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ARTICLE TYPE

Vanadium-catalyzed enantioselective Friedel-Crafts-type reactions

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The vanadium-mediated enantioselective Friedel-Crafts (FC) type reactions have been established with the dinuclear vanadium complex (R_a,S,S)-**1a**. The vanadium complex promoted the FC type reaction of imines with 2-naphthols or indoles to give the corresponding adducts with high enantioselectivities.

Chiral vanadium complexes are known to be effective catalysts¹ for enantioselective and chemoselective oxidative reactions such as oxidation of sulfides to sulfoxides,^{1a,b} epoxidation of allylic alcohols,^{1c,d} coupling of 2-naphthols^{1e-g} and oxidation of α -hydroxy carbonyl compounds.² In the vanadium mediated homo-coupling of 2-naphthols³ and the oxidation of alcohols,² O₂ or air can be used as a co-oxidant to promote the catalytic reactions. In 2000, North and co-worker reported the first Lewis acid vanadium-salen catalysts for enantioselective cyanosilylation reaction.⁴ Although except for the asymmetric cyanation of carbonyl derivatives,^{1h,5} chiral vanadium catalysts which function as Lewis acid have been inadequately studied until now. Asymmetric carbon-carbon bond-forming processes using vanadium complexes have been a challenge for the construction of chiral complicated molecules.^{6,7} Herein we report vanadium catalyzed enantioselective Friedel-Crafts (FC) type reactions of *N*-tosyl imines with 2-naphthols or indoles. The dinuclear vanadium complex (R_a,S,S)-**1a** which works as a chiral Lewis acid to promote the FC type reactions with high enantiocontrol (Figure 1).

Asymmetric FC type reaction between phenols and aldimines is an important approach for the preparation of optically active amine-phenol motif (e.g. Betti base)^{8,9} which is frequently encountered in biologically active compounds¹⁰ and widely used in asymmetric transformations.¹¹ The first asymmetric FC

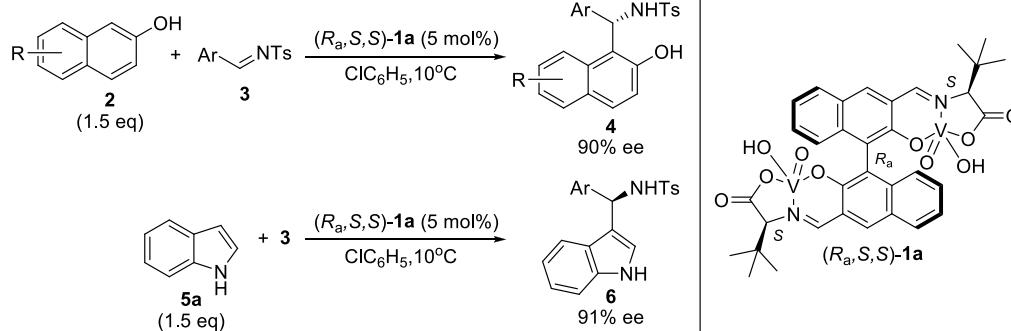


Figure 1 Vanadium-mediated enantioselective Friedel-Crafts (FC) type reactions of imines with 2-naphthols or indoles

reaction of 2-naphthols and aldimines was presented by Hui^{8a} in 2010, using stoichiometric amount of a chiral zinc complex. In 2011, Wang^{8b} and Chimni^{8c} independently reported the catalytic enantioselective processes using 15–20 mol% of organocatalysts derived from *Cinchona* alkaloids.

We previously reported the chiral dinuclear vanadium complexes for enantioselective oxidative homo-coupling of 2-naphthols with dual activation mechanism.^{3n-p} We assumed that in the dinuclear vanadium catalyzed reaction, activation of 2-naphthol and imine by each vanadium metals in the chiral template could lead to make smooth hetero-coupling (Figure 2), giving Betti adduct with high enantioselectivity.

