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Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

Synthesis of chiral fluorescence active probe and its application as an efficient catalyst in asymmetric Friedel-Crafts alkylation of indole derivatives with nitroalkenes

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

The novel chiral Zn(II) Complexes were synthesized and these complexes showed the fluorescence behaviour. The chiral Zn(II) complex was tested in asymmetric Friedel-Crafts alkylation reaction of indole derivatives with nitroalkenes. In all cases, the desired product was obtained with high yield (up to 93%) and good enantioselectivity (up to 78% ee) under the optimized reaction conditions. The effect of solvent, metallic salt and piperidine ratio on the fluorescence intensity of catalyst and on enantioselectivity of desired products was discussed.

Introduction

The Friedel-Crafts alkylation is a key reaction in organic synthesis for the formation of new carbon-carbon bonds.[1] This reaction requires aromatic substrate and electron deficient alkenes such as α,β-unsaturated ketones,[2] ketone enolates,[3] arylidene malonates,[4] α-hydroxy enones,[5] 3-nitro-2H-chromenes,[6] α-Substituted β-Nitroacrylates[7], nitrodienes and 2-Propargyloxy-β-nitrostyrenes.[8] The asymmetric version of Friedel-Crafts alkylation reaction of indoles with electron-deficient alkenes is of vital importance,[9] as enantiomerically pure indole skeleton is widely used for the synthesis of natural products, active pharmaceutical intermediates (APIs), agrochemicals and functional materials.[10] The potential examples of indole skeleton alkaloids are Uleine, Hapalindole G, Deethylibophyllidine, Brevicolline and physostigmine which exhibit important biological activities (Figure 1).[11] Furthermore, nitroalkenes are very efficient Michael acceptors where the nitro group can easily converted into expensive amino functional group and variety of different functionalities;[12] because of this speciality nitroalkenes are widely observed in many organic transformations.

The increasing demand of the indole containing compounds in pharmaceutical sciences has lead to the development of new strategies for the synthesis of enantiomerically pure indole derivatives with high selectivity. Several reports have appeared in the literature using chiral Lewis acids derived from chiral ligands and metal salts for the asymmetric Friedel-Crafts alkylation reaction of indole derivatives with trans β-Nitrostyrene.[13] In addition, some organocatalysts are also applied for asymmetric Friedel-Crafts alkylation reaction.[14] The above protocol gave good yield and enantiomeric excess of products; however few protocols have some drawbacks such as low enantioselectivity, a long reaction time, use of additives, low selectivity and multistep designed ligands. This limits the practical applications of reported protocols.

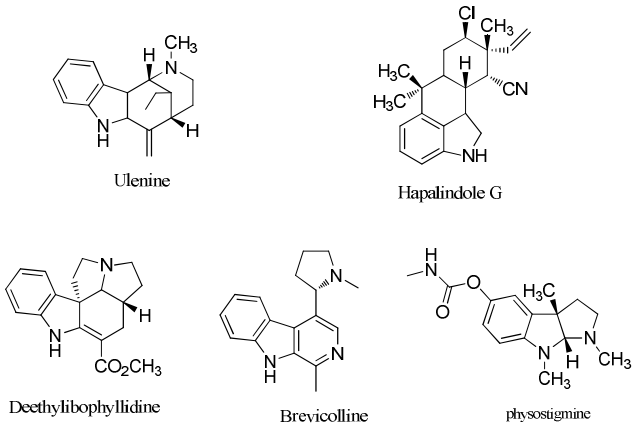

Fig. 1 Enantiopure indole skeleton in bioactive compounds

In the past, several methods have been developed for the synthesis of molecule-based highly selective and sensitive enantioselective fluorescence sensor for chiral recognition of bioactive enantiomers.[15] Chiral recognition of enantiomers also helps us to know more about interactions of bioloactive molecules, separation process, designing asymmetric catalysis systems and screening of high-throughput chiral catalysts.[16] In 2002, Lin *et al.* reported the chiral molecular squares bipyridyl bridging ligands and fac-$Re(CO)_3Cl$ corners for enantioselective Sensing,[17] subsequently they prepared chiral organometallic triangles Pt-acetylide linkage and utilized as a chiral catalyst for enantioselective additions of diethyl zinc to aromatic aldehydes.[18]

In the last two decades in combination of various chiral ligands and achiral or meso ligands have been successfully applied as a combinatorial complex in many reactions[19] which showed good results as compared to original chiral ligands. In the present study we are applying this fluorescence sensor and combinatorial ligand concept to prepare the enantiomerically pure fluorescence sensor of novel Schiff base zinc(II) complex with piperidine as an

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achiral combinatorial ligand. The prepared fluorescence active Schiff base zinc(II) complex is successfully applied for asymmetric Friedel-Crafts alkylation reaction of indole with trans β-nitrostyrene. This reaction is carried out at -15 °C for 40 h and afforded enantiomerically pure 3-substituted indole derivatives in high yields (up to 90%) with excellent enantiomeric excess (up to 78% ee) (figure 2).

