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High Throughput Screening of Asymmetric Bidentate Ligands/Zn^{+2} Catalysts for Hydrogenation during Pharmaceutical Processes

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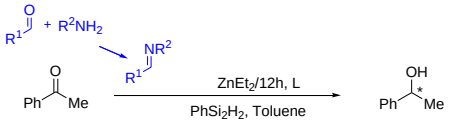
Abstract-Development in the field of asymmetric catalysis is driven by the importance of stereo chemically pure compounds in the field of pharmaceutical industry, agrochemicals and flavors. The unpredictable results given by new catalysts make the design of effective ones a long and costly work. Combinatorial asymmetric catalysis is the fastest and most efficient tools for finding best catalysts and it helps for many catalytic systems to be screened in a short period of time to decide about their effectiveness in synthesizing enantiomerically pure products. This work describes rapid screening of chiral asymmetric oxazoline, imine, aminal and bisimine bidentate ligands and their in situ use for catalytic transfer hydrogenation of ketone in the presence of zinc. The ligands thus prepared in situ gave nearly same results with that of the purified version. The ligands which gave more than 80% enantiomeric excesses (ee) with excellent conversions (<90%) were readily identified. Thus ligands with excellent results can be purified in bulk to save time and money.

Key Words: **High throughput screening, asymmetric catalysis, transfer hydrogenation, diethyl zinc, instant ligand libraries.**

I. INTRODUCTION

Stereo chemically pure compounds are required in the field of pharmaceutical industry, agrochemicals and flavors which can be synthesized by asymmetric catalysis [1]. The synthesis of molecules containing one or more chiral centers is remained active in the field of catalysis for chemists [2] who are generally sourced from natural products or by the resolution of racemic compounds [3]. According to W. S. Knowles the final structure cannot be predicted theoretically due to the small difference of energy (~2kcal/mol for 95% ee) between two diastereomeric transition states [4]. Finding new catalysts can both be time consuming, cost expensive and an inefficient method for bulk production [5]. High throughput screening creates a new methodology for the search of a vast variety of potential ligands which can be categorized in libraries, screened and then tuned to a particular substrate [6].



Scheme 1. Synthesis of bidentate ligands

The first comparison was made by De Vries by introducing instant libraries of MonoPhose [7-8] during which chiral ligands were synthesized both in situ and in pure giving results with slightly difference. In spite of the advances in the field, Bidentate ligands remains a problem that require purification of resulting ligands [9-10] for which solid phase [11-13] and supramolecular [14-17] methods have been employed so for. Due to the greater synthetic difficulties [18] of bidentate ligands, its use in combinatorial screening was stopped until E. Bergin and co-workers used it with appreciable enantiomeric excesses [19-20]. Herein we present a library of bidentate ligands for the in situ transfer hydrogenation of ketones and the comparison of results with the purified version.

I.

II. RESULTS AND DISCUSSIONS

In the beginning equimolar of aldehyde and amine were allowed to react together for 24 hours in toluene with 4A^{o} molecular sieves and luckily a pure ligand was obtained after column chromatography. The beauty of this method is the available variation in both starting materials and the formation of by product (water, HCl) which can easily be removed with the help of molecular sieves. Four families of ligands imines, aminals, oxazolines and bisimines were synthesized and used in situ. These ligands were easily obtained by combining aldehyde with amine [21], diamine [21-22] and amino alcohol [23-24] respectively Sch. 1.

