Proline-β3-Amino-Ester Dipeptides as Efficient Catalysts and Their Application

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During the past decade organocatalysis, which indeed has been known for more than a century, has emerged as one of the hot topics in organic chemistry[1]. In this contest a great deal of attention has been paid to the catalytic power of naturally occurring amino acids, due to both their low cost and availability in highly enantiopure form. Rather recently, Singh’s group have reported[2], along the line of former reports[3] by Wu et al., some new l-proline amides having an extra chiral center at the R position of the amide nitrogen atom and a polar, bulky group at the β position. They are highly efficient organocatalysts carrying out diastereo- and enantioselective direct aldol reactions in both organic and (much better) aqueous medium.

![Figure 1](https://example.com/figure1.png)

Figure 1. Dipeptide catalysts for asymmetric direct aldol reaction

Those new molecules aroused our attention because of their amino moieties that reminded of C-2 substituted β3-amino acids whose chemistry is our current interest. Therefore, we investigated[4] the behavior of real dipeptides coming from coupling of l-proline with miscellaneous C-2 substituted and unsubstituted β3-l-amino acids as catalysts in the model direct aldol reaction of cyclohexanone and 4-nitrobenzaldehyde. Our results were interesting and thoroughly consistent with the mechanism generally accepted for catalyzed aldol reactions. A curiosity remained unsatisfied as to the role played by the C-2 substituent (when present) in affecting the whole catalytic power of the various dipeptides tested: as a matter of fact, which aspect of the dual nature of any C-2 substituents, namely hydrogen bond-donor ability vs steric hindrance, would prevail at the transition state and consequently shape it? Therefore, we planned to modify our model catalyst, namely H-l-Pro-β3-l-Phe-OMe by inserting at the C-2 position of the β3-phenylglycine both a polar substituent, like –OH, a nonpolar, like –CH3 and a nonpolar as cumbersome, like CH2Ph. In the present work, we report the synthesis of the catalysts, that were obtained in good yields, 17 % 14 % and 28 %, respectively.

REFERENCES


