Solvent-Free Synthesis of Chiral Schiff-Base Ligands Based on Ferrocene under Microwave Irradiation and Application to Enantioselective Nitroaldol (Henry) Reaction

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ABSTRACT Chiral Schiff-bases **3a-f** based on ferrocene were designed and synthesized using solvent-free methods by mixing ferrocene carbaldehyde 1 with amino alcohols and amines **2a-f** under microwave irradiation and classical method for the enantioselective nitroaldol (Henry) reaction. The Schiff-bases were obtained in shorter reaction times and improved yield under microwave irradiation method over classical method. The highest enantioselectivity was observed in ligand **3e** (95% ee) when CH_2Cl_2 was used as solvent. *Chirality 23:374–378, 2011.*

KEY WORDS: ferrocene; microwave irradiation; chiral Schiff-bases; nitro aldol reaction; Henry reaction

INTRODUCTION

Studying Schiff bases derived from ferrocene carboxyaldehyde and their metal complexes is a quite attractive subject. Many studies on this class of ferrocene containing molecules have been reported recently. Synthesis of imines have been achieved by using several reagents such as zinc chloride, titanium chloride, molecular sieves or alumina.[1–3]

The main research in our group involves activation of organic reaction using microwave irradiation under solvent-free conditions, including the development of an efficient and practical method for ferrocene-derived chiral Schiff bases by simple condensation of ferrocene carboxyaldehyde with chiral amines in absence of any catalyst or solvent. This class of compounds may be potential catalysts for various asymmetric induction reactions, including enantioselective nitroaldol reaction, named as Henry reaction.[4–29]

The nitroaldol or Henry reaction is one of the classical named reactions in organic synthesis. Essentially the coupling of the nucleophile generated from a nitroalkane with a carbonyl electrophile is a widely used transformation, since its discovery in 1895. The resulting product of this reaction is a β-nitroalcohol, which is a versatile intermediate in synthetic organic chemistry. However, the wide applicability of this transformation, until recently, was impaired due to the nonavailability of suitable catalysts for imparting a definite stereochemistry to the newly generated stereogenic centres. The first asymmetric version of the Henry reaction was reported by Shibasaki in 1992.[4] Since then, interest in the asymmetric Henry reaction has been considerably expanded and various reports have been continuously appearing in the literature on development of various metal and non metal based catalysts.

In these processes, different chiral catalysts were developed such as those based upon BINOL by Shibasaki,[4] Bis(oxazoline) by Evans and Jørgensen,[5] dinuclear zinc complexes by Trost,[6] Salen–Cocomplexes by Yamada[7] and amino alcohols by Palomo.[8,9] Chiral Schiff-bases are the frequently used as a catalyst especially in asymmetric cyclopropanation.[10,11] The first asymmetric nitroaldol (Henry) reaction catalyzed by chiral copper Schiff-base complexes was first reported by Zhou.[12] Three reviews were appeared in literature on recent advances in asymmetric nitroaldol (Henry) reaction.[13–15] Moreover, Organic catalysts[16–18] and organometallic catalysts[19–29] have been continuously appearing in literature.

Chiral ligands based on ferrocene have been widely used in asymmetric catalysis of various reactions such as asymmetric allylation,[30] enantioselective diketene addition to bezaldehyde,[31] enantioselective addition of diethylzinc to *N*-diphenylphosphinoylimines,[32] enantioselective addition of diethylzinc to aldehydes,[33,34] hydroformylation, allylic substitution, organometallic cross-coupling,[35] catalytic enantioselective reduction of prochiral ketones,[36] hydrostlylation of olefins,[37] and enantioselective hydroboration of 2,5-dihydrofuran.[38] Ferrocene offers a variety of properties when introduced to ligands due to appropriate rigidity, planer chirality, steric bulkiness and stability. It is also readily available and can be easily derivatized.

This work was designed to synthesise chiral ligands based on ferrocene and their catalytic effects on asymmetric induction of C—C bond formation *via* the addition reaction of nitro methane with aldehydes. Amino alcohols of chiral ligands **2** (*R*) and **3** (*S*) have been already prepared in situ and hence were not fully characterized[36–39] and **1** has been already prepared and also characterized by Vasily et al.[31] However, there is no publication on asymmetric nitroaldol reaction as catalyst.