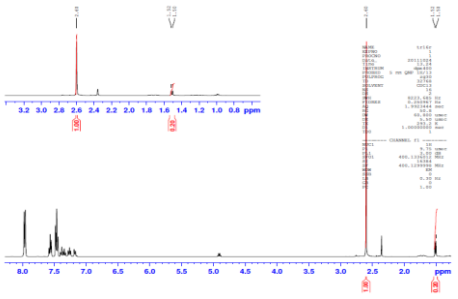


Fig 1: Conversion by Proton NMR

The enantiomers were separated by using HPLC, (High Performance Liquid Chromatography) by using chiral column. The two enantiomers R ans S has different retention times and thus not only was separated but also graduated to find out the %ee. Proton NMR (Nuclear Magnetic Resonance) spectroscopy was used for the first time to find out conversion by comparing reactants and products. Singlets of 3H belonging to ketones were

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gradually disappeared taking over by alcohol peak and the singlet was replaced by duplet Fig. 1. The structural variations and cheap availability of the above mentioned compounds helped us the synthesis of a library of ligands to be tested both in situ and in pure form Fig. 2.

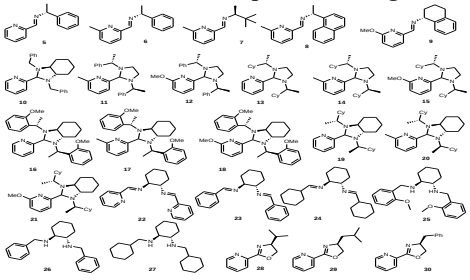
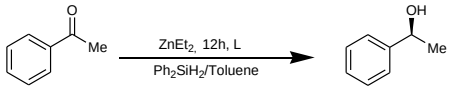


Fig. 2: Ligands employed in this study

At first we compare the results of ligands prepared in situ with that of purified one and found almost same results, 71% vs. 70% ee and 91% vs. 90% conversion for **5** Table 1 (entries 1 and 2) which encouraged us for the evaluation of other ligands by using one pot synthesis without the need of column chromatography i.e.; we made a small library and tested it in transfer hydrogenation of acetophenone Table 1, Fig. 1. Such ligands could be carried out in modular and parallel way that could easily be produced overnight. Substituents on the aldehyd had positive effect on both the conversion and selectivity (entries 8 versus 10, 13 versus 14 and 16 versus 17) due to presence of methyl group aiding the availability to metal atom while bisimine having the methoxy and phenyl group give positive effect due to resonance (entries 19 versus 20 and 21). Oxazoline ligands were both used in situ and in the purified form and maximum ee 78% and conversion 95% (entry 27) were recorded for **29**.

Table 1: Asymmetric transfer hydrogenation



Entry	L	Conv. %	ee %	Conf.
1	5	91	71	S
2	5*	90	70	S
3	6	65	58	R
4	7	80	56	R
5	8	99	86	R
6	8*	97	85	R
7	9	76	55	S
8	10	78	65	S
9	10*	78	53	S
10	11	92	78	R
11	11*	89	73	R
12	12	98	82	S
13	13	71	55	S
14	14	92	77	S
15	15	97	80	R
16	16	90	73	R
17	17	98	83	R
18	18	85	58	R
19	19	80	63	S
20	20	90	85	S
21	21	95	73	S
22	22	65	44	S
23	23	60	45	R
24	24	82	56	R
25	25	68	53	R
26	26	70	54	S
27	27	95	78	R
28	28*	45	48	S
29	29*	67	51	S
30	30*	76	62	S

*Ligands isolated and purified prior to use

The phenyl group seems to be an important feature since replacement of this with cyclohexyl group showed a significant drop in enantioselectivity (Entry 11, 14 and 12 vs. 15). Steric effect played an important role in complex formation and achieving goodees as the enantiomeric excess of 1-phenylethanol obtained was maximum 86% for **8** (entry 5), which helped us to access structure of the ligands in easy way. Honestly speaking none of our ligand is able to give product with exemplary conversion and ee, but we were able to improve the literature by combining easily available raw materials for synthesizing a small library of four classes of ligands and which can directly be used for combinatorial asymmetric syntheses. Furthermore, it is not necessary in the beginning to synthesize ligands in bulk quantities and thorough purification which waste time and money but can easily be tested in microlitre ranges of the two fragments and thus reducing cost, and time. Once finding a hit for the best ligand it can be synthesized and purified easily on large scale. Studies to find optimum conditions for the successful ligands are underway in our group.

