ORGANIC LETTERS

2005
Vol. 7, No. 9
1757−1759

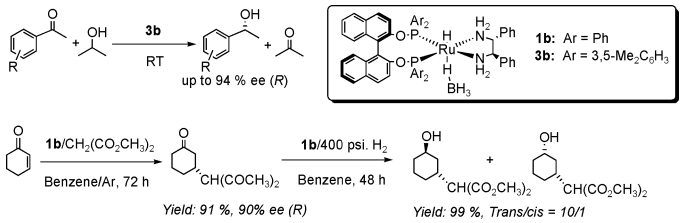
Applications of Ruthenium Hydride Borohydride Complexes Containing Phosphinite and Diamine Ligands to Asymmetric Catalytic Reactions

Rongwei Guo, Xuanhua Chen, Christian Elpelt, Datong Song, and Robert H. Morris*

Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, Ontario M5S 3H6, Canada
rmorris@chem.utoronto.ca

Received February 17, 2005

ABSTRACT



A series of novel *trans*-ruthenium hydride borohydride complexes with chiral phosphinite and diamine ligands were synthesized. They can be used in the asymmetric transfer hydrogenation of aryl ketones, including base-sensitive ones, to give chiral alcohols in moderate to good enantioselectivities (up to 94% ee). They are also efficient catalysts for the Michael addition of malonates to enones with enantioselectivities of up to 90%. This kind of catalyst allows a one-pot tandem Michael addition/H_2 hydrogenation protocol to build structures with multiple chiral centers.

Combinatorial catalyst discovery is recognized as a powerful method for the development of homogeneous enantioselective reactions.[1] This usually involves creating a library of catalysts by using ligands of modular design and combining them with transition-metal precursors. This approach is readily applicable to the catalytic asymmetric hydrogenation of prochiral ketones and olefins.[2−12] Noyori's group used ruthenium catalysts composed of chelating diamine and binap-type ligand modules to discover H_2-hydrogenation reactions that convert prochiral aryl ketones to alcohols with high enantioselectivity.[2a−2c] For example, they recently reported that among hydride borohydride complexes of the type RuH(BH_4)(diphosphine)(diamine) the combination of

(1) (a) Reetz, M. T. *Angew. Chem., Int. Ed.* **2001**, *40*, 284−310. (b) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40−73. (c) Dahlenburg, L. *Eur. J. Inorg. Chem.* **2003**, *30*, 2733−2747. (d) Delacroix, O.; Gladysz, J. A. *Chem. Commun.* **2003**, *38*, 665−675. (e) Carmona, D.; Pilar Lamata, M.; Oro, L. A. *Coord. Chem. Rev.* **2000**, 717−772. (f) McMorn, P.; Hutchings, G. J. *Chem. Soc. Rev.* **2004**, *33*, 108−122. (g) Chelucci, G.; Thummel, R. P. *Chem. Rev.* **2002**, *102*, 3129−3170. (h) Nicolaou, K. C., Hanko, R., Hartwig, W., Eds. *Handbook of Combinatorial Chemistry*; Wiley-VCH: Weinheim, 2002. (i) Hagemeyer, A., Strasser, P., Volpe, A. F., Jr., Eds. *High Throughput Screening in Chemical Catalysis*; Wiley-VCH: Weinheim, 2004. (j) de Vries, J. G.; de Vries, A. H. M. *Eur. J. Org. Chem.* **2003**, 799−811.

(2) (a) Ohkuma, T.; Ooka, H.; Ikariya, T.; and Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 10417−10418. (b) Ohkuma, T.; Koizumi, M.; Doucet, H.; Pham, T.; Kozawa, M.; Murata, K.; Katayama, E.; Yokozawa, T.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1998**, *120*, 13529−13530. (c) Doucet, H.; Ohkuma, T.; Murata, K.; Yokozawa, T.; Kozawa, M.; Katayama, E.; F. England, A. F.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 1703−1706. (d) Crepy, K. V. L.; Imamoto, T. *Adv. Synth. Catal.* **2003**, *345*, 79−101.

