SAMPLE PROBLEM:

Consider the structure below. Develop two enantioselective, retrosynthetic solutions to the synthetic problem and describe one forward synthesis in detail.
**Retrosynthetic analysis 1:**

This retrosynthetic analysis uses tartaric acid-derived 6 as a source of the stereogenic centers needed in the 1,2-diamine functionality in 1. The optically pure (R,R) and the (S,S) stereoisomers of tartrate are both available commercially. The triple bonds in structure 5 are convenient to acidify the termini of the three carbon unit bearing the primary amine to allow nucleophilic substitution. In the processes described by retroarrow a, protection of the amines (NH-Proc) that allows transformations from structures 5 to 2 will be sought. Nucleophilic substitution will be used to displace the oxygen atoms after the chain is elongated in retrosynthetic arrow b. OAct indicates activation of the oxygen atoms as leaving groups.

Since I have chosen to present this retrosynthesis as a forward synthesis I will leave the description sketchy and refer to referenced literature in the forward synthesis.

**Retrosynthetic analysis 2:**

Another feasible stereoselective retrosynthesis involves net addition of two nitrogen atoms across the double bond which should generate structure 8 from 9. The diastereoselectivity is controlled at this point but there will be a racemic mixture (two enantiomers in the reaction vessel) once the synthesis is complete. The resolution of similar mixtures to a single enantiomer has been accomplish for a variety of chiral 1,2-diamines. This protocol reduces the molecular complexity to the stereo control of a 1,2-disubstituted alkene. Stereocontrol can be effectively accomplished by the selective coupling of ylide 10 with aldehyde 11.

Retrosynthetic analysis 2 is less atom economical than retrosynthetic analysis 1 because half the material is discarded in the resolution. Resolving the 1,2-dimamine at the earliest possible stage in the synthesis would be desirable from the standpoint of atom economy.
FORWARD SYNTHESIS of retrosynthetic analysis 1.

The synthesis begins with compound 12 available from a three-step synthesis starting with the (l) isomer of tartaric acid. Upon triflation the primary alcohols are activated to SN2 displacement by carbanions. In the cited example the sodium salt of an amide enolate displaces the triflate of 13. Homologation of the chains in two directions simultaneously takes advantage of the fact that the structure is C2 symmetric. Hydrolysis of the 1,3-dioxolane protection of the 1,2-diol, mesylation and substitution with sodium azide should furnish 15. These operations were performed on 16 to furnish 17 in the cited reference. Note that the substitution reaction occurs with inversion at the carbinol carbon atom. In the last step all three functionalities azide, triple bond and benzylamine should reduce under heterogeneous catalysis with H2 and Pd.

2 Mash, E. A.; Nelson, K. A.; Van Deusen, S.; Hemperly, S. B. "1,4-Di-O-Alkyl Threitols From Tartaric Acid: 1,4-Di-O-Benzyl-L-Threitol [2,3-Butanediol, 1,4-bis(phenylmethoxy)- [S-(R,R)""] Organic Synthesis, Coll. Vol. 8, 155.