Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 48 (2007) 2687–2690

Catalytic, enantioselective allylation of α-iminoesters promoted by silver(I) complexes of chiral imines

Federica Colombo, Rita Annunziata and Maurizio Benaglia*

Dipartimento di Chimica Organica e Industriale, Università degli Studi di Milano, via Golgi 19, 20133 Milano, Italy

Received 18 January 2007; revised 14 February 2007; accepted 14 February 2007
Available online 17 February 2007

Abstract—The catalytic enantioselective addition of allyltributylstannane to N-protected α-iminoesters promoted by silver(I) trifluoromethanesulfonate in the presence of chiral imine ligands was studied. After testing several chiral imines derived from 1,2-diaminocyclohexane and binaphthyl diamine a very simple experimental procedure was developed that allowed us to obtain optically active homoallylic amines in very high yields and enantioselectivities up to 71%.

The synthesis of enantiomerically enriched homoallylic amines is a topic of paramount importance since they represent useful synthetic intermediates that may be converted in different functional groups.[1] In this context the enantioselective catalytic allyl addition to α-iminoesters is of special interest because this conversion provides an efficient route to optically active, nonnatural α-amino acids for use in natural products, peptide and pharmaceutical chemistry.[2] While the catalytic enantioselective allyl addition to carbonyl compounds is well developed,[3] few examples of the analogous reaction with imino esters are known, despite their utility in organic synthesis.[4] Lectka[5] and Jorgensen[6] reported an efficient addition of allylsilane and allylstannane, respectively, to *N*-tosyl iminoesters catalysed by Cu(I)/Binap complexes.[7] More recently Kobayashi[8] employed a 1,2-diphenyl-diamine/Cu(II) catalyst to successfully promote the addition of a properly functionalised allylsilane to *N*-acyliminoesters.[9] Unfortunately the known methods suffer from substrate limitation or require very special experimental procedures, like slow addition of one reagent in order to achieve high enantioselectivities.

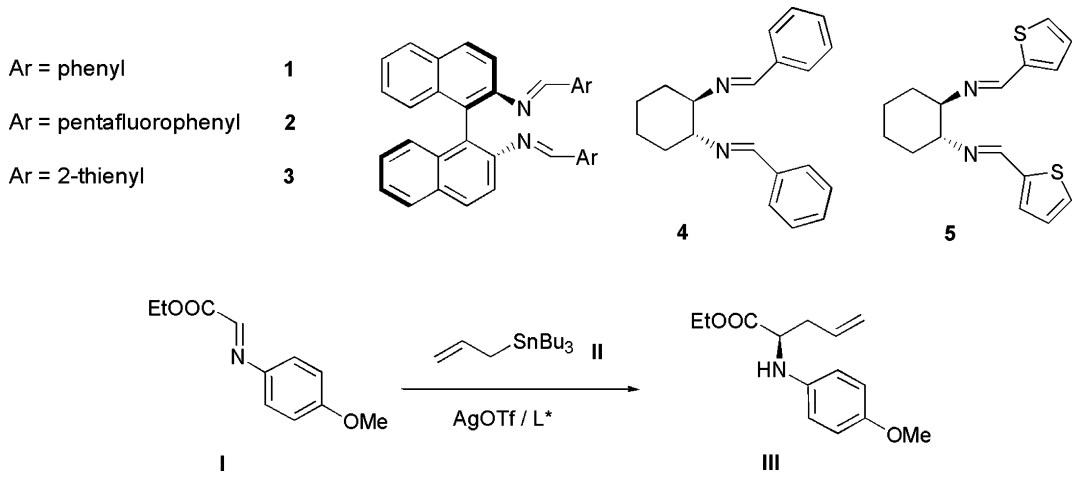
Hence the development of new, general, less expensive and practical enantioselective catalytic methods is strongly desired. Herein we report here the preliminary results of a study of the catalytic enantioselective addition of allyltributylstannane to N-protected α-iminoesters promoted by silver(I) trifluoromethanesulfonate in the presence of chiral bis-imine ligands. Our group has recently started a programme devoted to the development of new catalytic systems, readily prepared from commercially available and possibly cheap chiral reagents, easy to handle, and using very simple experimental procedures.[10] Following our interest in chiral bis-imines as ligands in asymmetric catalysis[11] we reasoned that imines derived from 1,2-diaminocyclohexane and binaphthyldiamine represent good candidates as possible promoters of allyl addition to α-iminoesters.

