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Optically Active Dinuclear Palladium Complexes Containing a Pd−Pd Bond: Preparation and Enantioinduction Ability in Asymmetric Ring-Opening Reactions

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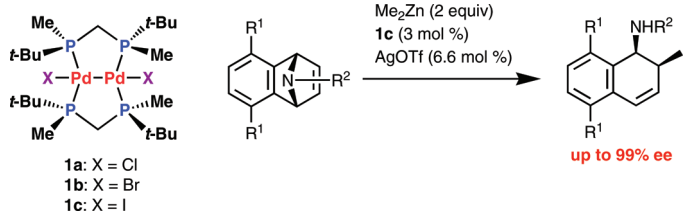
ABSTRACT



Optically active dinuclear palladium complexes containing a Pd−Pd bond were prepared by using (*R*,*R*)-bis(*tert*-butylmethylphosphino)methane ((*R*,*R*)-*t*-Bu-MiniPHOS). The dinuclear palladium complexes coupled with silver triflate exhibited good to excellent enantioselectivities up to 99% in palladium-catalyzed alkylative ring-opening reactions of azabenzonorbornadienes.

Among many transition-metal-catalyzed asymmetric reactions, chiral palladium complexes are known to be powerful and frequently employed catalysts for the synthesis of various kinds of optically active compounds.[1] Almost all of the chiral palladium complexes reported hitherto consist of a mononuclear metal center, and as far as we know, there is no report of chiral dinuclear complexes containing a Pd−Pd bond.[2,3] On the other hand, chiral dinuclear rhodium or ruthenium complexes have been extensively investigated in the field of asymmetric catalysis, and some of the explored reactions have been employed for the large-scale production of useful optically active compounds.[4,5] Such preceding successful results motivated us to study the preparation and application

(1) For excellent reviews dealing with Pd-catalyzed asymmetric reactions, see: (a) Tsuji, J. *Palladium Reagents and Catalysts*; Innovations in Organic Synthesis; Wiley, Chichester, 1995. (b) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395–422. (c) Sodeoka, M.; Hamashima, Y. *Pure Appl. Chem.* **2008**, *80*, 763–776. (d) Mohr, J. T.; Stoltz, B. M. *Chem. Asian J.* **2007**, *2*, 1476–1491. (e) Tietze, L. F.; Ila, H.; Bell, H. P. *Chem. Rev.* **2004**, *104*, 3453–3516. (f) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley: Hoboken, 2002. (g) Ogasawara, M.; Hayashi, T. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley: New York, 2000; pp 651−674.

(2) For representative papers dealing with dinuclear palladium complexes containing a Pd−Pd bond, see: (a) Balch, A. L.; Benner, L. S. *Inorg. Chem.* **1982**, *21*, 47. (b) Kullberg, M. L.; Lemke, F. R.; Powell, D. R.; Kublak, C. P. *Inorg. Chem.* **1985**, *24*, 3589–3593. (c) Krafft, T. E.; Hejna, C. I.; Smith, J. S. *Inorg. Chem.* **1990**, *29*, 2682–2688.

(3) Many interesting reactions of dinuclear palladium complexes including catalytic reactions have been reported. (a) Benner, L. S.; Olmstead, M. M.; Hope, H.; Balch, A. L. *J. Organomet. Chem.* **1978**, *153*, C31−C35. (b) Balch, A. L.; Hunt, C. T.; Lee, C.-L.; Olmstead, M. M.; Farr, J. P. *J. Am. Chem. Soc.* **1981**, *103*, 3764–3772. (c) Kullberg, M. L.; Kublak, C. P. *Organometallics* **1984**, *3*, 632–634. (d) Yamamoto, H.; Shinoda, S.; Saito, Y. *J. Mol. Catal.* **1985**, *30*, 259–266. (e) Kullberg, M. L.; Kubiak, C. P. *Inorg. Chem.* **1986**, *25*, 26–30. (f) Young, S. J.; Kellenberger, B.; Reibenspies, J. H.; Himmel, S. E.; Manning, M.; Anderson, O. P.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 5744–5753. (g) Davies, J. A.; Dutremez, S.; Pinkerton, A. A.; Vilmer, M. *Organometallics* **1991**, *10*, 2956–2958. (h) Davies, J. A.; Kirschbaum, K.; Kluwe, C. *Organometallics* **1994**, *13*, 3664–3670. (i) Besenyei, G.; Párkányi, L.; Foch, I.; Simándi, L. I.; Kálmán, A. *Chem. Commun.* **1997**, 1143–1144. (j) Ishii, H.; Ueda, M.; Takeuchi, K.; Asai, M. *J. Mol. Catal. A: Chem.* **1999**, *144*, 477–480. (k) Stambili, J. P.; Kuwano, R.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 4746–4748. (l) Richmond, M. K.; Scott, S. L.; Yap, G. P. A.; Alper, H. *Organometallics* **2002**, *21*, 3395–3400. (m) Besenyei, G.; Párkányi, L.; Szalontai, G.; Holly, S.; Pápai, I.; Keresztury, G.; Nagy, A. *J. Chem. Soc., Dalton Trans.* **2004**, 2041–2050. (n) Hama, T.; Hartwig, J. F. *Org. Lett.* **2008**, *10*, 1545–1548.