(3) (a) Pai, C. C.; Lin, C. W.; Lin, C. C.; Chen, C. C.; Chan, A. S. C. *J. Am. Chem. Soc.* **2000**, *122*, 11513−11514. (b) Wu, J.; Chen, H.; Kwok, W.; Guo, R.; Zhou, Z.; Yeung, C.; Chan, A. S. C. *J. Org. Chem.* **2002**, *67*, 7908−7910. (c). Wu, J.; Ji, J. X.; Guo, R.; Yeung, C. H.; Chan, A. S. C. *Chem. Eur. J.* **2003**, *9*, 2963−2968. (d) Xie, J. H.; Wang, L. X.; Fu, Y.; Zhu, S. F.; Fan, B. M.; Duan, H. F.; Zhou, Q. L. *J. Am. Chem. Soc.* **2003**, *125*, 4404−4405.

(4) (a) Jiang, Q.; Jiang, Y.; Xiao, D.; Cao, P.; Zhang, X. *Angew. Chem., Int. Ed.* **1998**, *37*, 1100−1103. (b) Lei, A.; Wu, S.; He, M.; Zhang, X. *J. Am. Chem. Soc.* **2004**, *126*, 1626−1627.

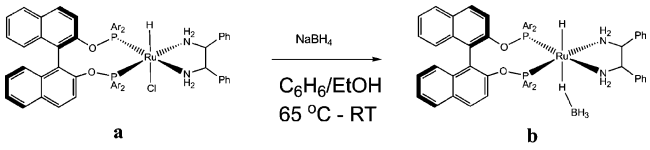
(5) (a) Burk, M. J.; Feaster, J. E.; Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 10125−10138. (b) Dobbs, D. A.; Vanhessche, K. P. M.; Brazi, E.; Rautenstrauch, V.; Lenoir, J. Y.; Genet, J. P.; Wiles, J.; Bergens, S. H. *Angew. Chem., Int. Ed.* **2000**, *39*, 1992−1995.

10.1021/ol050336j CCC: $30.25
Published on Web 04/07/2005

(*R*)-xylbinap ((*R*)-2,2′-bis[di(3,5-xylyl)phosphino]-1,1′-binaphthyl) and (*R*,*R*)-dpen ((1*R*,2*R*)-1,2-diphenylethylenediamine) ligands produce catalysts for the asymmetric H_2-hydrogenation of base-sensitive ketones.[7] Our group has shown that combinations of binap, aminophosphine, and diamine ligands with the precursor $RuHCl(PPh_3)_3$ lead to a wide variety of active catalysts for the H_2-hydrogenation or transfer hydrogenation of ketones and imines[8] and for Michael addition.[8f] We show here that a diverse set of catalysts can be created by use of phosphinite ligands based on the binol module, one of the cheapest chiral auxiliaries currently available. These ligands are attractive and also widely used in rhodium, iridium, and palladium complexes for asymmetric catalytic reactions.[6a,9−12]

The reaction of the complexes *trans*-RuHCl(phosphinite)(diamine) **1a**−**4a**[8e] with $NaBH_4$ in benzene/alcohol produces the complexes *trans*-RuH(η^1-BH_4)(phosphinite)(diamine) **1b**−**4b** in excellent yields (up to 99%), [phosphinite = (*R*)-2,2′-bis(diphenylphosphinoyl)-1,1′-binaphthyl ((*R*)-binop) or (*R*)-2,2′-bis[bis(3,5-dimethylphenyl)phosphinoyl]-1,1′-binaphthyl ((*R*)-xylbinop); diamine = (1*R*,2*R*)-1,2-diphenylethylenediamine ((*R*,*R*)-dpen) or (1*S*,2*S*)-1,2-diphenylethylenediamine ((*S*,*S*)-dpen)] (Scheme 1).

Scheme 1



1b: diphosphinite = (*R*)-BINOP (Ar = Ph), diamine = (*R*,*R*)-DPEN
2b: diphosphinite = (*R*)-BINOP (Ar = Ph), diamine = (*S*,*S*)-DPEN
3b: diphosphinite = (*R*)-xylBINOP (Ar = 3,5-$Me_2C_6H_3$), diamine = (*R*,*R*)-DPEN
4b: diphosphinite = (*R*)-xylBINOP (Ar = 3,5-$Me_2C_6H_3$), diamine = (*S*,*S*)-DPEN

The pale yellow solid products consist of two diastereomers in a ratio of 3/1 for **1b** and 2/1 for **2b** but only one for **3b** and **4b**. The source of the isomerism is the placement of the trans hydride and borohydride groups relative to the folded backbone of the diphosphinite ligand. The isomers interconvert readily in solution and it is assumed that both are present during catalysis.