Compounds **1**–**3** were prepared from the commercially available (*R*)-binaphthyl diamine by reaction with different aromatic and heteroaromatic aldehydes[11] and molecules **4**–**5** were synthesised by condensation of the proper aldehyde with (1*R*,2*R*)-diamino cyclohexane in quantitative yield. The behaviour of such ligands in the silver(I) trifluoromethanesulfonate catalysed reaction between *N*-4-methoxyphenyl imine of ethyl glyoxylate **I** and allyltributyl stannane **II** to afford the optically active homoallylic amine **III** was investigated (Scheme 1).[12]

The reaction was run with ligands **1**–**3** at 0 °C in the presence of 10 mol % catalyst for 20 h in DCM (Table 1). Ligands **1** and **2** which had offered the best performances in the enantioselective catalytic addition of aryl acetylenes to imines[11] afforded the product in low yields and enantioselectivities. Interestingly, better results were

Keywords: Silver complex; Homoallylic amines; Enantioselective catalysis; Chiral imines; Chiral catalysts.
* Corresponding author. Tel.: +39 0250314171; fax: +39 0250314159; e-mail: Maurizio.Benaglia@unimi.it

0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.02.071



Scheme 1.

Table 1. Addition of allyltributyl stannane to iminoester **I**

Entry	Ligand	Solvent	*T* (°C)	Time (h)	Yield[a] (%)	ee[b] (%)
1	**1**	DCM	0	20	50	11
2	**2**	DCM	0	20	70	7
3[c]	**3**	DCM	0	20	98	37
4[c]	**3**	DCM	−40	20	100	43
5[c]	**3**	THF	−40	20	77	18
6[c]	**3**	Toluene	−40	20	21	<5
7	**4**	DCM	0	20	87	<5
8	**5**	DCM	0	20	100	65
9	**5**	DCM	25	1	100	47
10	**5**	THF	25	1	72	51
11	**5**	Toluene	25	1	40	<5

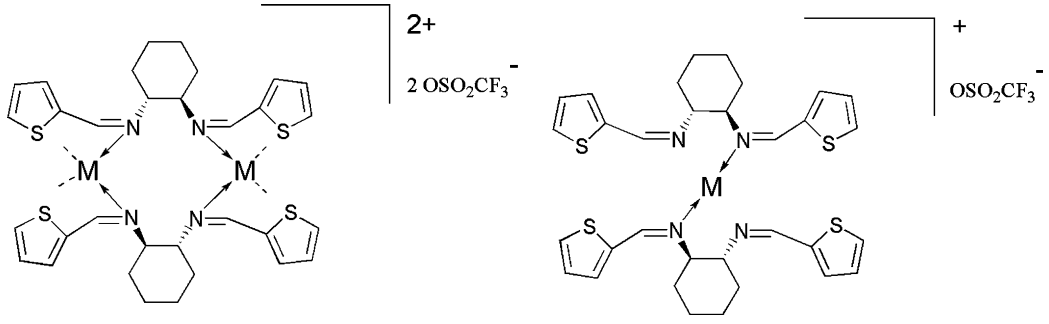
[a] Determined by ^{1}H NMR and confirmed after chromatographic purification.
[b] Determined by HPLC on chiral stationary phase (Chiracel AD column (hexane–isopropanol 95:5; flow rate 0.8 ml/min; λ 254 nm: $t_{major} = 13.1$ min, $t_{min} = 17.9$ min).
[c] With ligand **3** the product with absolute configuration opposite to that afforded by ligands **5**–**15** was obtained.

obtained with 2-thiophene carboxaldehyde derived bis-imine **3** that catalysed the reaction in 98% yield and a 37% ee that was increased to 43% at −40 °C (entries 3–4 vs entries 1–2). In other solvents the reaction was shown to be less stereoselective (entries 5–6).

A similar trend was observed with diaminocyclohexane-based ligands. Silver(I) complex of benzaldehyde derived bis-imine **4** catalysed at 0 °C the addition of stannane **II** to iminoester **I** with poor enantioselection; by employing 2-thiophene carboxaldehyde derivative **5** the product was isolated in quantitative yield with 65% ee and at 25 °C after only 1 h the homoallylic amine **III** was obtained in 47% ee in DCM and 51% ee in THF (entries 8–10 vs entry 7).[13]

It is known that copper complexes of bis-imines derived from C_2-symmetric biaryl diamine may exist as 'monomeric' or 'dimeric' forms, depending on the steric hindrance of the substituents in 2,6 positions of the aldehyde aromatic ring.[14] Also silver(I) complex of ligand **5** has already been shown to exist in equilibrium between two species (Scheme 2).[15]

In order to understand if different catalytic species, monometallic or bimetallic, were present in the reaction medium, the allylation was performed at 0 °C in DCM with different metal/ligand ratios (Table 2). Binaphthyl diamine derived ligand **3** always afforded similar level of stereoselectivity either when an excess of ligand or an excess of metal was used (entries 1–3). Also bis-imine **5** showed little dependence on the metal/ligand ratio, affording the best result with a 1/2 Ag(I)/**5** ratio (67% ee), not very different from the result obtained with 1/1 ratio (65% ee, entries 4–6). A lower reaction temperature did not bring any appreciable improvement to the stereoselectivity (71% ee, entry 7). Ag(OTf) alone is able to catalyse the reaction (70% yield after 20 h at 0 °C).



