Exercise 1: Proximity Effect

1-A) Considering the deuterium labeling experiment (vide infra), please provide a plausible mechanism accounting for the formation of bicyclic alcohol A.

1-B) Upon treatment under identical conditions, trans-cyclooctene oxide is converted into a mixture of cycloheptanecarboxaldehyde 7 and exo-A. Provide a mechanism for the formation of 7.

Exercise 2: Synthesis of (-)-Galanthamine

Galanthamine is a natural product isolated from snowdrop Galanthus Caucasicus (Bulgaria, Turkey, Caucasus mountains). Its use in traditional medicine likely dates back to antiquity. Researchers even suggested that Homer's "Moly" referred to Galanthus (Moly is a magical herb mentioned in Homer's Odyssey). It is currently used as a medicine for the treatment of cognitive decline associated with Alzheimer's disease. The first total synthesis of Galanthamine was reported by Sir. D. H. R. Barton (JCS, 1962, 806). In the 1990's, requirements of kg-quantities of material for clinical trials urged the development of a scaleable route. Building-up on Barton's strategy, a process-chemistry group reported the following synthesis (OPRD, 1999, 425).

2-A) Provide a mechanism for the transformation A -> B.

2-B) rac-Narwedine is converted in (-)-Narwedine in 80% yield by crystallisation. Please explain why yield exceeds 50%. Can this process be called a chiral resolution?
Exercice 3 : Shenvi’s Total Synthesis of (-)-Bilobalide

3-A) Determine the structure of all missing intermediates (D, F, I, J & L). Provide a mechanism for the transformation of D -> E and K -> L.
3-B) Compounds D and F are unstable under basic conditions. Why?
3-C) During the final step, identify competing positions for oxidation. In addition to the regioselectivity issue, what side reaction could be observed upon treatment of M with KHMDS?

![Chemical structures and reactions](image-url)