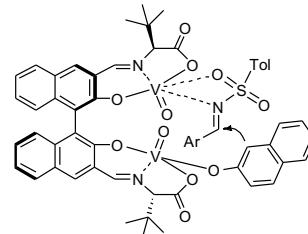


Figure 2 Plausible transition state for hetero-coupling of imine with 2-naphthol

To avoid a homo-coupling of 2-naphthol, the FC type reaction between 2-naphthol (**2a**) and 4-chlorophenyl *N*-tosylimine (**3a**) by vanadium catalysts was carried out at 10°C under N₂ atmosphere (Table 1).¹² Among the vanadium catalysts we tested, the dinuclear vanadium complexes (R_a,S,S)-**1a** possessing *t*Bu groups near to the active center, and (R_a,S,S)-**7** bearing H8-BINOL backbone exhibited high asymmetric induction ability (Table 1, Entries 1 and 4). The mononuclear vanadium complex (*S*)-**8** led to drastically decreasing enantiocontrol (Entry 5). The

optimal result (84% ee) was obtained when the reaction of **2a** (1.5 eq) with **3a** was performed in chlorobenzene (ClC_6H_5) at 10°C under N_2 atmosphere (Entry 12). After the 100% conversion of the imine **3a**, the product **4a** was obtained in 70% isolated yield with 85% ee (Table 2, Entry 1).

Table 1 Coupling reaction of **2a** with **3a** mediated by vanadium catalysts^a

10			vanadium catalyst (5 mol%) 10°C, N_2 50% conv. of 3a	
Entry	Catalyst	Solvent	2a (eq)	% Ee ^b
1	(<i>R_a,S,S</i>)- 1a	Toluene	1.5	83
2	(<i>S_a,S,S</i>)- 1a	Toluene	1.5	63
3	(<i>R_a,S,S</i>)- 1b	Toluene	1.5	70
4	(<i>R_a,S,S</i>)- 7	Toluene	1.5	80
5	(<i>S</i>)- 8^c	Toluene	1.5	19
6	(<i>R_a,S,S</i>)- 9	Toluene	1.5	64
7	(<i>R_a,S,S</i>)- 10	Toluene	1.5	48
8	(<i>R_a,S,S</i>)- 1a	THF or MeCN	1.5	(no reaction)
9	(<i>R_a,S,S</i>)- 1a	CH_2Cl_2	1.5	75
10	(<i>R_a,S,S</i>)- 1a	CCl_4	1.5	30
11	(<i>R_a,S,S</i>)- 1a	ClC_6H_5	1.0	82
12	(<i>R_a,S,S</i>)- 1a	ClC_6H_5	1.5	84
13	(<i>R_a,S,S</i>)- 1a	ClC_6H_5	2.0	80
14	(<i>R_a,S,S</i>)- 1a	ClC_6H_5	3.0	70

^aTrace amount of BINOL was formed. ^bDetermined by chiral HPLC (Daicel Chiraldak IC). ^c10 mol % of (*S*)-**8** was used.

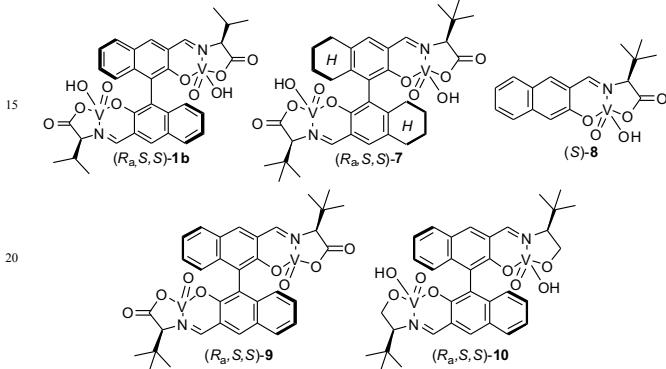


Table 2 Dinuclear vanadium complex (*R_a,S,S*)-**1a** catalyzed enantioselective Friedel-Crafts (FC) type reactions^a

