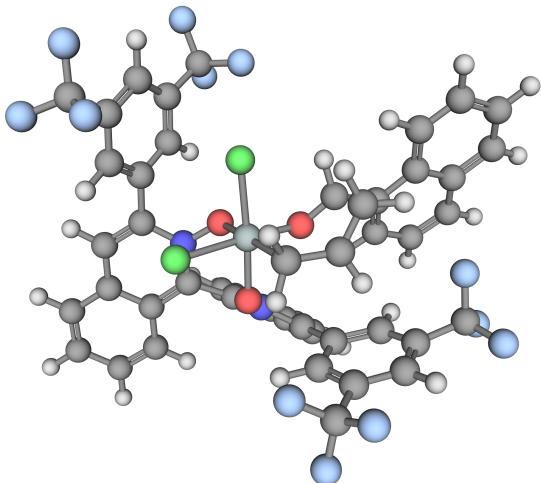
Cis-2-Chair-Si



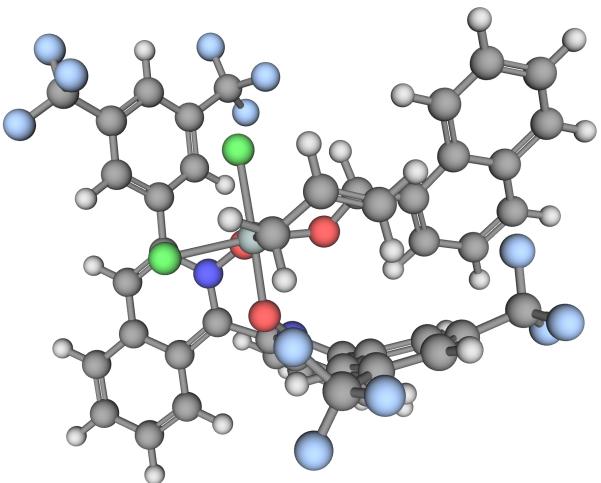
Cis-3-Boat-Re



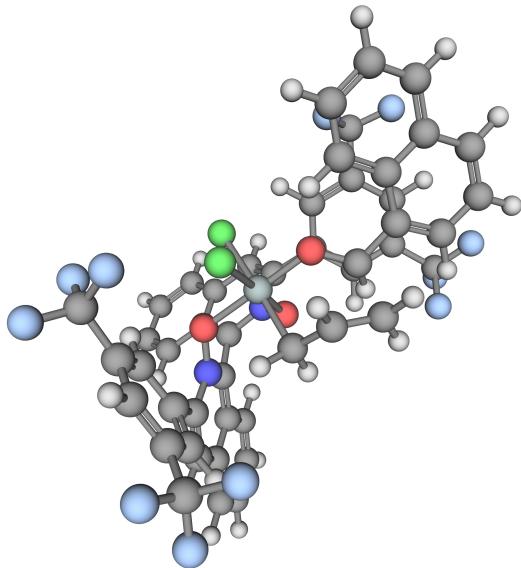
Cis-3-Chair-Re



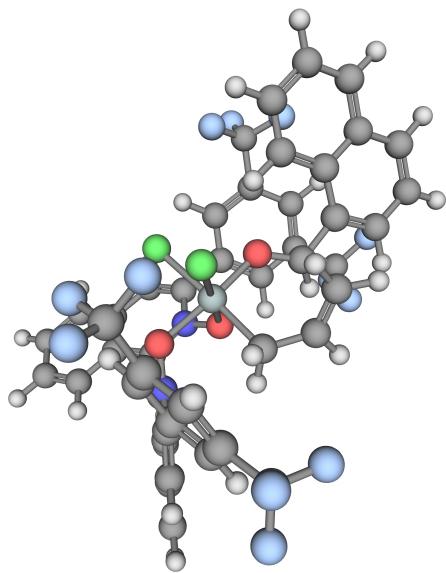
Cis-3-Boat-Si



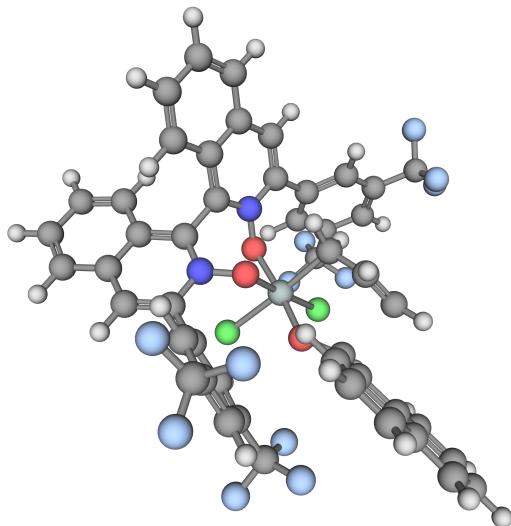
Cis-3-Chair-Si



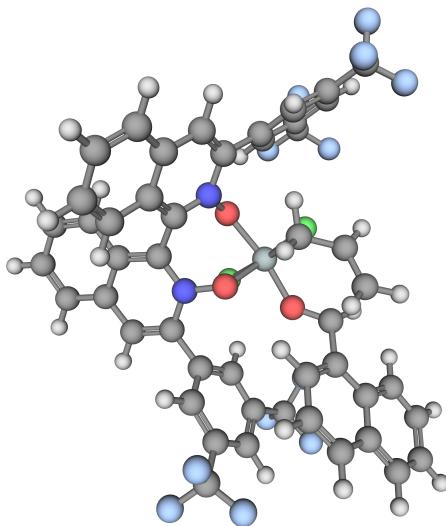
Cis-4-Boat-Re



Cis-4-Chair-Re

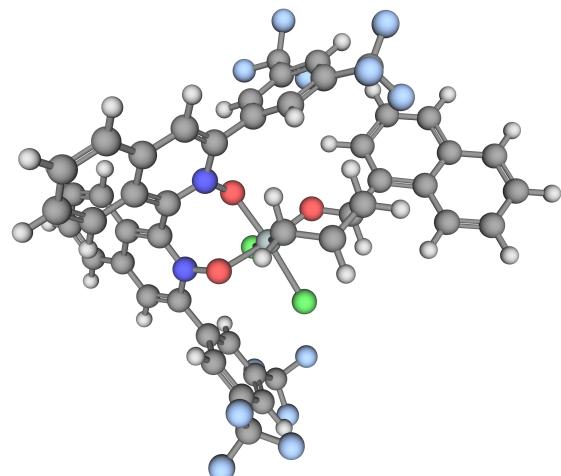


Cis-4-Boat-Si

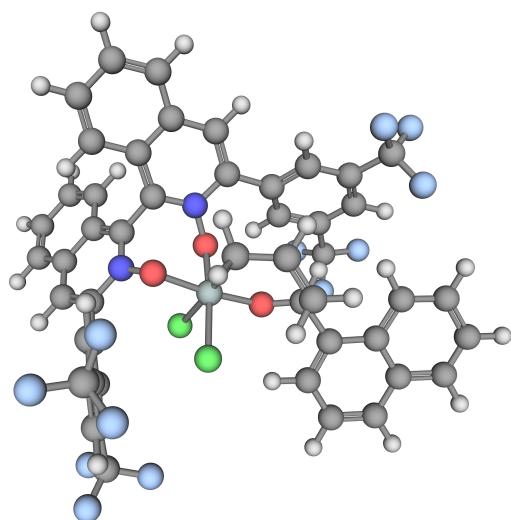


Cis-4-Chair-Si

Could not be located

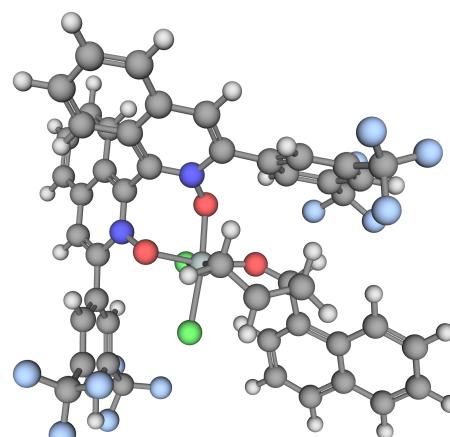


***Cis*-5-Boat-Re**



***Cis*-5-Boat-Si**

***Cis*-5-Chair-Re**



***Cis*-5-Chair-Si**

Section S3: Corrections for the *Cis*-4-Boat-Si structure.

The characterization of the *Cis*-4-Boat-Si structure revealed two negative eigenvalues of the Hessian matrix (two negative frequencies). The unwanted normal mode has a frequency of -4.25 cm^{-1} . We tried to re-optimize this transition structure using different algorithms implemented in the Gaussian

program,³² but they were all unsuccessful. We decided to correct the values of Gibbs free energy by removing the entropy contribution due to the normal mode corresponding to the CF₃ rotation, as reported in **Table 1** of the main text.

Molecule	Electronic energy, a.u.	Enthalpy correction, a.u.	Entropy, a.u.	Corrected entropy, a.u.	Corrected Gibbs free energy, a.u.
Cis-4-Boat-Si	-4585.17055721	0.738542	0.000487021	0.000476222	-4584.57400

Optimization of structure *Cis*-5-Boat-Re instead did not converge, despite multiple attempts.

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