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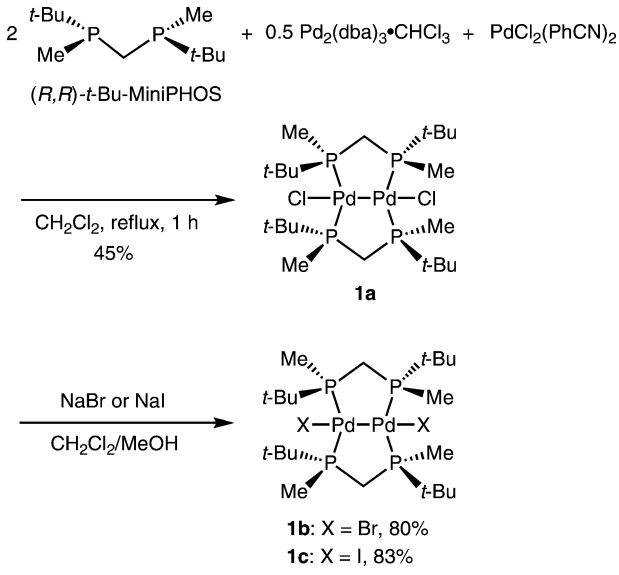
of chiral dinuclear palladium complexes. Herein we describe the first example of optically active dinuclear palladium complexes with a chiral diphosphine ligand and their potential utility as chiral catalysts in asymmetric carbon−carbon bond-forming reactions.

Our idea was based on the preparation of achiral dinuclear palladium(I) complexes with methylene-bridged diphosphine ligands, which was reported by Balch and Benner.[2a] We envisioned that the use of an optically active diphosphine instead of an achiral one would provide the desired palladium complex. This idea was realized by the use of (*R*,*R*)-bis(*tert*-butylmethylphosphino)methane (abbreviated as (*R*,*R*)-*t*-Bu-MiniPHOS), which was previously synthesized in our laboratory and was proven to be an efficient ligand in several representative asymmetric catalyses.[6] The preparation of the target dinuclear palladium complexes is shown in Scheme 1. Initially obtained chloride complex **1a** was converted into

Scheme 1. Preparation of Dinuclear Palladium Complexes **1a**−**c**



the corresponding bromide complex **1b** and iodide complex **1c** by reacting with NaBr and NaI, respectively.[7]

The molecular structure of bromide complex **1b** was determined by single-crystal X-ray analysis. The ORTEP drawing shown in Figure 1 clearly indicates that the complex

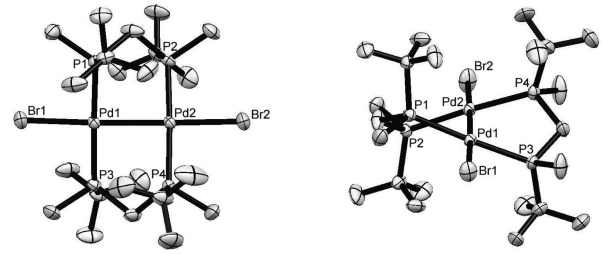


Figure 1. Crystal structure of complex **1b**; hydrogen atoms are omitted for clarity.

consists of two fused five-membered palladacycles containing a Pd−Pd bond. In this complex, each palladium metal forms a square planar structure, and the two five-membered rings have almost the same conformational geometries, being largely distorted each other.[8] A notable fact is that the bulky *tert*-butyl groups occupy quasi-axial positions rather than quasi-equatorial spaces, avoiding the steric repulsion between the *tert*-butyl group and the bromine atom. The complex possesses two stereochemically equivalent palladium atoms, and we expect that this imposed asymmetric environment may lead to high enantioselectivity in catalytic asymmetric reactions.