Entry	2 or 5a	3 (Ar)	Time (d)	% Yield ^b	% Ee ^c
1	2a (R = H)	3a (4-Cl-C ₆ H ₄)	7	4a , 70	85
2	2a	3b (4-Br-C ₆ H ₄)	9	4b , 70	85
3	2a	3c (4-F-C ₆ H ₄)	8	4c , 70	76
4	2a	3d (4-Et-C ₆ H ₄)	9	4d , 67	81
5	2a	3e (4-MeO-C ₆ H ₄)	8	4e , 70	71
6	2a	3f (3-Cl-C ₆ H ₄)	6	4f , 70	89
7	2a	3g (2-Cl-C ₆ H ₄)	7	4g , 70	90
8	2a	3h (Ph)	8	4h , 70	71
9	2a	3i (2-thiophenyl)	6	4i , 80	60
10	2b (R = 6-Br)	3a	6	4j , 77	88
11	2c (R = 7-Me)	3a	6	4k , 82	61
12	5a	3a	4	6a , 80	76
13	5a	3b	3	6b , 80	76
14	5a	3j (2-Br-C ₆ H ₄)	9	6c , 77	91
15	5a	3k (2-naphthyl)	2	6d , 90	64

^aReaction conditions: **2** or **5** (0.15 mmol), **3** (0.10 mmol), catalyst (*R_a,S,S*)-**1a** (5 mol %), ClC_6H_5 (0.4 mL), 10°C, N_2 . ^bIsolated yield. ^cDetermined by HPLC (Daicel Chiraldak IC for **4a**, **d**, **f**, **g**, **i**; Daicel Chiraldak AS-H for **4b**, **c**, **h**, **j**, **k**; Daicel Chiraldak AD-H for **4e**; Daicel Chiralcel OD for **6a**, **c**; Daicel Chiralcel OD-H for **6b**, **d**).

Under the optimal conditions, (*R_a,S,S*)-**1a** promoted the FC type reaction with high enantiocontrol for various substituted aromatic *N*-tosylimines with **2a** (Table 2). 2-Thiophenyl *N*-tosylimine (**3i**), 6-bromo-2-naphthol (**2b**) and 7-methyl-2-naphthol (**2c**) were suitable substrates (Entries 9-11). The dinuclear vanadium complex (*R_a,S,S*)-**1a** was also found to be effective for the FC type reactions of imines with indole **5a** (Entries 12-15). In the vanadium catalyzed FC reactions of **5a**, no bis-indole formation as a main side-reaction¹³ was observed at all. The highest enantiomeric excess value of product was obtained when the reaction of **5a** with 2-bromophenyl *N*-tosylimine (**3j**), affording the corresponding adduct **6c** with 91% ee (Entry 14). A non-substitution on indole nitrogen plays an important role in interaction with the chiral vanadium center leading to high asymmetric induction onto the product (Figure 3).

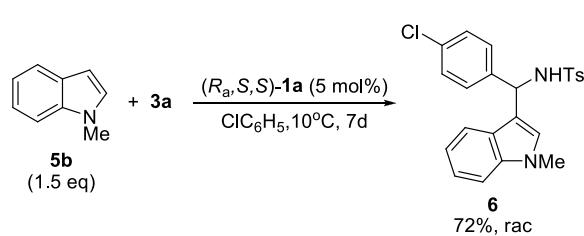


Figure 3 the FC type reaction of *N*-methyl indole (**5b**) with **3a**

In conclusion, we have discovered the first vanadium mediated enantioselective catalytic FC type reaction of *N*-tosyl imines with 2-naphthols or indoles. A wide variety of aryl aldimine substrates bearing either electron-withdrawing or electron-donating groups could be employed with 5 mol % of (*R_a,S,S*)-**1a** successfully. Gaining insights into the exact active vanadium species V(V) or V(IV) on the FC reactions and application of the dinuclear vanadium complexes for developing new asymmetric FC type reactions are in progress.

