Development of Efficient Methods for the Synthesis of Axially Chiral Compounds

Taichi Kano

Development of Efficient Methods for the Synthesis of Axially Chiral Compounds

Taichi Kano

Dedicated to my loving
parents, Masataka & Hiromi Kano
and all my friends
for their continuous encouragement

this thesis in token of gratitude and affection

Contents

Chapter 1

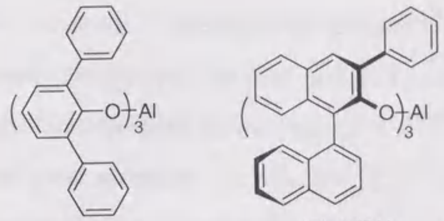
Introduction

The biaryl nucleus is a key subunit associated with many natural products and forms the basis of several nonracemic reagents of extraordinary value in synthetic chemistry. Owing to the substitution pattern on the ring(s) or other restraints, hindered rotation about the adjoining C-C bond gives rise to the stereochemical feature known as atropisomerism. Given the important of this structural type, there are relatively few chemical methods that directly yield nonracemic biaryls. This thesis describes efficient methods for the synthesis of axially chiral compounds

New Axially Chiral Phenols with C_2-Symmetry

Lewis acid-promoted carbon-carbon bond-forming reactions are some of the most important processes in organic synthesis. Traditionally, Friedel-Crafts reaction,[1] ene reaction,[2] Diels-Alder reaction,[3] and Mukaiyama aldol synthesis[4] are catalyzed by ordinary Lewis acids such as $AlCl_3$, $TiCl_4$, BF_3, and $SnCl_4$. These classical Lewis acids activate a wide variety of functional groups of substrates, and the reactions usually proceed efficiently but with relatively low stereo-, regio-, and chemoselectivities. Relatively simple design of the ligands of these Lewis acids leads to monomeric Lewis acids in organic solvent and consequently to high Lewis-acidity and reactivity. Furthermore, upon coordination with designed ligand(s), the well designed Lewis acid exhibits new selectivity. Aluminum tris(2,6-diphenylphenoxide) (ATPH),[5] which was developed in our laboratory, has been used as a typical designer Lewis acid catalyst for regio-, chemo- and stereoselective organic reactions, and the structure of ATPH has been successfully extended to the chiral analogue aluminum tris((*R*)-1-α-naphthyl-2-naphthoxide)((*R*)-ATBN) for asymmetric Claisen rearrangement (Fig. 1).[5c]

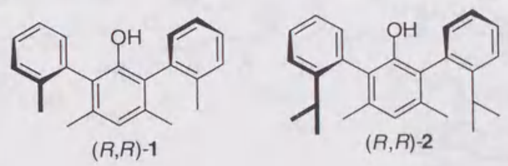
Fig. 1



ATPH (*R*)-ATBN

This result encouraged us to explore the possibility of a new chiral phenol with C_2-symmetry. Chapter 2 describes the synthesis and optical resolution of racemic 3,5-dimethyl-2,6-bis(2-methylphenyl)phenol (*dl*-**1**) and analogous 2,6-bis(2-isopropylphenyl)-3,5-dimethylphenol (*dl*-**2**) (Fig. 2).

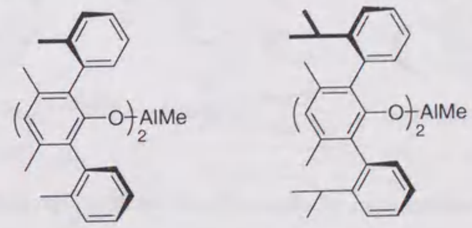
Fig. 2



(*R*,*R*)-**1** (*R*,*R*)-**2**

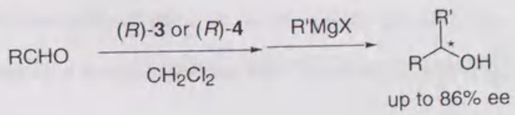
In addition, to determine the potential of chiral phenol **1** and **2**, asymmetric alkylation of aldehydes was demonstrated by the combined use of Grignard reagents and the optically active aluminum reagents **3** and **4** prepared from these chiral phenols (Fig. 3, Scheme 1).

Fig. 3



(*R*)-**3** (*R*)-**4**

Scheme 1

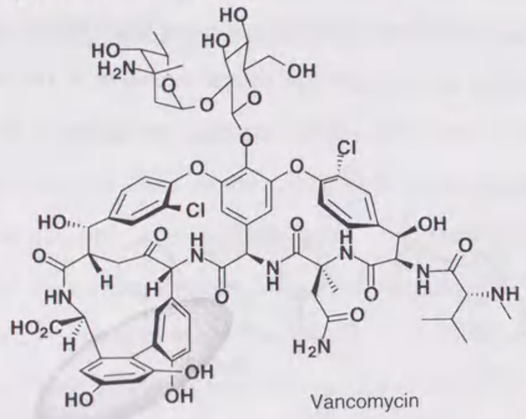


up to 86% ee

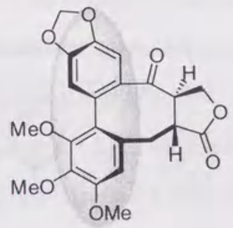
Asymmetric Coupling of Phenols with Arylleads

The optically pure biaryl axis has been the subject of increasing interest, due to its role as a pivotal element in a rapidly growing number of not only pharmacologically potent natural products[6] (e.g., vancomycin, steganone, etc.) but also nonracemic reagents[7] (e.g., BINAL-H, BINAP, etc.) and artificial helical polymers (Fig. 4).[8]

Fig. 4 (1) Natural Product

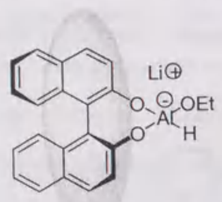


Vancomycin

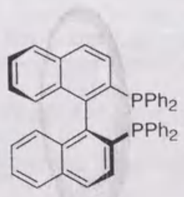


(-)-Steganone

(2) Chiral Metal Catalyst

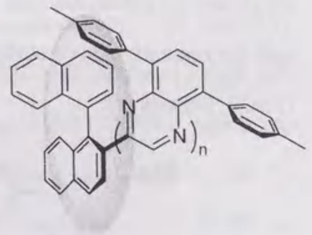


(*S*)-BINAL-H



(*S*)-BINAP

(3) Artificial Helical Polymer

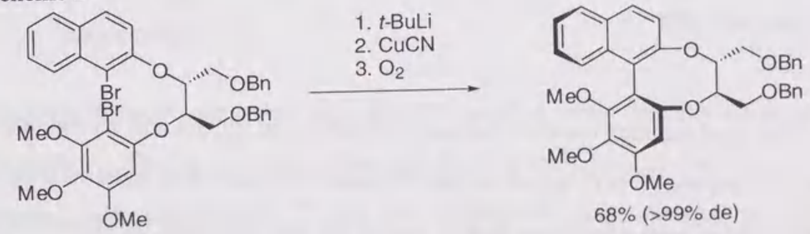


Despite a broad spectrum of classical[9] and modern[10] procedures for the chemical connection of aromatic moieties, the development of efficient aryl-coupling methods that enable the directed construction of even highly sterically demanding bi- and polyaryls in optically active form[11] has become of great importance.