EXPERIMENTAL

All chemicals were grade reagent unless otherwise specified. The START labstation (Milestone labstation for microwave enhanced chemistry) was used for synthesis of chiral Schiff bases. Melting points were determined with a GALLENKAMP Model apparatus with open capillaries and were uncorrected. Infrared spectra were recorded on a MATTSON Model 1000 spectrophotometer. The elemental analyses were obtained with CARLO-ERBA Model 1108 apparatus.^{1}H (400 MHz) and

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^{13}C (100 MHz) NMR spectra were recorded on a Bruker DPX-400 high performance digital FT NMR spectrometer, with tetramethylsilane as the internal standard for solutions in deuteriochloroform. *J* values are given in hertz. Optical rotations were recorded using an Perkin-Elmer Model 341 polarimeter. HPLC measurements were performed with BIO-RAD instrument. Separation were carried out on Chiralcel OD column (250 × 4.60 mm) with hexane/2-propanol (85:15) as eluent. TLC plates were purchased from Fluka.

General Classical Procedure for the Preparation of the Chiral Schiff-Base Ligands (3a-f) Based on Ferrocene

Chiral amines **(2a-f)** were added to a solution of ferrocene carbaldehyde **1** in 10 mL of ethanol. The reaction was then heated at reflux to 8 h. The ethanol was removed and the residue was washed three times with ether and then crystallized from mixture of chloroform and hexane to give a solid.

General Microwave Irradiation Procedure for the Preparation of the Chiral Schiff-Base Ligands (3a-f) Based on Ferrocene

General reaction protocol for the synthesis of imines: a mixture of ferrocene carbaldehyde **1** and the chiral amines **(2a-f)** was homogenized and subjected to microwave irradiation. At the end of irradiation, the reaction mixture was cooled to room temperature. The residue was washed with ether and then crystallized from mixture of chloroform and hexane to give the pure imine as a solid.

(1*S*, 2*R*)-2-(ferrocenylideneamino)-1,2-diphenylethan-1-ol 3a. (0,315 g, 77%), mp: 179-180 °C; $[\alpha]_D^{20} = +102.5°$ (c 2, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 2.64 (br s, 1H), 3.98 (s, 5H), 4.35 (s, 2H), 4.44-4.45 (d, 1H *J* = 6.4 Hz), 4.59-4.61 (d, 2H *J* = 6.8 Hz), 5.10-5.12 (d, 1H, *J* = 4.8 Hz), 7.27-7.37 (m, 10H), 8.06 (s, 1H) ^{13}C NMR (100 MHz, $CDCl_3$), δ 67.49, 67.92, 68.81, 69.02, 69.82, 70.53, 70.85, 73.18, 76.05, 79.96,126.45, 127.21, 127.34, 128.55, 128.65, 141.21, 1063; IR: ν 3140, 2954, 2864, 1645, 1496, 1452, 1375, 1259, 1060, 1041, 925, 822, 758, 713, 508, 483 Anal. Calcd for $C_{25}H_{23}FeNO$: C,73.36; H,5.66; N,3.42. Found: C,73.33; H,5.69; N,3,41.

(2*S*)-2-(ferrocenylideneamino)-2-phenylethan-1-ol 3b. (0.27 g, 80%), mp: 161–162 °C, $[\alpha]_D^{20} = +34.5°$ (c 2,CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 3.03 (br s, 1H), 4.10 (m, 7H), 4.38-4,39 (m, 4H), 4.85 (s, 1H), 7.48-7.28 (m, 5H), 8.27 (s 1H); ^{13}C NMR (100 MHz,$CDCl_3$), δ 69.13, 70.58, 71.04, 76.91, 78.81, 79.40, 116.40, 122.17, 127.51, 128.20, 161.84, 166.28; IR: ν 3249, 3089, 3056, 3024, 2921, 2915, 2858, 1638, 1496, 1458, 1394, 1391, 1342, 1252, 1201, 1092, 1027, 996, 829, 752, 701, 597, 539, 508, 496; Anal. Calcd for $C_{19}H_{19}FeNO$: C,68.49; H,5.75; N,4.20. Found: C,68.43; H,5.80; N,4.25.