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Notes and references

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- 1 For reviews on enantioselective reaction catalyzed by chiral vanadium complexes, see: Sulfoxidations (a) W. Plass *Coord. Chem. Rev.* 2011, **255**, 2378; (b) K. P. Volcho and N. F. Salakhutdinov, *Russ. Chem. Rev.* 2009, **78**, 457; Epoxidations (c) C. Bolm, *Coord. Chem. Rev.* 2003, **237**, 245; (d) Q.-H. Xia, H.-Q. Ge, C.-P. Ye, Z.-M. Liu and K.-X. Su, *Chem. Rev.* 2005, **105**, 1603; Oxidative couplings of 2-naphthols (e) S. Takizawa, T. Katayama and H. Sasai, *Chem. Commun.* 2008, 4113; (f) S. Takizawa, *Chem. Pharm. Bull.* 2009, **57**, 1179; (g) H. Wang, *Chirality* 2010, **22**, 827; Cyanation (h) M. North, D. L. Usanov, and C. Young, *Chem. Rev.* 2008, **108**, 5146.
- 2 (a) A. T. Radosevich, C. Musich and F. D. Toste, *J. Am. Chem. Soc.* 2005, **127**, 1090; (b) S.-S. Weng, M.-W. Shen, J.-Q. Kao, Y. S. Munot and C. T. Chen, *Proc. Natl. Acad. Sci. U.S.A.* 2006, **103**, 3522; (c) V. D. Pawar, S. Bettigeri, S.-S. Weng, J.-Q. Kao and C.-T. Chen, *J. Am. Chem. Soc.* 2006, **128**, 6308; (d) C.-T. Chen, S. Bettigeri, S.-S. Weng, V. D. Pawar, Y.-H. Lin, C.-Y. Liu and W.-Z. Lee, *J. Org. Chem.* 2007, **72**, 8175; (e) R. A. Shiels, K. Venkatasubbaiah and C. W. Jones, *Adv. Synth. Catal.* 2008, **350**, 2823; (f) C.-T. Chen, J.-Q. Kao, S. B. Salunke and Y.-H. Lin, *Org. Lett.* 2011, **13**, 26; (g) S. B. Salunke, N. S. Babu and C.-T. Chen, *Adv. Synth. Catal.* 2011, **353**, 1234.
- 3 (a) S.-W. Hon, C.-H. Li, J.-H. Kuo, N. B. Barhate, Y.-H. Liu, Y. Wang and C.-T. Chen, *Org. Lett.* 2001, **3**, 869; (b) C.-Y. Chu, D.-R. Hwang, S.-K. Wang and B.-J. Uang, *Chem. Commun.* 2001, 980; (c) N. B. Barhate and C.-T. Chen, *Org. Lett.* 2002, **4**, 2529; (d) Z. Luo, Q. Liu, L. Gong, X. Cui, A. Mi and Y. Jiang, *Chem. Commun.* 2002, 914; (e) Z. Luo, Q. Liu, L. Gong, X. Cui, A. Mi and Y. Jiang, *Angew. Chem., Int. Ed.* 2002, **41**, 4532; (f) C.-Y. Chu and B.-J. Uang, *Tetrahedron: Asymmetry* 2003, **14**, 53; (g) H. Somei, Y. Asano, T. Yoshida, S. Takizawa, H. Yamataka and H. Sasai, *Tetrahedron Lett.* 2004, **45**, 1841; (h) M. Tada, T. Taniike, L. K. Kantam and Y. Iwasawa, *Chem. Commun.