The major synthetic methods of these compounds can be divided into the following four categories: (1) the Ullmann coupling of aryl halides,[12] (2) oxidative coupling of electron-rich phenols,[13] (3) nucleophilic aromatic substitution on electron-deficient arenes with aryl Grignard compounds,[14] and (4) transition metal catalyzed cross coupling between aryl halides and organometallic species.[15]

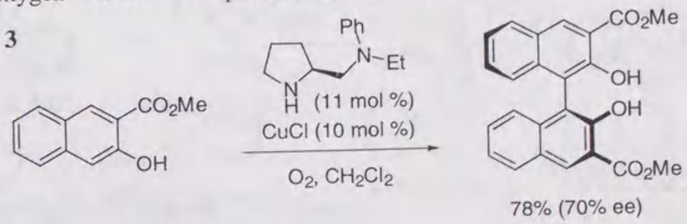
The optically active biaryls are often prepared by the intramolecular Ullmann coupling of two aryl halides linked by a chiral tether, which enabled the coupling between two different aromatics to give the unsymmetrical biaryls (Scheme 2).[12]

Scheme 2



In contrast, the intermolecular oxidative coupling of aromatic alcohols using metal salts ligated by optically active amines afford symmetrical biaryls such as BINOL with high enantioselectivity.[13c-f] Moreover, successful extension of this class of reaction to the catalytic process, which involves cross coupling between two different arenes[13h] or molecular oxygen[13i,j] have been reported recently (Scheme 3).

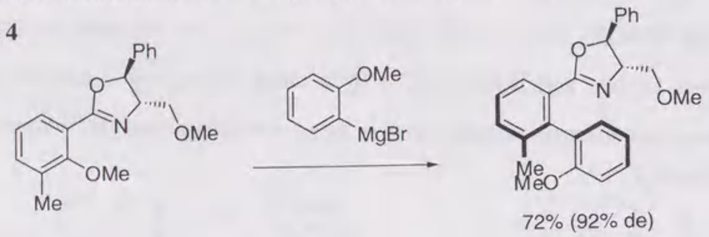
Scheme 3



The nucleophilic aromatic substitution on aromatic compounds, which have an activating group as well as a leaving group, with aryl Grignard reagents was extensively

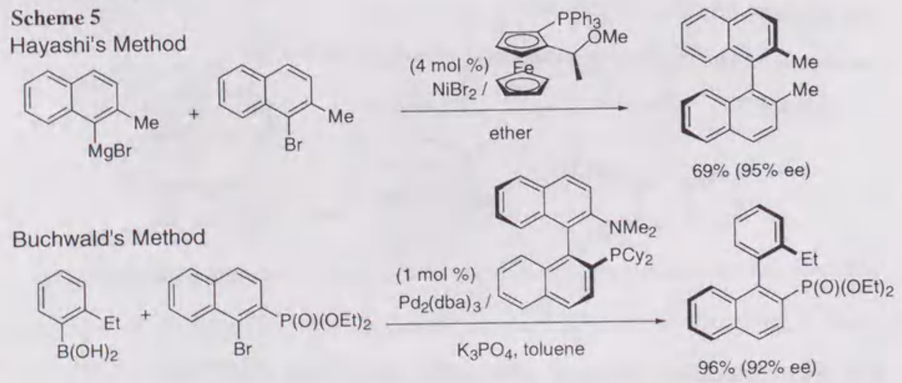
studied by Meyer.[14a-d] Using chiral oxazolines or chiral esters,[14f,g] sometimes accompanied by specific leaving groups such as menthol,[14e] unsymmetrical biaryls in an optically active form are synthesized diastereoselectively (Scheme 4). Unfortunately, however, very high atropisomeric excess is obtained merely with aromatic compounds in which the substituents *ortho* to the coupling position significantly differ in size.

Scheme 4



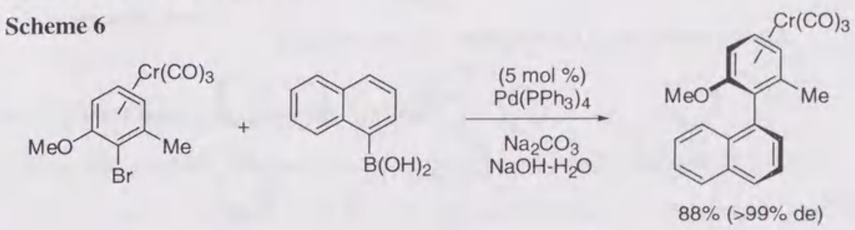
The cross coupling reactions between aryl halides or triflates and aryl boronic acid (Suzuki coupling)[10b] or Grignard reagent (Kumada coupling)[9a] with metal catalysts have been found of great significance to give various biaryls. Although the Hayashi's chiral Ni catalysts[15a,b] and subsequently reported Buchwald's recent method[15c] (Scheme 5) are among the most outstanding catalyses to date along this line, the use of sterically congested substrates frequently results in a significant decrease in yield and have shown limited scope.

Scheme 5



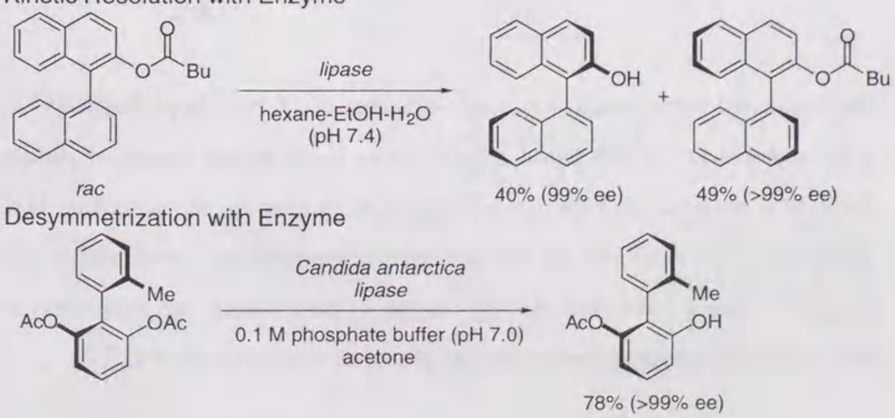
This indeed is an inherent disadvantage, since axially chiral compounds are required to have steric bulk proximal to the chiral axis around which the conformational rotation is highly restricted. Uemura reported that the Suzuki coupling using planar chiral arene chromium complexes gave relatively bulky biaryls in good yields with high diastereoselectivity (Scheme 6).[15e,f]

Scheme 6



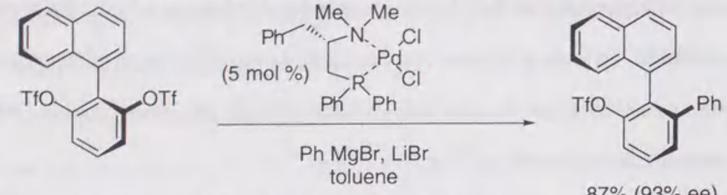
Entirely different approaches have also been used to create optically active biaryl frameworks. The optical resolution and kinetic resolution of racemates with enzymes,[16] desymmetrization,[17a,b] and the asymmetric ring opening of achiral lactones[11a,c] are those in which wide-ranging applications have been found (Scheme 7). Despite obvious usefulness of these methods, comparable success has not been achieved for the enantioselective cross coupling using an external chirality including asymmetric catalysts.

Scheme 7-1

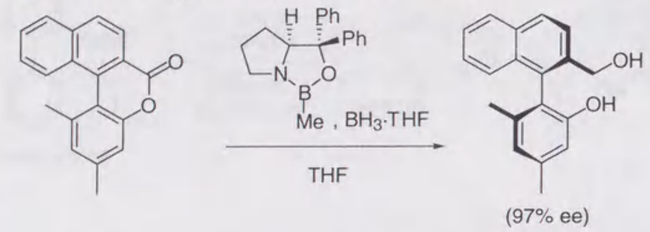


Scheme 7-2

Desymmetrization with Chiral Transition Metal Catalyst

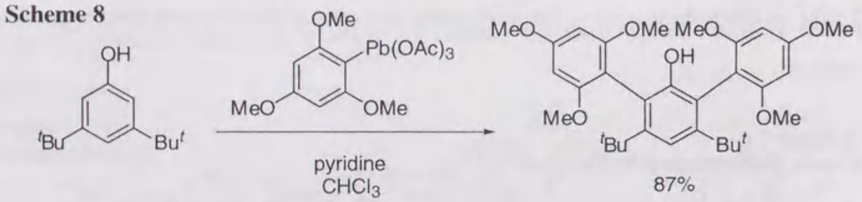


Asymmetric Ring Opening with Chiral Reagent



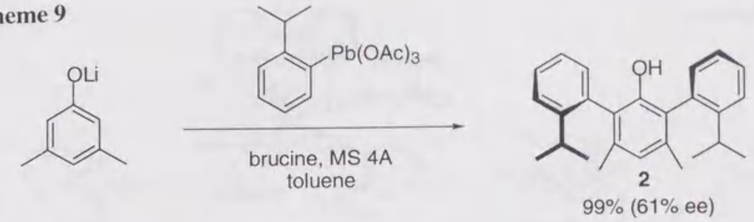
Barton has reported that the ligand coupling of phenols with arylleads is a powerful tool for the synthesis of sterically hindered products under mild conditions.[18] The reaction using arylleads as an equivalent of aryl cation was originally devised by Pinhey, who showed that the use of excess pyridine accelerated reaction rates (Scheme 8).[19]