(2*R*)-2-(ferrocenylideneamino)-1,1,3-triphenyl-propan–1-ol 3c. (0.390 g, 78%), mp: 197-198 °C, $[\alpha]_D^{20} = +117.1°$ (c 2, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 2.81 (br s, 1H), 3.74 (s, 5H), 4.16-4.44 (m, 4H), 4.53-4.51 (d,1H *J* = 8 Hz), 4.59-4.61 (d, 1H *J* = 8 Hz), 7.00-7.64 (m, 15H), 7.74 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$), δ 36.86, 53.45, 66.57, 68.87, 69.62, 69.93, 70.31, 77.72, 79.18, 125.53, 125.92,125.99, 126.44, 126.56,127.84, 128.09, 128.23, 128.39,144.72, 1601.90; IR: ν 3472, 3095, 3062, 3029,2956, 2883, 2930, 1635, 1503, 1456, 961, 716. Anal. Calcd. for $C_{32}H_{29}NOFe$: C,77.00; H,5.85; N,2.80. Found: C,76.89; H,5.95; N,2.75.

(1*R*)-2-(ferrocenylideneamino)-2-ethyl-cyclohexane 3d. (0,605g, 81%), mp: 76-77°C, $[\alpha]_D^{20} = -45°$ (C=1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.99-1.46 (m, 10H), 1.78 (m, 4H), 2.87 (m, 1H) 4.19(s, 5H), 4.36 (s, 2H), 4.70-4.62 (d, *J* = 31,6 Hz), 8.06 (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$), δ 20.16, 26.20, 26.63, 29.40, 30.40, 43.47, 68.84, 70.08, 72.38, 81.18, 158.22. Anal. Calcd. for $C_{19}H_{25}NFe$: C, 70.60; H,7.79; N,4.33. Found: C,70.69; H,7.95; N,4.25.

(1*S*)-2-(ferrocenylideneamino)-2-ethyl-napthlane 3e. (0,650g, 76%), mp: 137-138°C, $[\alpha]_D^{20} = -64,5°$ (C=1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.75-1.77 (d, 3H *J* = 6.8 Hz), 4.04 (s, 5H), 4.37 (s, 2H) , 4.66 (s, 1H), 4.72 (s, 1H), 5.29 (q, 1H, J 6.4 Hz), 7.49-8.24 (m, 7H), 8.26 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$), δ 23.77, 68.31, 68.78, 69.93, 68.93, 70.39, 123,98, 124.01, 125.40, 125.70, 127.39, 128.91, 130.87, 134.05, 159.87. Anal. Calcd. for $C_{23}H_{21}NFe$: C,75.24; H,3.81; N,5.73. Found: C,75.89; H,3.85; N,5.70.

TABLE 1. Optimization of the reaction between 1 and 2a under microwave irradiation (800 W)

Entry	Amine	Equ.	Temp. (°C)	Time (min)	Yield (%)[a]
1	**2a**	1.1	110	4	91
2	**2a**	1.1	120	4	96
3	**2a**	1.1	150	4	100

[a]Yields determined by ^1H NMR.

(1*S*, 2*S*)-*N*,*N*′-Cyclohexane-1,2-bis((ferrocenylmethylene)amine 3f. (0.450g, %75), mp: 137°C, $[\alpha]_D^{20} = +45°$ (C=1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.46 (m, 4H), 1.73 (m, 4H), 3.27 (m, 2H), 4.19 (s, 10H), 4.38 (s, 4H), 4.68 (d, 4H *J* = 7 Hz), 8.22 (s, 2H); ^{13C}NMR (100 MHz, $CDCl_3$), δ 24.59, 33.50, 68.26, 69.09, 69.93, 73.20, 160.52. Anal. Calcd. for $C_{28}H_{30}N_2Fe_2$: C,66.27; H,5.92; N,4.73. Found: C,66.89; H,5.95; N,4.75.

General procedure for the asymmetric Henry reaction. Asymmetric Henry Reaction was performed according to our previous method procedure published in literature.[27,29]

RESULTS AND DISCUSSION

2a was used to achieve optimization reaction conditions for preparation of chiral Schiff-bases. Thus, ferrocene carbaldehyde **1** and **2a** were mixed and irradiated by the START lab station. Reaction time and reaction temperature were decided based on previous literature studies.[1] Hence, optimum reaction conditions were selected as a temperature of 150°C and a reaction time of 4 min (entry 3, Table 1). The high yields were obtained under these optimized conditions for all the reactions.

Results show that microwave heating offers advantages over conventional heating such as shorter reaction times and improved yields (Table 2).