III. EXPERIMENTAL

All chemicals were obtained from commercial sources and used as received. Flash chromatography was carried out using silica gel; particle size 0.04-0.063 mm. Analytical TLC was performed using Merck Kieselgel 60 F_{254} silica gel plates. Visualization was by UV light (254 nm) or I_2 staining. NMR spectra were recorded in a Bruker DPX-400 Advance spectrometer, operating at 400.13 MHz for 1H-NMR, 100.61 MHz for 13C-NMR and 162.12 MHz for 31P-NMR. Shifts are referenced to the internal solvent signals (1H: δ 7.26 ppm, 13C: δ 77.0 ppm for $CDCl_3$ or 1H: δ 4.79 ppm for D_2O. Analytical CSP-HPLC was performed using Chiralpak IB (4.6 mm x 25 cm) columns. Electrospray mass spectra were recorded on a Mass Lynx NT V 3.4 on a Waters 600 controller connected to a 996 photodiode array detector with methanol, water or ethanol as carrier solvents. Melting points were determined using an Electro thermal IA9000 digital melting point apparatus and are uncorrected. Infrared spectra were recorded on a Mattson Genesis II FTIR spectrometer equipped with a Gateway 2000 4DX2-

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66 workstation and on a Perkin Elmer Spectrum One FT-IR Spectrometer equipped with Universal ATR sampling accessory. THF was distilled from sodium/benzophenone and toluene from calcium hydride.

A.Imine 5

A vial was charged with aldehyde (0.085 mmol) and amine (0.085mmol) and anhydrous toluene (0.2 ml). To this was added 4Å molecular sieves and the vial was sealed. The reaction was then stirred at 70°C overnight. ^{1}H NMR δ (400 MHz, $CDCl_3$) 8.60 (d, 1H, J = 4.5 Hz), 8.51 (s, 1H), 8.10 (d, 1H, J = 7.2 Hz), 7.65 (ap t, 1H), 7.50-7.45 (m, 2H), 7.40-7.30 (m, 2H), 7.25-7.17 (m, 2H), 4.63 (q, 1H, J = 6.6 Hz), 1.63 (d, 3H, J = 6.6 Hz), ^{13}C NMR (100MHz, $CDCl_3$) δ 160.0, 154.3, 148.9, 144.1, 136.1, 128.1, 126.6, 126.3, 124.3, 121.0, 69.2, 24.2. Consistent with literature values [19]

B. Imine 6

Prepared via the above procedure, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H, CH=N), 7.95 (d, 1H, J = 7.7 Hz, Ar), 7.62-7.68 (m, 1H, Ar), 7.42-7.51 (m, 2H, Ar), 7.33-7.40 (m, 2H, Ar), 7.20 (d, 1H, J = 7.7 Hz, Ar), 4.65 (q, 1H, J = 6.7 Hz, $CHCH_3$), 2.61 (s, 3H, $PyrCH_3$), 1.63 (d, 3H, J = 6.7 Hz, $CHCH_3$). ^{13}C NMR (100MHz, $CDCl_3$) δ 160.4 (CH=N), 157.5, 153.8, 144.1, 136.3, 128.0, 126.5, 126.3, 125.4, 123.9, 117.9, 69.1 (CH), 24.1 (CH_3), 23.9 (CH_3). IR (NaCl-disk) v/cm^{-1} 3388, 3061, 2971, 2926, 2861, 1711, 1645, 1591, 1453. HRMS calcd for $C_{15}H_{16}N_2$ $[M + H]^+$, 225.1392, found 225.1395, consistent with literature values [25].

