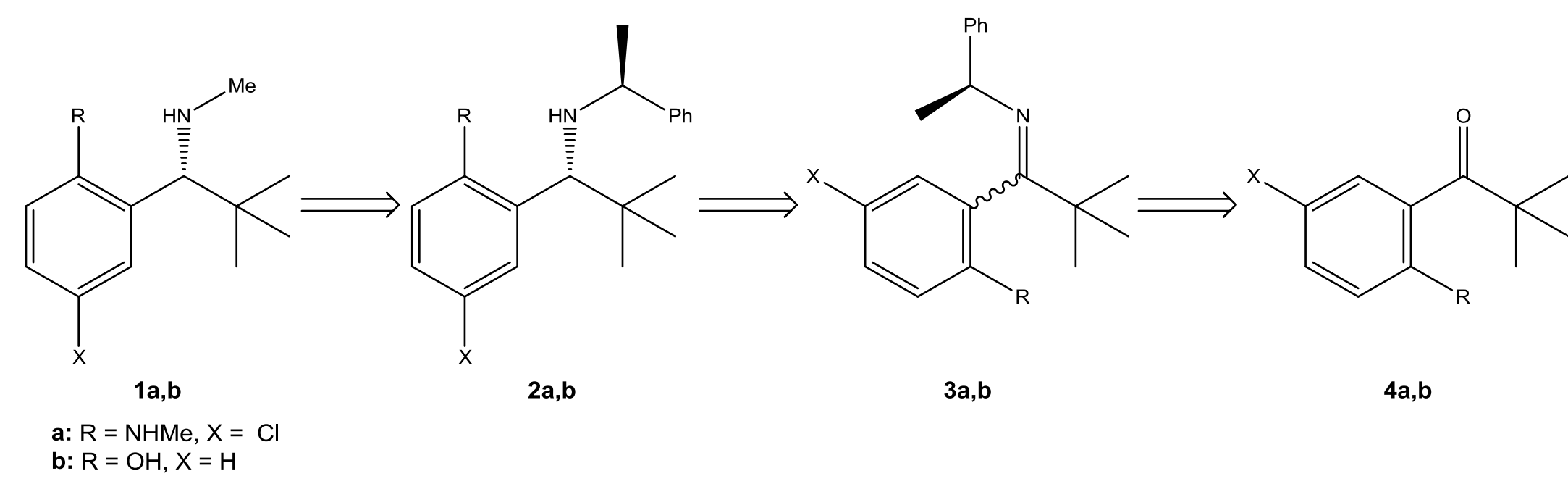
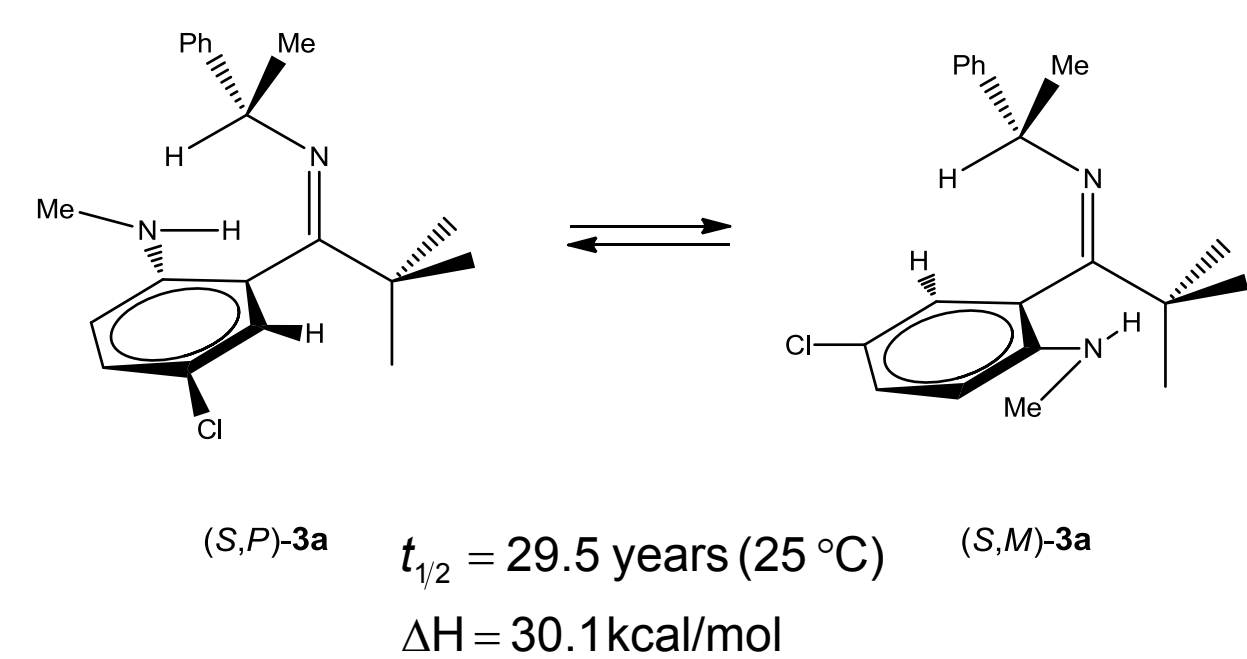