Scheme 8



We thus started with a search on synthetic efficiency of 2,6-bis(2-isopropylphenyl)-3,5-dimethylphenol (**2**) by this ligand coupling using chiral amines instead of pyridine, since chiral phenol **2** has been demonstrated to be an effective chiral auxiliary in the diastereoselective aldol and the Mannich type reaction of the corresponding chiral acetate.[20] Chapter 3 describes the first example of the diastereo- and enantioselective direct coupling of aryllead compounds with phenol derivatives (Scheme 9).[21]

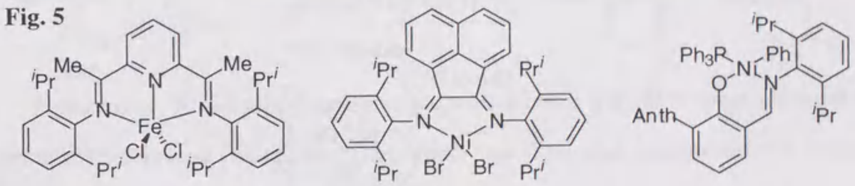
Scheme 9



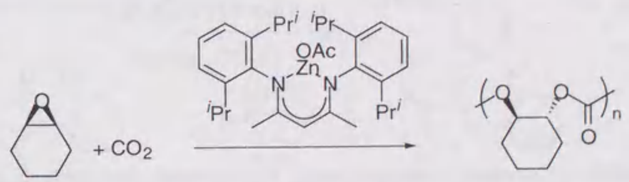
Direct Coupling of Anilines with Arylleads

Over the past few years, increased interest in *ortho*-substituted anilines and their derivatives as metal ligands has led to many advances in several catalytic transformations. Aniline frameworks are often found not only in diiminopyridine,[22] diimine[23] and iminophenol[24] ligands for polymerization (Fig. 5, Scheme 10) but also in imidazolylidene[25] and dialkylaniline[26] ligands for olefin metathesis (Scheme 11).

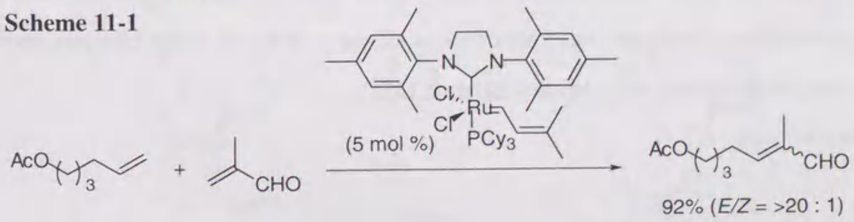
Fig. 5



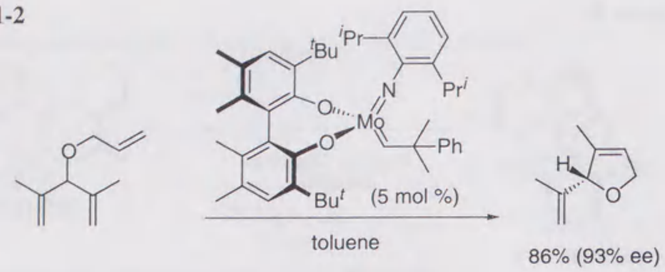
Scheme 10



Scheme 11-1

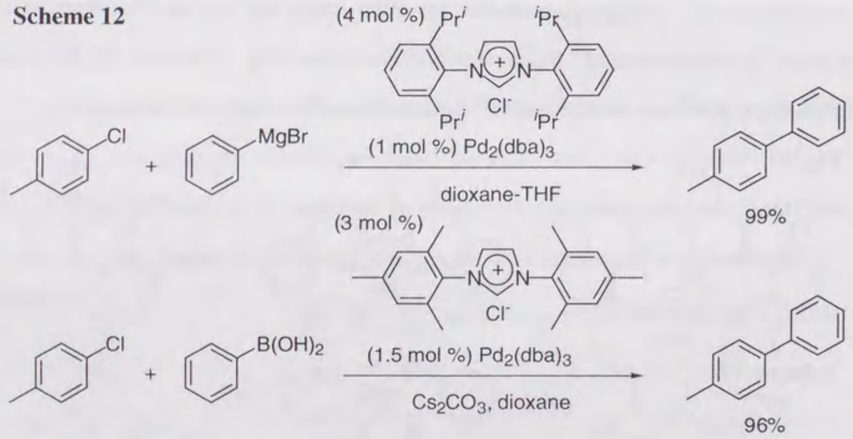


Scheme 11-2



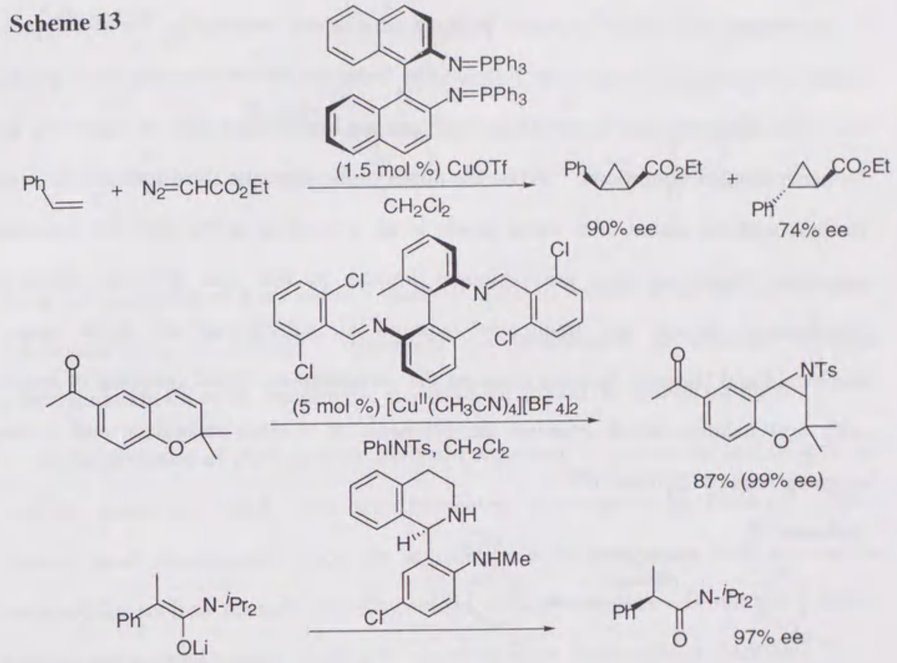
Very recently, imidazolium salts,[27] derived from anilines, have been used with several late transition metals and in highly active catalytic reactions such as Kumada-Tamao coupling and Suzuki-Miyaura coupling (Scheme 12).

