Appendix 1

A. In the case that both substituents are the same for addition to the piperidine nitrogen, then 2 moles of alkylating component (e.g. iodoethane) are reacted with 1 mole of piperidine derivative and 1 mole of KHCO3 in methanol at room temperature for several days. The progress of the alkylation can be followed by thin-layer chromatography. After the reaction has made good progress, the methanol is removed. Then the solids are extracted 3 times with portions of chloroform. The chloroform is then dried several hours over magnesium sulfate. The chloroform is filtered from the drying agent, also then removed and the extracted material is recrystallized in a minimum of hot methanol.

In the case where we form a spiro derivative, the same procedure is followed with both halogen reactive centers coming from each end of the C4 or C5 chain.

B. If the goal is to add two different substituents to nitrogen then it is done in stepwise fashion with the larger group added first. So for example a reaction can be carried out with 2-brompropane and an equal amount of a piperidine compound. The reaction is run in methanol. Once TLC shows good progress on the product formation, the reaction can be concentrated down until there is a clear solution and then chilled. The crystals that form and are isolated will be the HBr salt of the tertiary amine (from the secondary amine piperidin). The product is dissolved in water, the solution made basic with NaOH to pH = 12, and then extracted several times with diethyl ether. This extracts the free tertiary amine from the basic aqueous phase. The ether fractions are dried with sodium sulfate and then the ether is stripped off, leaving an oil. Dissolve the oil in acetone and then add the second alkylating reagent (e.g. methyl iodide) and collect the crystals that eventually form.

Appendix 2