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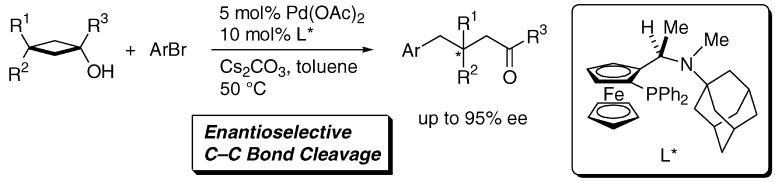

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Palladium-Catalyzed Asymmetric Arylation, Vinylation, and Allenylation of *tert*-Cyclobutanols via Enantioselective C−C Bond Cleavage

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Abstract: A novel enantioselective C−C bond cleavage has been achieved using palladium catalysts and chiral N,P-bidentate ligands in the asymmetric arylation, vinylation, and allenylation of *tert*-cyclobutanols. In these reactions, the enantioselective β-carbon elimination of Pd(II) alcoholate formed in situ is the key step. Treatment of *tert*-cyclobutanols with arylating reagents in toluene in the presence of $Pd(OAc)_2$, a chiral ferrocene-containing N,P-bidentate ligand, and Cs_2CO_3 affords optically active γ-arylated ketones in excellent yields with high enantioselectivity (up to 95% ee). When vinylating reagents are used in place of arylating ones, the asymmetric vinylation also proceeds to afford optically active γ-vinylated ketones in high yields with good to high enantioselectivity. When propargylic acetates are used, which are known to generate (σ-allenyl)palladium complexes with Pd(0) species, asymmetric allenylation occurs to afford optically active γ-allenylated ketones in moderate to good yields with moderate to high enantioselectivity.

Introduction

Selective C−C bond cleavage by transition metals has been considered to be one of the most challenging goals in organic and organometallic chemistry.[1] Catalytic reactions are especially of interest as they provide useful synthetic tools for various transformations, and several studies have appeared.[2−25] Two approaches of C−C bond cleavage by transition metals are known: one involves oxidative addition of C−C bonds to low-valent transition metals,[2−15] and the other uses β-carbon elimination of carbon-metal species such as M−C−C−C or heteroatom-metal species such as M−O−C−C.[16−24] Although many catalytic reactions via C−C bond cleavage has been developed, examples of the reactions involving β-carbon

(1) For reviews of C−C bond cleavage reactions, see: (a) Bishop, K. C., III. *Chem. Rev.* **1976**, *76*, 461. (b) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245. (c) Jennings, P. W.; Johnson, L. L. *Chem. Rev.* **1994**, *94*, 2241. (d) Rybtchinski, B.; Milstein, D. *Angew. Chem., Int. Ed.* **1999**, *38*, 870. (e) Murakami, M.; Ito, Y. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S., Ed.; Springer: New York, 1999; pp 97−129.

(2) Kaneda, K.; Azuma, H.; Wayaku, M.; Teranishi, S. *Chem. Lett.* **1974**, 215.

(3) (a) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1991**, *113*, 2771. (b) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 4895.

(4) (a) Murakami, M.; Amii, H.; Ito, Y. *Nature* **1994**, *370*, 540. (b) Murakami, M.; Amii, H.; Shigeto, K.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 8285. (c) Murakami, M.; Takahashi, K.; Amii, H.; Ito, Y. *J. Am. Chem. Soc.* **1997**, *119*, 9307. (d) Murakami, M.; Itahashi, T.; Amii, H.; Takahashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1998**, *120*, 9949. (e) Murakami, M.; Tsuruta, T.; Ito, Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 2484. (f) Murakami, M.; Itahashi, T.; Ito, Y. *J. Am. Chem. Soc.* **2002**, *124*, 13976.

(5) (a) Mitsudo, T.; Zhang, S.-W.; Watanabe, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 435. (b) Mitsudo, T.; Suzuki, T.; Zhang, S.-W.; Imai, D.; Fujita, K.; Manabe, T.; Shiotsuki, M.; Watanabe, Y.; Wada, K.; Kondo, T. *J. Am. Chem. Soc.* **1999**, *121*, 1839. (c) Kondo, T.; Nakamura, A.; Okada, T.; Suzuki, N.; Wada, K.; Mitsudo, T. *J. Am. Chem. Soc.* **2000**, *122*, 6319. (d) Kondo, T.; Kaneko, Y.; Taguchi, Y.; Nakamura, A.; Okada, T.; Shiotsuki, M.; Ura, Y.; Wada, K.; Mitsudo, T. *J. Am. Chem. Soc.* **2002**, *124*, 6824.

(6) (a) Suggs, J. W.; Jun, C.-H. *J. Chem. Soc., Chem. Commun.* **1985**, 92. (b) Jun, C.-H.; Lee, H. *J. Am. Chem. Soc.* **1999**, *121*, 880. (c) Jun, C.-H.; Lee, H.; Lim, S.-G. *J. Am. Chem. Soc.* **2001**, *123*, 751. (d) Liou, S.-Y.; van der Boom, M. E.; Milstein, D. *Chem. Commun.* **1998**, 687. (e) Gandelman, M.; Milstein, D. *Chem. Commun.* **2000**, 1603. (f) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1999**, *121*, 8645.

(7) Nilsson, Y. I. M.; Andersson, P. G.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1993**, *115*, 6609.

(8) (a) Noyori, R.; Odagi, T.; Takaya, H. *J. Am. Chem. Soc.* **1970**, *92*, 5780. (b) Noyori, R.; Kumagai, Y.; Umeda, I.; Takaya, H. *J. Am. Chem. Soc.* **1972**, *94*, 4018. (c) Lautens, M.; Ren, Y.; Delanghe, P. H. M. *J. Am. Chem. Soc.* **1994**, *116*, 8821. (d) Lautens, M.; Ren, Y. *J. Am. Chem. Soc.* **1996**, *118*, 10668. (e) Suginome, M.; Matsuda, T.; Ito, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11015.

(9) (a) Hayashi, M.; Ohmatsu, T.; Meng, Y.-P.; Saigo, K. *Angew. Chem., Int. Ed.* **1998**, *37*, 837. (b) Murakami, M.; Itami, K.; Ubukata, M.; Tsuji, I.; Ito, Y. *J. Org. Chem.* **1998**, *63*, 4.

(10) Iwasawa, N.; Matsuo, T.; Iwamoto, M.; Ikeno, T. *J. Am. Chem. Soc.* **1998**, *120*, 3903.

(11) (a) Ikura, K.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 1520. (b) Ryu, I.; Ikura, K.; Tamura, Y.; Maenaka, J.; Ogawa, A.; Sonoda, N. *Synlett* **1994**, 941. (c) Hoberg, J. O.; Jennings, P. W. *Organometallics* **1996**, *15*, 3902.

(12) Sugimura, T.; Futagawa, T.; Mori, A.; Ryu, I.; Sonoda, N.; Tai, A. *J. Org. Chem.* **1996**, *61*, 6100.

(13) Beyer, J.; Madsen, R. *J. Am. Chem. Soc.* **1998**, *120*, 12137.

(14) Miller, J. A. *Tetrahedron Lett.* **2001**, *42*, 6991.