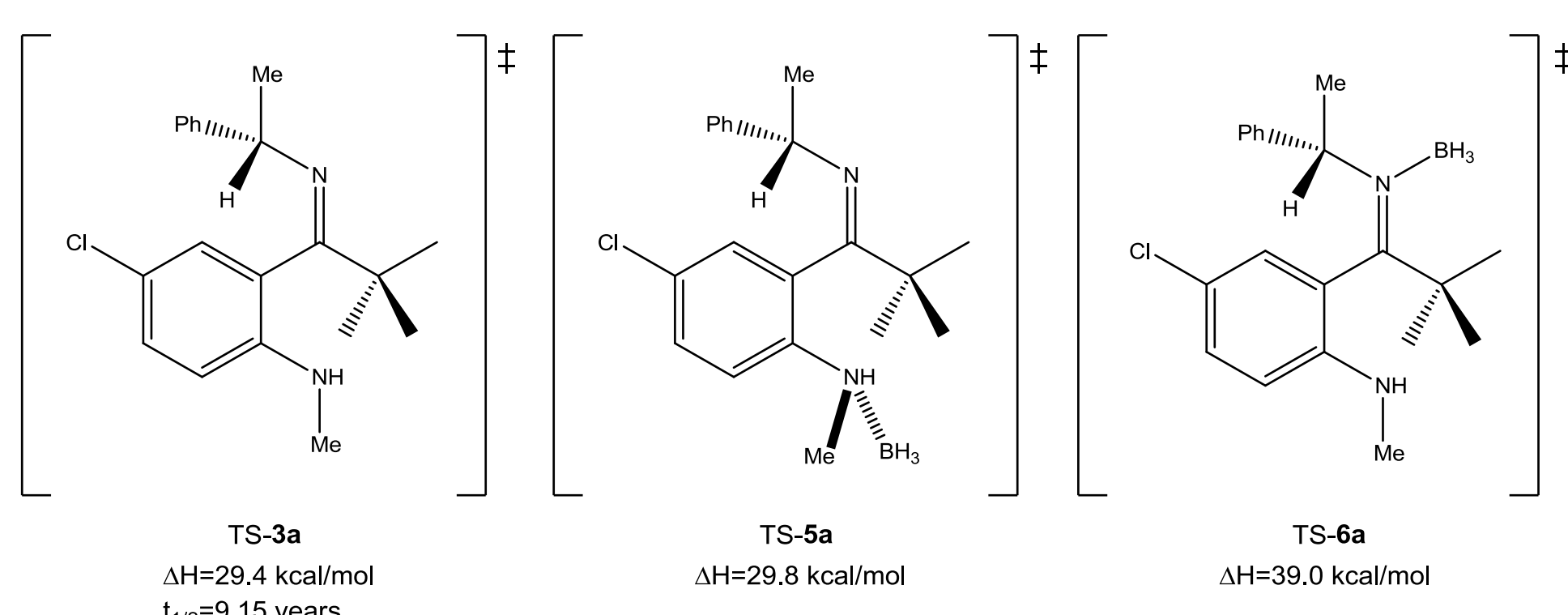
## Retrosynthetic analysis



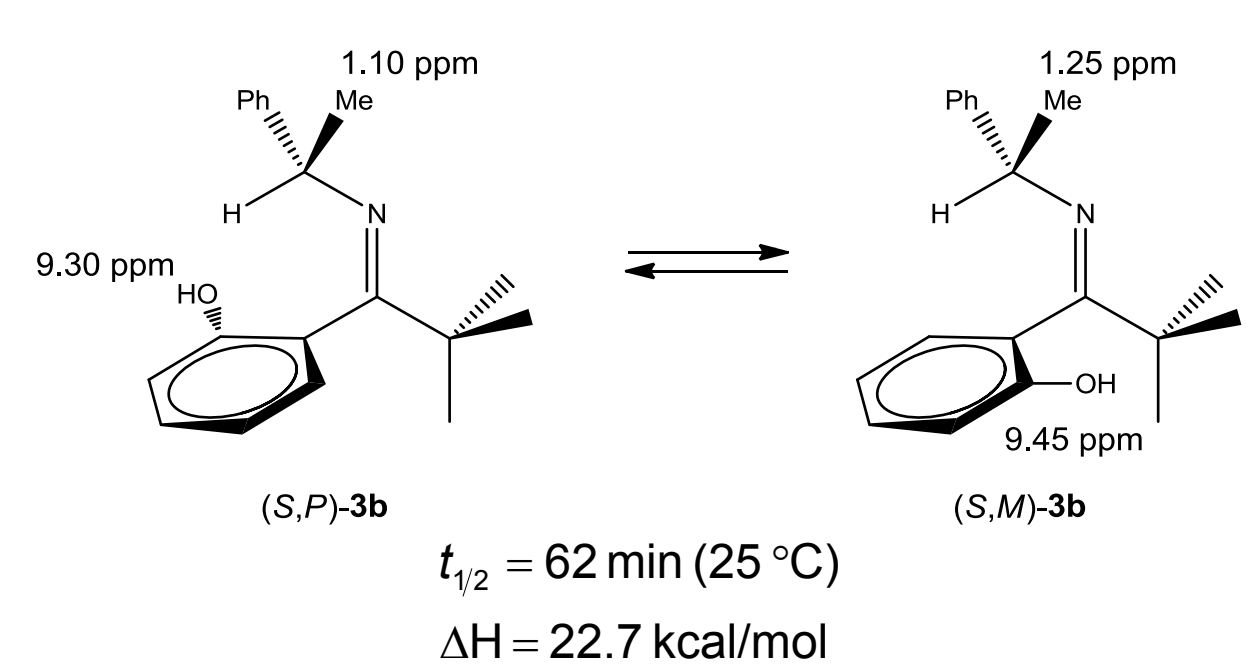
## Atropisomerization barriers



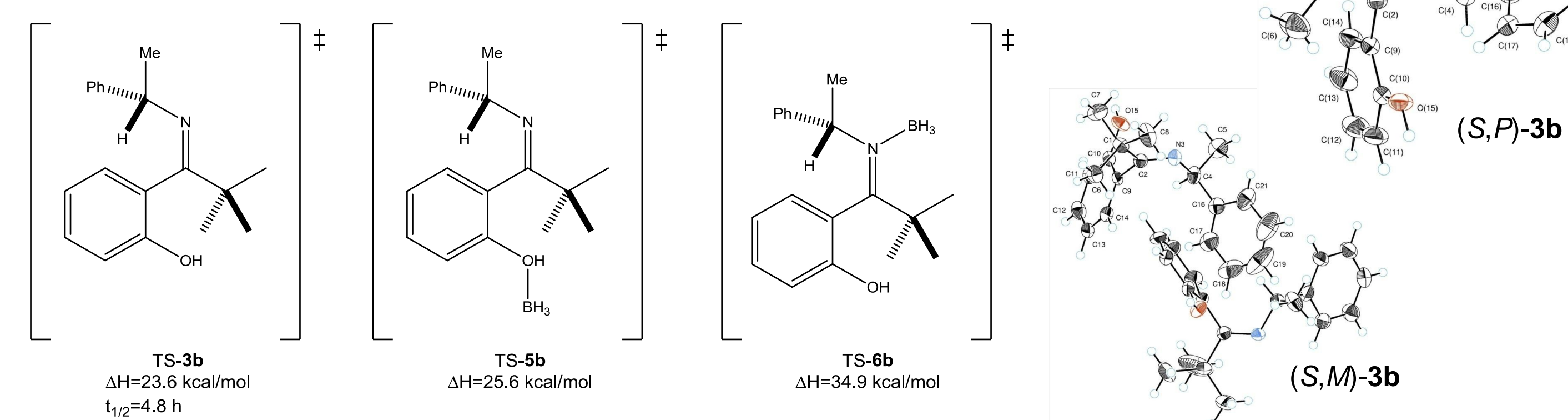
Atropisomers (S,P)-3a and (S,M)-3a were separated by column chromatography. They are stable at room temperature. *E* isomer of imine (S,P/M)-3a was not observed.



