Organic Cumulative Exam

Advisor: Name:

Please use separate paper for your answers.

- 1.) (30 points) The Nobel Prize in Chemistry was shared this year among three chemists for "their development of catalytic asymmetric synthesis." Please name the chemists, their affiliation, and their most significant contribution to chemistry.
- 2.) (10 points) Please identify one other chemist, not referred to above, or not at MU, that in your estimation could qualify for a high honor, *e.g.*, the Nobel Prize. Please identify the chemist's affiliation, and write a strong nomination for the chemist, describing his/her accomplishments to date (2-3 paragraphs). The nomination should contain keywords so that it would be possible to find papers co-authored by your nominee.
- 3.) (15 points) Many pharmaceutical drugs contain chiral carbons; however, these drugs are marketed in their racemic form. There has been much current interest in preparing enantiomerically pure forms of many of these medicines. One of these is Ritalin, used mainly for the treatment of attention deficit hyperactivity disorder. The trivial name for Ritalin is Methylphenidate. A more complete name for Ritalin is: Methyl 2-phenyl-2-(2'-piperdyl)acetate.

Draw all the stereoisomers of Ritalin, identifying the absolute configuration at each chiral carbon atom.

- 4.) (20 points) Enantiomers can be resolved into their separate antipodes by a variety of methods. Please explain two fundamentally different ways to accomplish this task. Explain in detail how you would verify that you were successful.
- 5.) Question 5 is on the next page.

6.) (25 points) -narcotine (1A) and -narcotine (1B) are identical except for having opposite configurations at the chiral center bearing oxygen. In order to establish their stereochemistry, they were each used as starting material in the following sequence of reactions:



The final product **4** was the same in both cases and was identical with tetrahydroprotoberberine, which is known to have the absolute configuration *S*. The ¹H nmr spectra of **3A** and **3B** in CDCl₃ showed complex multiplets in the 5.0-5.4 region. Washing the solutions with D₂O simplified this region in both cases. **3A** gave a doublet at 4.75 (J = 9 Hz); **3B** gave a doublet at 5.1 (J = 1.5 Hz). Rewrite the structure of narcotine indicating its absolute configuration at both chiral centers and show how you arrived at this conclusion. Include structures for compounds **2A**, **2B**, **3A**, and **3B**.