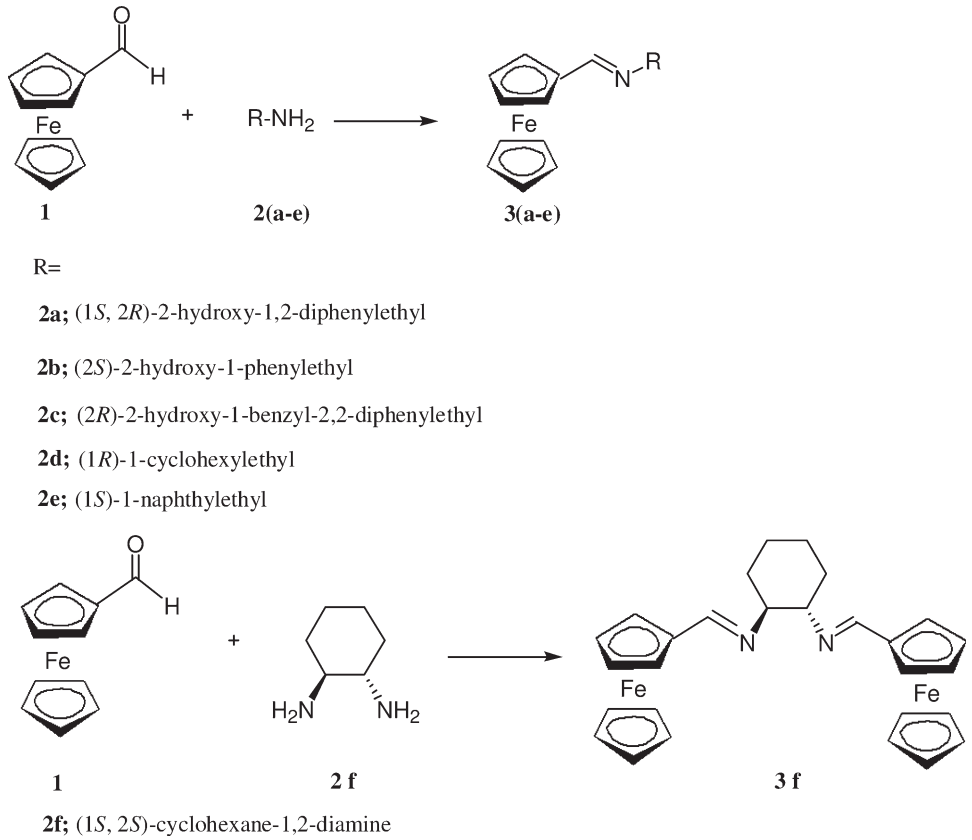
The ferrocene carbaldehyde was easily reacted with different chiral amino alcohols and amines in ethanol to provide chiral Schiff-bases **3a-f** based on ferrocene with high yield as shown in Scheme 1.

The catalytic activities of the chiral Schiff-bases **3a-c** were studied for the addition of nitro-methane to *p*-nitrobenzaldehyde. According to conditions previously reported[27,29] the reaction was initially carried out at room temperature using 10 mol % of catalyst and copper triflate as the source of metal ion for 40 h (Table 3). The experimental results show that using organic base (triethylamine) increases the reaction yield, but resulted in reduction of enantioselectivity as shown in Table 4.

TABLE 2. Synthesis of chiral Schiff-bases 3a-f under optimum microwave heating and classical conditions

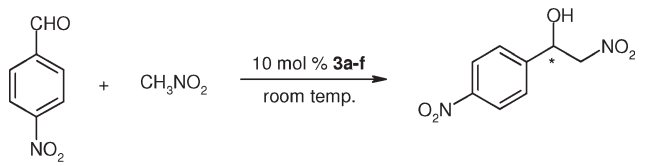
Entry	Amines	Microwave (Yield[a], %)	Thermal (Yield[b], %)
1	**2a**	100	77
2	**2b**	93	80
3	**2c**	99	78
4	**2d**	95	81
5	**2e**	93	76
6	**2f**	100	75

[a]Yields determined by ^1H NMR.
[b]Yields determined after purification.



Scheme 1. Synthesis of chiral Schiff-base ligands based on ferrocene.