Scheme 2.

Table 2. Studies on the Ag(I) catalysed allylation of imine **I**[a]

Entry	Ligand	M/L* Ratio	Yield[b] (%)	ee[c] (%)
1	**3**	1:1	100	37
2	**3**	2:1	100	36
3	**3**	1:2	100	38
4	**5**	1:1	100	65
5	**5**	2:1	100	57
6	**5**	1:2	100	67
7[d]	**5**	1:2	100	71

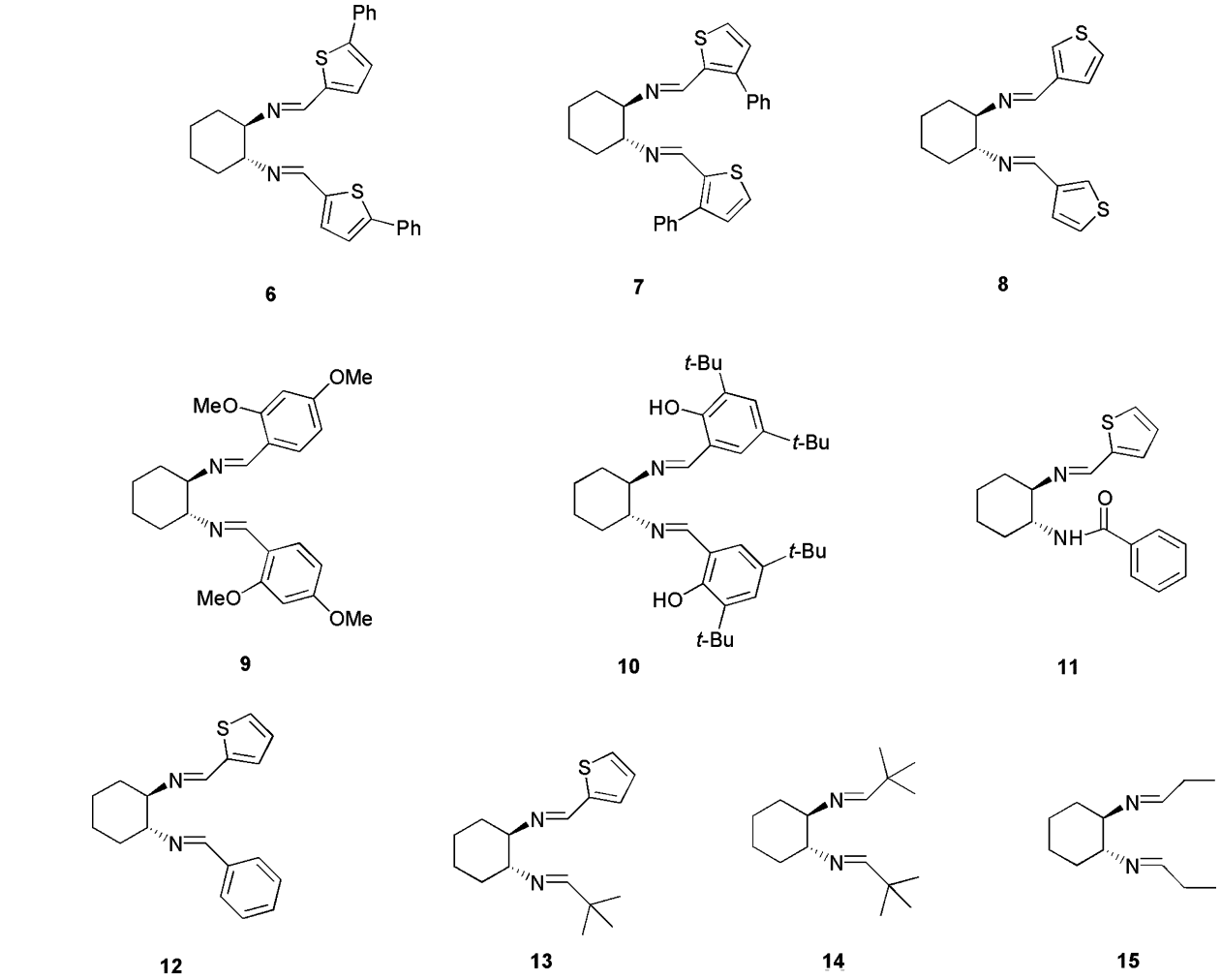
[a] Reaction run at 0 °C for 20 h in DCM.
[b] Determined by ^{1}H NMR and confirmed after chromatographic purification.
[c] Determined by HPLC on chiral stationary phase.
[d] Reaction run at −40 °C for 20 h.