The enantioinduction ability of these complexes was tested in the Pd-catalyzed asymmetric ring-opening reaction of oxabenzonorbornadiene (**2**).[9] Preliminary experimental results are summarized in Table 1. The reactions using **1a** as catalyst (3 mol %) without additives at 20 °C in dichloromethane, 1,2-dichloroethane, or toluene proceeded sluggishly, and after 24 h, the corresponding ring-opening product **3** was obtained in the indicated yields with low to moderate enantiomeric excesses (ee) (entries 1−3). The same reaction in toluene at higher temperatures afforded the product in good yields with improved ee (entries 4−6). Use of 1,2-dichloroethane or THF under refluxing conditions resulted in low yields and decreased enantioselectivities (entries 7 and 8), compared with the reaction using toluene as solvent. Complexes **1b** and **1c** were also used to examine the effects

(4) For asymmetric reactions catalyzed by rhodium dinuclear complexes, see: (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; VCH: Weinheim, 1998. (b) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911–935. (c) Takahashi, T.; Tsutsui, H.; Tamura, M.; Kitagaki, S.; Nakajima, M.; Hashimoto, S. *Chem. Commun.* **2001**, 1604–1605. (d) Davies, H. M. L.; Beckwith, R. E. *Chem. Rev.* **2003**, *103*, 2861–2904. (e) Minami, K.; Saito, H.; Tsutsui, H.; Nambu, H.; Anada, M.; Hashimoto, S. *Adv. Synth. Catal.* **2005**, *347*, 1483–1487. (f) Denton, J. R.; Davies, H. M. L. *Org. Lett.* **2009**, *11*, 787–790, and references cited therein.

(5) For diruthenium-catalyzed asymmetric reactions, see: (a) Nishibayashi, Y.; Onodera, G.; Inada, Y.; Hidai, M.; Uemura, S. *Organometallics* **2003**, *22*, 873–876. (b) Inada, Y.; Nishibayashi, Y.; Uemura, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 7715–7717. (c) Matsuzawa, H.; Miyake, Y.; Nishibayashi, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 6488–6491.

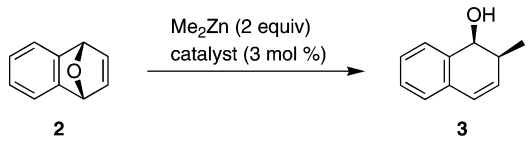
(6) (a) Yamanoi, Y.; Imamoto, T. *J. Org. Chem.* **1999**, *64*, 2988. (b) Gridnev, I. D.; Yamanoi, Y.; Higashi, N.; Tsuruta, H.; Yasutake, M.; Imamoto, T. *Adv. Synth. Catal.* **2001**, *343*, 118–136.

(7) The chloride complex **1a** was isolated as an orange powder that was proved to be a 57:43 mixture of two conformational isomers, and the bromide complex **1b** isolated was a 90:10 mixture of two conformers. The iodide complex **1c** was isolated as a single conformer.

(8) The dihedral angle between the two Pd-square planes is approximately 40°. CCDC-718690 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

(9) For representative papers dealing with asymmetric ring-opening reactions of oxabenzonorbornadienes and azabenzonorbornadienes, see: (a) Lautens, M.; Renaud, J.-L.; Hiebert, S. *J. Am. Chem. Soc.* **2000**, *122*, 1804–1805. (b) Lautens, M.; Fagnou, K.; Hiebert, S. *Acc. Chem. Res.* **2003**, *36*, 48–58. (c) Lautens, M.; Hiebert, S. *J. Am. Chem. Soc.* **2004**, *126*, 1437–1447. (d) Li, M.; Yan, X.-X.; Hong, W.; Zhu, X.-Z.; Cao, B.-X.; Sun, J.; Hou, X.-L. *Org. Lett.* **2004**, *6*, 2833–2835. (e) Cabrera, S.; Arrayás, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2004**, *43*, 3944–3947. (f) Cabrera, S.; Arrayás, R. G.; Alonso, I.; Carretero, J. *J. Am. Chem. Soc.* **2005**, *127*, 17938–17947. (g) Cho, Y.-H.; Zunic, V.; Senboku, H.; Olsen, M.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 6837–6846.

