

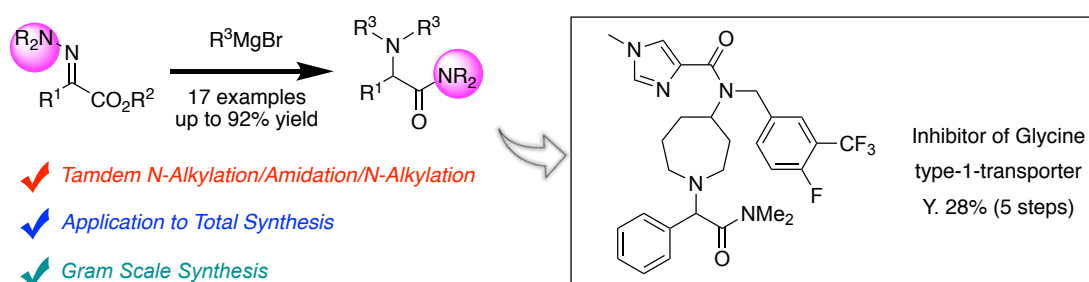
## Highly Selective Synthesis of $\alpha$ -Aminoamide Utilizing an Umpolung Reaction and Characteristics of $\alpha$ -Hydrazonoester

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Hydrazones are versatile synthetic intermediates in organic chemistry such as Wolff-Kishner reduction, Shapiro reaction, and Bamford-Stevens reaction. Since their C=N moieties behave as electrophiles of moderate reactivity with an availability of their chiral versions, e. g., SAMP and RAMP hydrazones, they have received considerable attention as stable and versatile imine derivatives and the development of various synthetic methodologies has been desired. During our research into  $\alpha$ -iminoester,<sup>1</sup> we have been interested in the reactivity of oxime derivatives as stable and useful substrates for the  $S_N2$  type reaction at the nitrogen atom and for the subsequent umpolung reactions to introduce plural substituents at the nitrogen.<sup>2</sup>

During the exploration into the  $S_N2$  type reaction at the nitrogen atom, we focused on a relatively strong N-N bond of the hydrazone moiety and found that once the N-N bond was cleaved, the cleaved nitrogen moiety behaved as a good nucleophile for the ester part to convert it to an amide. Herein, we would like to report an intriguing  $\alpha$ -aminoamide synthesis using an  $S_N2$  type reaction at the nitrogen atom followed by the subsequent amide formation and the second *N*-alkylation. Further extension of the present reaction to the synthesis of an inhibitor of the glycine type-1-transporter was also successfully carried out in an efficient manner.<sup>3</sup>



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- 2) I. Mizota, M. Maeda, M. Shimizu, *Tetrahedron* **2015**, 71, 5793.
- 3) I. Mizota, Y. Nakamura, S. Mizutani, N. Mizukoshi, S. Terasawa, M. Shimizu, *Org. Lett.* **2021**, 23, 4168.