TABLE 3. Asymmetric nitroaldol (Henry) reaction between nitromethane and *p*-nitrobenzaldehyde in the absence of triethylamine catalyzed by chiral Schiff-base ligands[a]

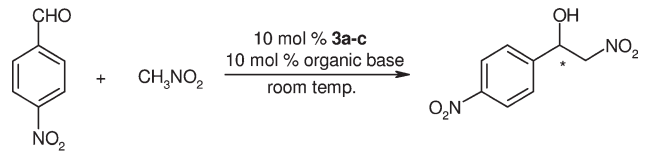


Entry	Cat.	M(OTf)$_2$	Time (h)	Solvent	Yield[b]	ee[c] (%)	Config.[d]
1	**3a**	Cu(OTf)$_2$	40	EtOH	63	10	*S*
2	**3a**	Cu(OTf)$_2$	40	CH_2Cl_2	54	37	*S*
3	**3a**	Cu(OTf)$_2$	40	PhMe	65	8	*S*
4	**3b**	Cu(OTf)$_2$	40	EtOH	56	20	*S*
5	**3b**	Cu(OTf)$_2$	40	CH_2Cl_2	52	30	*S*
6	**3b**	Cu(OTf)$_2$	40	PhMe	61	18	*S*
7	**3c**	Cu(OTf)$_2$	40	EtOH	68	7	*R*
8	**3c**	Cu(OTf)$_2$	40	CH_2Cl_2	58	17	*R*
9	**3c**	Cu(OTf)$_2$	40	PhMe	71	2	*R*
10	**3d**	Cu(OTf)$_2$	40	CH_2Cl_2	50	85	*R*
11	**3e**	Cu(OTf)$_2$	40	CH_2Cl_2	47	95	*S*
12	**3f**	Cu(OTf)$_2$	40	CH_2Cl_2	52	83	*R*

[a]All reactions were performed on a 0.2 mmol scale of 4-nitrobenzaldehyde and 0.6 mL of nitromethane
[b]After purification with TLC Ethylacetate/ Petroleum ether (30/70) Rf: 0.36 Lit[39]: 0.34
[c]Determined by chiral HPLC using a OD column.
[d]Determined by comparing the HPLC elution order of the enantiomers with an authentic sample according to the literature[40] and also determined by HP Chiral Detector.

These results were consistent with previously reported data.[27,29] It was shown that CH_2Cl_2 was solvent of choice for the enantioselective nitroaldol reaction catalyzed by chiral Schiff-bases. The chiral Schiff-base **3a** was found to be the best catalyst amongst the Schiff bases tested in CH_2Cl_2 with

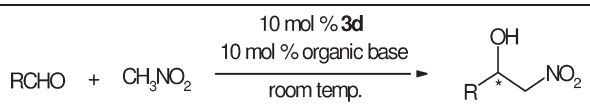
TABLE 4. Asymmetric nitroaldol (Henry) reaction between nitromethane and *p*-nitrobenzaldehyde in the presence of triethyl amine as the base catalyzed by chiral Schiff-base ligands[a]

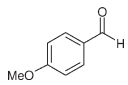
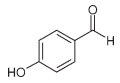


Entry	Cat.	M(OTf)$_2$	Time (h)	Solvent	Yield[b]	ee[c] (%)	Config.[d]
1	**3a**	Cu(OTf)$_2$	40	EtOH	67	27	*S*
2	**3a**	Cu(OTf)$_2$	40	CH_2Cl_2	73	7	*S*
3	**3a**	Cu(OTf)$_2$	40	PhMe	78	3	*S*
4	**3b**	Cu(OTf)$_2$	40	CH_2Cl_2	70	13	*S*
5	**3c**	Cu(OTf)$_2$	40	CH_2Cl_2	76	4	*R*

[a]All reactions were performed on a 0.2 mmol scale of 4-nitrobenzaldhyde, %10 mol organic base (triethyl amine) and 0.6 mL of nitromethane.
[b]After purification with TLC Ethyl acetate/ Petroleum ether (30/70) Rf: 0.36 Lit[39] : 0.34
[c]Determined by chiral HPLC using a OD column.
[d]Determined by comparing the HPLC elution order of the enantiomers with an authentic sample according to the literature[41] and also determined by HP Chiral Detector.

