Incorporation of the GEMs item: *A greener synthesis of creatine* submitted by Carl S. Lecher into the Organic Chemistry curriculum.

Summary prepared by **Carl S. Lecher**, Assistant Professor of Chemistry at Marian College, Indianapolis, Indiana (July 2008). Email: clecher@marian.edu

**Summary:** This simple procedure for the synthesis of creatine is a student favorite, especially for student athletes. The procedure demonstrates the preparation and isolation of a commonly known dietary supplement from sarcosine and cyanamide. Aqueous household ammonia functions both as the catalyst and the solvent. The experiment can be utilized for a variety of purposes within the organic chemistry curriculum, including the chemistry of nitriles, and is useful for starting a discussion of the impact of experimental design on the generation of impurities.

In other routes, creatine is typically synthesized from sarcosine and cyanamide as well. However, there are deficiencies in the usual routes. Cyanamide is used in excess (2 or more equivalents), concentrated ammonium hydroxide is used as the catalyst, and two equivalents NaCl are used as an additive to aid in the precipitation of the product. Students should be able to identify three ways to potentially improve both the greenness and quality of the creatine synthesized by this method. The first is to reduce the amount of cyanamide used from two equivalents to one equivalent. In addition to improving the effective mass yield of the reaction, it should greatly reduce the generation of the impurity dicyanodiamide, a dimer of cyanamide. The second is to eliminate use of NaCl. This would also improve the effective mass yield of the reaction, as well as eliminate the presence of any sodium chloride as an impurity in the product. The third would be to eliminate use of concentrated ammonium hydroxide, which presents a host of safety problems, including causing severe skin irritation, skin burns, and severe irritation to the upper respiratory tract. Replacing concentrated ammonium hydroxide with household ammonia (which can be further diluted) would eliminate these safety concerns and the need for a fume hood.