(15) (a) Schwager, H.; Spyroudis, S.; Vollhardt, K. P. C. *J. Organomet. Chem.* **1990**, *382*, 191. (b) Perthuisot, C.; Jones, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 3647. (c) Perthuisot, C.; Edelbach, B. L.; Zubris, D. L.; Jones, W. D. *Organometallics* **1997**, *16*, 2018. (d) Edelbach, B. L.; Lachicotte, R. J.; Jones, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 2843. (e) Satoh, T.; Jones, W. D. *Organometallics* **2001**, *20*, 2916. (f) Perthuisot, C.; Edelbach, B. L.; Zubris, D. L.; Simhai, N.; Iverson, C. N.; Müller, C.; Satoh, T.; Jones, W. D. *J. Mol. Catal. A: Chem.* **2002**, *189*, 157 and references therein.

(16) (a) Lautens, M.; Meyer, C.; Lorenz, A. *J. Am. Chem. Soc.* **1996**, *118*, 10676. (b) Bessmertnykh, A. G.; Blinov, K. A.; Grishin, Y. K.; Donskaya, N. A.; Tveritinova, E. V.; Yur'eva, N. M.; Beletskaya, I. P. *J. Org. Chem.* **1997**, *62*, 6069. (c) Tsukada, N.; Shibuya, A.; Nakamura, I.; Yamamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 8123. (d) Nakamura, I.; Itagaki, H.; Yamamoto, Y. *J. Org. Chem.* **1998**, *63*, 6458. (e) Camacho, D. H.; Nakamura, I.; Saito, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 3365. (f) Nakamura, I.; Saito, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 2661. (g) Camacho, D. H.; Nakamura, I.; Saito, S.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66*, 270. (h) de Meijere, A.; Bräse, S. *J. Organomet. Chem.* **1999**, *576*, 88. (i) Nüske, H.; Noltemeyer, M.; de Meijere, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 3411. (j) Knoke, M.; de Meijere, A. *Synlett* **2003**, *2*, 195. (k) Ma, S.; Zhang, J. *Angew. Chem., Int. Ed.* **2003**, *42*, 184.

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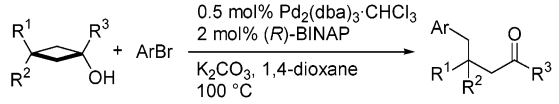
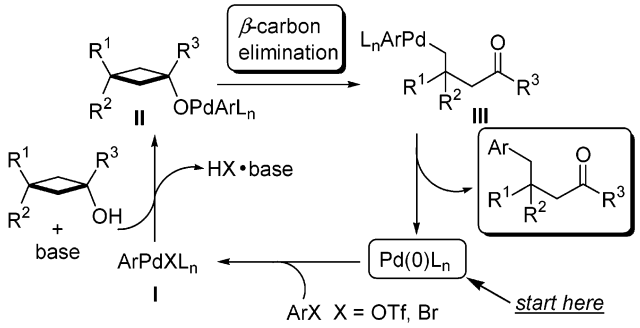
Scheme 1. Palladium-Catalyzed Arylation of *tert*-Cyclobutanols via C−C Bond Cleavage



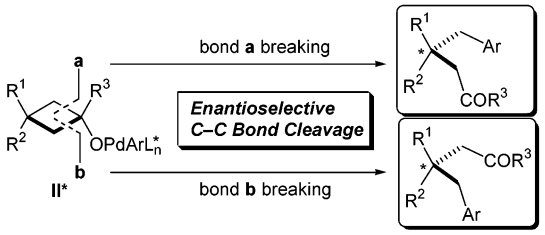
elimination from the late transition metal alcoholates[26] are still quite limited.[21−24]

In the course of our studies on the aerobic oxidation of alcohols in palladium catalysis,[27] we found the novel oxidative transformation of *tert*-cyclobutanols to a variety of organic compounds via β-carbon elimination of the Pd(II) alcoholate intermediate.[28] We also reported the Pd(0)-catalyzed arylation of *tert*-cyclobutanols to give γ-arylated ketones via β-carbon elimination of arylpalladium alcoholate intermediates (Scheme 1).[29] The plausible catalytic cycle of this arylation reaction of *tert*-cyclobutanols is shown in Scheme 2. An arylpalladium intermediate (**I**), formed by oxidative addition of aryl bromide to a palladium(0) phosphine complex, undergoes a ligand exchange with *tert*-cyclobutanol to afford a palladium(II)-alcoholate (**II**), which gives an alkylpalladium intermediate (**III**) by β-carbon elimination. The species **III** is prone to eliminate a palladium(0) phosphine complex reductively to give γ-arylated ketones.[30] When 3-substituted *tert*-cyclobutanols are used, it might be possible to produce optically active ketones if the enantioselective C−C bond cleavage could occur in the palladium(II)-alcoholate (**II***) (bond **a** or **b**) by use of some chiral ligands as shown in Scheme 3. A variety of catalytic reactions involving "regioselective" C−C bond cleavage have been achieved, but the example of "enantioselective" C−C bond cleavage has been scarcely reported to the best of our knowledge.[31] Here, we describe the detailed results of novel Pd-catalyzed asymmetric arylation, establishing nearly complete enantioselective C−C bond cleavage together with some mechanistic aspects of this reaction and also the results of novel asymmetric vinylation and allenylation of *tert*-cyclobutanols.[32]

Scheme 2. Plausible Catalytic Cycle for Arylation of *tert*-Cyclobutanols



Scheme 3. Enantioselective C−C Bond Cleavage



Results and Discussion

Asymmetric Arylation of *tert*-Cyclobutanols. In the Pd(0)-catalyzed arylation of *tert*-cyclobutanols, the addition of some phosphine ligands was necessary to obtain γ-arylated ketones, and (*R*)-BINAP was revealed to be more effective than other phosphine ligands such as PPh_3, dppe, dppb, and dppf[29a] (Scheme 1). However, almost no asymmetric induction was observed using (*R*)-BINAP and other chiral bisphosphine ligands such as (*R*)-Tol-BINAP, (*R*)-(*S*)-BPPFA, (+)-Me-DUPHOS, and (+)-DIOP.[33] The use of chiral monophosphine ligands such as (*R*)-MeO-MOP (**A**) and (*S*)-H-MOP (**B**)[34] (Figure 1), on the