Scheme 12



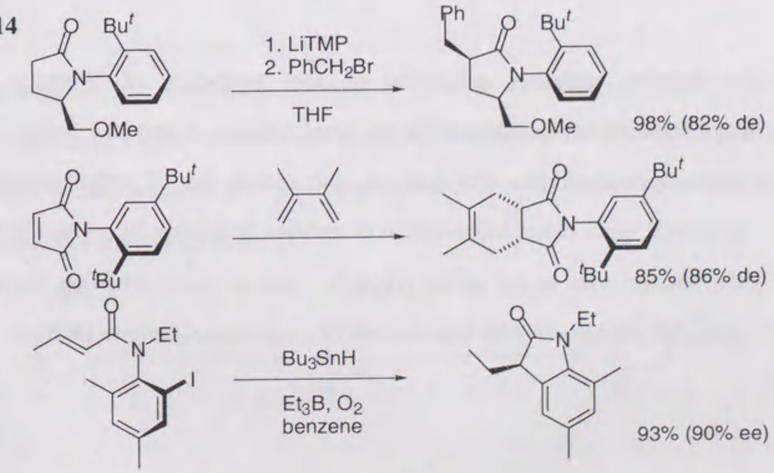
Several asymmetric reactions e.g., cyclopropanation, alkene aziridination and protonation of enolates, have also been achieved with chiral metal catalysts derived from biaryl amines with chirality (Scheme 13).[28]

Scheme 13



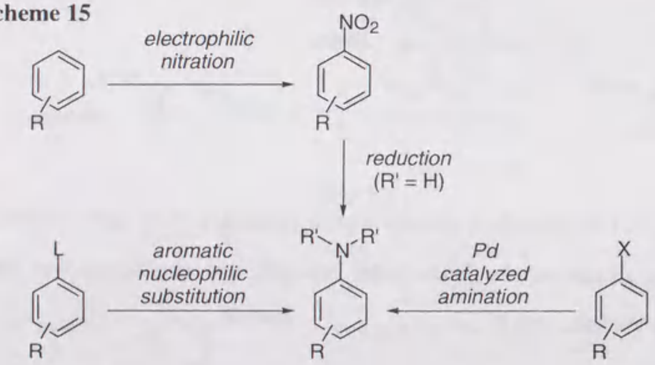
Furthermore, *N*,*N*-disubstituted anilines with a chiral axis have great potential in diastereoselective alkylation, the Diels-Alder reaction, and enantioselective radical addition reactions (Scheme 14).[29]

Scheme 14



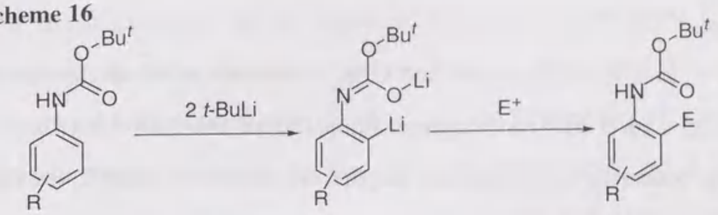
In general, substituted aromatic primary amines are prepared by the electrophilic nitration of aromatic compounds followed by reduction of the resulting nitro group.[30] However, these classical electrophilic reactions are limited by a lack of selectivity and by harsh reaction conditions. While the nucleophilic aromatic substitution of an arene nucleus with an amine or a metal amide is an alternative to the nitration-reduction sequence, these reactions are seriously limited in that one or more electron-withdrawing groups are frequently required as substituents on arene rings.[31] Buchwald and Hartwig recently reported the palladium-catalyzed coupling of amines with aryl halides, which enabled the synthesis of various secondary and tertiary aromatic amines (Scheme 15).[32]

Scheme 15



Despite numerous examples of the amination of aromatic compounds, regioselective functionalization at the arene nucleus of aromatic amines has remained relatively unexplored. For instance, the preparation of *ortho*-haloaniline is often nontrivial, since direct halogenation of anilines frequently takes place preferentially at the position para to the amino group.[33] Directed *ortho*-lithiation has emerged as a powerful technique for the construction of *o*-substituted anilines (Scheme 16).[34]

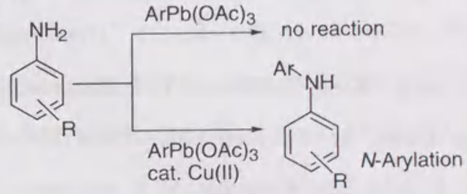
Scheme 16



With the exception of such indirect methods, little is known about the direct *ortho*-functionalization of anilines,[35] especially the introduction of a bulky aromatic substituent to build up an asymmetric environment around the aniline nitrogen.[36]

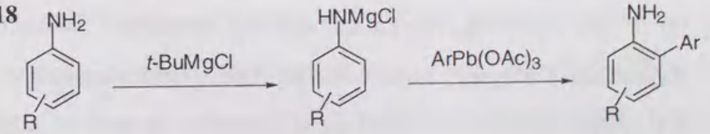
Ortho-arylation of phenols with aryllead compounds is a powerful tool in aryl-aryl coupling reactions, which have been intensively investigated by Pinhey.[19] These aromatic lead compounds, which are aryl cation equivalent, react with soft carbon nucleophiles such as phenols and the enolates of β-dicarbonyls. In marked contrast, anilines and anilides undergo neither *C*- nor *N*-arylation with aryllead triacetates.[37]

Scheme 17



Barton later exploited the $Cu(OAc)_2$-catalyzed *N*-arylation of anilines using aryllead triacetates, which gave various diphenylamines but did not lead to *C*-arylation (Scheme 17).[38] Chapter 4 deals with the aryl-aryl coupling reaction with aryllead triacetate at the *ortho*-position of anilines (Scheme 18).[39]

Scheme 18



References

(1) G. A. Olah, R. Krishnamurti, and G. K. S. Prakash in 'Comprehensive Organic Synthesis' ed. B. M. Trost, Pergamon Press, Oxford, vol. 3, ch. 1.8. (1991).

(2) B. B. Snider in 'Comprehensive Organic Synthesis' ed. B. M. Trost, Pergamon Press, Oxford, vol. 5, ch. 1.1. (1991).

(3) W. Oppolzer in 'Comprehensive Organic Synthesis' ed. B. M. Trost, Pergamon Press, Oxford, vol. 5, ch. 4.1. (1991).

(4) T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, **96**, 7503 (1974) ; T. Mukaiyama, *Angew. Chem. Int. Ed. Engl.*, **16**, 817 (1977).

(5) (a) K. Maruoka, H. Imoto, S. Saito, and H. Yamamoto, *J. Am. Chem. Soc.*, **116**, 4131 (1994). (b) K. Maruoka, H. Imoto, and H. Yamamoto, *J. Am. Chem. Soc.*, **116**, 12115 (1994). (c) K. Maruoka, S. Saito, and H. Yamamoto, *J. Am. Chem. Soc.*, **117**, 1165 (1995). (d) K. Maruoka, M. Ito, and H. Yamamoto, *J. Am. Chem. Soc.*, **117**, 9091 (1995). (e) S. Saito, M. Ito, and H. Yamamoto, *J. Am. Chem. Soc.*, **119**, 611 (1997).

(6) D. A. Evans, M. R. Wood, W. Trotter, T. I. Richardson, J. C. Barrow, and J. L. Katz, *Angew. Chem. Int. Ed. Engl.*, **37**, 2700 (1998). (b) K. C. Nicolaou, S. Natarajan, H. Li, N. F. Jain, R. Hughes, M. E. Solomon, J. M. Ramanjulu, C. N. C. Boddy, and M. Takayanagi, *Angew. Chem. Int. Ed. Engl.*, **37**, 2708 (1998). (c) A. I. Meyers, and J. J. Willemsen, *Chem. Commun.*, 1673 (1997). (d) P. Chau, I. R. Czuba, M. A. Rizzacasa, G. Bringmann, K.-P. Gulden, and M. Schäffer, *J. Org. Chem.* **61**, 7101 (1996). (e) K. Tomioka, T. Ishiguro, and K. Koga, *Tetrahedron Lett.*, **21**, 2973 (1980).