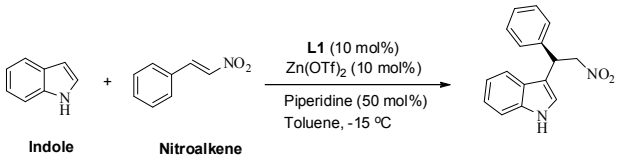

Fig. 2 Asymmetric Friedel-Crafts alkylation reaction of indole with trans β-nitrostyrene.

Result and Discussion

Initially we prepared the (1*S*,2*R*)-1-[(2-Hydroxy-3,5-di-tert-butyl-benzylidene)-amino]-indan-2-ol according to a reported procedure.[20] 3,5-Di-tert-butylsalicylaldehyde (10 mmol) was dissolved in 60 mL ethanol. (1*S*,2*R*)-1-Amino-2-indanol (10.5 mmol) was added in one portion. The solution instantly turned bright yellow in colour. The mixture was stirred for 2 h at room temperature; ethanol was removed on the rotary evaporator. The resulting solid was dried under vacuum to give **L1** (Figure 3).

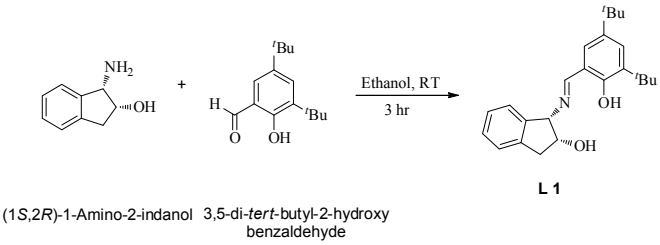

Fig. 3 Synthesis of chiral ligand **L1**

The chiral Zn(II) complex was prepared at room temperature by addition of **L1**(0.04 mmol) and $Zn(OTf)_2$ (0.04 mmol) in 3 mL toluene and stirred it for 10 min. Then, we added piperidine (0.2 mmol) and the resulting reaction mixture were stirred for 30 minutes at room temperature (30 °C) (see figure.4). The prepared chiral Zn(II) complex was studied by fluorescence spectroscopy. In this study, we investigated the effect of various parameters such as solvatochromic effect with different metal salts and effect of piperidine concentration on fluorescence intensity of chiral Zn(II) complex.

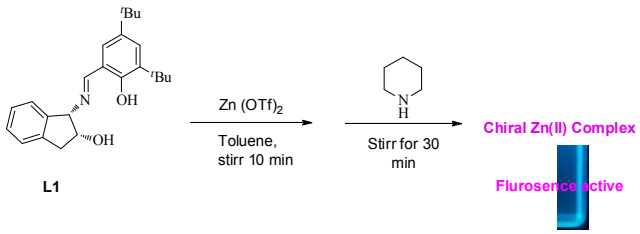

Fig. 4 Synthesis of chiral Zn(II) Complex

The fluorescence spectra of chiral Zn(II) complex were investigated in different solvents like toluene, dichloromethane (DCM), methyl tertbutyl ether (MTBE), chloroform ($CHCl_3$) , trifluorotoluene ($PhCF_3$). The most intense fluorescence was observed in toluene for ligand **L1**. The Ligand **L1** shows maximum fluorescence intensity at λ_{ex} = 471 nm (figure 5) in toluene. The fluorescence intensity for **L1** was found to decrease in different solvents with following order as Toluene > DCM > MTBE > $CHCl_3$ > $PhCF_3$.

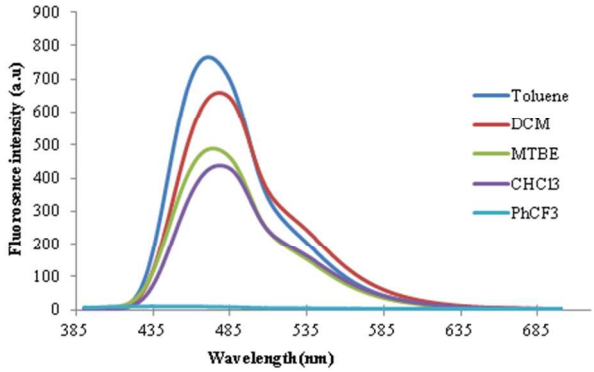

Fig. 5 Effect of solvent on fluorescence intensity chiral Zn(II) complex

Then the effects of metal salts such as $Zn(OTf)_2$, $Sc(OTf)_3$, $In(OTf)_3$, $Yb(OTf)_3$, $Cu(OTf)_2$ on the fluorescence intensity of ligand **L1** in toluene were studied; where we observed that ligand **L1** showed maximum fluorescence intensity in combination with $Zn(OTf)_2$. The Ligand **L1** showed fluorescence intensity at λ_{ex} =471 nm with $Zn(OTf)_2$ (figure 6). While the fluorescence intensity of ligand **L1** with $Sc(OTf)_3$ showed lower intensity as compared to $Zn(OTf)_2$ even in double concentration with decreasing wavelength (456 nm). The fluorescence intensity of the complex formed between $In(OTf)_3$, $Yb(OTf)_3$, $Cu(OTf)_2$ with ligand **L1** was negligible at same wavelength (471nm).