(17) (a) Wender, P. A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc*. **1995**, *117*, 4720. (b) Wender, P. A.; Husfeld, C. O.; Langkopf, E.; Love, J. A. *J. Am. Chem. Soc*. **1998**, *120*, 1940. (c) Wender, P. A.; Sperandio, D. *J. Org. Chem.* **1998**, *63*, 4164. (d) Wender, P. A.; Rieck, H.; Fuji, M. *J. Am. Chem. Soc*. **1998**, *120*, 10976. (e) Wender, P. A.; Glorius, F.; Husfeld, C. O.; Langkopf, E.; Love, J. A. *J. Am. Chem. Soc*. **1999**, *121*, 5348. (f) Wender, P. A.; Dyckman, A. J.; Husfeld, C. O.; Kadereit, D.; Love, J. A.; Rieck, H. *J. Am. Chem. Soc*. **1999**, *121*, 10442. (g) Wender, P. A.; Correa, A. G.; Sato, Y.; Sun, R. *J. Am. Chem. Soc*. **2000**, *122*, 7815.
(18) (a) Trost, B. M.; Toste, F. D.; Shen, H. *J. Am. Chem. Soc*. **2000**, *122*, 2379. (b) Trost, B. M.; Yasukata, T. *J. Am. Chem. Soc*. **2001**, *123*, 7162.
(19) Golden, H. J.; Baker, D. J.; Miller, R. G. *J. Am. Chem. Soc*. **1974**, *96*, 4235.
(20) (a) Yoshikawa, S.; Aoki, K.; Kiji, J.; Furukawa, J. *Tetrahedron* **1974**, *30*, 405. (b) Catellani, M.; Chiusoli, G. P.; Dradi, E.; Salerno, G. *J. Organomet. Chem*. **1979**, *177*, C29. (c) Catellani, M.; Chiusoli, G. P. *J. Organomet. Chem*. **1983**, *247*, C59. (d) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 119. (e) Catellani, M.; Cugini, F. *Tetrahedron* **1999**, *55*, 6595. (f) Lautens, M.; Piguel, S. *Angew. Chem., Int. Ed*. **2000**, *39*, 1045.
(21) Harayama, H.; Kuroki, T.; Kimura, M.; Tanaka, S.; Tamaru, Y. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 2352.
(22) Kondo, T.; Kodoi, K.; Nishinaga, E.; Okada, T.; Morisaki, Y.; Watanabe, Y.; Mitsudo, T. *J. Am. Chem. Soc*. **1998**, *120*, 5587.
(23) Terao, Y.; Wakui, H.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc*. **2001**, *123*, 10407.
(24) (a) Park, S.-B.; Cha, J. K. *Org. Lett*. **2000**, *2*, 147. (b) Okumoto, H.; Jinnai, T.; Shimizu, H.; Harada, Y.; Mishima, H.; Suzuki, A. *Synlett* **2000**, 629.
(25) For other approaches for C−C bond cleavage, in which a direct electrophilic attack of the palladium cationic complex to an electron-rich β-carbon atom of siloxycyclopropanes occurs, see: (a) Aoki, S.; Fujimura, T.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc*. **1988**, *110*, 3296. (b) Aoki, S.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett*. **1988**, *29*, 1541. (c) Aoki, S.; Nakamura, E. *Synlett* **1990**, 741. (d) Fujimura, T.; Aoki, S.; Nakamura, E. *J. Org. Chem*. **1991**, *56*, 2809. (e) Aoki, S.; Nakamura, E. *Tetrahedron* **1991**, *47*, 3935. (f) Kang, S.-K.; Yamaguchi, T.; Ho, P.-S.; Kim, W.-Y.; Yoon, S.-K. *Tetrahedron Lett*. **1997**, *38*, 1947. (g) Yasui, K.; Fugami, K.; Tanaka, S.; Tamaru, Y.; Ii, A.; Yoshida, Z.; Saidi, M. R. *Tetrahedron Lett.* **1992**, *33*, 789.
(26) (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1989; pp 59−61. (b) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*, 2nd ed.; Wiley: New York, 1994; pp 57−59. (c) Bryndza, H. E.; Tam, W. *Chem. Rev*. **1988**, *88*, 1163.
(27) (a) Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *Tetrahedron Lett*. **1998**, *39*, 6011. (b) Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *J. Org. Chem*. **1999**, *64*, 6750.
(28) (a) Nishimura, T.; Ohe, K.; Uemura, S. *J. Am. Chem. Soc*. **1999**, *121*, 2645. (b) Nishimura, T.; Ohe, K.; Uemura, S. *J. Org. Chem*. **2001**, *66*, 1455.
(29) (a) Nishimura, T.; Uemura, S. *J. Am. Chem. Soc*. **1999**, *121*, 11010. (b) Nishimura, T.; Matsumura, S.; Maeda, Y.; Uemura, S. *Tetrahedron Lett*. **2002**, *43*, 3037.
(30) Reverse process of the β-carbon elimination from palladium(II)-alcoholate has been reported. Quan, L. G.; Lamrani, M.; Yamamoto, Y. *J. Am. Chem. Soc*. **2000**, *122*, 4827. Detailed study of the β-aryl elimination from the [Pd−CH_2CMe_2Ph] complex, see: Cámpora, J.; Gutiérrez-Puebla, E.; López, J. A.; Monge, A.; Palma, P.; del Río, D.; Carmona, E. *Angew. Chem., Int. Ed.* **2001**, *40*, 3641.
(31) Rhodium-catalyzed asymmetric hydrogenolysis of the α-carbon−carbon bond of cyclobutanone involving an enantioselective C−C bond cleavage was presented by: Murakami, M.; Amii, H.; Ito, Y. Abstract II. *69th Annual Meeting of the Chemical Society of Japan*; Kyoto, Japan, March 1995; p 1127.
(32) A part of this work has been published in communication form: Nishimura, T.; Matsumura, S.; Maeda, Y.; Uemura, S. *Chem. Commun*. **2002**, 50.
(33) (*R*)-BINAP, dppe, dppb, and dppf stand for (*R*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, 1,2-bis(diphenylphosphino)ethane, 1,4-bis(diphenylphosphino)butane, and 1,1′-bis(diphenylphosphino)ferrocene, respectively. (*R*)-Tol-BINAP, (*R*)-(*S*)-BPPFA, (+)-Me-DUPHOS, and (+)-DIOP also stand for (*R*)-2,2′-bis(di-*p*-tolyl-diphenylphosphino)-1,1′-binaphthyl, (*R*)-*N*,*N*-dimethyl-1-[(*S*)-1′,2-bis(diphenylphosphino)ferrocenyl]ethylamine, (+)-1,2-bis(2,5-dimethylphospholano)benzene, and (+)-4,5-bis(diphenylphosphinomethyl)-2,2-dimethyl-1,3-dioxolane, respectively.

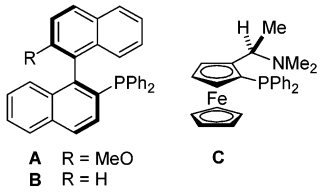
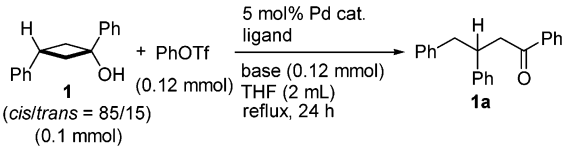


Figure 1. Chiral monophosphine ligands.

Table 1. Asymmetric Arylation of *tert*-Cyclobutanol **1** Using (*R*)-MeO-MOP (**A**)



entry	catalyst	ligand (mol %)	base	GLC yield (%)	ee (%)
1	$Pd_2(dba)_3{\cdot}CHCl_3$	**A** (20)	K_2CO_3	90	12
2	$Pd_2(dba)_3{\cdot}CHCl_3$	**B** (20)	K_2CO_3	75	19
3	$Pd_2(dba)_3{\cdot}CHCl_3$	**B** (10)	K_2CO_3	84	21
4	$Pd(OAc)_2$	**B** (10)	K_2CO_3	75	24
5	$Pd(OAc)_2$	**B** (20)	Cs_2CO_3	60	33
6[a]	$Pd(OAc)_2$	**B** (20)	Cs_2CO_3	64	35
7[a]	$Pd(OAc)_2$	**C** (20)	Cs_2CO_3	36	43

[a] THF (1 mL) was used.

