Pergamon

Tetrahedron Letters, Vol. 38, No. 16, pp. 2903-2906, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00499-1

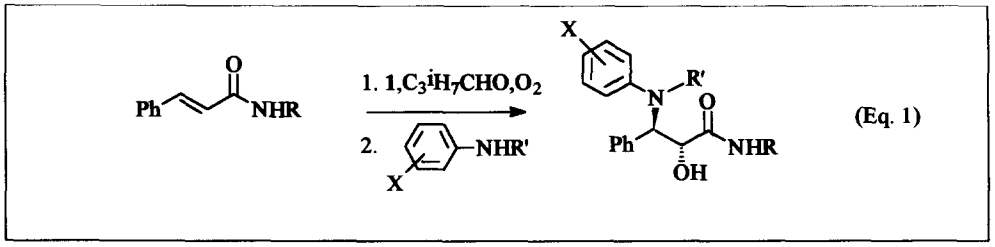
Polyaniline Supported Cobalt(II)-Salen Catalyst : One Pot Synthesis of β-Phenylisoserine Derivatives from Cinnamoyl Amide

Bhaskar C. Das and Javed Iqbal*

Department of Chemistry, Indian Institute of Technology, Kanpur 208 016, India

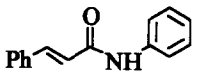
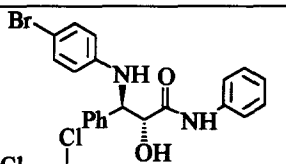
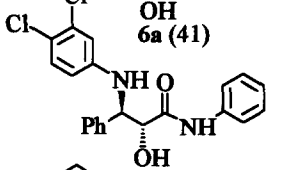
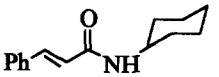
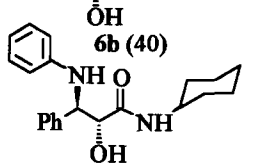
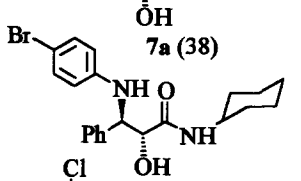
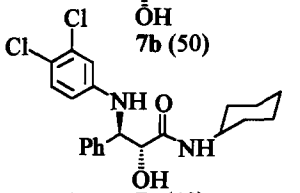
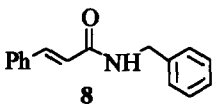
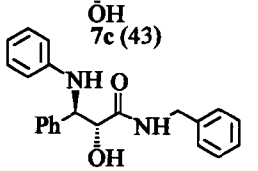
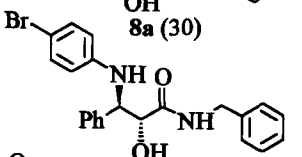
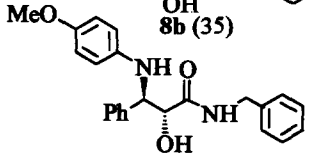
Abstract: *A novel one pot conversion of cinnamoyl amides to the corresponding β-phenylisoserine derivatives was developed by employing polyaniline supported cobalt(II)-salen catalysed formation of the epoxide followed by its opening with anilines at ambient conditions.* © 1997 Published by Elsevier Science Ltd.

Polymer supported metal complexes are gaining importance[1] as efficient heterogeneous catalyst in variety of organic transformations. The advantage of polymer supported catalyst over others is due to their recycleability, selectivity and tolerance to variety of reaction conditions. Recent advances in the polymer supported catalyst is highly promising as it opens up a wide array of applications in organic synthesis, particularly in combinatorial synthesis leading to diverse chemical libraries.[2] Polymer supported substrates are often being employed for variety of reactions in order to create a library of compounds, however, there are some disadvantages to this method. For example, the reaction of polymer supported substrates are sometimes slow and large amount of reagents are required to complete the reaction. Also, the loading capacity of polymer supported substrates is low and large scale preparation of compounds is not feasible. To circumvent this probelm we have developed a new methodology for the combinatorial synthesis.[3] This paper describes a method for the preparation of β-phenylisoserine derivatives using a novel polyaniline supported Co(II)-catalyst. These derivatives may be useful building blocks for the synthesis of dipeptide isosteres having potential[4] role as enzyme inhibitors. In an earlier study we have demonstrated[5a] that polyaniline supported Co(II)-acetate catalyzes the epoxidation of various alkenes under oxygen atmosphere at ambient conditions.