(7) (a) E. N. Jacobsen, A. Pfaltz, and H. Yamamoto Eds., "Comprehensive Asymmetric Catalysis," Springer-Verlag, Berlin Heidelderg (1999). (b) R. Noyori Ed., "Asymmetric Catalysis in Organic Synthesis," John Wiley & Sons, New York (1994).

(8) For recent examples: (a) T. Takata, Y. Furusho, K. Murakawa, T. Endo, H. Matsuoka, T. Hirasa, J. Matsuo, and M. Sisido, *J. Am. Chem. Soc.*, **120**, 4530 (1998), and references cited therein. (b) K. Nozaki, T. Terakawa, H. Takaya, and T. Hiyama, *Angew. Chem. Int. Ed. Engl.*, **37**, 131 (1998). (c) Y. Ito, T. Miyake, R. Ghima, T. Ohara, and M. Suginome, *J. Am. Chem. Soc.*, **120**, 11880 (1998).

(9) (a) K. Tamao, K. Sumitani, Y. Kiso, N. Zembayashi, A. Fujioka, S. Kodama, I. Nakajima, A. Minato, and M. Kumada, *Bull. Chem. Soc. Jpn.*, **49**, 1958 (1976). (b) J. K. Stille, *Angew. Chem. Int. Ed. Engl.*, **25**, 508 (1986).

(10) (a) P. Knochel, R. Singer, *Chem. Rev.*, **93**, 2117 (1993). (b) A. Miyaura and A. Suzuki, *Chem. Rev.*, **95**, 2457 (1995). For recent advances in this field, see: (c) D. W. Old, J. P. Wolfe, and S. L. Buchwald, *J. Am. Chem. Soc.*, **120**, 9722 (1998). (d) A. F. Littke and G. C. Fu, *Angew. Chem. Int. Ed. Engl.*, **37**, 3387 (1998).

(11) For recent reviews, see: (a) G. Bringmann, M. Breuning, and S. Tasler, *Synthesis*, 525 (1999). (b) G. Bringmann, R. Walter, and R. Weirich, "Methods of Organic Chemistry (Houben Weyl)," 4th ed., eds. G. Helmchen, R. W. Hoffmann, J. Mulzer, and E. Schaumann, Thieme, Stuttgart (1995), Vol. E21a, p 567. (c) G. Bringmann, R. Walter, and R. Weirich, *Angew. Chem. Int. Ed. Engl.*, **29**, 977 (1990).

(12) (a) S. Miyano, H. Fukushima, S. Hanada, H. Ito, and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, **61**, 3249 (1988). (b) B. H. Lipshutz, F. Kayser, and Z.-P. Liu, *Angew. Chem. Int. Ed. Engl.*, **33**, 1842 (1994). (c) T. Sugimura, H. Yamada, S. Inoue, and A. Tai, *Tetrahedron: Asymmetry*, **8**, 649 (1997). (d) G.-Q. Lin and M. Zhong, *Tetrahedron: Asymmetry*, **8**, 1369 (1997).

(13) (a) K. Tomioka, T. Ishiguro, Y. Iitaka, and K. Koga, *Tetrahedron*, **40**, 1303 (1984). (b) K. S. Feldman, and R. S. Smith, *J. Org. Chem.*, **61**, 2606 (1996). (c) M. Arisawa, S. Utsumi, M. Nakajima, N. G. Ramesh, H. Tohma, and Y. Kita, *Chem. Commun.*, 469 (1999). (d) B. Feringa and H. Wynberg, *J. Org. Chem.*, **46**, 2547

(1981). (e) J. Brussee and A. C. A. Jansen, *Tetrahedron Lett.*, **24**, 3261 (1983). (f) K. Yamamoto, H. Fukushima, and M. Nakazaki, *Chem. Commun.*, 1490 (1984). (g) T. Osa, Y. Kashiwagi, Y. Yanagisawa, and M. Bobbitt, *Chem. Commun.*, 2535 (1994). (h) M. Smrcina, J. Poláková, S. Vyskocil, and P. Kocovsky, *J. Org. Chem.*, **58**, 4534 (1993). (i) M. Nakajima, I. Miyoshi, K. Kanayama, S. Hashimoto, M. Noji, and K. Koga, *J. Org. Chem.*, **64**, 2264 (1999). (j) R. Irie, K. Masutani, and T. Katsuki, *Synlett*, 1433 (2000).

(14) (a) M. Reuman and A. I. Meyers, *Tetrahedron*, **41**, 837 (1985). (b) T. G. Gant and A. I. Meyers, *Tetrahedron*, **50**, 2297 (1994). (c) A. I. Meyers and K. A. Lutomski, *J. Am. Chem. Soc.*, **104**, 879 (1982). (d) A. I. Meyers and R. J. Himmelsbach, *J. Am. Chem. Soc.*, **107**, 682 (1985). (e) J. M. Wilson and D. J. Cram, *J. Am. Chem. Soc.*, **104**, 881 (1982). (f) T. Hattori, H. Hotta, T. Suzuki, and S. Miyano, *Bull. Chem. Soc. Jpn.*, **66**, 613 (1993). (g) T. Hattori, N. Koike, and S. Miyano, *J. Chem. Soc. Perkin Trans. 1*, 2273 (1994). (h) R. W. Baker, G. R. Pocock, and M. V. Sargent, *Chem. Commun.*, 1489 (1993). (i) R. W. Baker, G. R. Pocock, M. V. Sargent, and E. Twiss, *Tetrahedron: Asymmetry*, **4**, 2423 (1993).

(15) (a) T. Hayashi, K. Hayashizaki, T. Kiyoi, and Y. Ito, *J. Am. Chem. Soc.*, **110**, 8153 (1988). (b) T. Hayashi, K. Hayashizaki, and Y. Ito, *Tetrahedron Lett.*, **30**, 215 (1989). (c) J. Yin and S. L. Buchwald, *J. Am. Chem. Soc.*, **122**, 12051 (2000). (d) A. N. Cammidge and V. L. Crépy, *Chem. Commun.*, 1723 (2000). (e) M. Uemura and K. Kamikawa, *Synlett*, 938 (2000). (f) K. Kamikawa, T. Watanabe, and M. Uemura, *J. Org. Chem.*, **61**, 1375 (1996). (g) S. G. Nelson and M. A. Hilfiker, *Org. Lett.*, **1**, 1379 (1999).

(16) (a) S. Miyano, K. Kawahara, Y. Inoue, and H. Hashimoto, *Chem. Lett.*, 355 (1987). (b) Y. Tamai, T. Nakano, S. Koike, K. Kawahara, and S. Miyano, *Chem. Lett.*, 1135 (1989).

(17) (a) T. Konegawa, T. Nakamura, T. Matsumoto, and K. Suzuki, 76th National Meeting of the Chemical Society of Japan (1999). (b) T. Hayashi, S. Niizuma, T. Kamikawa, N. Suzuki, and Y. Uozumi, *J. Am. Chem. Soc.*, **117**, 9101 (1995).

(18) D. H. R. Barton, D. M. X. Donnelly, P. J. Guiry, and J.-P. Finet, *J. Chem. Soc. Perkin Trans. 1*, 2921 (1994).

(19) (a) H. C. Bell, J. T. Pinhey, and S. Sternhell, *Aust. J. Chem.*, **32**, 1551 (1979). (b) J. T. Pinhey, *Aust. J. Chem.*, **44**, 1353 (1991). (c) J. T. Pinhey, *Pure Appl. Chem.*, **68**, 819 (1996).

(20) (a) S. Saito, K. Hatanaka, T. Kano, and H. Yamamoto, *Angew. Chem. Int. Ed. Engl.*, **37**, 3378 (1998). (b) S. Saito, K. Hatanaka, and H. Yamamoto, *Org. Lett.*, **2**, 1891 (2000). For preliminary preparation of 3a-b, see: (c) S. Saito, T. Kano, K. Hatanaka, and H. Yamamoto, *J. Org. Chem.*, **62**, 5651 (1997).

(21) S. Saito, T. Kano, H. Muto, M. Nakadai, and H. Yamamoto, *J. Am. Chem. Soc.*, **121**, 8943 (1999).