C. Imine 7

Prepared via the above procedure, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H, CH=N), 7.90 (d, 1H, J = 7.8Hz, Py), 7.63 (ap t, 1H, Py-4-H), 7.17 (d, 1H, J = 7.6 Hz, Py), 3.07 (q, 1H J = 6.5Hz, CH), 2.60 (s, 3H, $ArCH_3$), 1.17 (d, 3H, J = 6.5Hz, CH_3), 0.94 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (100MHz, $CDCl_3$) 159.4, 157.3, 154.1, 136.2, 123.5, 117.5, 74.8, 33.8, 26.1, 23.8. IR (NaCl-disk) v/cm^{-1} 2964, 2868, 1653, 1647, 1591, 1575, 1457, 1363, 1120, 783. $[\alpha]^{20}$D = +51.1 (c 0.6, CHCl3). HRM calcd for $C1_3H_{20}N_2$ $[M + Na]^+$ 227.1524, found 227.1517, consistent with literature values [19].

D. Aminal 10

A vial was charged with aldehyde (0.085 mmol) and diamine (0.085mmol) and anhydrous toluene (0.2 mL). To this was added 4Å molecular sieves and the vial was sealed. The reaction was then stirred at 70 °C overnight. The ligand was purified through flash chromatography using a ratio of 5:1 (n-hexane:ethyl acetate) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 4.5 Hz, 1H, Py-6-H), 7.53 (td, J = 7.6, 1.6 H, 1H, Ar), 7.37 (d, J = 7.8 Hz, 1H, Ar), 7.23-7.02 (m, 11H, Ar), 4.74 (s, 1H, N-CH-N), 3.82 (d, J = 13.8 Hz, Ph-CHH), 3.50 (d, J = 14.5 Hz, Ph-CHH), 3.01 (d, J = 14.5 Hz, Ph-CHH), 3.05-2.95 (m, 1H, CHN), 2.59-2.45 (m, 1H, CHN), 1.90-1.61 (m, 4H, 2 x CH_2), 1.40-1.06 (m, 4H, 2 x CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) 161.1 (Py-6-C), 147.7, 140.4, 138.7, 134.9, 128.5, 127.5, 127.3, 127.2, 126.0, 125.8, 123.5, 121.5, 87.0 (N-C-N), 68.4 (benzyl), 67.1 (benzyl), 56.0 (CHN), 52.0 (CHN), 29.8, 29.7, 24.1. IR (NaCl-disk) v/cm^{-1} 3027, 2929, 2857, 1637, 1588, 1452, 1434, 736. HRMS calcd for $C_{26}H_{29}N_3$ $[M + H]^+$ 384.2448, found 384.2440, consistent with literature values [26].

E. Bisimine 22

Cyclohexane-1, 2 diamine (3.00 mmol) was dissolved in 6 mL of toluene at 0°C with stirring. O-anisaldehyde solution (6.00 mmol) was then added drop wise over 15 min. The resulting suspension was then stirred for 3 hours at RT. Water (5 mL) and diethyl ether (15 mL) were then added and the layers were separated. The organic layer was collected and the aqueous layer was washed with a further 100 mL of ether. The ether layers were then combined dried over $MgSO_4$ and the solvent was removed under reduced pressure to give of reddish oil (2.63 mmol, 87.6% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, 2H, J = 4.8 Hz, Py-6-H), 8.32 (s, 2H, CH=N), 7.88 (d,2H, J = 7.9 Hz, Py-3-H), 7.65 (ap t, 2H, Py), 7.25-7.20 (m, 2H, Py), 3.60-3.49 (m, 2H), 1.95-1.75 (m, 6H), 1.55-1.46 (m, 2H). ^{13}C NMR (100MHz, CDC_{l3}) δ 161.4, 154.5 (q), 149.2, 136.4, 124.4, 121.3, 73.5 (CH), 32.7 (CH_2), 24.3 (CH_2). IR (NaCl-disk) v/cm^{-1} 2928, 2842, 1714, 1644, 1587, 1467, 992. HRMS calculated for $C_{18}H_{20}N_4$ $[M + H]^+$ 293.1766, found 293.1759, consistent with literature values [22].