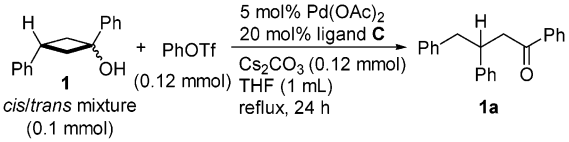
other hand, provided the arylated ketones in good yields with a slight enantioselectivity. Thus, the treatment of 1,3-diphenylcyclobutanol (**1**, cis/trans = 85/15, 0.1 mmol) with 1.2 equiv of both PhOTf and K_2CO_3 in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol % Pd) and ligand **A** (20 mol %) in THF at reflux temperature for 24 h under N_2 atmosphere afforded 1,3,4-triphenyl-1-butanone (**1a**) in 90% yield with 12% ee (Table 1, entry 1). With ligand **B**, an improvement of the ee value was observed, but the product yield slightly decreased (entry 1 vs 2). $Pd(OAc)_2$ can also be used, and in this case the use of Cs_2CO_3 as a base instead of K_2CO_3 gave a better enantioselectivity (entries 5 and 6). Here, other bases such as CH_3COONa and K_3PO_4 were not effective.

To find more effective ligands for this arylation, a N,P-bidentate ligand having a ferrocene, (*R*)-*N*,*N*-dimethyl-1-[(*S*)-2-(diphenylphosphino)ferrocenyl]ethylamine [(*R*)-(*S*)-PPFA, **C**], was next examined. As a result, a better selectivity (43% ee) was obtained for **1a** [entry 7: the absolute configuration was *S*[35]], encouraging us to examine this type of ligand more carefully.

Another factor affecting the enantioselectivity was the ratio of the isomeric alcohols (Table 2). When the arylation of **1** (cis/trans = 80/20) was carried out under the same conditions as entry 7 in Table 1, the ee value of **1a** decreased to 36% (entry 1). The more the ratio of cis alcohols increased, the higher the ee value of **1a** became, and thus the ee value increased to 59% when the alcohol of cis/trans = 98/2 was employed (entry 5). These results suggest that the enantioselective C−C bond cleavage occurs at the same direction in each arylpalladium(II)-alcoholate composed of cis and trans isomeric alcohols. That is, the C−C bond **b** cleavage preferentially occurs in the net reaction of both *cis*-**1** (R^1 = H; R^2, R^3 = Ph) and *trans*-**1** (R^2 = H; R^1, R^3 = Ph in Scheme 3), indicating that the lower cis ratio of **1** decreases the ee value of the product **1a** because the absolute configuration of **1a** obtained from *trans*-**1** and *cis*-**1** is opposite.

By using this alcohol (cis/trans = 98/2), the ligand **C**, and palladium acetate, more suitable reaction conditions were examined, typical results of which are shown in Table 3. It was revealed that the use of bromobenzene, Cs_2CO_3 as a base, and

Table 2. Relationship between the Cis/Trans Ratio of *tert*-Cyclobutanol **1** and the ee Value of Product **1a**



entry	cis/trans	GLC yield (%)	ee (%)
1	80/20	16	36
2	85/15	36	43
3	90/10	40	50
4	95/5	33	54
5	98/2	42	59

Table 3. Asymmetric Arylation of *tert*-Cyclobutanol **1** Using (*R*)-(*S*)-PPFA (**C**)[a]

entry	PhX	base	solvent (mL)	temp (°C)	time (h)	GLC yield (%)	ee (%)
1	PhOTf	Cs_2CO_3	THF (1)	reflux	24	42	59
2	PhOTf	Cs_2CO_3	1,4-dioxane (1)	90	24	12	52
3	PhOTf	Cs_2CO_3	toluene (1)	90	24	70	48
4	PhBr	K_2CO_3	toluene (1)	80	48	21	57
5	PhBr	K_2CO_3	toluene (0.5)	80	48	11	57
6	PhBr	Cs_2CO_3	toluene (0.5)	80	48	91	58

[a] Reaction conditions: alcohol **1** (cis/trans = 98/2, 0.1 mmol), $Pd(OAc)_2$ (5 mol %), (*R*)-(*S*)-PPFA (**C**) (20 mol %), base (0.12 mmol), phenyl triflate or bromobenzene (0.12 mmol).

Table 4. Asymmetric Arylation of *tert*-Cyclobutanol **1** Using Chiral Ferrocene-Containing N,P-Ligand[a]

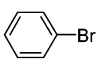
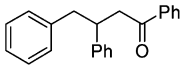
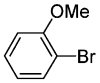
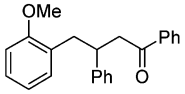
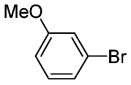
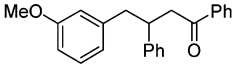
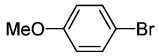
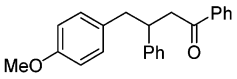
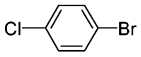
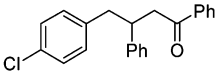
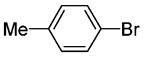
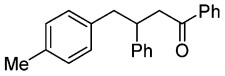
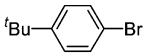
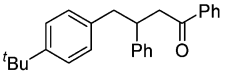
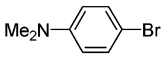
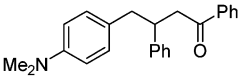
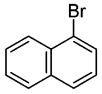
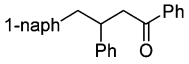
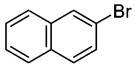
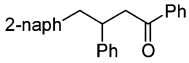
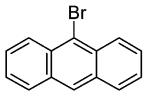
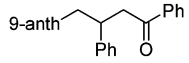
entry	ligand	time (h)	isolated yield (%)	ee (%)
1	**C**	24	70	58
2	**D**	24	90	57
3	**E**	24	72	47
4	**F**	24	98	45
5	**G**	24	77	45
6	**H**	48	58	58
7	**I**	48	20	83
8	**J**	24	95	77
9	**K**	12	90	83
10[b]	**L**	4	99	86
11[b,c]	**L**	12	99	93
12[b]	**M**	5	91	89
13[b,c]	**M**	24	86	92

[a] Reaction conditions: alcohol **1** (cis/trans = 98/2, 0.1 mmol), $Pd(OAc)_2$ (5 mol %), chiral ligand (20 mol %), Cs_2CO_3 (0.12 mmol), PhBr (0.12 mmol) in toluene (0.5 mL) at 80 °C under N_2. [b] Ligand (10 mol %) was used. [c] At 50 °C.

(34) (a) Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc*. **1991**, *113*, 9887. (b) Uozumi, Y.; Suzuki, N.; Ogiwara, A.; Hayashi, T. *Tetrahedron* **1994**, *50*, 4293.