The crystal structures of **3b** and **4b** were determined by use of X-ray diffraction (Figures 1 and 2). These structures

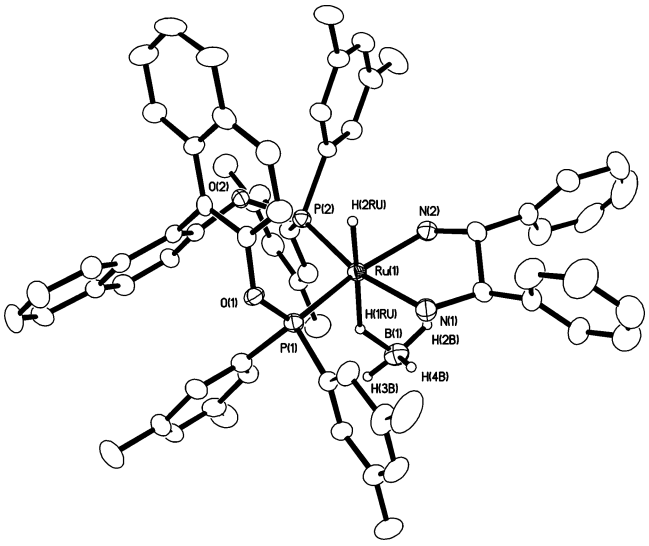


Figure 1. Structure of complex **3b**. Only hydrogen of the hydride and borohydride ligands are shown.

are similar to that of *trans*-RuHCl((*R*)-xylbinop)((*R*,*R*)-dpen)[8e] with the PPNN atoms in the equatorial plane of a slightly distorted octahedron and with the Ru−HBH_3 bond leaning toward the NN side to form BH−HN hydrogen bonds.

The complexes **1b**−**4b** were tested in the base-free asymmetric transfer hydrogenation of simple ketones and showed good activities and enantioselectivities (Table 1). They are less active for the H_2-hydrogenation of ketones.

The ruthenium complex **3b** with the (*R*)-xylbinop and matching diamine ligand (*R*,*R*)-dpen gives the best results for acetophenone (compare entries 1−5).

This complex was extensively investigated with a variety of substrates. The electronic properties of the substituent on the phenyl ring of the ketone changed the reduction rate but had little effect on the enantioselectivity. A para-substituted acetophenone with an electron-donor substituent, i.e., 4′-methyl or 4′-methoxyl, is reduced more slowly than acetophenone (entries 3, 12, and 16). The ortho-substituted acetophenone, 2′-chloroacetophenone, is reduced slowly and

(6) (a) Chen, Y.; Yekta, S.; Yudin, A. K. *Chem. Rev.* **2003**, *103*, 3155−3211. (b) RajanBabu, T. V.; Ayers, T. A.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 4101−4102. (c) RajanBabu, T. V.; Radetich, B.; You, K. K.; Ayers, T. A.; Casalnuovo, A. L.; Calabrese, J. C. *J. Org. Chem.* **1999**, *64*, 3429−3447.

(7) (a) Ohkuma, T.; Koizumi, M.; Muniz, K.; Hilt, G.; Kabuto, C.; Noyori, R. *J. Am. Chem. Soc.* **2002**, *124*, 6508−6509. (b) Sandoval, C. A.; Ohkuma, T.; Muñiz, K.; Noyori, R. *J. Am. Chem. Soc.* **2003**, *125*, 13490−13503.