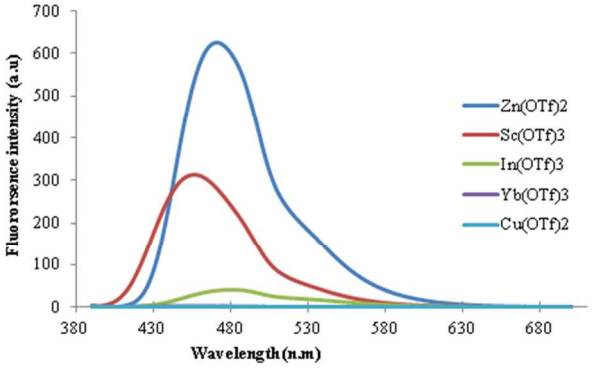

Fig.6 Effect of various metal salts on fluorescence intensity of ligand L1 in toluene

Furthermore, we studied the effect of ligand to piperidine ratio on fluorescence intensity of chiral Zn(II) complex. Different molar ratio was also screened ranging from 01:01, 01:02, 01:03 and 01:04. Herein, we synthesized the chiral Zn(II) complex with above mentioned ligand to piperidine ratio. The chiral Zn(II) complex with molar ratio 01:01gave slight fluorescence intensity, when we increase the molar ratio from 01:01 to 01:02 the fluorescence intensity increases dramatically, further increasing the molar ratio from 01:02 to 01:03, 01:04 the fluorescence intensity increases slightly. The molar ratio 01:04

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shows maximum fluorescence intensity λ_{ex} = 471 nm (figure 7).

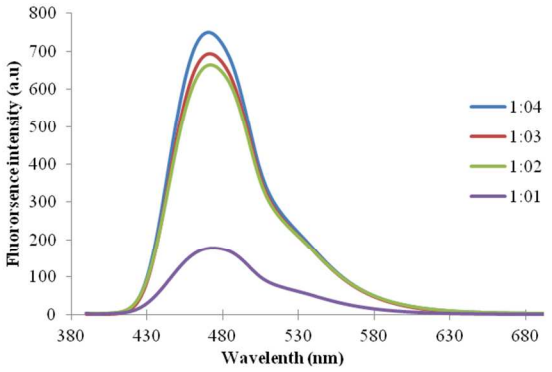

Fig.7 Effect of piperidine concentration on fluorescence intensity chiral Zn (II) complex in toluene

Based on these results, we focused on the experiments to check the role of every components of chiral Zn(II) complex on fluorescence behaviour. Initially, we omitted the metal from chiral complex and observed that the fluorescence intensity was decreases dramatically. Moreover the fluorescence intensity was not observed in absence of metal and piperidine. Later on, we performed the control experiments only with the piperidine and in combination of piperidine-metal which did not show fluorescence intensity. All these experiments proved that all components are necessary to from the active chiral Zn(II) complex. The complex showed maximum fluorescence intensity at λ_{ex} = 471 nm which confirms that there is strong interaction in the ligand **L1**, $Zn(OTf)_2$, and piperidine which is shown in figure 8.

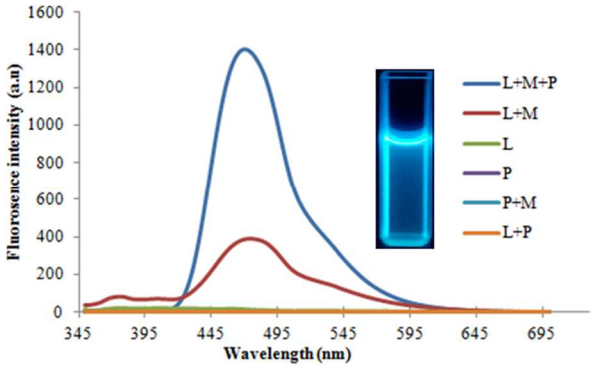

Fig. 8 Comparison of fluorescence intensity of piperidine (P) with $Zn(OTf)_2$ metal (M), L1 ligand (L), ligand with metal and combination of ligand, metal , piperidine (chiral Zn(II) complex) in toluene.

Fig. 8 Comparison of fluorescence intensity of piperidine (P) with $Zn(OTf)_2$ metal (M), **L1** ligand (L), ligand with metal and combination of ligand, metal , piperidine (chiral Zn(II) complex) in toluene