Therefore the results seem to suggest that under the present experimental conditions the allylation is a ligand-accelerated reaction but they do not allow to draw any definitive conclusion about how many catalytic species are present and eventually which is the real catalytically active enantioselective one.[16]

With the goal to clarify the role of thiophene ring in determining the enantioselectivity of the allylation several other C_1 and C_2 symmetric ligands with different steric and electronic characteristics were prepared and tested (Scheme 3).[17] C_2 symmetric bis-imines **6** and **7** featuring a phenyl group in the 3 or 5 position of the thiophene ring catalysed the reaction in quantitative yield, but not with increased enantioselectivity (Table 3, entries 2 and 3 vs entry 1). Interestingly the 3-thiophene carboxaldehyde derived bis-imine **8** afforded a racemic product, pointing at a decisive role of the 2-thiophene residue in controlling the enantioselective outcome of the reaction.[18]

Electron rich chiral bis-imine, as compound **9**, afforded the product with 39% ee, while the presence of 'acid' hydrogens (ligands **10** and **11**) dramatically decreased the stereoselectivity (entries 5–7). C_1 symmetric bis-imines bringing only one 2-thiophene ring were also tested. While ligand **12** promoted the reaction with 40% ee, slightly lower than **5**, ligand **13** afforded the product with comparable enantioselectivity (61% ee, entries 8–9). Noteworthy once again the analogous C_2 symmetric ligand **14**, and the less sterically demanding bis-imine **15**, both without any thiophene residue, catalysed the allylation with lower enantioselectivities (entries 10–11).

In conclusion, we have demonstrated that silver complexes of enantiomerically pure imines, readily prepared



Scheme 3.

Table 3. Addition of allyltributyl stannane to iminoester **I** promoted by Ag(I) complexes[a]

Entry	Ligand	Yield[b] (%)	ee[c] (%)
1	**5**	100	65
2	**6**	98	37
3	**7**	95	45
4	**8**	95	8
5	**9**	90	39
6	**10**	91	<5
7	**11**	90	11
8	**12**	93	40
9	**13**	91	61
10	**14**	93	35
11	**15**	97	33

[a] Reaction run at 0 °C for 20 h in DCM.
[b] Determined by ^{1}H NMR and confirmed after chromatographic purification.
[c] Determined by HPLC on chiral stationary phase.

in one step and in very high yields from commercially available chiral diamines are efficient catalysts for the allyl addition to α-iminoesters.[19] A very simple experimental procedure was developed that allowed us to obtain optically active homoallylic amines in very high yields and enantioselectivity up to 71%. Further work is underway to clarify the origin of the stereoselectivity of the process and improve the performance of the catalyst.

Acknowledgements

This work was supported by MIUR (Rome) within the national project 'Nuovi metodi catalitici stereoselettivi e sintesi stereoselettiva di molecole funzionali'. We thank Professor Cozzi for valuable discussion.