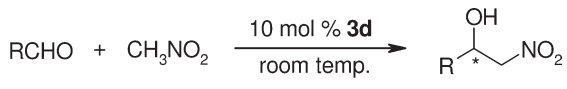
TABLE 5. Asymmetric nitro aldol (Henry) reaction between nitromethane and substitute aldehyde in the presence of triethyl amine as the base catalyzed by chiral Schiff-base ligand 3d[a]

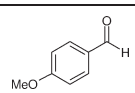
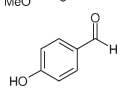


Entry	Aldehyde	$M(OTf)_2$	Time (h)	Yield[b]	ee[c] (%)	Config.[d]
1		$Cu(OTf)_2$	40	65	59	*S*
2		$Cu(OTf)_2$	40	70	40	*R*
3		$Cu(OTf)_2$	40	74	30	*S*
4		$Cu(OTf)_2$	40	70	34	*S*

[a]All reactions were performed on a 0.2 mmol scale of aldehyde in the mixture of 0.8 mL of ethanol and 0.6 mL of nitromethane.
[b]After purification with TLC lit.[15]
[c]Determined by chiral HPLC using an OD column.
[d]Determined by comparing the HPLC elution order of the enantiomers with an authentic sample according to the literature[14] and also determined by HP Chiral Detector.

TABLE 6. Asymmetric nitro aldol (Henry) reaction between nitromethane and substitute aldehyde catalyzed by chiral Schiff-base ligand 3d[a]



Entry	Aldehyde	$M(OTf)_2$	Time (h)	Yield[b]	ee[c] (%)	Config.[d]
1		$Cu(OTf)_2$	40	nr[e]	–	–
2		$Cu(OTf)_2$	40	25	82	*R*
3		$Cu(OTf)_2$	40	nr[e]	–	–
4		$Cu(OTf)_2$	40	nr[e]	–	–

[a]All reactions were performed on a 0.2 mmol scale of aldehyde in the mixture of 0.8 mL of ethanol and 0.6 mL of nitromethane.
[b]After purification with TLC lit.[15]
[c]Determined by chiral HPLC using an OD column.
[d]Determined by comparing the HPLC elution order of the enantiomers with an authentic sample according to the literature[14] and also determined by HP Chiral Detector.
[e]nr: No reaction.

an enantioselectivity (37% ee). The results also suggested that chiral Schiff-bases synthesised from amino alcohols act as a catalyst in enantioselective nitroaldol reaction, with a poor effectiveness in literature cited here.[7–42] Therefore, it was decided to synthesise the chiral Schiff base ligands with chiral amines (**2d, 2e, 2f**) instead of amino alcohols. Then the catalytic activities of these ligands **3d-f** were studied for the addition of nitromethane to *p*-nitrobenzaldeyhede. The reaction was carried out at room temperature using 10 mol % of catalyst and copper triflate as the source of metal ion for 40 h in CH_2Cl_2. Results indicated that ligands derived from amine have a dramatic improvement up to (95% ee) in enantioselective nitroaldol reaction over those derived from amino alcohols as shown in Table 3. Therefore, catalytic activity of chiral Schiff base **3d** were tested on the substitute aldehyde (4-metoxy benzaldehyde, 2-choloro benzaldehyde, isobutyl aldehyde, 4-hydroxy benzaldehyde). The moderate enantioselectivities were observed in the case using organic base (Table 5). Moreover, the aldol reaction of 4-hydroxy benzaldehyde and 4-nitrobenzaldehyde produced with nitromethane have a similar enantioselectivity (82% ee) as shown in Table 6 while the rest of aldehyde did not reacted with nitromethane.

CONCLUSION

In conclusion, ferrocene based on chiral Schiff base ligands **(3a-f)** prepared from the reaction of amino alcohols and amines (**2a-f**) with ferrocene carbaldehyde **1** were reported and their catalytic activity were tested in nitroaldol (Henry) reaction. Somehow, it was shown that ligands derived from amines had a better catalytic activity over these derived from amino alcohols. We suppose that this result would find immense use in asymmetric Henry catalysis of various reactions.