Initially we performed the Friedel-Crafts alkylation of indole **3a** with trans-β-nitrostyrene **4a** in toluene at room temperature using **L1**-$Zn(OTf)_2$-Piperdene complex as a catalyst. The desired product **5a** was obtained in 92 % yield with 60% ee (Table 1, entry 1). To compare the efficiency of ligand **L1**, we prepared another ligand **L2** by reaction of (1*S*,2*R*)-1-Amino-2-indanol and 4-(diethylamino)benzaldehyde using above mentioned procedure and applied on substrate indole **3a** with trans-β-nitrostyrene **4a** at room temperature; where we observed that the desired product **5a** was obtained with good yield but failed to provide high enantiomeric excess; therefore ligand **L1** was used for further experiments. In the **L1** is there are two sterically hindered *tert*-butyl groups on the phenol ring which act as donor group in the complex formation, because of this sterically hindered group ligand **L1** showed good enantiomeric excess as compared to ligand **L2**. Then, we screened various metallic salts such as $Cu(OTf)_2$, $Sc(OTf)_3$, $Yb(OTf)_3$, $In(OTf)_3$ (Table 1, entries 3-6). The $Cu(OTf)_2$, Sc $(OTf)_3$ provided good yields but failed to give high enantiomeric excess of desired product. In combination of ligand **L1** with $Yb(OTf)_3$, $In(OTf)_3$ provided desired product **5a** in racemic form with moderate yield (Table 1, entries 5-6). Thus in present study **L1** as a chiral ligand and $Zn(OTf)_2$ as the metallic salt was selected as the best catalyst for further optimization study (Table1, entry 1).

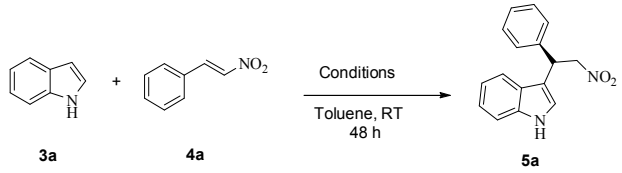

Table 1 Effect of ligands, metal salts and catalyst loading on the asymmetric Friedel- Crafts alkylation of indole.[a]

Entry	Ligand	Metal salt	% Yield[b]	%ee[c]
Ligand Screening				
1	**L1**	$Zn(OTf)_2$	92	60
2	**L2**	$Zn(OTf)_2$	88	19
Metal screening				
3	**L1**	$Cu(OTf)_2$	47	16
4	**L1**	$Sc(OTf)_3$	91	4
5	**L1**	$Yb(OTf)_3$	54	Racemic
6	**L1**	$In(OTf)_3$	47	Racemic

[a] Reaction conditions: nitrostyrene-0.5 mmol, indole-0.6 mmol, toluene-3mL, ligand-0.05 mmol, metal-0.05 mmol, piperidine-0.15 mmol, temperature- RT, time-48 h, [b] Isolated yield, [c] Determined by chiral HPLC analysis on a Chiralcel OD-H column..

The effect of catalyst loading ranging from 5-20 mol% of substrate for model reaction of indole **3a** with trans-β-nitrostyrene **4a** was studied (Table 2, entries1-4), and it was observed that increasing the catalyst loading from 5 mol% to 10 mol% led to remarkable increases in the yield and enantiomeric excess of desired product **5a**. Further increase in the catalyst loading did not show any profound effect on yield and enantiomeric excess of desired product.

Table 2 Effect of catalyst loading on the asymmetric Friedel-Crafts alkylation of indole.[a]

Entry	Ligand (mol %)	Metal (mol %)	Piperidine (mol %)	% Yield[b]	% ee[c]
1	5	5	15	87	54
2	10	10	30	92	60
3	15	15	45	92	60
4	20	20	60	94	58
5	10	--	30	16	50
6	--	10	30	25	Racemic
7	10	10	--	88	5
8	10	--	--	<10	8

[a] Reaction conditions: ligand -**L1**, Metal- $Zn(OTf)_2$, nitrostyrene-0.5 mmol, indole-0.6 mmol, toluene-3mL, [b] Isolated yield, [c] Determined by chiral HPLC analysis on a Chiralcel OD-H column.

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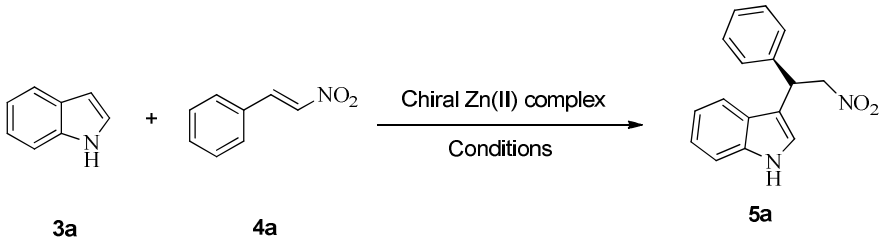
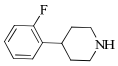
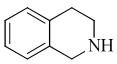
Table 3 Effect of reaction parameters on the asymmetric Friedel- Crafts alkylation of indole.[a]