Table 1. Asymmetric Ring-Opening Reaction of Oxabenzonorbornadiene (**2**) Catalyzed by **1a**−**c**



2 **3**

entry	catalyst	solvent	T (°C)	time (h)	yield[a] (%)	ee (%)
1	**1a**	CH_2Cl_2	20	24	71	30
2	**1a**	$Cl(CH_2)_2Cl$	20	24	19	28
3	**1a**	toluene	20	24	86	45
4	**1a**	toluene	50	4	74	53
5	**1a**	toluene	80	0.5	71	60
6	**1a**	toluene	reflux	0.5	66	55
7	**1a**	$Cl(CH_2)_2Cl$	reflux	0.5	56	46
8	**1a**	THF	reflux	4	13	24
9	**1b**	toluene	80	0.5	68	60
10	**1c**	toluene	80	0.5	28, 74[b]	63
11	**1a**[c]	toluene	80	0.5	92	60
12	**1a**[d]	toluene	80	0.5	63	51
13	**1a**[e]	toluene	80	0.5	73	59
14	**1a**[f]	toluene	80	0.5	70	59

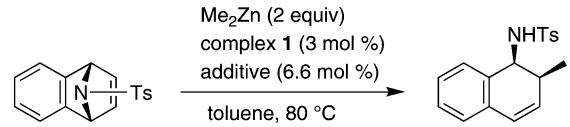
[a] Isolated yield. [b] After 4 h. [c] AgOTf (6.6 mol %) was added as an additive. [d] AgF (6.6 mol %) was added. [e] $AgBF_4$ (6.6 mol %) was added. [f] $AgPF_6$ (6.6 mol %) was added.

of bromide and iodide counterions, and the obtained results indicate that both chemical yields and enantioselectivities were not markedly affected by these halides (entries 9 and 10).[10] On the other hand, use of silver salts, especially silver triflate, as additive increased the chemical yields (entry 11).[11]

Based on the results mentioned above, the catalyst system (complexes **1a**−**c**/AgOTf) was applied to the ring-opening reaction of azabenzonorbornadiene derivative **4a** with dimethylzinc. The results are summarized in Table 2 together with those obtained by the use of **1a**−**c** alone. Remarkable rate acceleration was observed when AgOTf/**1a**−**c** was used in a 2:1 ratio (entries 2, 5, and 7). This is probably due to the formation of a dicationic palladium complex that is more reactive than the parent complexes.[12]

The scope of reaction with this catalytic system was examined by using variously substituted azabenzonorbornadienes. The summarized results are shown in Table 3. All reactions of substrates of *N*-tosyl series (**4a**−**e**) with dimethylzinc proceeded smoothly to give the expected products (**5a**−**e**) in high yields (entries 1−5). The enantioselectivities of these reactions are largely dependent on the substituent (R^1) on the benzene ring. Thus, excellent enantiomeric excesses of up to 99% were observed for MeO and BnO derivatives (entries 3 and 4), and the reactions of other derivatives (**4a**,**b**,**e**) resulted in 72−88% selectivities (entries 1, 2, and 5). The very high enantioselectivity of the reaction

Table 2. Effects of Silver Triflate in Ring-Opening Reaction of **4a**

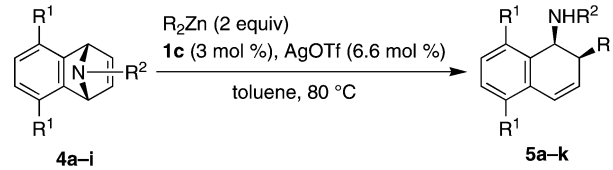


4a **5a**[a]

entry	complex	additive	time (h)	yield[b] (%)	ee (%)
1	**1a**		3	72	50
2	**1a**	AgOTf	0.5	91	73
3[c]	**1a**	AgOTf	3	75	67
4	**1b**		0.5	77	66
5	**1b**	AgOTf	0.5	87	72
6	**1c**		3	70	72
7	**1c**	AgOTf	0.5	88	72

[a] Absolute configuration was determined by comparison of the chiral HPLC retention time with the data described in the literature.[9e] [b] Isolated yield. [c] The reaction was carried out by the use of **1a** (3 mol %) and AgOTf (3.3 mol %).

Table 3. Asymmetric Ring-Opening Reactions of Azabenzonorbornadienes



4a–i **5a–k**

	substrate				time		yield[a]	ee
entry	**4**	R^1	R^2	R_2Zn	(h)	product	(%)	(%)
1	**4a**	H	Ts	Me_2Zn	0.5	**5a**	88	72
2	**4b**	Me	Ts	Me_2Zn	2	**5b**	79	88
3	**4c**	MeO	Ts	Me_2Zn	0.5	**5c**	94	99
4	**4d**	BnO	Ts	Me_2Zn	1	**5d**	91	95
5	**4e**	MOMO	Ts	Me_2Zn	0.5	**5e**	88	74
6	**4f**	MeO	$PhSO_2$	Me_2Zn	0.5	**5f**	83	99
7	**4g**	MeO	Ar^1SO_2[b]	Me_2Zn	0.5	**5g**	74	99
8	**4h**	MeO	Ar^2SO_2[c]	Me_2Zn	4.5	**5h**	66	26
9	**4i**	MeO	Ms	Me_2Zn	0.5	**5i**	75	98
10	**4c**	MeO	Ts	Et_2Zn	24	**5j**	72	80
11	**4d**	BnO	Ts	Et_2Zn	24	**5k**	70	91

[a] Isolated yield. [b] Ar^1SO_2 = 4-$O_2NC_6H_4SO_2$. [c] Ar^2SO_2 = 2,4,6-(*i*-Pr)$_3C_6H_2SO_2$.