(22) (a) B. L. Small, M. Brookhart, and A. M. A. Bennett, *J. Am. Chem. Soc.*, **120**, 4049 (1998). (b) B. L. Small and M. Brookhart, *J. Am. Chem. Soc.*, **120**, 7143 (1998). c) G. J. P. Britovsek, V. C. Gibson, B. S. Kimberley, P. J. Maddox, S. J. McTavish, G. A. Solan, A. J. P. White, and D. J. Williams, *Chem. Commun.*, 849 (1998)

(23) Polyolefin: (a) L. K. Johnson, C. M. Killian, M., and M. Brookhart, *J. Am. Chem. Soc.*, **117**, 6414 (1995). (b) L. K. Johnson, S. Mecking, and M. Brookhart, *J. Am. Chem. Soc.*, **118**, 267 (1996). (c) C. M. Killian, D. J. Tempel, L. K. Johnson, and M. Brookhart, *J. Am. Chem. Soc.*, **118**, 11664 (1996). (d) S. Mecking, L. K. Johnson, L. Wang, and M. Brookhart, *J. Am. Chem. Soc.*, **129**, 888 (1998). Polycarbonate: (e) M. Cheng, E. B. Lobkovsky, and G. W. Coates, *J. Am. Chem. Soc.*, **120**, 11018 (1998). Polyester: (f) M. Cheng, A. B. Attygalle, E. B. Lobkovsky, and G. W. Coates, *J. Am. Chem. Soc.*, **121**, 11583 (1999).

(24) T. R. Younkin, E. F. Connor, J. I. Henderson, S. K. Friedrich, R. H. Grubbs, and D. A. Bansleben, *Science*, **287**, 467 (2000).

(25) (a) M. Scholl, S. Ding, C. W. Lee, and R. H. Grubbs, *Org. Lett.*, **1**, 953 (1999). (b) A. K. Chatterjee and R. H. Grubbs, *Org. Lett.*, **1**, 1751 (1999). (c) A. K. Chatterjee, J. P. Morgan, M. Scholl, and R. H. Grubbs, *J. Am. Chem. Soc.*, **122**, 3783 (2000).

(26) (a) O. Fujimura and R. H. Grubbs, *J. Am. Chem. Soc.*, **118**, 2499 (1996) and references therein. (b) J. B. Alexander, D. S. La, D. R. Cefalo, A. H. Hoveyda, and R. R. Schrock, *J. Am. Chem. Soc.*, **120**, 4041 (1998). (c) D. S. La, J. B. Alexander, D. R. Cefalo, D. D. Graf, A. H. Hoveyda, and R. R. Schrock, *J. Am. Chem. Soc.*, **120**, 9720 (1998). (d) S. S. Zhu, D. R. Cefalo, D. S. La, J. Y. Jamieson, W. M. Davis, A. H. Hoveyda, and R. R. Schrock, *J. Am. Chem. Soc.*, **121**, 8251 (1999). (e) D. S. La, J. G. Ford, E. S. Sattely, P. J. Bonitatebus, R. R. Schrock, and A. H. Hoveyda, *J. Am. Chem. Soc.*, **121**, 11603 (1999). (f) G. S. Weatherhead, J. G. Ford, E. J. Alexanian, R. R. Schrock, and A. H. Hoveyda, *J. Am. Chem. Soc.*, **122**, 1828 (2000).

(27) Kumada coupling: (a) J. Huang and S. P. Nolan, *J. Am. Chem. Soc.*, **121**, 9889 (1999). (b) V. P. W. Böhm, T. Weskamp, C. W. K. Gstöttmayr, and W. A. Herrmann, *Angew. Chem. Int. Ed. Engl.*, **39**, 1602 (2000). Suzuki coupling: (c) C. Zhang, J. Huang, M. L. Trudell, and S. P. Nolan, *J. Org. Chem.*, **64**, 3804 (1999).

(28) (a) M. T. Reetz, E. Bohres, and R. Goddard, *Chem. Commun.*, 935 (1998). (b) C. J. Sanders, K. M. Gillespie, D. Bell, and P. Scott, *J. Am. Chem. Soc.*, **122**, 7132 (2000). (c) E. Vedejs, A. W. Kruger, N. Lee, S. T. Sakata, M. Stec, and E. Suna, *J. Am. Chem. Soc.*, **122**, 4602 (2000) and references therein.

(29) (a) M. Fujita, O. Kitagawa, Y. Yamada, H. Izawa, H. Hasegawa, and T. Taguchi, *J. Org. Chem.*, **65**, 1108 (2000). (b) D. P. Curran, H. Qi, S. J. Geib, and N. C. DeMello, *J. Am. Chem. Soc.*, **116**, 3131 (1994). (c) D. P. Curran, W. Liu, and C. H.-T. Chen, *J. Am. Chem. Soc.*, **121**, 11012 (1999). (d) K. Kondo, H. Fujita, T. Suzuki, and Y. Murakami, *Tetrahedron Lett.*, **40**, 5577 (1999). (e) T. Bach, J. Schröder, and K. Harms, *Tetrahedron Lett.*, **40**, 9003 (1999). (f) A. D. Hughes and

N. S. Simpkins, *Synlett*, 967 (1998). (g) C. R. A. Godfrey, N. S. Simpkins, and D. Walker, *Synlett*, 388 (2000).

(30) J. March, "Advanced Organic Chemistry," Wiley, New York (1992), p. 1216.

(31) Review: A. J. Belfield, G. R. Brown, A. J. Foubister, *Tetrahedron*, **55**, 11399 (1999)

(32) Review: (a) J. Hartwig, *Synlett*, 329 (1997). (b) J. Hartwig, *Angew. Chem. Int. Ed. Engl.*, **37**, 2046 (1998). (c) J. P. Wolfe, S. Wagaw, J.-F. Marcoux, and S. J. Buchwald, *Acc. Chem. Res.*, **31**, 805 (1998). (d) B. H. Yang and S. L. Buchwald, *J. Organomet. Chem.*, **576**, 125 (1999).

(33) S. Gervat, E. Léonel, J.-Y. Barraud, and V. Ratovelomanana, *Tetrahedron Lett.*, **34**, 2115 (1993) and references therein.

(34) (a) W. Fuhrer and H. W. Gschwend, *J. Org. Chem.*, **44**, 1133 (1979). (b) J. M. Muchowski and M. C. Venuti, *J. Org. Chem.*, **45**, 4798 (1980).

(35) (a) T. Sugasawa, T. Toyoda, M. Adachi, and K. Sasakura, *J. Am. Chem. Soc.*, **100**, 4842 (1978). (b) P. D. Johnson and P. A. Aristoff, *J. Org. Chem.*, **55**, 1374 (1990).

(36) (a) J. A. Aeschlimann, N. D. Lees, N. P. McCleland, and G. N. Nicklin, *J. Chem. Soc.*, **127**, 66 (1925). (b) Q.-Y. Chen and Z.-T. Li, *J. Org. Chem.*, **58**, 2599 (1993). (c) Q.-Y. Chen and Z.-T. Li, *J. Chem. Soc., Perkin Trans. 1*, 1705 (1993). (d) A. B. Pierini, M. T. Baumgartner, and R. A. Rossi, *Tetrahedron Lett.*, **28**, 4653 (1987). (e) A. B. Pierini, M. T. Baumgartner, and R. A. Rossi, *J. Org. Chem.*, **56**, 580 (1991).

(37) J. T. Pinhey, "Comprehensive Organometallic Chemistry II," ed by E. W. Abel, F. G. A. Stone, and G. Wilkinson, Pergamon, Oxford (1995), Vol. 11, p. 461.

(38) (a) D. H. R. Barton, N. Yadav–Bhanagar, J.-P. Finet, and J. Khamsi, *Tetrahedron Lett.*, 28, 3111 (1987). (b) D. H. R. Barton, D. M. X. Donnelly, J.-P. Finet, and P. J. Guiry, *J. Chem. Soc., Perkin Trans. 1*, 2095 (1991).