Entry	Solvent	Amines	**L1** : Piperidine ratio	Temp. (°C)	Time (h)	% Yield [b]	% ee [c]
Effect of solvent							
1	ACN	Piperidine	1:3	RT	48	85	53
2	MTBE	Piperidine	1:3	RT	48	72	44
3	THF	Piperidine	1:3	RT	48	78	44
4	DCM	Piperidine	1:3	RT	48	82	53
5	$CHCl_3$	Piperidine	1:3	RT	48	90	51
6	*n*-hexane	Piperidine	1:3	RT	48	70	46
7	Toluene	Piperidine	1:3	RT	48	92	60
Effect of amines							
8	Toluene		1:3	RT	48	38	45
9	Toluene		1:3	RT	48	91	31
10	Toluene		1:3	RT	48	86	39
11	Toluene		1:3	RT	48	79	47
12	Toluene		1:3	RT	48	84	50
Effect of piperidine ratio							
13	Toluene	Piperidine	1:1	RT	48	94	11
14	Toluene	Piperidine	1:2	RT	48	94	53
15	Toluene	Piperidine	1:3	RT	48	92	60
16	Toluene	Piperidine	1:4	RT	48	91	63
17	Toluene	Piperidine	1:5	RT	48	92	64
18	Toluene	Piperidine	1:6	RT	48	92	64
19	Toluene	Piperidine	1:7	RT	48	90	64
20	Toluene	Piperidine	1:8	RT	48	89	63
21[d]	Toluene	Piperidine	1:5	RT	48	92	64
22[e]	Toluene	Piperidine	1:5	RT	48	92	64
23[f]	Toluene	Piperidine	1:5	RT	48	90	64
Effect of temperature							
24	Toluene	Piperidine	1:5	0	48	91	70
25	Toluene	Piperidine	1:5	-15	48	91	75
26	Toluene	Piperidine	1:5	-20	48	90	73
Effect of time							
27	Toluene	Piperidine	1:5	-15	14	34	58
28	Toluene	Piperidine	1:5	-15	20	46	60
29	Toluene	Piperidine	1:5	-15	24	76	67
30	Toluene	Piperidine	1:5	-15	28	89	68
31	Toluene	Piperidine	1:5	-15	40	92	75
32	Toluene	Piperidine	1:5	-15	48	92	75

[a] Reaction conditions: a nitrostyrene-0.5 mmol, indole-0.6 mmol, toluene-3mL, **L1**-0.05 mmol, $Zn(OTf)_2$-0.05 mmol, [b] Isolated yield, [c] Determined by chiral HPLC analysis on a Chiralcel OD-H column, [d] 150mg 3Å MS, [e] 150mg 4 Å MS, [f] 150mg 5 Å MS

Based on these results, we performed the test experiments to check the roles of every component in the catalytic system. These experiments showed that ligand L1, Zn(OTf)2 and piperidine were necessary for the efficient catalytic system (Table 2, entries

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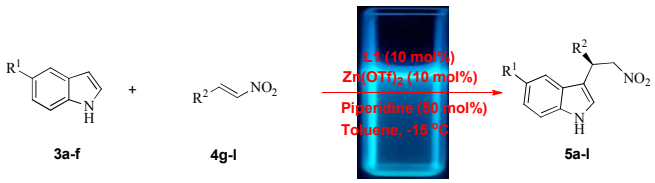
5-8). To get the optimal reaction conditions, we studied the effect of the various reactions parameters such as effect of solvents, amines, piperidine ratio, molecular sieves, temperature and time on the yield and enantiomeric excess of desired product (Table 3). The influence of solvent on the asymmetric Friedel-Crafts reaction was investigated (Table 3, Entries 1-7). Solvents such as ACN (Acetonitrile), MTBE (methyl tertiary butyl ether), THF (tetrahydrofuran), DCM (dichloromethane), $CHCl_3$ (chloroform), toluene and *n*-hexane were screened. Our catalyst showed high activity in toluene with 92% yield and 60% ee of desired product **5a** (Table 3, entry 7). Other solvents gave low enantioselectivity as compared to toluene (Table 3, entries 1-6), therefore, toluene was used for further studies. The chiral Zn(II) complex with amines plays an important role on the enantioselectivity of desired product **5a**.Various amines such as 2,2,6,6-tetramethylpiperidine (45% ee), cis-3,5-dimethylmorpholine (31% ee), 4-(2-fluorophenyl)piperidine(39% ee), 1,2,3,4-tetrahydro isoquinoline (47% ee), pyrrolidine (50% ee) were screened (Table 3, entries 8-12). Out of these amines piperidine provided (60% ee) good enantioselectivity; hence it was used for remaining experiments.