F. Bisimine 23

Prepared via the procedure above using Cyclohexane-1, 2 diamine (2.72 mmol) and cyclohexanecarbaldehyde (5.44 mmol) to give dark-yellow oil (0.698 g, 6.40 mmol, 78.4% yield) 10 The spectral data was consistent with that reported in the literature, ^{1}H NMR (400MHz $CDCl_3$)δ 8.24 (2H, s, CH=N), 7.65 – 7.55 (4H, m, Ar-H), 7.40 – 7.25 (6H, m, Ar-H), 3.48 (2H, m, CH), 1.98 – 1.76 (6H, m, Cy), 1.64 – 1.43 (2H, m, Cy), ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 135.9, 129.7, 127.9, 127.4, 73.7, 32,5, 24.0, consistent with literature values [27].

G. Bisimine 24

Prepared via the procedure above using Cyclohexane-1, 2 diamine (0.321 g, 2.81 mmol) and cyclohexanecarbaldehyde (0.630 g, 630 mg 0.680 mL 5.62 mmol) to give pale-yellow oil (0.721 g, 7.32mmol, 75.8% yield). ^{1}H NMR (400MHz $CDCl_3$) δ 7.42 (2H, d,J = 5.65 Hz, CyCH=N), 3.05 – 2.95 (2H, m, Cy), 2.15 – 2.05 (2H, m, Cy), 1.82 – 1.51 (16H, m, Cy), 1.39 – 1.10 (14H, m, Cy). ^{13}C NMR (100 MHz $CDCl_3$) δ 168.2, 72.9, 42.9, 32.5, 29.5, 25.4, 24.9, 24.9, 24.0, consistent with literature values [28].

H. Oxazoline 28

A vial was charged with imidate (0.085 mmol) and amino alcohol (0.085mmol) and anhydrous toluene (0.2 mL). To this was added 4Å molecular sieves and the vial was sealed. The reaction was then stirred at 70°C overnight. The product was then extracted with DCM (3×15ml), dried over $MgSO_4$ and concentrated. The compound was then purified using silica gel flash chromatography (EtOAc:n-hexane:Et3N, 7:5:0.01) to

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yield a colorless oil. (327 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d,1H, J =4.2 Hz, o-CHpy), 8.09 (d,1H, J = 8.2 Hz, o-CHpy), 7.80 (t, 1H, J = 1.6 Hz, m-CHpy), 7.42 (dd, 1H, J = 4.7 Hz, J = 6.8 Hz, p-CHpy), 4.54 (t, 1H, J = 8.6 Hz, -CHN), 4.27-4.20(m,1H, $-CH(CH_3)_2$), 1.92-1.88 (m, 2H,$-CH_2$-O), 1.10-1.06 (m, 3H, $-CH_3$), 0.99-0.96 (m, 3H, $-CH_3$).^{13}C NMR (100MHz $CDCl_3$) δ 162.1, 149.2, 146.4, 136.1, 125.0, 123.4, 72.4, 70.3, 32.3, 18.6, 17.7. IR (NaCl-disk) v/cm^{-1}, HRMS calcd for $C_{11}H_{14}N_2O$ $[M + H]^+$ 191.1184 found 239.1177, consistent with literature values [19].