(Eq. 1)

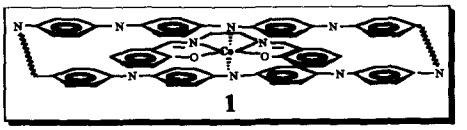
Table 1. Cobalt Complex (1) Catalysed Transformation of Cinnamoyl Amides to β–Phenyl isoserine Derivatives

Entry	Amide	Amine	Product(s) (yield, %)[a]
1.	 **6**	**3**	 **6a** (41)
2.		**4**	 **6b** (40)
3.	 **7**	**2**	 **7a** (38)
4.		**3**	 **7b** (50)
5.		**4**	 **7c** (43)
6.	 **8**	**2**	 **8a** (30)
7.			 **8b** (35)
8.		**5**	 **8c** (40)

2 = aniline, 3 = 4-bromoaniline, 4 = 3,4-dichloro aniline, 5=4-methoxyaniline

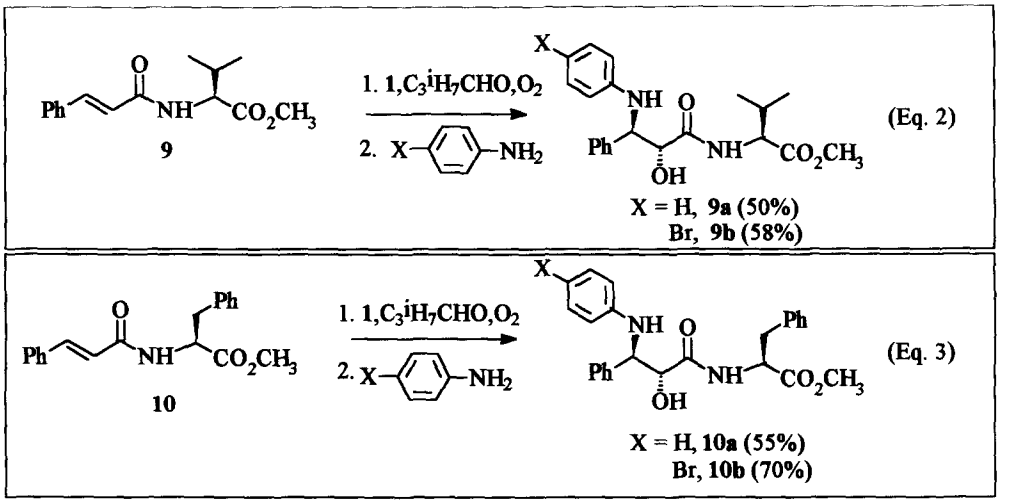
a)Yield of the purified product based on the corresponding cinnamoyl amide.

We now demonstrate a dual role of polyaniline supported Co(II)-salen complex first as a catalyst during the epoxidation of cinnamoyl amides and later during the opening of the correspondings epoxide[5b] with anilines (Eq. 1). This one pot procedure offers a versatile route to β-phenylisoserine derivatives from cinnamoyl amides. The polyaniline supported Co(II)-salen was prepared by stirring an equal mixture (*w/w*) of polyemeraldine[6] base and cobalt(II)-salen[7] in acetonitrile at ambient conditions for 36 h. The filtration and washing with acetonitrile and acetic acid followed by drying at 110-120°C afforded a crystalline solid which showed the presence of cobalt in UV-Vis spectra. The supported Co-salen complex may have the structure **1** as shown below:



1

Typically, cinnamoyl amide (5 mmol) was dissolved in acetonitrile (25 ml) and 2-methylpropanal (15 mmol) was added to it and the resulting mixture was stirred in the presence of catalytic amount of **1** (≈25 mg) under oxygen balloon at ambient temperature (16 to 22 h). The progress of the reaction was monitored by TLC and as soon as the starting cinnamoyl amide disappeared the oxygen baloon was removed and aniline (5 mmol) and catalyst **1** (≈10 mg) was added to this reaction mixture. After an additional stirring for 6 to