In the fluorescence study of chiral Zn(II) complex it was observed that when we increase the ratio of **L1** to piperidine the fluorescence intensity of catalyst increases, hence we checked the effect of molar ratio on enantioselectivity of the desired product. Therefore we screened the piperidine molar ratio ranging from 1: 1 to 1: 8 (ligand L1: piperidine) and observed that when we increase the molar ratio from 1:1 to 1:5, there was increase in the enantioselectivity desired product **5a** from 11% ee to 64% ee (Table 3, entries 13-17). These experiments was clearly indicates that when increase the fluorescence intensity of the chiral Zn(II) complex increases the enantioselectivity of desired product **5a**. With further increase in the piperidine ratio from 1:6 to 1:8 there is no effect on the enantioselectivity of desired product. Furthermore, we screened the role of molecular sieves on the yield and enantioselectivity of desired product **5a** (Table 3, Entries 21-23) and it was observed that there is no effect on the yield and enantioselectivity of product **5a**. Then we checked the effect of acid additives on yield and enantioselectivity of desired product **5a**. We screened the various racemic and enantiomerically pure acids such as para-trifluoro benzoic acid, D- camphor sulphonic acid, N-boc proline, L- lactic acid, triflic acid, (*R*)-tetrahydrofuran-2-carboxylic acid and tartaric acid, but they failed to increase the enantiomeric excess of desired product **5a**(see ESI† Table 1). Thus the next experiments were carried out without acid additives. The effect of temperature on the yield and enantioselectivity of the product **5a** was studied and the reactions were carried out at various temperatures ranging from room temperature to -20 °C (Table 3, entries 25-27). At room temperature, the enantioselectivity of **5a** was low, whereas decreasing the temperature to 0 °C leads to increase in enantioselectivity up to 70% ee. Further decrease in the temperature to -15 °C increases the enantioselectivity up to 75% ee. A further decrease in the temperature to -20 °C decreases the enantioselectivity to 73% ee. Hence optimized temperature is -15 °C.

Finally, we examined the effect of time on the model reaction (Table 3, entries 28-32). After 40 h, the maximum yield and enantioselectivity of the desired product **5a** was obtained. Thus the optimized reaction conditions are indole (**3a**, 0.5 mmol), trans-β-nitrostyrene (**4a**, 0.6mmol), Ligand (**L1**, 0.05mmol), $Zn(OTf)_2$ (0.05mmol), piperidine (0.15mmol) at -15°C for 40 h.

With the optimal reaction conditions in hand, we performed the asymmetric Friedel-Crafts alkylation reaction between indole derivatives and nitrostyrene derivatives (Table 4, entries 1-12). We first surveyed a variety of indoles **5a-5f** bearing different substituents (Table 4, entries 1-6) which could react with nitrostyrene in good yields with high enantioselectivity. The substitution on the C-5 position of indole, with halogen (-Br, -Cl, -F) substituent provided good enantioselectivities (78-76% ee, Table 4, entries 2-4). Further, electron donating (-OMe, -Me) substituent at C-5 of indole provided good enantioselectivities with **5e**:70% ee, **5f**:76% ee (Table 4, entries 5-6). The substituent effect on the nitrostyrene ring was also studied. The nitrostyrene with halogen (-Br, -Cl, -F) substituent at para position gave corresponding products with good enantiomeric excess (69-76 % ee, Table 4, entries 7-9).

Table 4 Asymmetric Friedel-Crafts alkylation of indole derivatives with nitroalkenes.[a]



Entry	R_1	R_2	Product	% Yield[b]	% ee[c]
1	H	Ph	**5l**	92	76
2	Br	Ph	**5b**	85	78
3	Cl	Ph	**5c**	87	75
4	F	Ph	**5d**	91	74
5	OMe	Ph	**5e**	90	70
6	Me	Ph	**5f**	89	76
7	H	4-BrC_6H_4	**5g**	87	69
8	H	4-ClC_6H_4	**5h**	91	76
9	H	4-FC_6H_4	**5i**	93	76
10	H	4-MeC_6H_4	**5j**	88	70
11	H	4-$OMeC_6H_4$	**5k**	85	72
12	H		**5l**	94	72

[a] Reaction conditions: **L1**-(10 mol %), $Zn(OTf)_2$-(10 mol %), piperidine (50 mol %), toluene-(3ml), nitrostyrene-(1mmol), indole-(1.2 mmol), temperature- (-15 °C), [b] Isolated yield, [c] Determined by chiral HPLC analysis on a Chiralcel OD-H column.

Electron-rich (-Me, -OMe) aromatic nitrostyrene at para position furnished desired product with good enantioselectivity as **5j**: 70% ee and **5k**: 72% ee was obtained. It is notable that a heterocyclic nitrostyrene derivative provides good enantioselectivity as 5l: 72% ee.

Conclusions

In conclusion, the novel and efficient catalytic asymmetric protocol for Friedel-Crafts alkylation reaction of indoles with nitroalkene derivatives by chiral Zn(II)-Schiff base complex was developed. The Chiral Zn(II)complex was showed excellent fluorescence behaviour. The developed novel catalyst provides

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high yields (up to 93%) with good enantiomeric excess (up to 78%) for wide range of indoles and aromatic nitrostyrene derivatives under mild reaction conditions. The developed protocol offers high yields, good enantioselectivities, short reaction time, mild reaction conditions and inexpensive catalytic system.

Acknowledgements

G.V.M. is thankful to the Council of Scientific and Industrial Research (CSIR), New Delhi for providing a senior research fellowship. The authors also thanks to Department of Science and 60 Technology (DST)-SERB, India (project file NO.SR/S1/OC-09-2012) for financial support.

References

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† Electronic Supplementary Information (ESI) available: general experimental procedure, Copies of the ^{1}H and ^{13}C NMR spectra and the Chiral HPLC chromatograms of the products.