(35) (−)-Sparteine-mediated enantioselective lithiation of *N*-Boc-*N*-(*p*-methoxyphenyl)-cinnamylamine followed by treatment with benzyl bromide provided (*S*)-*N*-Boc-*N*-(*p*-methoxyphenyl)-3,4-diphenyl-(*Z*)-1-butene-1-amine. Subsequent hydrolysis with HCl to the corresponding aldehyde followed by Grignard reaction with PhMgBr afforded the corresponding alcohol which was then oxidized to give (*S*)-(−)-**1a**. The *S*-configuration of **1a** obtained in this asymmetric arylation was confirmed by both the specific rotation and the retention time of HPLC. Absolute configurations of (*S*)-(−)-**5a** and (*S*)-(+)-**1o** were confirmed in the same way. (a) Weisenburger, G. A.; Beak, P. *J. Am. Chem. Soc*. **1996**, *118*, 12218. (b) Whisler, M. C.; Soli, E. D.; Beak, P. *Tetrahedron Lett*. **2000**, *41*, 9527.

Table 5. Asymmetric Arylation of *tert*-Cyclobutanol **1** with Aryl Bromide[a]

entry	ArBr	time (h)	product		isolated yield (%)	ee (%)
1		20		**(*S*)-(-)-1a**	93	91
2		22		**(-)-1b**	94	75
3		22		**(-)-1c**	93	92
4		20		**(-)-1d**	87	90
5		22		**(-)-1e**	97	88
6		18		**(-)-1f**	95	91
7		48		**(-)-1g**	99	94
8		48		**(-)-1h**	89	95
9		22		**(-)-1i**	99	77
10		15		**(-)-1j**	91	90
11		28			72	0
12[b, c]		12		**(+)-1k**	79	26
13[c, d]		31			87	48

[a] Reaction conditions: alcohol **1** (cis/trans = 98/2, 0.2 mmol), $Pd(OAc)_2$ (5 mol %), ligand **L** (10 mol %), Cs_2CO_3 (0.24 mmol), ArBr (0.24 mmol) in toluene (1.0 mL) at 50 °C under N_2. [b] Ligand **J** (10 mol %) was used. [c] At 80 °C. [d] (*R*)-(*S*)-PPFA (**C**) (20 mol %) was used.

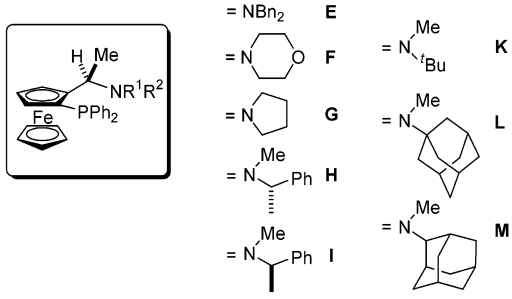


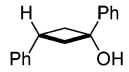
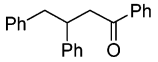
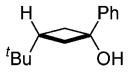
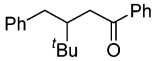
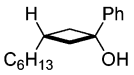
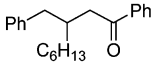
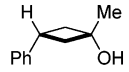
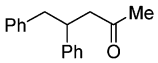
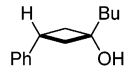
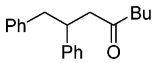
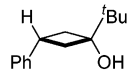
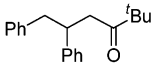
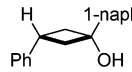
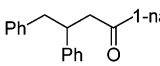
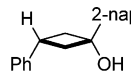
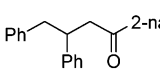
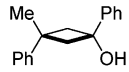
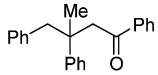
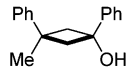
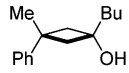
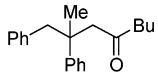
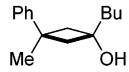
Figure 2. Chiral ferrocene-containing N,P-ligands.

toluene as a solvent at 80 °C for 2 days afforded a high yield of **1a** without a decrease of enantioselectivity (entry 6). Under this reaction condition, a variety of chiral N,P-ligands such as (*R*)-(*S*)-PPFA (**C**)[36] (Figure 2), which possess the ferrocene and the different amino groups on the side chain, were then applied to this asymmetric arylation in the hopes of accomplishing a higher selectivity (Table 4). First, some ligands **D**−**G**, which possess symmetric acyclic or cyclic amino groups, were employed, but the ee values of **1a** were lower than that in the case of (*R*)-(*S*)-PPFA (**C**) (entries 2−5). Next, several ligands containing nonsymmetrical amino groups having a methyl group as one substituent on the N atom such as **H**−**M** were examined. When **H** was used, the enantioselectivity was the same as that when using **C**, but a significant increase of enantioselectivity was observed using **I** as a chiral ligand (entry 6 vs 7). Furthermore, when ligands having one bulkier substituent on the N atom, such as cyclohexyl (**J**), *tert*-butyl (**K**), and adamantyl (**L** and **M**), were used, the ee value as well as the product yield markedly increased (entries 8−13). It is noteworthy that the arylation of **1** proceeded completely within only 4 h at 80 °C by using even 10 mol % **L** (entry 10). Finally, **1a** was obtained in 99% yield with 93% ee even at 50 °C (entry 11). Therefore, we decided that the optimum reaction condition was the use of *tert*-cyclobutanol, $Pd(OAc)_2$ (5 mol %), chiral ligand **L** (10 mol %), aryl bromide (1.2 equiv), and Cs_2CO_3 (1.2 equiv) in toluene (0.2 M) at 50 °C under N_2. Under this optimum condition, arylation using a variety of aryl bromides and *tert*-cyclobutanols was further examined.

The results of the asymmetric arylation of **1** (cis/trans = 98/2) with various aryl bromides are listed in Table 5. Generally, most of the aryl bromides, which have various substituents on

(36) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, N.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M.; Yamamoto, K.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138.

Table 6. Asymmetric Arylation of *tert*-Cyclobutanols with PhBr[a]

entry	alcohol	*cis*/*trans*	temp. (°C) / time (h)	product		isolated yield (%)	ee (%)
1		**1**, 98/2	50/20		**(*S*)-(-)-1a**	93	91
2		**2**, 97/3	50/24		**(+)-2a**	99	75
3		**3**, 96/4	50/24		**(+)-3a**	99	82
4		**4**, 97/3	50/48		**(-)-4a**	79	73
5			80/10			69	64
6		**5**, 99/1	50/48		**(*S*)-(-)-5a**	13	67
7			80/18			91	66
8		**6**, 99/1	50/48		**(-)-6a**	23	33
9			80/48			74	22
10[b]			80/72			36	36
11		**7**, 98/2	50/24		**(+)-7a**	95	86
12		**8**, 99/1	50/16		**(-)-8a**	99	93
13		***cis*-9**, 99/1	50/48		**(-)-9a**	83	90
14		***trans*-9**, 1/99	50/48		**(+)-9a**	84	55
15			80/13			95	43
16		***cis*-10**, 99/1	50/72		**(-)-10a**	50	15
17			80/48			83	8
18[b]			80/72			88	22
19		***trans*-10**, 1/99	80/48		**(+)-10a**	97	7

[a] Reaction conditions: alcohol (0.2 mmol), $Pd(OAc)_2$ (5 mol %), ligand **L** (10 mol %), Cs_2CO_3 (0.24 mmol), PhBr (0.24 mmol) in toluene (1.0 mL) at 50 °C under N_2. [b] (*R*)-(*S*)-PPFA (**C**) (20 mol %) was used.