I. Oxazoline 29

Prepared via the procedure above and collected as colorless oil. (299 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d,1H, J =3.5 Hz, o-CHpy), 8.08 (d,1H, J = 8.0 Hz, o-CHpy), 7.82-7.78 (dd, 1H, J = 5.88 Hz, J = 15.5 Hz m-CHpy), 7.43-7.40 (dd, 1H, J = 4.66 Hz, J = 8.74 Hz, p-CHpy), 4.70-4.60 (m, 1H, -CHN), 4.48-4.37 (m,1H, CH_2-O), 4.15-4.05 (m,1H, CH_2-O), 1.96-1.85(m, 2H,$-CH_2$), 1.78-1.68 (m, 2H, $-CH_2$), 1.45 (m, 1H, -CH), 1.00 (6H, d, J = 2.20 Hz, CH_3). ^{13}C NMR (100MHz, $CDCl_3$) δ 162.4, 149.6, 146.8, 136.5, 125.4, 123.8, 73.6, 65.3, 45.4, 25.3, 22.7. IR (NaCl-disk) v/cm^{-1}. HRMS calcd for $C_{12}H_{16}N_2O$ $[M + Na]^+$ 227.1160 found 227.1167.

J. Oxazoline 30

Prepared via the procedure above and collected as colourless oil. (350 mg, 89%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, 1H, J = 4.7 Hz, Py-6-H), 8.08 (d, 1H, J = 7.9 Hz, Py-3-H), 7.82-7.72 (m, 1H, Py-4-H), 7.40 (dd, 1H J = 7.5, 4.7 Hz, Py-5-H), 7.35-7.27 (m, 2H, Ph), 7.28-7.20 (m, 3H, Ph), 4.71-4.61 (m, 1H, CH, 4-H), 4.45 (ap t, 1H, CH, 5-H), 4.23 (ap t, 1H, CH, 5-H), 3.30 (dd, 1H, J = 13.8, 5.0 Hz, CH_2), 2.76 (dd, 1H, J = 13.8, 9.1 Hz, CH_2). ^{13}C NMR (100MHz, $CDCl_3$) δ 162.6 (q), 149.3, 146.2 (q), 137.3 (q), 136.2, 128.7, 128.1, 126.1, 125.1, 123.4, 72.0 (CH_2), 67.6 (CH), 41.2 (CH_2). IR (NaCl-disk) v/cm^{-1} 3084, 2860, 1641, 1469, 1440, 1363, 1099. HRMS calcd for $C_{15}H_{14}N_2O$ $[M + H]^+$ 239.1184 found 239.1189, consistent with literature values [19].

K. General procedure for asymmetric transfer hydrogenation

In a vial 42 µmol of the electrophile and nucleophile were added in toluene (0.4 mL) in the presence of molecular sieves. The reaction stirred at 70°C for 12 h. The solvent was removed under reduced pressure to give the ligand. A mixture of the ligand (42 µmol) and $ZnEt_2$ (12.4 mg, 21 µmol) in absolute MeOH (20 mL) was stirred at 40°C overnight under N_2. The solvent was removed to give the crude complex. A mixture of the crude complex and ketone (4.0 mmol) in degassed solution of Ph_2SiH_2 (30 mL, pH 3.5) was stirred vigorously at 40°C for 12 h under N_2. The reaction mixture was extracted with ethyl acetate (2 x 15 mL). The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure giving a mixture of products.

II.

IV. CONCLUSION

In conclusion we have applied the instant library to the transfer hydrogenation of acetophenone with zinc in water. After the comparison of results obtained from purified vs. in-situ ligands it was found that the technique is suitable for rapid recognition of best catalytic system. Four different types of ligands were tested and the ee > 80% was easily identified. The positive trend of the results was explained due to presence of phenyl group and substituents on aldehyde.

V. ACKNOWLEGMENT

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REFERENCES

[1] M. T. Reetz, Combinatorial Transition Metal Catalysis: Mixing Monodentate Ligands to Control Enantio-, Diastereo-, and Regioselectivity. Angewandte Chemie International Edition, 47, Issue 14, pp. 2556-2588, March 2008.

[2] T.L. Church, P.G. Andersson, Iridium Catalysts for the Asymmetric Hydrogenation of Olefins with Nontraditional Functional Substituents. Coordination Chemistry Reviews, 252, pp. 513-531 March 2008.