(8) (a) Abdur-Rashid, K.; Lough, A. J.; Morris, R. H. *Organometallics* **2001**, *20*, 1047−1049. (b) Rautenstrauch, V.; Hoang-Cong, X.; Churlaud, R.; Abdur-Rashid, K.; Morris, R. H. *Chem. Eur. J.* **2003**, *9*, 4954−4967. (c) Guo, R.; Lough, A. J.; Morris, R. H.; Song, D. *Organometallics* **2004**, *23*, 5524−5529. (d) Li, T.; Churlaud, R.; Lough, A. J.; Abdur-Rashid, K.; Morris, R. H. *Organometallics* **2004**, *23*, 6239−6247. (e) Guo, R.; Elpelt, C.; Chen, X.; Song, D.; Morris, R. H. Submitted for publication. (f) Guo, R.; Morris, R. H.; Song, D. *J. Am. Chem. Soc.* **2005**, *126*, 516−517.

(9) (a) Jerphagnon, T.; Renaud, J.-L.; Bruneau, C. *Tetrahedron: Asymmetry* **2004**, *15*, 2101−2111. (b) Reetz, M. T.; Mehler, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3889−3890. (c) Reetz, M. T.; Sell, T.; Meiswinkel, A.; Mehler, G. *Angew. Chem., Int. Ed.* **2003**, *42*, 790−793. (d) Reetz, M. T.; Ma, J. A.; Goddard, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 412−415.

(10) (a) van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 11539−11540. (b) Pena, D.; Minnaard, A. J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *Org. Lett.* **2003**, *5*, 475−478.

(11) (a) Zhang, F. Y.; Kwok, W. H.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2001**, *12*, 2337−2342. (b) Guo, R.; Au−Yeung, T. T. L.; Wu, J.; Choi, M. C. K.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2002**, *13*, 2519. (c) Guo, R.; Wu, J.; Kowk, W. H.; Chen, J.; Choi, M. C. K.; Zhou, Z. Y. *Acta Crystallogr.* **2002**, *E58*, o270. (d) Tietze, L. F.; Ila, H.; Bell, H. P. *Chem. Rev.* **2004**, *104*, 3453−3516.

(12) (a) Zhou, Y. G.; Tang, W. J.; Wang, W. B.; Li, W.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 4952−4953. (b) Zhou, Y. G.; Zhang, X. *Chem. Commun.* **2002**, 1124−1125. (c) Tang, W. J.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029−3069.

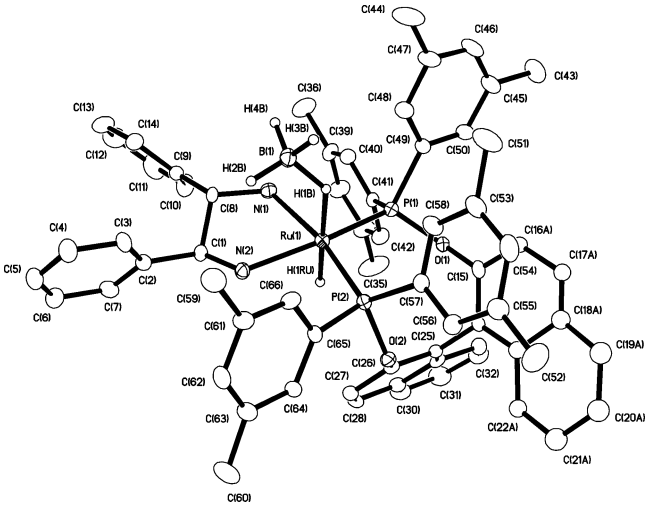
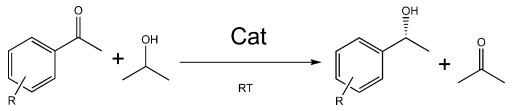


Figure 2. Structure of complex **4b**.

shows a lower enantioselectivity (entries 6 and 7). The enantioselectivities dropped with the extended reaction time (entry 3 vs 4, entry 6 vs 7, entry 12 vs 13, entry 16 vs 17).

The catalyst **3b** is also efficient for the hydrogenation of the base-sensitive substrate 4-acetylbenzoate ethyl ester[7a] by transfer hydrogenation from 2-propanol. Only the ethyl ester of alcohol is produced in 98% conversion and 92% ee (*R*) in less than 20 h. No transesterification product was observed (Scheme 2).