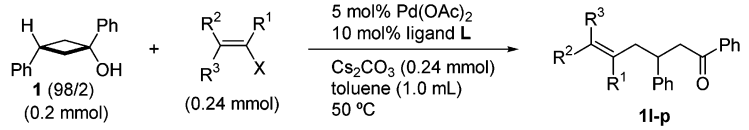
aromatic nuclei, gave the corresponding desired ketones in excellent yield with high enantioselectivity. 2-Bromoanisole showed a slightly lower selectivity as compared to that from 3- and 4-bromoanisoles probably due to its steric effect (entry 2 vs 1, 3, and 4). *p*-Bromochlorobenzene afforded **1e** without affecting the chloro substituent in 97% yield with 88% ee (entry 5). Bromoarenes having other substituents such as methyl, *tert*-butyl, or dimethylamino afforded the corresponding ketones **1f**−**1h** in high yield without the reduction of ee value (entries 6−8). The reactions using 1- and 2-bromonaphthalene also occurred smoothly to give **1i** and **1j**, respectively, in high yield with high enantioselectivity (entries 9 and 10). Surprisingly, when 9-bromoanthracene was used as an arylating reagent, **1k** was obtained as a racemate under this condition (entry 11), but the use of sterically less hindered chiral ligands such as **J** and **C** improved the ee value up to 48% (entries 12 and 13). The dissociation of the N atom of the ligand having a bulkier substituent from the palladium metal may reduce the enantioselectivity.[37]

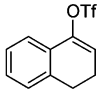
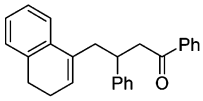
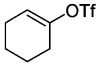
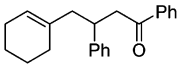
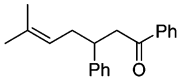
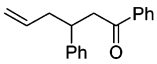
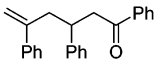
The results of the asymmetric arylation of several monocyclic *tert*-cyclobutanols using bromobenzene leading to chiral γ-arylated ketones under the optimized conditions described above are listed in Table 6. 3-Substituted cyclobutanols **1**−**8** gave the corresponding ketones **1a**−**8a** in moderate to excellent yield with high enantioselectivity. 3-Alkyl-substituted cyclobutanols **2** and **3** gave the corresponding γ-arylated ketones **2a** and **3a** in excellent yield with 75% ee and 82% ee, respectively (entries 2 and 3). It should be noted that this arylation could also be applied to 1-alkyl-substituted cyclobutanols **4**−**6**, but the ee values of **4a**−**6a** were slightly lower, and a longer reaction time or higher reaction temperature was required (entries 4−10). The absolute configuration of **5a** was also *S* as in the case of **1a**.[35] In the case of cyclobutanols **7** and **8**, which have naphthyl groups at the 1-position, the reactions proceeded smoothly to afford the corresponding ketones **7a** and **8a**, respectively, in excellent yield with high enantioselectivity (entries 11 and 12). 3,3-Disubstituted cyclobutanols can give the corresponding ketones having chiral quaternary carbon centers.[38] Treatment

(37) (a) Hayashi, T.; Konishi, M.; Fukushima, M.; Mise, T.; Kagotani, M.; Tajika, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 180. (b) Schnyder, A.; Hintermann, L.; Togni, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 931.

(38) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 388.

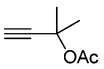
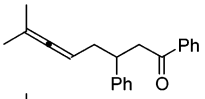
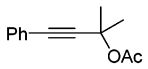
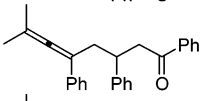
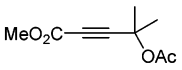
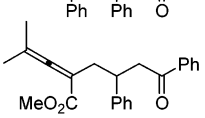
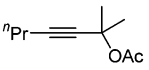
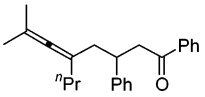
Table 7. Asymmetric Vinylation of *tert*-Cyclobutanol **1**



entry	vinylating reagent	time (h)	product		isolated yield (%)	ee (%)
1		48		**(+)-1l**	93	73
2		36		**(+)-1m**	65	88
3		30		**(+)-1n**	45	70
4[a]		36			87	73
5[a]		48		**(*S*)-(+)-1o**	27	73
6[a, b]		27			17	49
7		48		**(+)-1p**	21	82
8[a]		48			36	78

[a] Cs_2CO_3 (0.4 mmol) was used. [b] At 80 °C.

Table 8. Asymmetric Allenylation of *tert*-Cyclobutanol **1**[a]

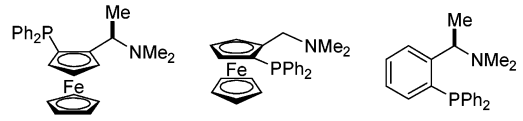
entry	propargylic acetate	time (h)	product		isolated yield (%)	ee (%)
1		45			trace	—
2		48		**(+)-1q**	79	78
3		24		**(+)-1r**	37	84
4		48			trace	—

[a] Reaction conditions: alcohol **1** (cis/trans = 98/2, 0.2 mmol), $Pd(OAc)_2$ (5 mol %), ligand **L** (10 mol %), Cs_2CO_3 (0.4 mmol), propargylic acetate (0.24 mmol) in toluene (1.0 mL) at 50 °C.

of cyclobutanol *cis*-**9**[39] under the same conditions for 48 h afforded (−)-**9a** with 90% ee, while the isomer *trans*-**9**[39] gave (+)-**9a** with 55% ee after 48 h (entries 13 and 14). These results also indicate that the enantioselective C−C bond cleavage preferentially occurs at the C−C bond in the same direction in the ligand **L** ligated palladium(II)-alcoholates (Scheme 3), irrespective of the substituents at the 3-position on the cyclobutane ring. In the case of *cis*- and *trans*-**10**,[39] the reaction was very slow, and **10a** was obtained with a low level of enantioselectivity (entries 16−19), suggesting that the substituent at the 1-position of *tert*-cyclobutanol plays an important role and that the presence of the aromatic group at the 1-position is essential for obtaining both the high reaction rate and the high enantioselectivity.

(39) Each of the alcohols *cis*-**9** and *trans*-**9** was separated by HPLC, while each of the alcohols *cis*-**10** and *trans*-**10** was separated by column chromatography on SiO_2. The exact stereochemistry of *cis*-**9** and *trans*-**9** was determined by X-ray single-crystal analysis of the 4-chlorobenzoate ester of *trans*-**9**. The stereochemistry of *cis*-**10** and *trans*-**10** was assumed to be so by comparison with ^1H NMR spectra of *cis*-**9** and *trans*-**9**.