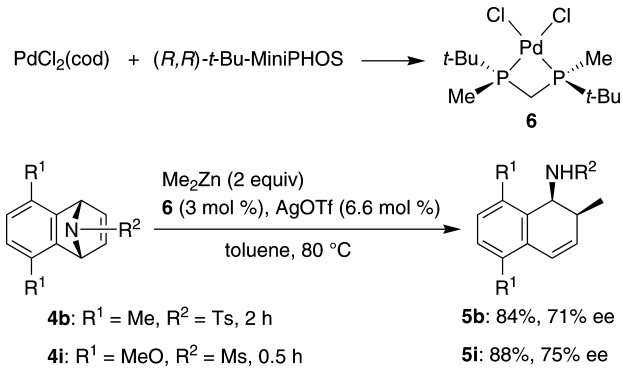
(10) Fagnou, K.; Lautens, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 26–47.

(11) Carretero and co-workers generated cationic Pd complexes by treatment of palladium chloride complexes with $NaB(Ar^F)_4$ or $AgPF_6$ and demonstrated their high catalytic activities in alkylative ring opening of oxabenzonorbornadienes and azabenzonorbornadienes. See refs 9d and 9e.

(12) Addition of 2 equiv of AgOTf to each solution of **1a**−**c** in toluene-d_8 afforded the same NMR signals (^{1}H NMR (400 MHz) δ 1.12 (m, 36H), 1.28 (br s, 12H), 1.70 (quin, J = 42.5 Hz, 4H); ^{31}P NMR (161 MHz) δ 2.68). On the other hand, addition of 1 equiv of AgOTf to a solution of **1c** in toluene-d_8 gave different signals (^{1}H NMR (400 MHz) δ 1.16 (m, 36H), 1.60 (br s, 12H), 2.15 (quin, J = 39.5 Hz, 4H); ^{31}P NMR (161 MHz) δ −3.62 (s)). A monocationic species was probably generated in the latter case.

(13) In order to confirm the existence of a dimeric palladium species throughout the course of the reaction, we carried out the reaction in toluene-d_8 using a stoichiometric amount of **1c**/AgOTf (1:2). After the mixture was kept at 80 °C for 0.5 h, NaI was added. The ^{1}H and ^{31}P NMR spectra of the mixture showed almost the same signals as those of dimeric complex **1c**.

of the methoxy derivative was not affected by changing the sulfonyl substituent on the nitrogen atom (entries 6−9), except the substrate had a bulkier substituent (entry 8). These enantioselectivities compare well with the highest value reported hitherto for this transformation.[9] On the other hand, reactions of these substrates with diethylzinc required longer reaction times (24 h) to obtain acceptable chemical yields; the enantiomeric excesses of the products were found to be 80% and 91%, respectively (entries 10 and 11).



It is also of interest to compare these dimeric palladium-catalyzed reactions with those catalyzed by a mononuclear palladium complex **6**, which was prepared by the reaction of $PdCl_2$(cod) with (*R*,*R*)-*t*-Bu-MiniPHOS. The complex **6** coupled with silver triflate exhibited similar catalytic activity as dimeric species in the reactions of **4b** and **4i** with dimethylzinc, but considerable differences in ee's of the products (71% vs 88%; 75% vs 98%) were observed. These results indicate that the actual catalytic species generated from the dimeric palladium complex **1c** is not the same as that generated from the monomeric palladium complex **6**.[13]

In summary, we prepared optically active dipalladium complexes containing a Pd−Pd bond using a methylene-bridged P-chiral diphosphine ligand ((*R*,*R*)-*t*-Bu-MiniPHOS). The complexes that coupled with silver triflate exhibited high catalytic activity in the asymmetric ring-opening reactions of azabenzonorbornadienes with dimethylzinc. These findings demonstrate the potential utility of the dinuclear palladium complexes as chiral catalysts in other catalytic asymmetric reactions.

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Supporting Information Available: Experimental procedures and characterization data of new compounds and details of X-ray crystallographic analysis for **1b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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