Literature Cited

1. Öztürk G, Petit A, Kouklovsky C. Synthesis of ferrocenyl Schiff bases under solvent-free conditions using microwave irradiation. Synth Commun 2008;38:2707–2713.
2. Varma RS, Dahiya R, Kumar S. Clay catalyzed synthesis of imines and enamines under solvent-free conditions using microwave irradiation. Tetrahedron Lett 1997;38:2039–2042.
3. Li J-R, Ma S-L, Sun YJ, Zhao JM, Zhou Z-M. New synthesis of 2H-3,1-benzoxazine derivatives: zinc chloride-catalyzed cyclocondensation of 2-amino-5-nitrobenzonitrile with aldehydes under microwave conditions. Synth Commun 2006:36;1537–1542.
4. Sasai H, Suzuki T, Arai S, Arai T, Shibasaki M. Basic character of rare earth metal alkoxides. Utilization in catalytic carbon-carbon bond-forming reactions and catalytic asymmetric nitroaldol reactions. J Am Chem Soc 1992;114:4418–4420.
5. Evans DA, Seidel D, Rueping M, Lam HW, Shaw JT, Downey CW. A new copper acetate-bis(oxazoline)-catalyzed, enantioselective Henry reaction. J Am Chem Soc 2003;125:12692–12693.
6. Trost BM, Yeh VS. C. A dinuclear Zn catalyst for the asymmetric nitroaldol (Henry) reaction. Angew Chem Int Ed 2002;41:861–863.
7. Yamada T. Enantioselective Henry reaction catalyzed by salen-cobalt complexes. Synth Stuttgart 2004;12:1947–1950.
8. Palomo C, Oiarbide M, Laso A. Enantioselective Henry reactions under dual Lewis acid/amine catalysis using chiral amino alcohol ligands. Angew Chem Int Ed 2005;44:3881–3884.
9. Palomo C, Oiarbide M, Mielgo A. Unveiling for the reliable catalysts asymmetric nitroaldol (Henry) reaction. Angew Chem Int Ed 2004;43:5442–5444.
10. Li ZN, Zheng Z, Chen H. Highly efficient and enantioselective cyclopropanation of styrene with diazoacetates using a new copper-(Schiff-base) catalyst. Tetrahedron: Asymmetry 2000;11:1157–1163.