(39) S. Saito, T. Kano, Y. Ohyabu, and H. Yamamoto, *Synlett*, 1676 (2000).

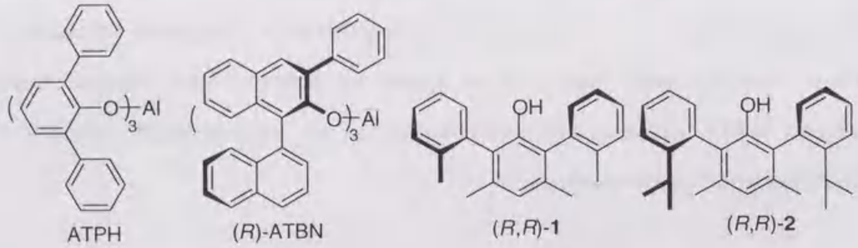
Chapter 2

New Chiral Phenol with C_2-Symmetry

Abstract: A new C_2-symmetric phenol, 3,5-dimethyl-2,6-bis(2-methylphenyl)phenol, was synthesized and the optical resolution of its racemic form was achieved using (+)-camphorsulfonyl chloride. The optical resolution of its derivative 2,6-bis(2-isopropylphenyl)-3,5-dimethylphenol was also successful in a similar manner. The absolute configuration of these phenols was determined by an X-ray crystal analysis of the corresponding (+)-(*S*)-camphorsulfonate together with CD-spectral measurement. These chiral auxiliaries were used as ligands for optically active organoaluminum reagents, which served as effective promoters of the enantioselective alkylation of aldehydes with Grignard reagents.

The desire to control the selectivity of carbon-carbon bond-forming reactions in organic synthesis has led to the design of various Lewis acid catalysts, which are required to attach the proper ligands to an acidic metal center. Various Lewis acid catalysts have been used for this purpose in our laboratory,[1] and each reagent has characteristic features due to its unique steric factors. In particular, aluminum tris(2,6-diphenylphenoxide) (ATPH)[2] has been used as a typical designer Lewis acid catalyst for regio-, chemo- and stereoselective organic reactions, and the structure of ATPH has been successfully extended to the chiral analogue aluminum tris((*R*)-1-α-naphthyl-2-naphthoxide)((*R*)-ATBN) for asymmetric Claisen rearrangement.[2c] This result encouraged us to explore the possibility of a new chiral phenol with C_2-symmetry. We report here the synthesis and optical resolution of racemic 3,5-dimethyl-2,6-bis(2-methylphenyl)phenol (*dl*-**1**) and analogous 2,6-bis(2-isopropylphenyl)-3,5-dimethylphenol (*dl*-**2**) for chiral aluminum reagents, which were found to be effective for the enantioselective alkylation of aldehydes (Figure 1).

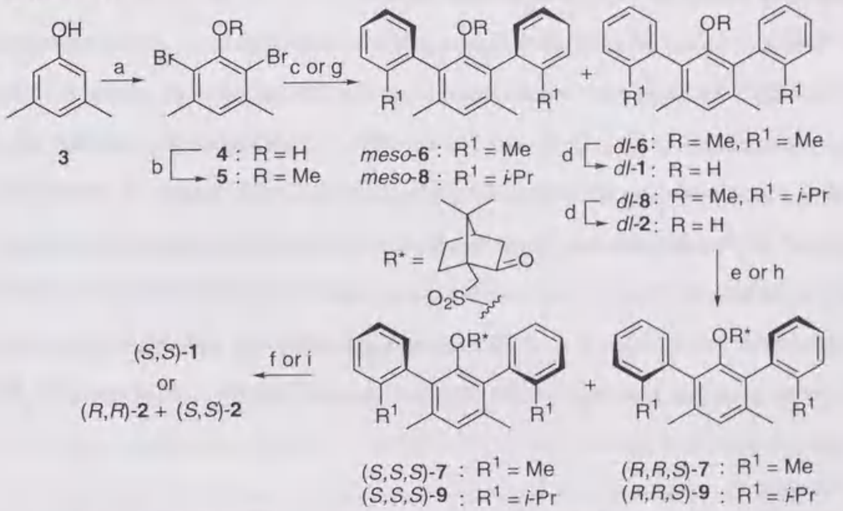
Figure 1



Optically active **1** and **2** were synthesized as follows. Regioselective dibromination of commercially available 3,5-dimethylphenol (**3**) with Br_2 in the presence of 4 equiv of *t*-$BuNH_2$, followed by methylation of **4** with MeI and K_2CO_3 in MeOH gave methyl ether **5** (68% yield from **3**). Subsequent Suzuki coupling[3] of **5** with 2-methylphenyl boronic acid [$Pd(OAc)_2$, (*o*-tolyl)P, $Ba(OH)_2$, DME-H_2O (10 : 1); reflux for 4h] gave racemic *dl*-**6** and *meso*-**6** in a ratio of 1 : 1, which was then

recrystallized from methanol to give *meso*-**6** in a yield of 45% as a colorless crystal. The filtrate, which contained a 10 : 1 mixture of *dl*- and *meso*-**6**, was purified by column chromatography on silica gel to give *dl*-**6** in a yield of 38%, which was demethylated (BBr_3, CH_2Cl_2), and the resulting *dl*-**1** was converted into camphorsulfonyl esters (*R,R,S*)-**7** and (*S,S,S*)-**7** (94%) by sequential treatment with NaH and (+)-(*S*)-camphorsulfonyl chloride. The mixture of diastereomers (*R,R,S*)-**7** and (*S,S,S*)-**7** were separated by fractional recrystallization from ether to give enantiomerically pure (*S,S,S*)-**7** (17%), which was subjected to desulfonylation (Na, naphthalene, THF; -78 °C for 30 min) to furnish (*S,S*)-**1** (>99% ee)[4] in 68% yield (Scheme 1).

Scheme 1



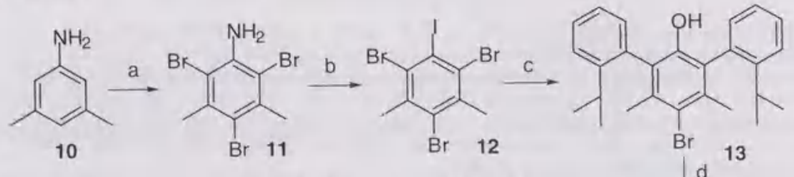
For (*S,S*)-**1**: (a) Br_2, *t*-$BuNH_2$, toluene, 0 °C, 70% (b) MeI, K_2CO_3, MeOH, reflux, 97% (c) (2-methyl)phenyl boronic acid, $Pd(OAc)_2$, (*o*-tolyl)$_3$P, $Ba(OH)_2$, DME-H_2O (10 : 1), reflux, 97% (*dl*-**6** = 38%) (d) BBr_3, CH_2Cl_2, 0 °C, 99% (e) NaH, (+)-camphorsulfonyl chloride, THF, rt, 75% ((*S,S*)-**8** = 17%) (f) Na, naphthalene, THF, -78 °C, 68%. For (*R,R*)- and (*S,S*,)-**2**: (g) (2-isopropyl)phenyl boronic acid, $Pd(OAc)_2$, (*o*-tolyl)$_3$P, $Ba(OH)_2$, DME-H_2O (10 : 1) in a sealed tube, reflux, 46% (h) *n*-BuLi, (+)-camphorsulfonyl chloride, THF, rt, 88% ((*S,S*)-**10** = 38%, (*R,R*)-**10** = 46%) (i) $LiAlH_4$, THF, 50 °C, 82%.