* 2004, 2542; (i) M. Tada, N. Kojima, Y. Izumi, T. Taniike and Y. Iwasawa, *J. Phys. Chem. B* 2005, **109**, 9905; (j) S. Habaue, S. Murakami and H. Higashimura, *J. Polym. Sci. Part A: Polym. Chem.* 2005, **43**, 5872; (k) M. Tada and Y. Iwasawa, *Chem. Commun.* 2006, 2833; (l) M. Tada, R. Bai and Y. Iwasawa, *Catal. Today* 2006, **117**, 141; (m) Q.-X. Guo, Z.-J. Wu, Z.-B. Luo, Q.-Z. Liu, J.-L. Ye, S.-W. Luo, L.-F. Cun and L.-Z. Gong, *J. Am. Chem. Soc.* 2007, **129**, 13927; (n) S. Takizawa, T. Katayama, C. Kameyama, K. Onitsuka, T. Suzuki, T. Yanagida, T. Kawai and H. Sasai, *Chem. Commun.* 2008, 1810; (o) S. Takizawa, T. Katayama, H. Somei, Y. Asano, T. Yoshida, C. Kameyama, D. Rajesh, K. Onitsuka, T. Suzuki, M. Mikami, H. Yamataka, D. Jayaprakash and H. Sasai, *Tetrahedron* 2008, **64**, 3361; (p) S. Takizawa, D. Rajesh, T. Katayama and H. Sasai, *Synlett* **2009**, 1667. Y. N. Belokon, M. North and T. Parsons, *Org. Lett.* 2000, **2**, 1617. (a) Y. N. Belokon, B. Green, N. S. Ikonomikov, M. North, V. Parsons and V. I. Tararov, *Tetrahedron*, 2001, **57**, 771; (b) Y. N. Belokon, P. Carta, A. V. Gutnov, V. Maleev, M. A. Moskalenko, L. V. Yashkina, N. S. Ikonomikov, N. V. Voskoboev, V. N. Khristalev and M. North, *Helv. Chim. Acta*, 2002, **85**, 3301; (c) A. Watanabe, K. Matsumoto, Y. Shimada and T. Katsuki, *Tetrahedron Lett.* 2004, **45**, 6229; (d) J. Blacker, L. A. Clutterbuck, M. R. Crampton, C. Grosjean and M. North, *Tetrahedron: Asymmetry* 2006, **17** 1449; (e) S. Hanessian, G. J. Reddy and N. Chahal, *Org. Lett.* 2006, **8**, 5477; (f) Y. N. Belokon, V. I. Maleev, M. North and D. L. Usanov, *Chem. Commun.* 2006, 4614; (g) Y. N. Belokon, J. Hunt and M. North, *Tetrahedron: Asymmetry* 2008, **19**, 2804; (h) J. Takaki, H. Egami, K. Matsumoto, B. Saito and T. Katsuki, *Chem. Lett.* 2008, **37**, 502; (i) Y. N. Belokon, W. Clegg, R. W. Harrington, M. North and C. Young, *Inorg. Chem.* 2008, **47**, 3801; (j) Y. N. Belokon, W. Clegg, R. W. Harrington, V. I. Maleev, M. North, M. O. Pujol, D. L. Usanov and C. Young, *Chem. Eur. J.* 2009, **15**, 2148; (k) M. North, M. Omedes-Pujol and C. Williamson, *Chem. Eur. J.* 2010, **16**, 11367; (l) Y. Sakai, J. Mitote, K. Matsumoto and T. Katsuki, *Chem.*