11. Jarvo ER, Lawrence BM, Jacobsen EN. Highly enantio- and regioselective quinone diels-alder reaction catalyzed by a tridentate [(Schiff Base)-CrIII] complex. Angew Chem Int Ed 2005;44:6043–6046.
12. Gan C, Lai G, Zhang Z, Wang Z, Zhou M-M. Efficient and enantioselective nitroaldol reaction catalyzed by copper Schiff-base complexes. Tetrahedron: Asymmetry 2006;17;725–728.
13. Luzzio F. The Henry reaction: recent examples. Tetrahedron 2001;57: 915–945.
14. Boruwa J, Gogoi N, Saikia PP, Barua Nabin C. Catalytic asymmetric Henry reaction. Tetrahedron: Asymmetry 2006;17:3315–3326.
15. Palomo C, Oiarbide M, Laso A. Recent advances in the catalytic asymmetric nitroaldol (Henry) reaction. Eur J Org Chem 2007:16;2561–2574.
16. Hirata N, Hayashi M. Nitroaldol reaction catalyzed by tris(2,4,6-trimethoxyphenyl) phosphine (TTMPP). Synth Commun 2007;37:1653–1664.
17. Mandal T, Samanta S, Zhao CG. Organocatalytic highly enantioselective nitroaldol reaction of α-ketophosphonates and nitromethane. Org Lett 2007;9:943–945.
18. Rampalakos C, Wulff WD. A novel bis-thiourea organocatalyst for the asymmetric aza-Henry reaction. Adv Synth Catal 2008;350:1785–1790.
19. Mansawat W, Saengswang I, U-prasitwong P, Bhanthumnavin W, Vilaivan T. Novel thiolated amino-alcohols as chiral ligands for copper-catalyzed asymmetric nitro-aldol reactions. Tetrahedron Lett 2007;48:4235–4238.
20. Jiang JJ, Shi M. Development of new chiral phosphine-salen type ligands and their application in the Cu(I)-catalyzed enantioselective Henry reaction. Tetrahedron: Asymmetry 2007;18:1376–1382.
21. Blay G, Climent E, Fernandez I, Hernandez-Olmos V, Pedro JR. Enantioselective Henry reaction catalyzed with copper(II)–iminopyridine complexes. Tetrahedron: Asymmetry 2007;18:1603–1612.
22. Trost BM, Lupton DW. Dinuclear zinc-catalyzed enantioselective aza-Henry reaction. Org Lett 2007;9:2023–2026.
23. Ma KY, You JS. Rational design of sterically and electronically easily tunable chiral bisimidazolines and their applications in dual Lewis acid/Brønsted base catalysis for highly enantioselective nitroaldol (Henry) reactions. Chem A Eur J 2007;13:1863–1871.
24. Bandini M, Piccinelli F, Tommasi S, Umani-Ronchi A, Ventrici C. Highly enantioselective nitroaldol reaction catalyzed by new chiral copper complexes. Chem Commun 2007;6;616–618.
25. Arai T, Watanabe M, Yanagisawa A. Practical asymmetric Henry reaction catalyzed by a chiral diamine-Cu(OAc)$_2$ complex. Org Lett 2007;9:3595–3597.
26. Kowalczyk R, Sidorowicz L, Skarz˙ ewski J. Asymmetric nitroaldol reaction catalyzed by a chromium(III)–salen system. Tetrahedron: Asymmetry 2007;18:2581–2586.
27. Çolak M, Aral T, Hoşgören H, Demirel ,N. Synthesis of novel chiral Schiff-base ligands and their application in asymmetric nitroaldol (Henry) reaction. Tetrahedron: Asymmetry 2007;18:1129–1133.
28. Pandya SU, Dickins RS, Parker D. Enantioselective catalysis of the Henry reaction by a chiral macrocyclic ytterbium complex in aqueous media. Org Biomol Chem 2007;5:3842–3846.
29. Çolak M, Demirel N. Enantioselective nitroaldol (Henry) reaction catalyzed by chiral Schiff-base ligands. Tetrahedron: Asymmetry 2008; 19:635–639.
30. Bandini M, Cabiddu S, Cadoni E, Olivelli P, Sinisi R, Umani-Ronchi A, Usai M. New adaptive chiral thiophene ligands for copper-catalyzed asymmetric Henry reaction. Chirality 2009;21:239–244.
31. Tsarev VN, Lyubimov SE, Bondarev OG, Korlykov AA, Antipin MY, Petrovskii PV, Shiyaev AA, Benetsky EB, Vologzhanin PA, Gavrilov KN. Novel higly efficient *P*-chiral ferrocenylimino diamidophosphite ligands for Pd-catalysed asymmetric allylation. Eur J Org Chem 2005; 10:2097–2105.
32. Moreno RM, Moyano A. Salicylaldehyde Schiff bases derived from 2-ferrocenyl-2-amino alcohols. Part 2: Stereochemical divergence in the titanium-promoted enantioselective diketene addition to benzaldehyde. Tedrahedron: Asymmetry 2006;17:1104–1110.
33. Wang MC, Xu CL, Cheng XF, Ding X. Chiral ferrocenyl amidophosphine ligand for highly enantioselective addition of diethylzinc to *N*-diphenylphosphinoylimines. Tedrahedron 2006;62:12220–12226.
34. Freng GJ, Xuan SZ, Wen ZY. Synthesis of chiral *N*-ferrocenylmethylamino alcohols and their application in enantioselective addition of diethylzinc to aldehydes. Chin Chem Lett 2004;15:1025–1028.
35. Bolm C, Muñiz K, Hildebrand JP. Planar−chiral ferrocenes in asymmetric catalysis: the impact of stereochemically inhomogeneous ligands. Org Lett 1999;1:491–494.
36. Atkinson CJR, Gibson VC, Long NJ. The syntheses and catalytic applications of unsymmetrical ferrocene ligands. Chem Soc Rev 2004;33:313–328.
37. Wei-Yi C, Jun L, Zong-Xuan S, Ya-Wen Z. Catalytic enantioselective reduction of prochiral ketones with chiral ferrocenyl amino alcohols. Chin J Chem 2004;22:306–309.
38. Togni A, Dorta R, Köllner C, Pioda G. Some new aspects of asymmetric catalysis with chiral ferrocenyl ligands. Pure Appl Chem 1998;70:1477–1485.
39. Togni A, Bieler N, Burckhardt U, Köllner C, Pioda G, Schneider R, Schnyder A. Recent studies in asymmetric catalysis using ferrocenyl ligands. Pure Appl Chem 1999;71:1531–1537.
40. Weeden JA, Chisholm John D. Phosphine-catalyzed nitroaldol reactions. Tetrahedron Lett 2006;47:9313–9316.
41. Blachet J, Bonin M, Husson HP. Synthesis of enantiomerically pure and α-substituted propargylic amine by reaction of organoaluminum reagents with oxazolidines. J Org Chem 2000;65:6423–6426.
42. Xiong Y, Wang F, Huang X, Wen Y, Feng X. A new copper(I)-tetrahydrosalen-catalyzed asymmetric Henry reaction and its extension to the synthesis of (*S*)-norphenylephrine. Chem Eur J 2007;13:829–833.