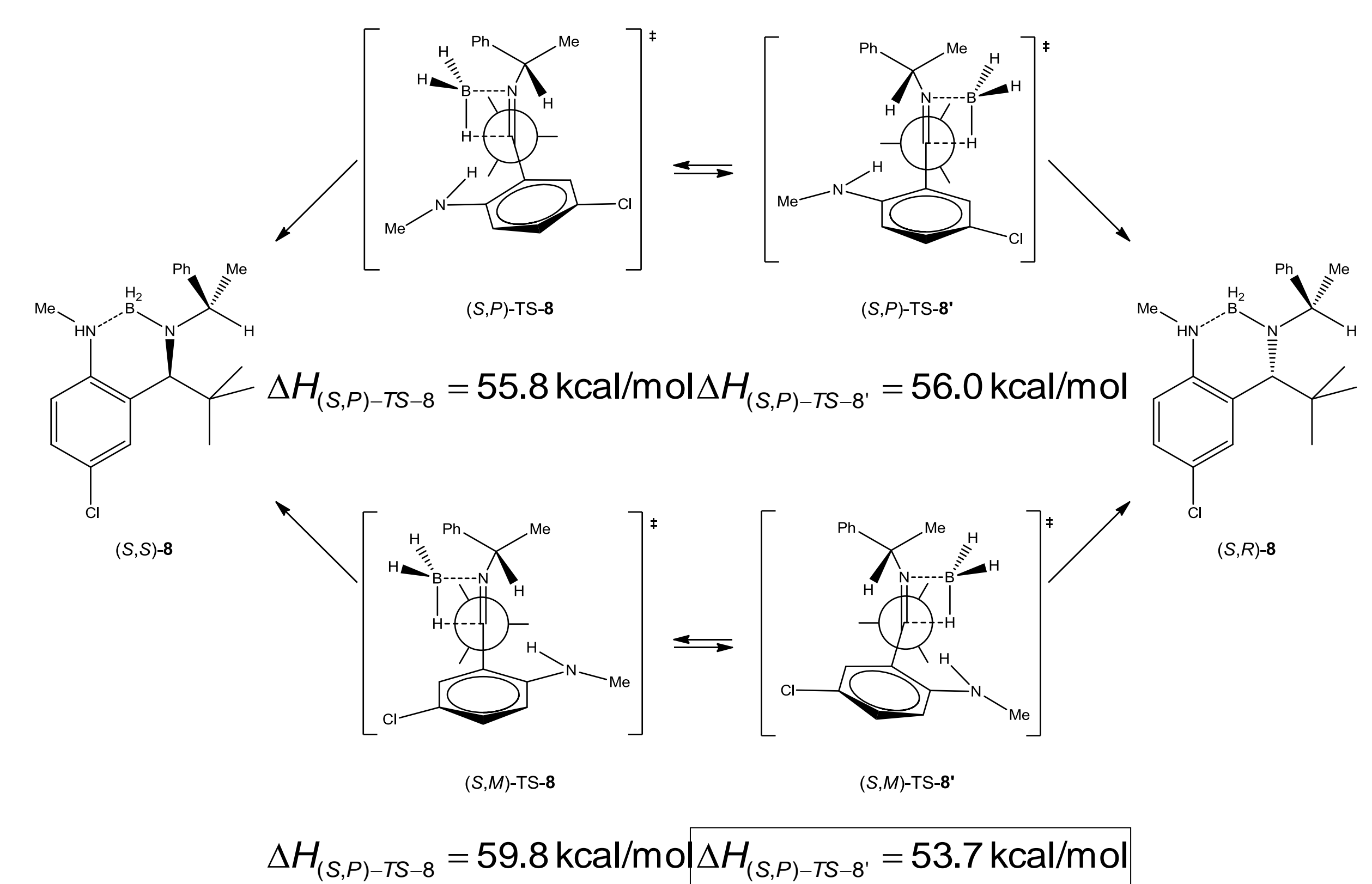
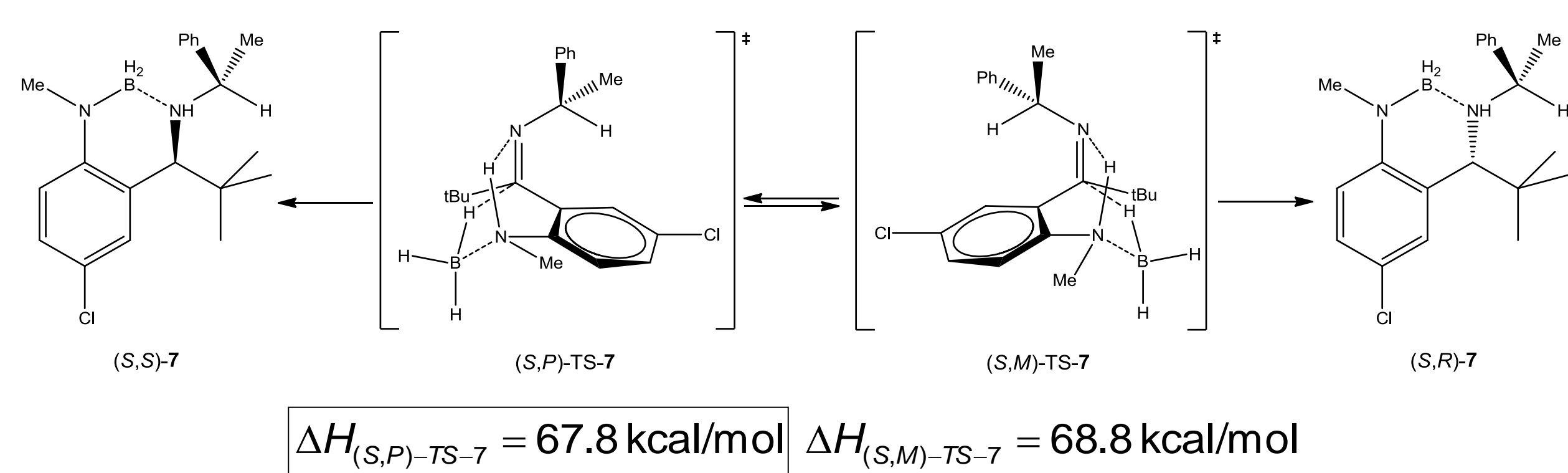
DFT calculations at the b3lyp/6-31g(d,p) level show that complexation with Lewis acid further increases barrier for interconversion of atropisomers.



Atropisomers (S,P)-3b and (S,M)-3b were separated by HPLC. Atropisomers are stable as solids at -10 °C. While isomerization occurs in solutions at room temperature.