See DOI: 10.1039/b000000x/

1 For reviews on Friedel-Crafts alkylation reactions, see: a) Olah, G. A.; Khrisnamurti, R.; Prakash, G. K. S. *In Comprehensive Organic Synthesis,* 1st ed.; Pergamon: New York, 1991; Vol. 3, pp 293-339, b) Olah, G. A. In Friedel-Crafts and Related Reactions; Wiley Interscience: New York, 1964; Vol. 2. Part 1.

2 a) T. Sakamoto, J. Itoh, K. Mori, and T. Akiyama, *Org. Biomol. Chem.,* 2010, **8**, 5448-5454, b) G. Bartoli, M. Bosco, A. Carlone, F. Pesciaioli, L. Sambri, and P. Melchiorre, *Org. Lett.,* 2007, **9**, 1403-1405, c) G. Blay, I. Fernández, J. R. Pedro, and C. Vila, *Org. Lett.,* 2007, **9**, 2601-2604.

3 a) B. M. Trost and G. M. Schroeder, *J. Am. Chem. Soc*, 1999, **121**, 6759-6760, b) B. M. Trost, J. Xu, and T. Schmidt, *J. Am. Chem. Soc.,* 2009, **131**, 18343-18357.

4 J. Wu, D. Wang, F. Wu, and B. Wan, *J. Org. Chem.*, 2013, **78**, 5611-5617.

5 C. Palomo, M. Oiarbide, B. G. Kardak, J. M. García, and A. Linden, *J. Am. Chem. Soc*., 2005, **127**, 4154-4155.

6 Y. Jia, W. Yang, and D.-M. Du, *Org. Biomol. Chem.*, 2012, **10**, 4739.

7 J. Q. Weng, Q. M. Deng, L. Wu, K. Xu, H. Wu, R. R. Liu, J. R. Gao, and Y. X. Jia, *Org. Lett.,* 2014, **16**, 776-779.

8 J. Peng and D.-M. Du, *Eur. J. Org. Chem.,* 2012, 4042-405.

9 K. A. Jørgensen, *Synthesis* 2003, 1117-1125, b) M. Bandini, A. Melloni, and A. Umani-Ronchi, *Angew. Chemie - Int. Ed.*, 2004, **43**, 550-556, c) M. Bandini, A. Melloni, S. Tommasi, A. Umani-Ronchi, *Synlett* 2005, 1199-1222, d) T. B. Poulsen, K. A. Jørgensen, *Chem. Rev.*, 2008, **108**, 2903-2915.

10 For a review of pharmacology, see: a) N. H. Greig, X.F. Pei, T. T. Soncrant, D. K. Ingram, A. Brossi, *Med. Res. Rev.,* 1995, **15**, 3, b) D. J. Faulkner, *Nat. Prod. Rep.*, 2001, **18**, 1-49, c) K. S. Jandu, V. Barrett, M. Brockwell, D. Cambridge, D. R. Farrant, C. Foster, H. Giles, R. C. Glen, A. P. Hill, H. Hobbs, A. Honey, G. R. Martin, J. Salmon, D. Smith, P. Woollard, and D. L. Selwood, *J. Med. Chem*., 2001, **44**, 681-693, d) K. H. Lim, O. Hiraku, K. Komiyama, T. Koyano, M. Hayashi, and T. S. Kam, *J. Nat. Prod.*, 2007, **70**, 1302-1307.

11 a) T. Fukuyama and X. Chen, *J. Am. Chem. Soc.*, 1994, **116**, 3125-3126, b) R. E. Moore, C. Cheuk, X. G. Yang, G. M. L. Patterson, R. Bonjouklian, T. A. Smitka, J. S. Mynderse, R. S. Foster, N. D. Jones, J. K. Swartzendruber, and J. B. Deeter, *J. Org. Chem.*, 1987, **291**, 1036-1043, c) R. E. Moore, C. Cheuk, and G. M. L. Patterson, *J. Am. Chem. Soc.*,1984, **106**, 6456-6457, d) B. Robinson, Alkaloids 1971, 13, 213, e) S. Takano, K. Ogasawara, *Alkaloids* 1989, **36**, 225.

12 a) O. M. Berner, L. Tedeschi, and D. Enders, *European J. Org. Chem.*, 2002, 1877-1894, b) W. Zhuang, R. G. Hazell, and K. A. Jørgensen, *Org. Biomol. Chem.,* 2005, **3**, 2566-2571, c) R. Ballini and M. Petrini, *Tetrahedron*, 2004, **60**, 1017-1047, d) N. Ono (Ed.), The Nitro Group in Organic Synthesis, Wiley-VCH, New York, 200.