[3] H. Fenniri, Combinatorial Chemistry, A practical approach, ISBN 0199637547, 9780199637546, Oxford University Press, 2000.

[4] W. S. Knowles, Asymmetric Hydrogenations (Nobel Lecture) Angewandte Chemie International Edition, 41, Issue 12, pp. 1998-2007, June 2002.

[5] K. Ding, H. Du, Y. Yuan and J. Long, Combinatorial Chemistry Approach to Chiral Catalyst Engineering and Screening: Rational Design and Serendipity Chemistry - A European Journal, 10, Issue 12, pp. 2872-2884, March 2004.

[6] C. Gennari, U. Piarulli. Combinatorial Libraries of Chiral Ligands for Enantioselective Catalysis. Chemical Reviews, 103, Issue 8, pp. 3071-3100 June 2003.

[7] L. Lefort, J. A. F. Boogers, A. H. M. de Vries and J.G. de Vries, Instant Ligand Libraries. Parallel Synthesis of Monodentate Phosphoramidites and in Situ Screening in Asymmetric Hydrogenation. Organic Letters, 6, Issue 11, pp. 1733-1735, May 2004.

[8] R. B. C. Jagt, P. Y. Toullec, E. P. Schudde, J. G. de Vries, B. L. Feringa and A. J. Minnaard, Synthesis of Solution-Phase Phosphoramidite and Phosphite Ligand Libraries and Their In Situ Screening in the Rhodium-Catalyzed Asymmetric Addition of Arylboronic Acids. Journal of Combinatorial Chemistry, 9, Issue 3, pp. 407-414, May 2007.

[9] C. Jakel and R. Paciello, High-Throughput and Parallel Screening Methods in Asymmetric Hydrogenation. Chemical Reviews, 106, Issue7, pp. 2912-2942, July 2006.

[10] J. R. Porter, J. F. Traverse, A. H. Hoveyda and M. L. Snapper, Enantioselective Synthesis of Arylamins Through Zr-Catalyzed Addition of Dialkylzincs to imines by Screening of Parallel Libraries. Journal of American

ISSN: 2277-3754
ISO 9001:2008 Certified
International Journal of Engineering and Innovative Technology (IJEIT)
Volume 3, Issue 3, September 2013

Chemical Society, 123, Issue 5, pp. 984-985, February 2001.

[11] R. den Heeten, B. H. G. Swennenhuis, P.W. N. M. van Leeuwen, J. G. de Vries and P. C. J. Kamer, Parallel Synthesis and Screening of Polymer Supported Phosphorus-Stereogenic Aminophosphane-Phosphite and Phosphinite Ligands. Angewandte Chemie International Edition, 47, Issue 35, pp. 6602-6605, July 2008.

[12] C. M. Sprout, M. L. Richmond and C. T. Seto, Solid Phase Synthesis of Chiral N-Acylethylene diamines and their Use of Lignads for the Asymmetric Addition of Alkylzinc Reagents to Aldehydes. Journal of Organic Chemistry, 69, Issue 20, pp. 6666-6673, October 2004.

[13] J. F. Jensen, K. Worm-Leonhard and M. Meldal. Optically Active (Peptido-carbene) palladium Complexes: Towards True Solid-Phase Combinatorial Libraries of Transition Metal Catalysts. European Journal Organic Chemistry, 2008, Issue 22, pp. 3785-3797, August 2008.

[14] J. Meeuwissen, M. Kuil, A. M. van der Burg, A. J. Sandee and J. N. H. Reek, Application of a Supramolecular-Ligand Library for the Automated Search for Catalysts for the Asymmetric Hydrogenation of Industrially Relevant Substrates. Chemistry - A European Journal, 15, Issue 39, pp. 10272-10279, October 2009.

[15] P. A. R. Breuil, F. W. Patureau and J. N. H. Reek, Singly Hydrogen Bonded Supramolecular Ligands for Highly Selective Rhodium Catalyzed Hydrogenation Reactions. Angewandte Chemie International Edition, 48, Issue 12, pp. 2162-2165, February 2009.