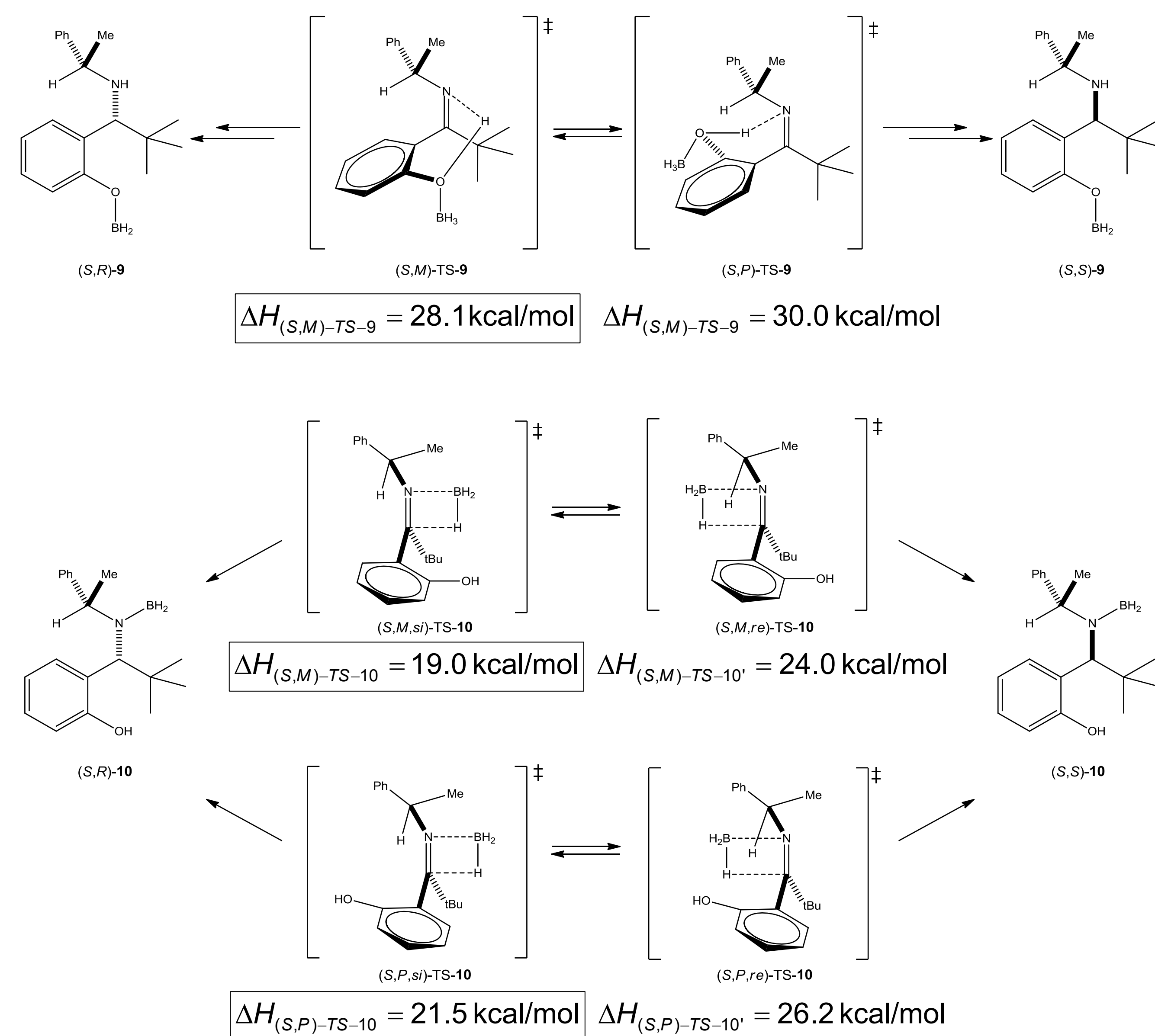


## Calculated transition states for the reduction of 3a



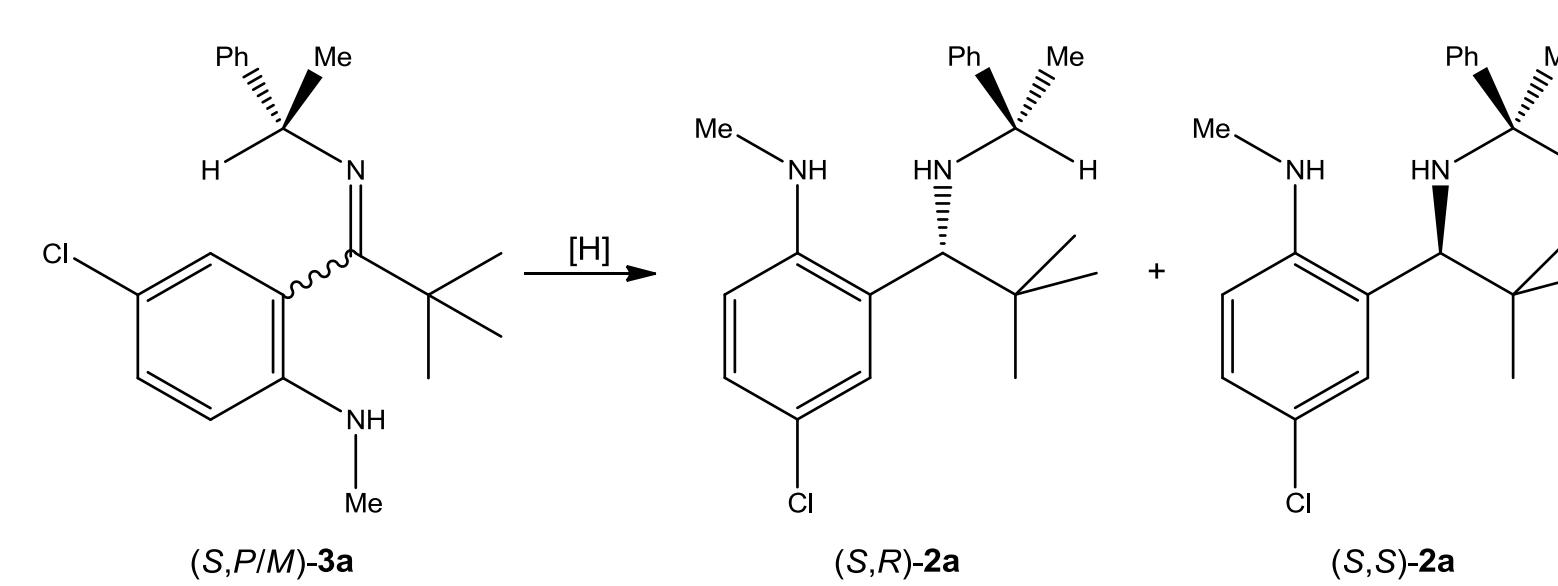
Intramolecular 6-membered transition state (S,P/M)-TS-7 is higher in energy compared to 4-membered transition state (S,P/M)-TS-8 ( $\Delta H = 14.1$  kcal/mol). Hence, aniline nitrogen complex with borane does not control reactions diastereoselectivity. Diastereoselectivity of the reaction of 3a is controlled by the chiral auxiliary.

## Calculated transition states for the reduction of 3b



Computational investigation of possible reduction pathways for imine (S,P/M)-3b showed that reduction transition state barriers are lower than rotation barriers. As demonstrated above diastereoselectivity of imine (S,M)-3b and (S,P)-3b reduction is controlled solely by steric hindrance of chiral  $\alpha$ -methylbenzylamine auxiliary. Hydroxyl group doesn't act as directing group for borane attack. This is in agreement with experimental data