13 a) S.-F. Lu, D.-M. Du, and J. Xu, *Org. Lett.*, 2006, **10**, 2115-2118, b) Y. X. Jia, S. F. Zhu, Y. Yang, and Q. L. Zhou, *J. Org. Chem*., 2006, **71**, 75-80, c) P. K. Singh, A. Bisai, and V. K. Singh, *Tetrahedron Lett*., 2007, **48**, 1127-1129, d) Z. L. Yuan, Z. Y. Lei, and M. Shi, *Tetrahedron Asymmetry*, 2008, **19**, 1339-1346, e) H. Liu, S-F. Lu, J. Xu, D-M. Du, *Chem. Asian J.,* 2008, **3**, 1111-1121, f) S. C. McKeon, H. Müller-Bunz, and P. J. Guiry, *European J. Org. Chem*., 2009, 4833-4841, g) H. Y. Kim, S. Kim, and K. Oh, *Angew. Chem. Int. Ed.*, 2010, **49**, 4476-4478, h) H. Liu and D.-M. Du, *Adv. Synth. Catal.*, 2010, **352**, 1113-1118, i) H. Liu and D.-M. Du, *European J. Org. Chem*., 2010, 2121-2131, j) J. F. Schneider, F. C. Falk, R. Fröhlich, and J. Paradies, *European J. Org. Chem.*, 2010, 2265-2269, k) S. C. McKeon, H. M. Bunz and P. J. Guiry, *European J. Org. Chem.*, 2011, 7107-7115, l) J. Wu, X. Li, F. Wu, and B. Wan, *Org. Lett*., 2011, **18**, 4834-4837.

14 a) R. P. Herrera, V. Sgarzani, L. Bernardi, and A. Ricci, *Angew. Chemie - Int. Ed.*, 2005, **44**, 6576-6579, b) M. Ganesh and D. Seidel, *J. Am. Chem. Soc.,* 2008, **130**, 16464-16465, c) J. Itoh, K. Fuchibe, and T. Akiyama, *Angew. Chemie - Int. Ed.,* 2008, **47**, 4016-4018.

15 a) G. A. Hembury, V. V. Borovkov and Y. Inoue, *Chem. Rev.,* 2008, **108**, 1-73, b) L. Pu, *Chem. Rev.,* 2004, **104**, 1687-1716, c) X. Meia and C. Wolf, *Chem. Commun*., 2004, 2078-2079, d) G. W. Gokel, W. M. Leevy, and M. E. Weber, *Chem. Rev.,* 2004, **104**, 2723-2750, e) D. Leung, S. O. Kang, and E. V. Anslyn, *Chem. Soc. Rev*., 2012, **41**, 448-479, f) F. Song, N. Fei, F. Li, S. Zhang, Y. Cheng, and C. Zhu, *Chem. Commun*., 2013,**49**, 2891-2893.

16 a) K. Ding, A. Ishii and K. Mikami, *Angew. Chemie - Int. Ed*., 1999, **38**, 497-501, b) M. Matsushita, K. Yoshida, N. Yamamoto, P. Wirsching, R. A. Lerner, and K. D. Janda, *Angew. Chemie - Int. Ed*., 2003, **42**, 5984-5987, c) G. A. Korbel, G. Lalic, and M. D. Shair, *J. Am. Chem. Soc.*, 2001, **123**,361-362, d) S. Yu and L. Pu, *J. Am. Chem. Soc.*, 2010, **132**, 17698-17700.

17 S. J. Lee and W. Lin, *J. Am. Chem. Soc.,* 2002, **124**, 4554-4555.

18 S. J. Lee, A. Hu, and W. Lin, *J. Am. Chem. Soc.*, 2002, **124**, 12948-12949.

19 a) S. Kobayashi, I. Hachiya, H. Ishitani, M. Araki, *Tetrahedron Lett*., 1993, **34**, 4535-4538, b) P. J. Walsh, A. E. Lurain, and J. Balsells, *Chem. Rev.,* 2003, **103**, 3297-3344, c) M. T. Reetz, *Angew. Chem. Int. Ed.*, 2008, **47**, 2556-2588, d) B. Breit, *Angew. Chem. Int. Ed.*, 2005, **44**, 6816-6825, e) K. Ding, H. Du, Y. Yuan, and J. Long, *Chem. Eur. J.*, 2004, **10**, 2872-2884, f) G. V. More, B. M. Bhanage, *Eur. J. Org. Chem*., 2013, 6900-6906.

20 R. T. Ruck and E. N. Jacobsen, *J. Am. Chem. Soc*.,2002, **124**, 2882-2883

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Synthesis of chiral fluorescence active probe and its application as an efficient catalyst in asymmetric Friedel-Crafts alkylation of indole derivatives with nitroalkenes

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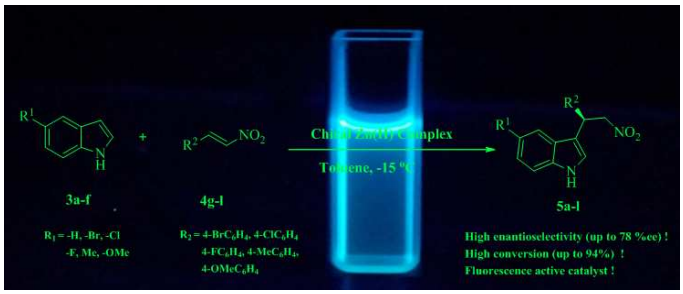

Green protocol for the asymmetric Friedel-Crafts alkylation using fluorescence active Zn(II) chiral catalyst with high conversion and enantiomeric excess has been developed.

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