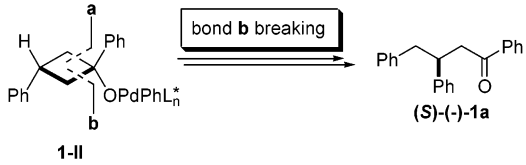
Asymmetric Vinylation of *tert*-Cyclobutanols. Asymmetric vinylation of organic compounds is one of the useful reactions in synthetic organic chemistry due to the production of optically active vinylated compounds, which allow further transformations of the vinyl group. Thus, the asymmetric vinylation of *tert*-cyclobutanols using vinylating reagents such as vinyl halides or vinyl triflates was next investigated (Table 7). Treatment of **1** (cis/trans = 98/2) with 1.2 equiv of both 3,4-dihydronaphthalen-1-yl triflate and Cs_2CO_3 in the presence of 5 mol % $Pd(OAc)_2$ and 10 mol % ligand **L** in toluene (1.0 mL) at 50 °C for 48 h afforded **1l** in 93% yield with 73% ee (entry 1). When cyclohex-1-enyl triflate was used, the reaction also proceeded smoothly to give **1m** in 65% yield with 88% ee (entry 2). 1-Bromo-2-methylpropene afforded **1n** in moderate yield with high enantioselectivity (entry 3). The increase of the yield of **1n** was observed when 2.0 equiv of Cs_2CO_3 was used (entry 4). The vinylating reagents such as vinyl bromide and α-bromostyrene gave the corresponding vinylated ketone (*S*)-**1o**[35] and



(*R*)-(*R*)-PPFA (*S*)-FcPN (*R*)-AMPHOS

Figure 3. Chiral N,P-ligands.

Scheme 4. The Direction of Enantioselective C−C Bond Cleavage



1-II **(*S*)-(-)-1a**

1p in low yield, respectively, but with high enantioselectivity (entries 5−8).

Asymmetric Allenylation of *tert*-Cyclobutanols. It is known that propargylic compounds oxidatively add to Pd(0) species to generate (σ-allenyl)palladium(II) complexes which can be used for various transformations.[40] Considering the results of the vinylation described above, we expected that the analogous allenylation may occur when (σ-allenyl)palladium(II) complexes could be generated in the reaction media.

When **1** (cis/trans = 98/2, 0.2 mmol) was treated with 1.2 equiv of 1,1-dimethyl-2-propynyl methyl acetate and 2.0 equiv of Cs_2CO_3 in the presence of 5 mol % $Pd(OAc)_2$ and 10 mol % ligand **L** in toluene (1.0 mL) at 50 °C for 45 h, the reaction did not proceed (Table 8, entry 1). On the other hand, treatment of **1** with 1,1-dimethyl-3-phenyl-2-propynyl acetate afforded **1q** in 79% yield with 78% ee (entry 2). Propargylic acetate having a methoxylcarbonyl moiety afforded the corresponding ketone **1r** (entry 3), but no reaction occurred with that having an alkyl moiety at the terminal position (entry 4).

The Role of a Chiral Ferrocene-Containing N,P-Ligand. To confirm the real active palladium species in these reactions, phenylation of **1** was carried out by changing the ratio between Pd(0) and ligand **L**. In the case of the ratio of Pd/L = 1/2, **1a** was obtained in 68% yield with 91% ee, while even in the case of the ratio of Pd/L = 2/1, **1a** was produced in almost the same yield and enantioselectivity (Table S3). This result shows that the active palladium catalyst species is consisting of the ligand and the metal in a one-to-one ratio forming "PdL",[37a] the ferrocene-containing N,P-ligand working as a bidentate ligand and bound to Pd metal on both the P and the N atoms.

As described above, the absolute configuration of **1a** obtained by using (*R*)-(*S*)-PPFA derivatives **C**−**M** was revealed to be *S* by comparison with the sample prepared separately,[35] and this fact showed that the C−C bond **b** of the palladium(II)-alcoholate **1-II** was preferentially cleaved (Scheme 4). To clarify the reason why the PPFA derivatives cause a high asymmetric induction in these reactions, arylation using several types of chiral ligands containing structures similar to that of (*R*)-(*S*)-PPFA, such as (*R*)-(*R*)-PPFA, (*S*)-FcPN, and (*R*)-AMPHOS, was examined (Figure 3). (*R*)-(*R*)-PPFA[36,41] is a diastereomer of (*R*)-(*S*)-PPFA, in which both the planar and the central chirality is *R*. (*S*)-FcPN[42] lacks the central chirality, but it still has the planar chirality *S*. (*R*)-AMPHOS[43] has the central chirality *R*, but it lacks the planar chirality because it has the benzene ring in place of the ferrocene ring. Typical results are shown in Table 9. (*R*)-(*R*)-PPFA gave the desired ketone **1a** in 37% yield with 25% ee at 80 °C for 48 h, the absolute configuration of the obtained **1a** being *R* opposite to that obtained with (*R*)-(*S*)-PPFA (entry 2). This result clearly indicates that the ferrocene planar chirality plays a dominant role in controlling the direction of enantioselective C−C bond cleavage of *tert*-cyclobutanols. In the use of (*S*)-FcPN, the reaction proceeded faster than that with (*R*)-(*S*)-PPFA, but a dramatic decrease of the ee value was observed (entry 3). On the other hand, when (*R*)-AMPHOS was used, this arylation proceeded slowly to afford **1a** in 22% yield with only 5% ee (entry 4). These results suggest that both the central chirality on the side chain and the planar chirality are essential for obtaining the high enantioselectivity.

Table 9. Asymmetric Arylation of *tert*-Cyclobutanol **1** Using Chiral N,P-Ligand[a]

entry	ligand	isolated yield (%)	ee (%)
1[b]	(*R*)-(*S*)-PPFA	70	58 (*S*)
2	(*R*)-(*R*)-PPFA	37	25 (*R*)
3	(*S*)-FcPN	86	13 (*S*)
4	(*R*)-AMPHOS	22	5 (*S*)

[a] Reaction conditions: alcohol **1** (cis/trans = 98/2, 0.2 mmol), $Pd(OAc)_2$ (5 mol %), chiral ligand (20 mol %), Cs_2CO_3 (0.24 mmol), PhBr (0.24 mmol) in toluene (1.0 mL) at 80 °C for 48 h under N_2. [b] Alcohol **1** (0.1 mmol) was used.

Conclusion

A novel enantioselective C−C bond cleavage in asymmetric arylation, vinylation, and allenylation of *tert*-cyclobutanols using palladium catalysts and chiral N,P-bidentate ligands is described. The high enantioselective β-carbon elimination of Pd(II) alcoholate occurred to give various optically active γ-arylated, γ-vinylated, and γ-allenylated ketones, respectively, in these reactions. It was revealed that the planar chirality of chiral ferrocene-containing N,P-ligands played a dominant role in controlling the direction of the enantioselective C−C bond cleavage. Although more detailed studies are required to solve the question of mechanism for some steps involving β-carbon elimination, these reactions demonstrate a new approach for constructing chiral carbon centers in asymmetric organic synthesis.