8 h at 25°C the solvent was removed to yield a residue which was washed with CCl_4 to afford the corresponding β-phenylisoserine derivatives as a solid in > 90% purity (HPLC). The generality of this reaction is demonstrated by converting phenyl (**6**), cyclohexyl (**7**) and benzyl cinnamoylamids (**8**) using aniline (**2**), p-bromoaniline (**3**), 3, 4-dichloroaniline (**4**) and p-methoxyaniline (**5**) to the corresponding β-phenylisoserine derivatives in good to excellent yields (Table 1). It is interesting to note that the stereochemistry of these amides is found to be *anti* in all the cases, however, the ^{1}H NMR of the crude reaction mixture showed the presence of small amount (15%) of the coressponding *syn* diastereomer.The one pot synthesis of β-phenylisoserine derivatives and the recycleability of catalyst **1** offers an attractive route to the generation of library of compounds in a combinatorial fashion. The noteworthy feature of this reaction

is the simplicity involved during the isolation of the product as the latter can be obtained by merely washing the crude reaction mixture with CCl_4 which removes the unchanged anilines and other nonpolar byproducts. A TLC analysis of the CCl_4 wash also showed the presence of the β-phenylisoserine derivatives apart from the unreacted anilines. It is also noteworthy that the polyaniline supported Co(II)-salen catalyst **1** can be reused after filtering followed by washing and drying. The recovered catalyst **1** was found to be equally active during the conversion of benzyl-cinnamoyl amide with p-bromoaniline to the corresponding β-phenylisoserine derivatives in reproducible yields (Table 1, entry 7).

Similarly the reaction of valinyl cinnamoyl amide **9** and phenylalinyl cinnamoyl amide **10** with amines (**2**) and (**3**) proceeded efficiently to afford the corresponding β-phenylisoserine-valine and phenylalanine dipeptide isosteres derivatives **9a-b** and **10a-b** respectvely in good yields (Eq. 2 and 3). Once again the *anti* diastereomer was found to be the major product, however, small amount of the corresponding *syn* diasteromer was also present in the mother liquor. ***However, no attempts were made to check the optical purity of dipeptide 9a-b and 10a-b and only the relative stereochemistry for these diastereomers have been shown in equation 2 and 3.***

In conclusion, polyaniline supported Co(II)-salen complex is an extremerly versatile catalyst for a one pot conversion of cinnamoyl amides to the corresponding β-phenylisoserine derivatives by a combined use of epoxidation and aniline opening sequence. The purification of these derivatives by CCl_4 washing circumvents the use of column chromatography and therefore offers an attractive protocol for the application in generating a library of α-hydroxy-β-amino acid derivatives and dipeptide isoteres derived from the corresponding amino acids.

Acknowledgements: One of us (BCD) is grateful to CSIR, New Delhi for Senior Research Fellowship.

REFERENCES

1. a) Itsuno, S.; Sakurai, Y.; Ifo, K.; Maruyama, T; Nakahama, S.; Frechot, J. M. J. *J. Org. Chem.* **1990**, *55*, 304. b) Tang, H. G.; Shrrington, D. C. *Polymer*, **1993**, *34*, 2821. c) Miller, M. M.; Shrrrington, D. C. *J. Catalysis*, **1995**, *152*, 368. d) Ahn, J. H.; Sherrington, D. C.; *J. Chem. Soc., Chem. Comm.* **1996**, 643. e) Altava, B.; Burguete, M. I.; Luis, S. U.; Mayoral, J.A. *Tetrahedron* **1994**, *50*, 7535. f) Brock, T.; Sherrington, D. C. *Polymer*, **1992**, *33*, 1773.
2. Kobayashi, S.; Nagayama, S. *J. Am. Chem. Soc.*, **1996**, *118*, 8977.
3. a) Thompson L. A.; Ellman, J. A. *Chem. Rev.* **1996**, *96*, 555. b) Fruchtel, J. S.; Jung, G.; Angew; *Int. Ed. Engl.* **1996**, *35*, 17. c) Terret, N. K.; Gardner, M.; Gordon, D. W.; Kobylecki, R. J.; Steele, J. *Tetrahedron*, **1995**, *51*, 8135.
4. Abbenante, G.; March, D. R.; Bergman, D. A.; Hunt, P. A.; Garnham, B.; Dancer, R. J.; Martin, J. L.; Fairlie, D. P. *J. Am. Chem. Soc.* **1995**, *117*, 10220.
5. a) Das, B.C.; Iqbal, J. *Tetrahedron Lett.* **1997**, (*in press*). b) Bhatia, B.; Jain, S.; De, A.; Bagchi, I.; Iqbal, J. *Tetrahedron Lett.*, **1996**, 37, 7311.
6. Hasik, M.; Turek, W.; Stochmal, E.; Lalkowski, M.; Pron, A.; *Journal of Catalysis* **1994**, *147*, 544.
7. Bailes, R. H.; Calvin. M. *J. Am. Chem. Soc.* **1947**, *69*, 1886.

(*Received in UK* 7 *January* 1997; *revised* 11 *March* 1997; *accepted* 14 *March* 1997)