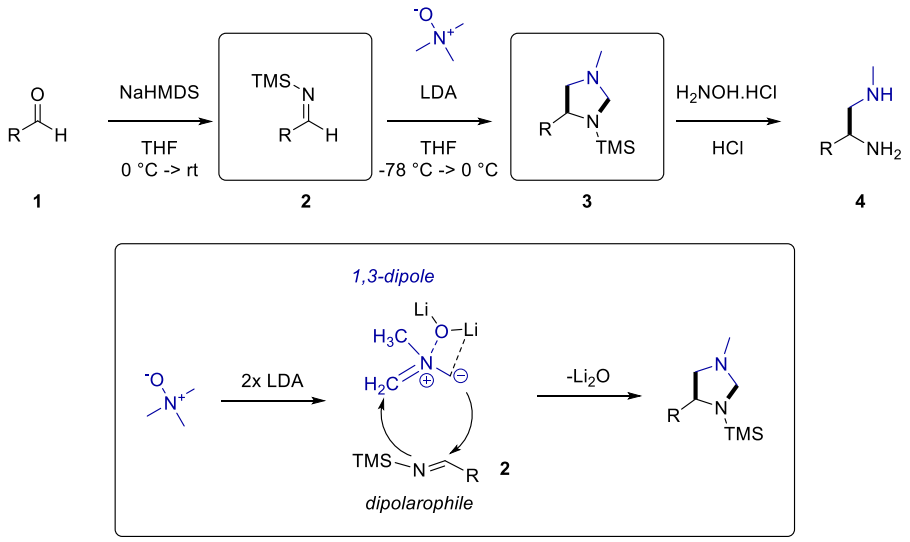
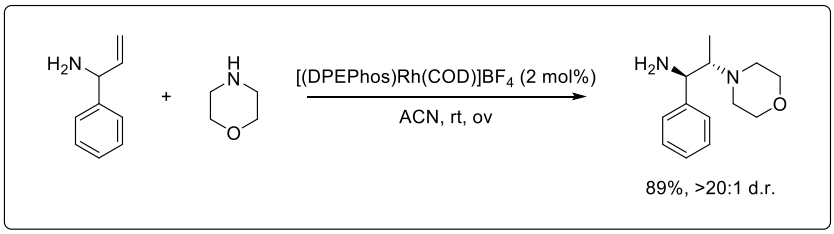
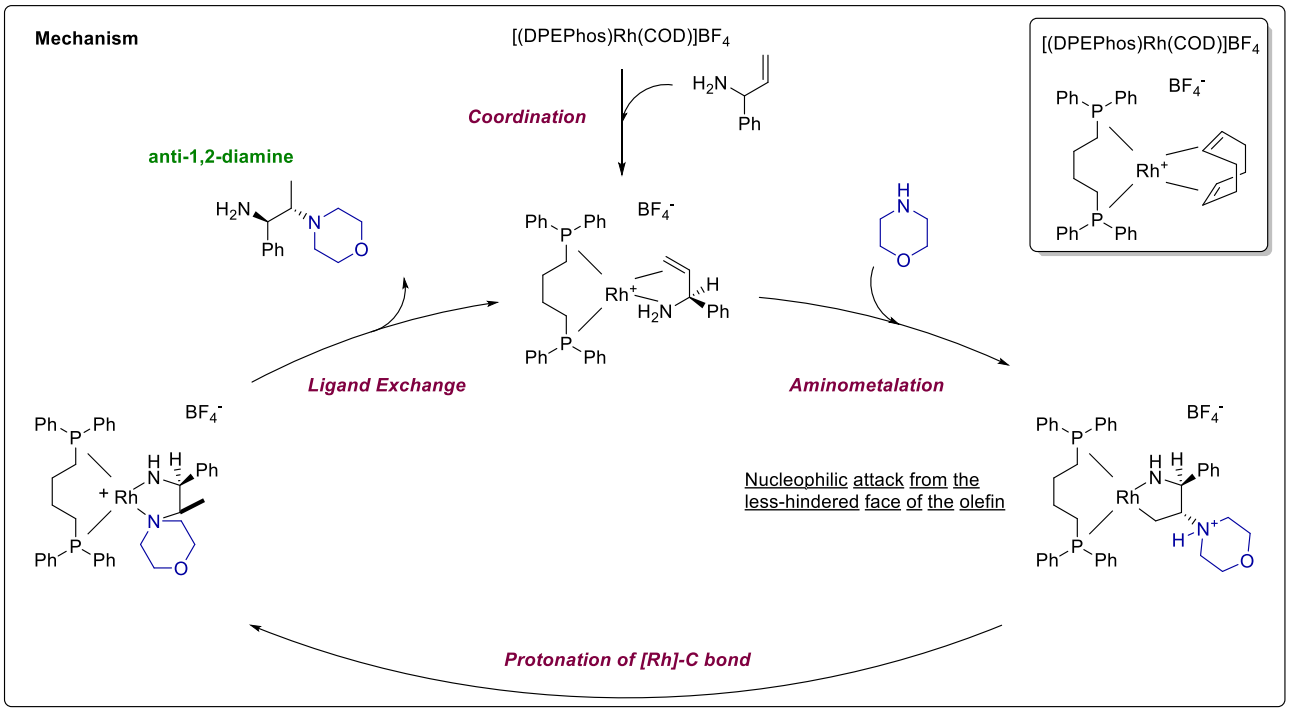
1. Based on the starting material **1** and product **4** propose a structure for intermediates **2** and **3**. Draw the mechanism to go from intermediate **2** to intermediate **3**.