## Diastereoselective reduction of imines 3a and 3b

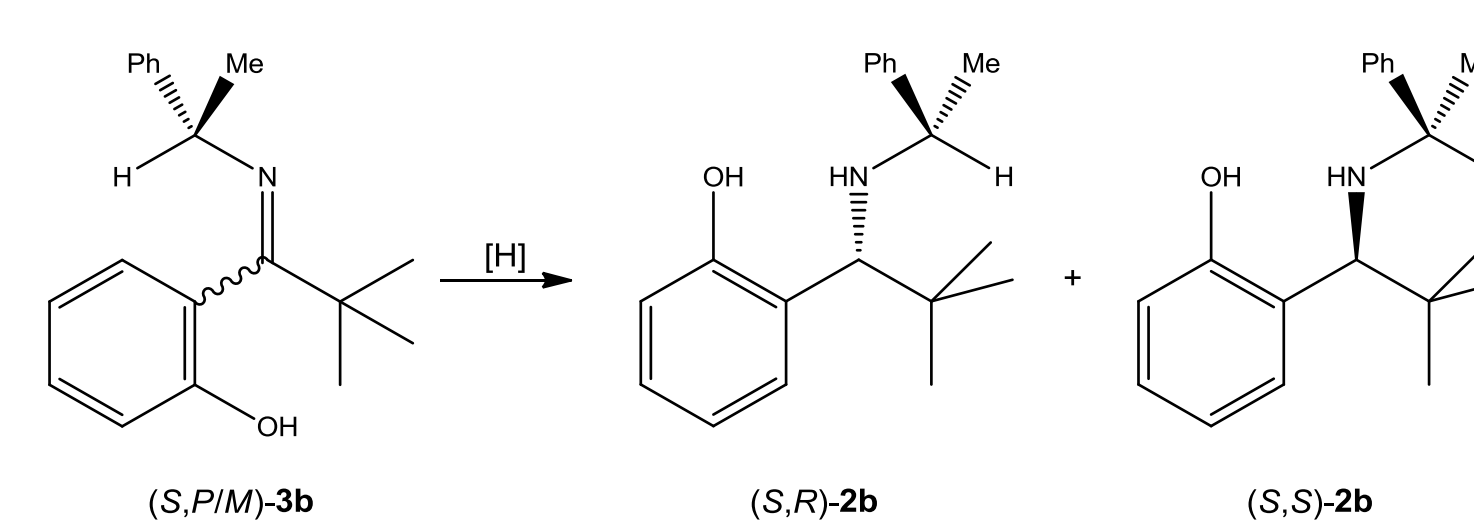


No.	(S,P)-3a:(S,M)-3a	Reaction conditions <sup>a</sup>	(S,R)-2a:(S,S)-2a <sup>b</sup>	Absolute configuration	Yield, %
1	99:1	A	99.5:0.5	R	95
2	1:99	A	96:4	R	76
3	1:1	A	99:1	R	93
4	99:1	B	99:1	R	91
5	1:99	B	99:1	R	90
6	99:1	C	81:19	R	96
7	1:99	C	99:1	R	96

(a) Reaction conditions: A: NaBH<sub>4</sub>, CeCl<sub>3</sub>·7H<sub>2</sub>O, MeOH, -78 °C; B: NaBH<sub>4</sub>, Ti(OEt)<sub>4</sub>, MeOH, -78 °C; C: BH<sub>3</sub>·THF, THF, -78 °C.

(b) Determined by chiral HPLC

Reduction of both (S,P)-3a and (S,M)-3a atropisomers gives diamine (S,R)-2a with R configuration



No.	(S,P)-3b:(S,M)-3a	Reaction conditions <sup>a</sup>	(S,R)-2b:(S,S)-2b <sup>b</sup>	Absolute configuration	Yield, %
1	99:1	A	99:1	R	92
2	1:99	A	1:1	-	93
3	99:1	B	97:3	R	96
4	1:99	B	1:1	-	84
5	99:1	C	99:1	R	95
6	1:99	C	93:7	R	93

(a) Reaction conditions: A: NaBH<sub>4</sub>, CeCl<sub>3</sub>·7H<sub>2</sub>O, MeOH, -78 °C; B: NaBH<sub>3</sub>CN, AcOH, r.t.; C: BH<sub>3</sub>·THF, THF, -78 °C.

(b) Determined by chiral HPLC

Reduction of imine (S,P)-3b gives diamine (S,R)-2b with R configuration, but reduction of imine (S,M)-3b gives mixture of diamines (S,R)-2b and (S,S)-2b with ratio 1:1.