- Commun.
- 75 *2010*, **46**, 5787; (m) N. H. Khan, S. Saravanan, R. I. Kureshy, S. H. R. Abdi, A. Sadhukhan and H. C. Bajaj, *J. Organomet. Chem.* 2010, **695**, 1133; (n) C.-Y. Chu, C.-T. Hsu, P. H. Lo and B.-J. Uang, *Tetrahedron: Asymmetry* 2011, **22**, 1981.
- 6 (a) P. P. Reddy, C.-Y. Chu, D.-R. Hwang, S.-K. Wang and B.-J. Uang, *Coord. Chem. Rev.* 2003, **237**, 257; (b) T. Hirao, *Pure Appl. Chem.* 2005, **77**, 1539.
- 80 A few vanadium mediated enantioselective pinacol couplings have been reported, see: (a) R. Annunziata, M. Cinquini, F. Cozzi and P. Giaroni, *Tetrahedron: Asymmetry* 1990, **1**, 355; (b) R. Annunziata, M. Cinquini, F. Cozzi, P. Giaroni and M. Benaglia *Tetrahedron* 1991, **47**, 5737; (c) J. Sun, Z. Dai, C. Li, X. Pan and C. Zhu, *J. Organomet. Chem.* 2009, **694**, 3219.
- 85 (d) L.-F. Niu, Y.-C. Xin, R.-L. Wang, F. Jiang, P.-F. Xu and X.-P. Hui, *Synlett* 2010, 765; (b) G. Liu, S. Zhang, H. Li, T. Zhang and W. Wang, *Org. Lett.* 2011, **13**, 828; (c) P. Chauhan and S. S. Chimni, *Eur. J. Org. Chem.* 2011, 1636; (d) G.-X. Li and J. Qu, *Chem. Commun.* 2012, **48**, 5518.
- 90 C. Cardelluccio, M. A. M. Capozzi and F. Naso, *Tetrahedron: Asymmetry* 2010, **21**, 507.
- 10 (a) J. A. Beutler, J. H. Cardellina II, J. B. Mcmahon and M. R. Boyd, *J. Nat. Prod.* 1992, **55**, 207; (b) S.-B. Chen, G.-Y. Gao, H.-W. Leung, H.-W. Yeung, J.-S. Yang and P.-G. Xiao, *J. Nat. Prod.* 2001, **64**, 85; (c) C. Hirayama, H. Ono, Y. Tamura and M. Nakamura, *Phytochemistry* 2006, **67**, 579.
- 11 (a) C. Cardelluccio, G. Ciccarella, F. Naso, F. Perna and P. Tortorella, *Tetrahedron* 1999, **55**, 14685; (b) J. Lu, X. Xu, C. Wang, J. He, Y. Hu and H. Hu, *Tetrahedron Lett.* 2002, **43**, 8367; (c) X. Wang, Y. Dong, J. Sun, X. Xu, R. Li and Y. Hu, *J. Org. Chem.* 2005, **70**, 1897; (d) K. E. Metlushka, B. A. Kasheirov, V. F. Zheltukhin, D. N. Sadkova, B. Buechner, C. Hess, O. N. Kataeva, C. E. McKenna and V. A. Alfonsov, *Chem. Eur. J.* 2009, **15**, 6718; (e) H. Liu, D. Su, G. Cheng, J. Xu, X. Wang and Y. Hu, *Org. Biomol. Chem.* 2010, **8**, 1899; (f) T. Kanemitsu, E. Toyoshima, M. Miyazaki, K. Nagata and T. Itoh, *Heterocycles* 2010, **81**, 2781; (g) T. Kanemitsu, Y. Asajima, T. Shibata, M. Miyazaki, K. Nagata and T. Itoh, *Heterocycles* 2011, **83**, 2525; (h) S. Bhatt and B. Trivedi, *Polyhedron* 2012, **35**, 15; (i) H.-P. Deng and M. Shi, *Eur. J. Org. Chem.* 2012, 183.
- 12 The reaction of **2a** with **3a** was carried out in ClC_6H_5 at 10°C under air to give hetero-coupling **4a** in 37% with 82% ee, accompanied by (S)-BINOL as a homo-coupling in 63% yield with 73% ee.
- 13 For recent reviews and reports on enantioselective FC reaction, see: (a) S.-L. You, Q. Cai and M. Zeng, *Chem. Soc. Rev.* 2009, **38**, 2190; (b) Z. Liu and M. Shi, *Tetrahedron: Asymmetry* 2009, **20**, 1119; (c) M. Terada, *Synthesis* 2010, 1929; (d) M. Zeng and S.-L. You, *Synlett* 2010, 1289; (e) J. Lv, X. Li, L. Zhong, S. Luo and J.-P. Cheng, *Org. Lett.* 2010, **12**, 1096; (f) F. Xu, D. Huang, C. Han, W. Shen, X. Lin and Y. Wang, *J. Org. Chem.* 2010, **75**, 8677; (g) Y. Qian, G. Ma, A. Lv, H.-L. Zhu, J. Zhao and V. H. Rawal, *Chem. Commun.* 2010, **46**, 3004; (h) L. Liu, Q. Zhao, F. Du, H. Chen, Z. Qin and B. Fu, *Tetrahedron: Asymmetry* 2011, **22**, 1874; (i) B.-L. Wang, N.-K. Li, J.-X. Zhang, G.-G. Liu, T. Liu, Q. Shen and X.-W. Wang, *Org. Biomol. Chem.* 2011, **9**, 2614; (j) C.-H. Xing, Y.-X. Liao, J. Ng and Q.-S. Hu, *J. Org. Chem.* 2011, **76**, 4125; (k) L.-Y. Chen, H. He, W.-H. Chan and A. W. M. Lee, *J. Org. Chem.* 2011, **76**, 7141; (l) Y. Huang, S. Suzuki, G. Liu, E. Tokunaga, M. Shiro and N. Shibata, *New J. Chem.* 2011, **35**, 2614; (m) C. Wang, Y. Li, G. Jia, Y. Liu, S. Lu and C. Li, *Chem. Commun.* 2012, **48**, 6232.