The sequence shown here was presented in the associated research spotlight episode. The imine **2** was formed from the corresponding aldehyde via an aza-Brook rearrangement. Mixing of compound **2** with an *N*-oxide in strong basic media resulted in the imidazolidine compound **3** via a [3+2] cycloaddition reaction. Subsequent ring opening by acidic hydrolysis resulted in the 1,2-diamine **4**. Different mechanisms could be proposed for the formation of the 1,3-dipole from the *N*-oxide. A detailed look into the mechanism of the 1,3-dipole formation was report by Montgomery et al. (J. Org. Chem. 2021, 86, 11502−11518).

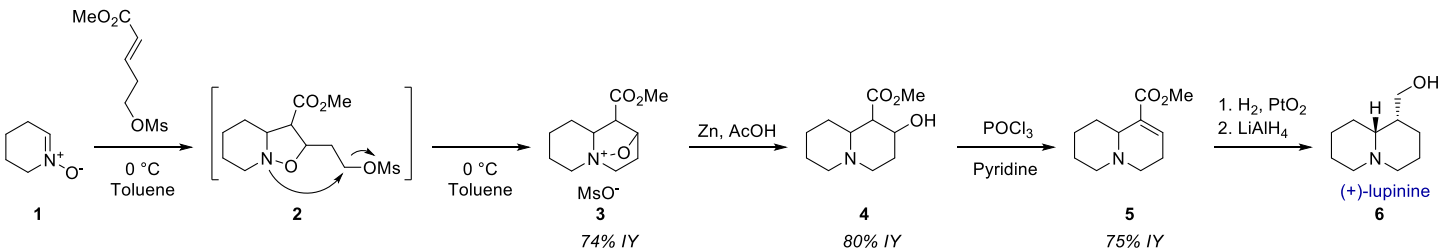
2. Based on the conditions shown draw the structure of the product and propose a catalytic cycle. Based on the catalytic cycle explain the diastereoselectivity of the product.





Similar to the research spotlight episode the product of the reaction shown here is a 1,2-diamine. However, in this report by Hull and co-workers a rhodium-catalyzed strategy was used (J. Am. Chem. Soc. 2014, 136, 11256−11259 and Org. Lett. 2022, 24, 5513−5518). The catalytic cycle proposed involves four steps. First, coordination of the allyl amine with cationic [Rh]. Secondly, nucleophilic attack of the amine which occurs in such a way that the nucleophile attacks the less-hindered face of the activated olefin. Thirdly, direct protonation of the [Rh]-C bond or alternatively (not shown) proton transfer followed by reductive elimination. Finally, ligand exchange liberates the *anti*-1,2-diamine product.