[16] P. E. Goudriaan, X.-B. Jang, M. Kuil, R. Lemmens, P.W. N.M. van Leeuwen and J. N. H. Reek, Synthesis of Building Blocks for the Development of the SUPRAPhos Ligand Library and Examples of Their Application in Catalysis. European Journal of Organic Chemistry, 2008, Issue 36, pp. 6079-6092, September 2008.

[17] B. Breit, Supramolecular Approaches to Generate Library of Chelating Bidentate Ligands for Homogeneous Catalysis. Angewandte Chemie International Edition, 44, Issue 36, pp. 6816-6825, October 2005.

[18] A. J. Minnaard, B. L. Feringa, L. Lefort and J. G. de Vries, Asymmetric Hydrogenation Using Monodentate Phosphoramidite Ligands. Accounts of Chemical Research, 40, Issue 12, pp. 1267-1277, December 2007.

[19] R. Frauenlob, M. M. McCormak, C. M. Walsh, E. Bergin, Rapid, In-Situ Synthesis of bidentate ligands: Chromatography free generation of catalyst libraries. Organic Bimolecular Chemistry, 9, pp. 6934-6937, August 2011.

[20] T. Zaman, R. Frauenlob, R. McCarthy, C. Walsh and E. Bergin, Application of Rapidly Generated Bidentate Ligand Linraries to zinc catalyzed reduction. Journal of Organ metallic Chemistry, 716, pp. 159-166, October 2012.

[21] G. J. Kim, S. H. Kim, P. H. Chong and M. A. Kwon, N-N'-Dialkylated 1, 2-Diamine Derivatives as a new Efficient Ligands for $RuCl_2$ $(PPh_3)_3$ Catalyzed Asymmetric Transfer Hydrogenation of Aromatic Ketones. Tetrahedron Letters, 43, Issue 45, pp. 8059-8062, November 2002.

[22] V. Jurcik, R. Wilhelm, Preparation of Aminals in Water, Tetrahedron, 60, Issue 14, pp. 3205-3210, March 2004.

[23] H. Brunner, U. Obermann and P. wimmer, Asymmetric Catalysis, Enantioselective Monophenylation of Diols with cupric acetate/pyridinyloxazoline catalysts. Organometallics, 8, Issue 3, pp. 821-826, March 1989.

[24] H. A. McManus and P. J. Guiry, Recent Developments in the Application of Oxazoline-Containing Ligands in Asymmetric Catalysis. Chemical Reviews, 104, Issue 9, pp. 4151-4202, September 2004.

[25] R. V. Ottenchaber, K. P. Brylivakov, E. P. Talsi, Nonheme Manganese-Catalyzed Asymmetric Oxidation. Lewis Acid Activation versus Oxygen Rebound Mechanism: Evident for Third Oxidant. Inorganic Chemistry, 49, Issue 18, pp. 8620-8628, September 2010.

[26] J. Y. Wu, B. N. Stanzl, T. Ritter, A Strategy for the Synthesis of well-Defined Iron Catalysts and Application to Regioselective Diene Hydrosylilation. Journal of American Chemical Society, 132, Issue 38, pp. 13214-13216, September 2010.

[27] Kylmälä, T., Kuuloja, N., Xu, Y., Rissanen, K. & Franzén R, Synthesis of Chlorinated Biphenyls by Suzuki Cross-Coupling Using Diamine or Diimine-Palladium Complexes. European Journal of Organic Chemistry, 2008, Issue 23, pp. 4019-4025, August 2008.

[28] Jones, M.D. & Mahon, M.F, Synthesis of RhI Diamine Complexes and their Exploitation for Asymmetric Hydrogen Transfer Processes. Journal of Organ metallic Chemistry, 693, Issue 13, pp. 2377-2382, August 2008.

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