Experimental Section

General Methods. NMR spectra were recorded on JEOL EX-400 (^{1}H NMR, 400 MHz; ^{13}C NMR, 100 MHz; ^{31}P NMR, 161.9 MHz), JNM AL-300 (^{1}H NMR, 300 MHz; ^{13}C NMR, 75.5 MHz), and JEOL GSX-270 (^{1}H NMR, 270 MHz; ^{13}C NMR, 67.5 MHz) instruments for solutions in $CDCl_3$ with Me_4Si as an internal standard. The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet. FT-IR spectra (thin film for liquids, KBr disk for solids) were recorded on a Nicolet Impact 400 spectrometer. Melting points are uncorrected. Recycling preparative high performance liquid chromatography (HPLC) was performed on a JAI LC-908-G30 instrument (600 mm × 20 mm × 2, JAIGEL-1H and JAIGEL-2H dual

(40) (a) Tsuji, J. *Palladium Reagents and Catalysis; Innovations in Organic Synthesis*, Wiley: Chichester, 1995. (b) Tsuji, J.; Mandai, T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2589.
(41) Marquarding, D.; Klusacek, H.; Gokel, G.; Hoffmann, P.; Ugi, I. *J. Am. Chem. Soc*. **1970**, *92*, 5389.
(42) Nishibayashi, Y.; Arikawa, Y.; Ohe, K.; Uemura, S. *J. Org. Chem*. **1996**, *61*, 1172.
(43) (a) Rauchfuss, T. B.; Patino, F. T.; Roundhill, D. M. *Inorg. Chem*. **1975**, *14*, 652. (b) Yamamoto, K.; Tomita, A.; Tsuji, J. *Chem. Lett*. **1978**, 3.

styrene polymer columns) equipped with an ultraviolet (UV) and refractive-index (RI) detector and $CHCl_3$ as an eluent. HPLC analyses were performed on a L-7000 instrument (HITACHI) using Daicel Chiralcel AD and OD columns (4.6 × 250 mm) at 25 °C. Column chromatography on SiO_2 was performed with Merck silica gel 60. Elemental analysis was carried out at the Microanalytical Center of Kyoto University.

Materials. Commercially available organic and inorganic compounds were used without further purification except for the solvent, which was distilled by the known method before use. $Pd_2(dba)_3 \cdot CHCl_3$ (dba = dibenzylideneacetone) was synthesized by the literature method.[44] Cyclobutanols **1**−**10** were prepared according to the reported procedures from the corresponding cyclobutanones and Grignard reagents or alkyllithiums. (*R*)-MeO-MOP, (*S*)-H-MOP,[34] and PPFA derivatives **D**−**M**[36] were prepared according to the reported procedures. Vinyl triflate was prepared according to the reported procedures[45] from the corresponding ketones and trifluoromethanesulfonic anhydride, while vinyl bromides are commercial products. Propargylic acetates were prepared according to known procedures[40b] from the corresponding propargylic alcohols.

Preparation of Cis-Rich *tert*-Cyclobutanols. A typical procedure for preparing cis-rich *tert*-cyclobutanol **1** is as follows: to a mixture of **1**, pyridine (3.0 equiv), and a catalytic amount of 4-*N*,*N*-(dimethylamino)pyridine (5 mol %) in CH_2Cl_2 was added acetic anhydride (0.7−0.8 equiv) at 0 °C, and the resulting mixture was stirred for 6 h. After the general workup, the produced acetate ester of **1** (cis/trans = 98/2) was separated from unreacted **1** and isolated in a pure form by column chromatography on SiO_2. Deacetylation of the ester was performed by the known method (excess K_2CO_3 in MeOH at room temperature). Cis-rich **1** was obtained after column chromatography on SiO_2 in ca. 45% yield from the initial **1**. Other alcohols **2**, **3**, **4**, **6**, **7**, and **8** were prepared by the same procedure, except for **5**, which could be purified in the alcohol form by column chromatography on SiO_2. Each of the alcohols *cis*-**9** and *trans*-**9** was separated by HPLC, while each of the alcohols *cis*-**10** and *trans*-**10** was separated by column chromatography on SiO_2. The ratio of cis and trans isomers of each substrate was determined by ^1H NMR.

Preparation of (*R*)-*N*,*N*-Dimethyl-1-[(*S*)-2-(diphenylphosphino)-ferrocenyl]ethylamine [(*R*)-(*S*)-PPFA] Derivatives. PPFA derivatives were prepared according to the reported procedures[36] from (*R*)-1-[(*S*)-2-(diphenylphosphino)ferrocenyl]ethyl acetate [(*R*)-(*S*)-PPFOAc] and the corresponding amines. A typical procedure for preparing ligand **D** is as follows: a mixture of (*R*)-(*S*)-PPFOAc and diethylamine (30 equiv) in MeOH (0.2 M) was stirred for 6 h at reflux temperature. The solvent was evaporated, and the crude residue was purified by column chromatography on SiO_2 to afford the desired product **D** as a yellow solid. Other ligands **E**−**M** were prepared by the same procedure using corresponding secondary amines. Ligands **H**−**M** are new compounds.

Typical Procedure for Palladium-Catalyzed Asymmetric Arylation of *tert*-Cyclobutanols. A mixture of $Pd(OAc)_2$ (0.01 mmol), (*R*)-(*S*)-**L** (0.02 mmol), Cs_2CO_3 (0.24 mmol), and toluene (0.5 mL) in a 10-mL two-necked round-bottomed flask was stirred at room temperature under N_2. After 0.5 h, a mixture of aryl bromide (0.24 mmol) and alcohol (0.20 mmol) in toluene (0.5 mL) was added, and the resulting mixture was stirred at 50 °C until the reaction had reached completion by monitoring with TLC analysis. The reaction mixture was cooled to room temperature and then filtered through a pad of Florisil. The filtrate was concentrated under vacuum to give an oil, which was subjected to column chromatography on SiO_2 with EtOAc−hexane (2/98) as eluent. The enantiomeric excess was determined by HPLC.

Typical Procedure for Palladium-Catalyzed Asymmetric Vinylation and Allenylation of *tert*-Cyclobutanols. A mixture of $Pd(OAc)_2$ (0.01 mmol), (*R*)-(*S*)-**L** (0.02 mmol), Cs_2CO_3 (0.4 mmol), and toluene (0.5 mL) in a 10-mL Schlenk tube was stirred at room temperature under N_2. After 0.5 h, a mixture of alcohol (0.20 mmol) and vinylic bromide (0.24 mmol) or propargylic acetate (0.24 mmol) in toluene (0.5 mL) was added, and the resulting mixture was stirred at 50 °C until the reaction had reached completion, which was monitored by TLC analysis. The reaction mixture was cooled to room temperature and then filtered through a pad of Florisil. The filtrate was concentrated under vacuum to give an oil, which was subjected to column chromatography on SiO_2 with EtOAc−hexane (2/98) as eluent. The enantiomeric excess was determined by HPLC.

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Supporting Information Available: Experimental procedures, characterization data for all unknown compounds, and tables for X-ray crystal structures of esters of **1** and *trans*-**9** (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(44) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253.
(45) Ritter, K. *Synthesis* **1993**, 735.