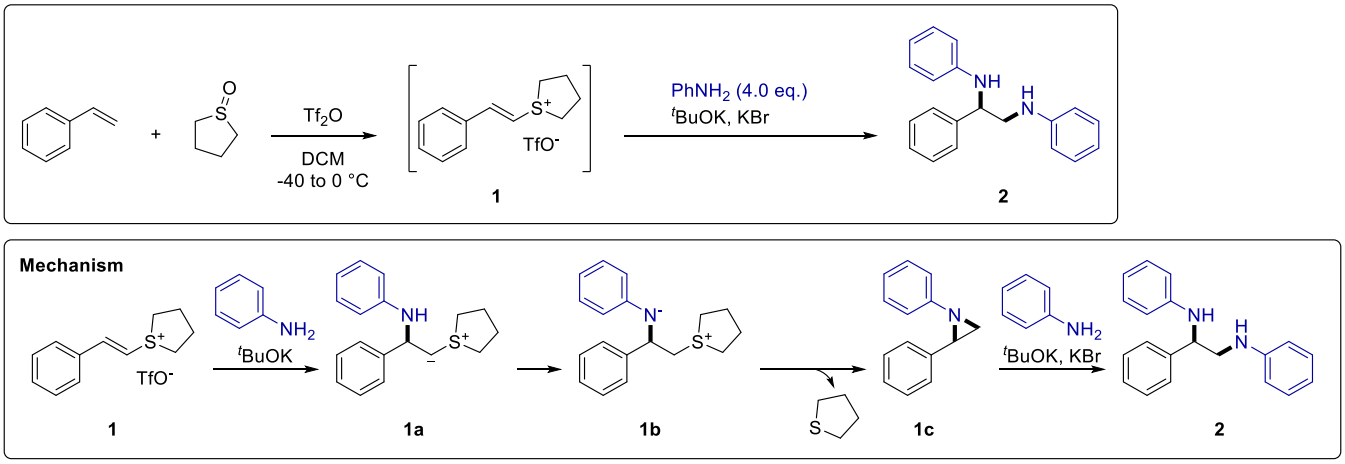
3. Draw the structures of the intermediates and final natural product.



The synthesis of dl-lupine was reported by Tufariello and co-workers (Tetrahedron Lett. 1976, 45, 4037-4040). Central to their route is the [3+2] cycloaddition with 2,3,4,5-tetrahydropyridine-1-oxide **1**. First nitrone cyclization forms an unstable

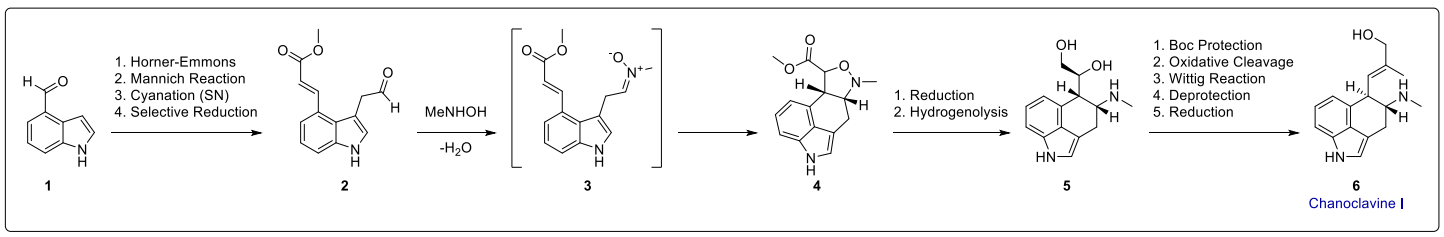
intermediate **2** which undergoes a ring expanding rearrangement providing rapid access to the fused ring system **3**. The salt was isolated and subsequently ring-opened **4**, dehydrated **5**, and reduced to obtain the natural product (+)-Lupine **6**.

4. Propose a structure for both the intermediate and final product. Propose a mechanism for the last step and propose a drawback of this methodology.



Similar to the research spotlight episode the product of the reaction is a 1,2-diamine **2**. The protocol reported by Wen and co-workers starts with the synthesis of a vinyl sulfonium salt **1** which can be isolated or directly reacted in-situ. Addition of base and excess of aniline results in the 1,2-diamine product **2**. The proposed mechanism involves first conjugate addition of the aniline to the vinyl sulfonium salt **1a**, followed by intramolecular proton transfer **1b**, intramolecular cyclization **1c** and finally a second nucleophilic attack by aniline to generate the final 1,2-diamine product **2**. Only identical aryl amines can be used in this strategy.

5. Propose a cycloaddition strategy from indole **2**, via a reactive intermediate, to obtain the *N*-methylated 1,3-aminoalcohol **5** an important precursor in the total synthesis of Chanoclavine I.



The total synthesis of Chanoclavine was reported by Grayson and co-workers (Helv. Chim. Acta 1980, 63, 1706-1710). The key step (**2** to **4**) involves a transient reactive nitrone intermediate **3** which undergoes a regio- and stereo-selective intramolecular cycloaddition to a disubstituted olefinic bond. The nitrone-olefin [3+2]-cycloaddition results in an Isoxazolidine **4** which is converted to the *N*-methylated 1,3-aminoalcohol **5** after reduction of the ester moiety and ring-opening. The potential to ring-open the Isoxazolidine ring system makes it useful in the total synthesis of multiple natural products (for more examples see org. reactions **doi**: 10.1002/0471264180.or036.01).