PROBLEM 1

[SUPPL Problem 1 # 2]

Arabic compound numbers in TAPSOC,
Roman numerals in Supplementary material

About the LiHMDS effect on the stereochemical outcome of 1 → 2 + 3.

Rather than causing more trouble to the mechanism solver, stereochemical preference is an invaluable source of information.

Stereochemical outcome not only needs to be accounted for in your answer but the absolute configuration of reaction products is generally the result of critical transition states whereby the combined stereoelectronic interplay of substrate substituents, catalysts and other reagents constitutes a decision making point in the entire scheme.

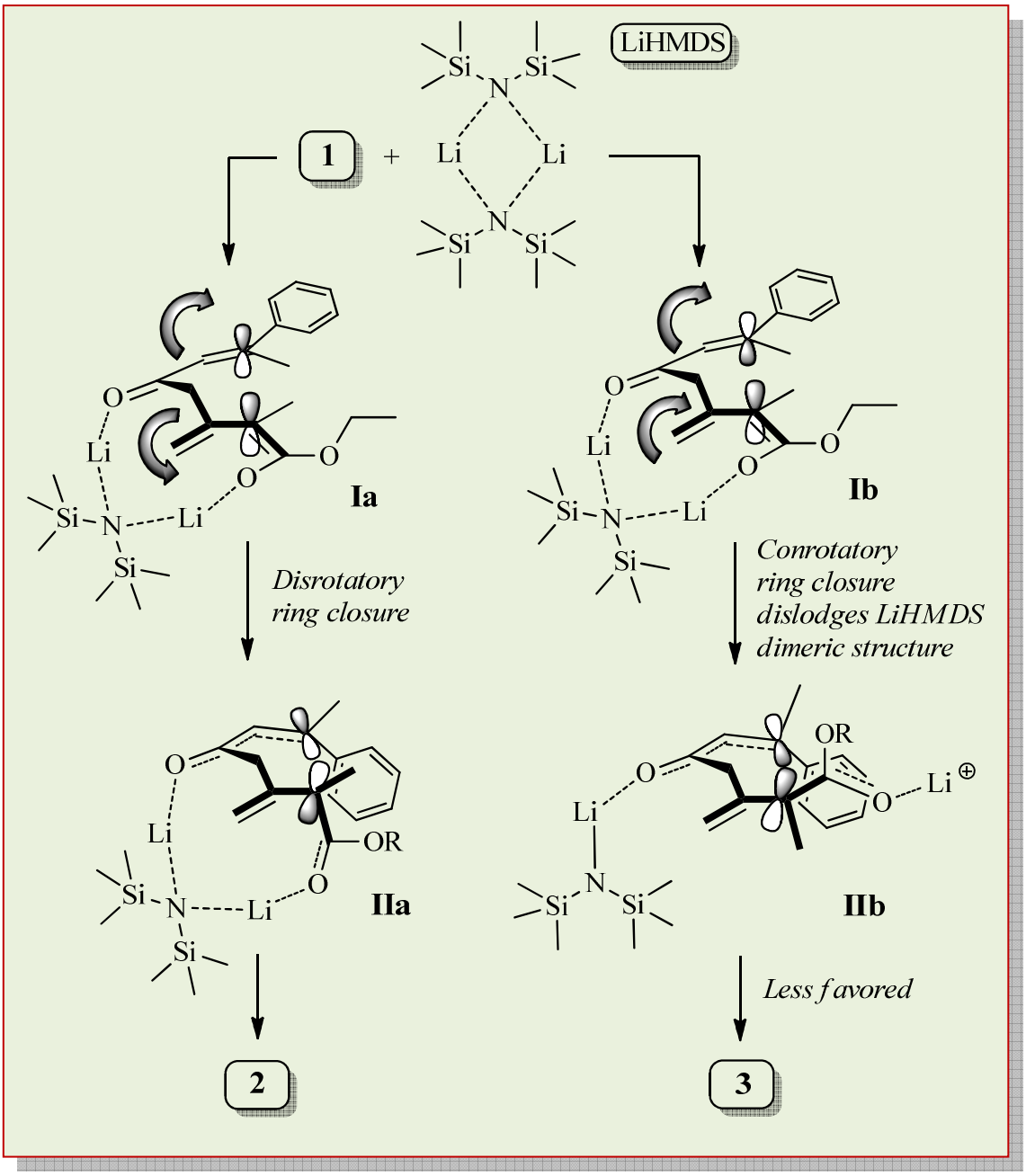
In reaction Scheme 1.1 (TAPSOC) the additional data provided by replacing MeLi with LiHMDS with an enormous impact on product distribution offers the opportunity to refine your mechanistic sequence.

This change in the Li species leads to this primary conclusion: there ought to be active participation of this species in a critical transition state. We should look at **10a**

and **10b** in Scheme 1.2 of TAPSOC for clues. There, MeLi is depicted as a Lewis acid enhancing the reactivity of the α,β–unsaturated ketone in the face of the ester enolate.

Observe that the organic substrate in **10a,b** performs as a **monodentate** ligand as a result of the monovalence of Li in the MeLi model. However, LiHMDS is a much more complex species of dimeric structure with two Li^+ equivalents bridging the bulkyl hexamethyl disilazane sections (Scheme SP1.3 - top).

Alternatively, the organic substrate (**10a/b**) can impinge on LiHMDS in a **bidentate** manner as shown in **Ia** and **Ib**. This pseudo rigid structure offers resistance to the conrotatory cyclization mode, because it forces the disentanglement of the Li complex to allow for **IIb**. This step should be energetically costly relative to **Ia** → **IIa**. A few kcal mol^{-1} difference in $\Delta G^{\ddagger}$ would suffice to throw the reaction in the direction of end product *cis*-**2**


LiHMDS
1
+
Ia
Ib
Disrotatory ring closure
Conrotatory ring closure dislodges LiHMDS dimeric structure
IIa
IIb
Less favored
2
3

SCHEME SP1.3