References and notes

1. Miller, S. J.; Blackwell, H. E.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 9606–9614, and references cited therein.
2. Groger, H. *Chem. Rev.* **2003**, *103*, 2795–2828; Burk, M. J. *Acc. Chem. Res.* **2000**, *33*, 363–372; Alvaro, G.; Savoia, D. *Synlett.* **2002**, 651–673.
3. Denmark, S. E. *Chem. Rev.* **2003**, *103*, 2763–2794; Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200–206.
4. The difficulty in developing catalytic systems for the organometallic addition to imines is also due to the fact that Lewis acids may be deactivated or decomposed by the nitrogen atom of the reagents or of the products.
5. Ferraris, D.; Dudding, T.; Young, B.; Drury, W. J., III; Lectka, T. *J. Org. Chem.* **1999**, *64*, 2168–2169; Ferraris, D.; Young, B.; Cox, C.; Dudding, T.; Drury, W. J., III; Lectka, T. *J. Am. Chem. Soc.* **2002**, *124*, 67–77.
6. Fang, X.; Johannsen, M.; Yao, S.; Gathergood, N.; Hazell, R. G.; Jorgensen, K. A. *J. Org. Chem.* **1999**, *64*, 4844–4849.
7. These catalytic systems promoted the allylation reaction up to 80% ee, and it must be noted that from a synthetic point of view the deprotection of a *N*-sulfonyl may result quite problematic.
8. Kiyohara, H.; Nakamura, Y.; Matsubara, R.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 1615–1617.
9. For catalytic enantioselective allylations of imines and their equivalents see: Nakamura, H.; Nakamura, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4242–4243; Fernandes, R. A.; Stimac, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 14133–14139; Fernandes, R. A.; Yamamoto, Y. *J. Org. Chem.* **2004**, *69*, 735–739; Gastner, T.; Ishitani, H.; Akiyama, R.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 1896–1897; Hamada, T.; Manabe, K.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 3927–3929.
10. Puglisi, A.; Benaglia, M.; Annunziata, R.; Bologna, A. *Tetrahedron Lett.* **2003**, *44*, 2947–2950; Colombo, F.; Annunziata, R.; Benaglia, M.; Raimondi, L. *Chirality* **2006**, *18*, 446–453; For an example of chiral organic catalyst see: Pignataro, L.; Benaglia, M.; Annunziata, R.; Cozzi, F.; Cinquini, M. *J. Org. Chem.* **2006**, *71*, 1458.
11. Benaglia, M.; Negri, D.; Dell'Anna, G. *Tetrahedron Lett.* **2004**, *45*, 8705–8708; Orlandi, S.; Colombo, F.; Benaglia, M. *Synthesis* **2005**, 1689–1691; Colombo, F.; Benaglia, M.; Orlandi, S.; Usuelli, F.; Celentano, G. *J. Org. Chem.* **2006**, *71*, 2064–2070; Colombo, F.; Benaglia, M.; Orlandi, S.; Usuelli, F. *J. Mol. Catal., A: Chemicals* **2006**, 128–134.
12. The catalytic behaviour of several metals was studied under the same experimental conditions (Zn(II), Cu(II), Ir(I), Ni(II), Ag(I)), but Ag(OTf) gave the best performances; among different silver(I) salts tested in the reaction silver trifluoromethanesulfonate was selected.
13. By further lowering the reaction temperature to −40 °C the enantioselectivity of the process was not appreciably improved.
14. Sanders, C. J.; Gillespie, K. M.; Bell, D.; Scott, P. *J. Am. Chem. Soc.* **2000**, *122*, 7132–7133; Gillespie, K. M.; Sanders, C. J.; O'Shaughnessy, P.; Westmoreland, I.; Thickitt, C. P.; Scott, P. *J. Org. Chem.* **2002**, *67*, 3450–3458; O'Shaughnessy, P.; Scott, P. *Tetrahedron: Asymmetry* **2003**, *14*, 1979–1985; O'Shaughnessy, P.; Knight, P. D.; Morton, C.; Gillespie, K. M.; Scott, P. *Chem. Commun.* **2003**, 1770–1771; O'Shaughnessy, P.; Gillespie, K. M.; Knight, P. D.; Munslow, I. J.; Scott, P. *J. Chem. Soc., Dalton Trans.* **2004**, 2251–2257, See also Ref. 11.
15. van Stein, G. C.; van Koten, G.; Vrieze, K.; Spek, A. L.; Klop, E. A.; Brevard, C. *Inorg. Chem.* **1985**, *24*, 1367–1372.
16. NMR investigation showed the presence of at least two species at the equilibrium (see also Ref. 15). On the basis of the present data it is very difficult to clearly indicate the catalytically active species. Further mechanistic studies are underway.
17. For a recent article about the steric and electronic tuning of chiral bis(oxazoline)s with 3,3′-bithiophene backbone see: Benaglia, M.; Benincori, T.; Mussini, P.; Pilati, T.; Rizzo, S.; Sannicolo', F. *J. Org. Chem.* **2005**, *70*, 7488–7494.
18. For the use of chiral diamino-oligothiophenes as ligands in asymmetric catalysis see: Albano, V. G.; Bandini, M.; Barbarella, G.; Melucci, M.; Monari, M.; Piccinelli, F.; Tommasi, S.; Umani-Ronchi, A. *Chem. Eur. J.* **2006**, *12*, 667–675, and references cited therein. For a recoverable catalyst see: Bandini, M.; Benaglia, M.; Quinto, T.; Tommasi, S.; Umani-Ronchi, A. *Adv. Synth. Catal.* **2006**, *348*, 1521–1524.
19. Preliminary studies showed that the present catalytic system is not able to promote the allylation to imines derived from aromatic or aliphatic aldehydes. Further work is in progress.