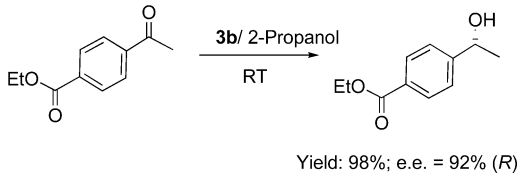
Table 1. Transfer Hydrogenation of Ketones Catalyzed by Complexes **1b**−**4b**[a]



entry	cat.	R	time (h)	conv (%)	ee (%)
1	**1b**	H	6	92	80 (*R*)
2	**2b**	H	6	94	49 (*R*)
3	**3b**	H	8	92	93 (*R*)
4	**3b**	H	76	97	88 (*R*)
5	**4b**	H	8	91	60 (*R*)
6	**3b**	2′-Cl	8	47	86 (*R*)
7	**3b**	2′-Cl	76	98	84 (*R*)
8	**3b**	3′-Cl	8	70	88 (*R*)
9	**3b**	3′-Cl	76	99	85 (*R*)
10	**3b**	4′-Cl	6	92	91 (*R*)
11	**3b**	4′-Cl	8	98	90 (*R*)
12	**3b**	4′-Me	8	80	94 (*R*)
13	**3b**	4′-Me	76	96	87 (*R*)
14	**3b**	3′-MeO	6	90	91 (*R*)
15	**3b**	3′-MeO	8	96	91 (*R*)
16	**3b**	4′-MeO	8	64	93 (*R*)
17	**3b**	4′-MeO	76	79	82 (*R*)

[a] The reactions were carried out in an Ar glovebox at room temperature. The molar ratio of substrate/catalyst = 100/1. The concentration of aryl methyl ketone is 0.1 M.

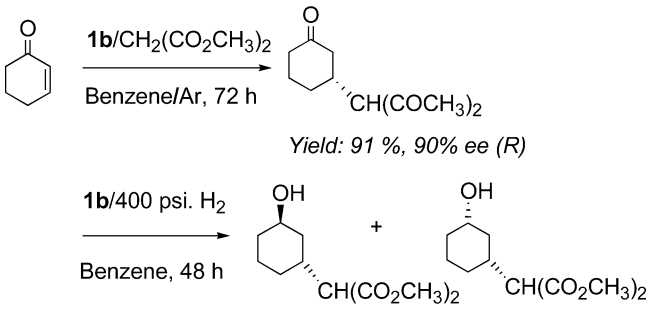
Scheme 2



Yield: 98%; e.e. = 92% (*R*)

Complexes **1b**−**4b** are also efficient catalysts for the enantioselective Michael addition of malonates to enones. The complex **1b** is the most enantioselective and provides the product in 90% ee in the *R*-form when THF or benzene is the solvent (Scheme 3).[13]

Scheme 3



Yield: 91 %, 90% ee (R)

Yield: 99 %, Trans/cis = 10/1

When the protic solvents ethanol or 2-propanol were used, the enantioselectivity dropped sharply. The complexes **2b**, **3b**, and **4b** gave Michael addition products with the enantiomeric excess of 30% in the *S*-form (**2b**), 44% in the *R*-form (**3b**), and 52% in the *S*-form (**4b**), respectively. They allow a one-pot tandem Michael addition/H_2-hydrogenation protocol as in our previously disclosed research results with *trans*-RuH(η^1-BH_4)(binap)((*R*,*R*)-Pnor) complexes (Scheme 3).[8f]

In conclusion, we have developed a new catalytic system for the base-free transfer hydrogenation of simple ketones and this system is also effective for the asymmetric Michael addition. The modular construction of these catalysts and their flexibility toward hydrogenation, transfer hydrogenation, Michael addition, and tandem reaction make these promising systems to pursue.

Acknowledgment. R.H.M. thanks NSERC and the PRF, administrated by the American Chemical Society, for research grants.

Supporting Information Available: Experimental procedures and characterization data of all new compounds and crystallographic data for **3b** and **4b** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

OL050336J

(13) (a) Watanabe, M.; Murata, K.; Ikariya, T. *J. Am. Chem. Soc.* **2003**, *125*, 7508−7509. (b) Watanabe, M.; Ikagawa, A.; Wang, H.; Murata, K.; Ikariya, T. *J. Am. Chem. Soc.* **2004**, *126*, 11148−11149.