(*R,R*)-**1** can be obtained readily by using (-)-camphorsulfonyl chloride. The synthesis of (*R,R*)-**2** and (*S,S*)-**2** was initiated with the introduction of sterically hindered (2-isopropyl)phenyl groups to **5** by Suzuki coupling, which was carried out using a

sealed tube to give *dl*-**8** in 45% yield.[5] It should be noted that no *meso*-**8** could be detected. Sulfonylation of *dl*-**2** with *n*-BuLi and (+)-camphorsulfonyl chloride after treatment of *dl*-**8** with BBr_3 gave a diastereomixture of (*R*,*R*,*S*)-**9** and (*S*,*S*,*S*)-**9**, which were separated by silica gel column chromatography to furnish (*R*,*R*,*S*)-**9** in 46% yield together with a slightly impure (*S*,*S*,*S*)-**9**, which was recrystallized from EtOAc to give enantiomerically pure (*S*,*S*,*S*)-**9** in 38% yield. Subsequent reduction of (*R*,*R*,*S*)-**9** or (*S*,*S*,*S*)-**9** with $LiAlH_4$ in THF at reflux gave rise to (*R*,*R*)-**2** or (*S*,*S*)-**2** in 82% yield. The absolute configuration of (*S*,*S*)-**2** was rigorously established by X-ray crystal analysis of (*S*,*S*,*S*)-**9**,[6] and those of (*R*,*R*)-**2**, (*R*,*R*)-**1** and (*S*,*S*)-**1** could be assigned by correlating among the CD-spectra of these phenols.[6]

Scheme 2 shows an alternative approach to this type of phenol. Tribromination of aniline **10**, followed by diazotization and iodination[7] of **11** with KI gave tribromoiodobenzene **12** in an overall yield of 88%. The successive generation of two different benzynes from **12** was promoted by treatment with 2 equiv of the Grignard reagent,[8] and transmetallation of the resulting 2,6-diarylphenyl magnesium species to BH_3 was followed by hydrolysis with H_2O_2-*aq*. NaOH[9] to give bromophenol **13** in 42% yield in a *dl* : *meso* ratio of ca. 2 : 1. Subsequent reduction with Bu_3SnH proceeded smoothly to give *dl*-**2** and *meso*-**2** (66 : 34) in 70% yield (overall yield of *dl*-**2** from **10** = 17%).

Scheme 2

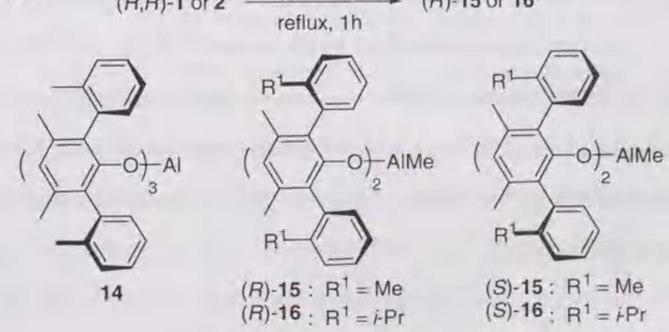


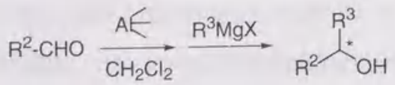
(a) Br_2, CCl_4, CH_2Cl_2, 0 °C, 90% (b) (i) $NaNO_2$, H_2SO_4-AcOH, 0 °C (ii) KI, 80 °C, 98% (c) (i) (2-isopropylphenyl)-magnesium iodide, THF, rt (ii) BH_3, rt (iii) H_2O_2, NaOH, rt, 42% (d) Bu_3SnH, 140 °C, 70%

Neither the reaction of (*R*,*R*)-**1** with Me_3Al in CH_2Cl_2 or toluene upon reflux gave

aluminum trisphenoxide **14**, but resulted in the formation of aluminum bisphenoxide methylaluminum bis((*R*,*R*)-3,5-dimethyl-2,6-bis(2-methylphenyl)phenoxide) [(*R*)-**15**], which was rigorously confirmed by ^{1}H-NMR measurement.[10] A similar trend was also observed with sterically more-hindered (*R*,*R*)-**2** upon reaction with Me_3Al to produce methylaluminum bis((*R*,*R*)-2,6-bis(2-isopropylphenyl)-3,5-dimethylphenoxide) [(*R*)-**16**] as a sole product (Scheme 3).[10] To determine the potential of chiral phenols **1** and **2**, asymmetric alkylation of aldehydes[11] was demonstrated by the combined use of Grignard reagents and the optically active aluminum reagents **15** and **16** (Equation 1), and the results are summarized in Table 1. This reaction had several characteristic features: (1) Asymmetric induction of aliphatic aldehydes was most highly promoted by using 3 equiv of **15**, i.e. the % ee decreased with less **15** (<3 equiv) or with 3 equiv of **16**. In contrast, reagent **16** was more efficient for conjugated aldehydes such as benzaldehyde or cinnamaldehyde (**17**). Vinylation of **17** gave allylic alcohols **24** and **25** with low to moderate selectivities. (2) The choice of the solvent for Grignard reagents is crucial for obtaining higher % ee. For instance, alkylation of **17** complexed with (*R*)-**16** with a THF solution of vinylmagnesium bromide gave alcohol **25** with 42% ee, whereas replacing THF with diglyme gave **25** with 6% ee. (3) The alkylation of aliphatic aldehydes and (*E*)-2-hexenal with (*S*)-**15** or (*S*)-**16** proceeded favorably from the *si* face of the carbonyl plane, while the *re* face was preferred with benzaldehyde and **17**. The origin of this face-reversibility is now under investigation in our laboratory.[12]

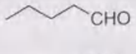
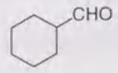
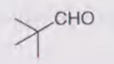
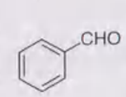
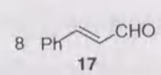
Scheme 3



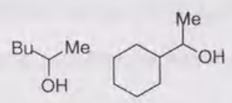


(1)

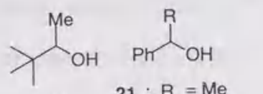
Table 1. Asymmetric alkylation of aldehydes with Grignard reagents in the presence of the optically active **15** or **16** [a]

entry	aldehyde	aluminum reagent (equiv)	Grignard reagent (equiv, solvent)	alcohol	yield [b] %	ee [c] % absolute config [d] (rotation)
1		(*S*)-**15** (3.0)	MeMgI (3.0, ether)	**18**	99	52 [f] *S* (+)
2		(*S*)-**15** (3.0)	MeMgI (3.0, ether)	**19**	99	84 [f] *S* (+)
3		(*S*)-**15** (3.0)	MeMgI (3.0, ether)	**20**	90 [e]	86 [f] *S* (+)
4		(*S*)-**15** (1.2)	MeMgBr (2.0, ether)	**21**	83	42 *R* (+)
5		(*R*)-**16** (1.2)	MeMgBr (2.0, ether)	**21**	61	65 *S* (-)
6		(*R*)-**16** (1.2)	BuMgCl (2.0, ether)	**22**	99	73 *S* (-)
7		(*R*)-**16** (1.2)	BuMgCl (2.0,THF)	**22**	90	75 *S* (-)
8	 **17**	(*R*)-**16** (2.0)	BuMgCl (2.0, ether)	**23**	86	83 *S*(+)
9		(*R*)-**16** (1.2)	 (2.0, THF)	**24**	95	80 [g] (-) [h]
10		(*R*)-**16** (1.2)	 (2.0, THF)	**25**	82	42 [g] *S* (+)
11		(*S*)-**16** (1.2)	BuMgBr (2.0, ether)	**26**	99	82 [f] *S* (+)

[a] Unless otherwise specified, the reactions were carried out using **15** or **16**, an aldehyde, and a Grignard reagent in CH_2Cl_2 at -78 °C for 30 min-2 h under the conditions as indicated in Table 1. [b] Isolated yields. [c] Determined by chiral HPLC (column: OB-H) analysis. [d] Determined by comparison of reported optical rotation. [e] GC-yield. [f] Determined by HPLC using OD-H after converting the products into phenyl carbamate (pyridine, phenyl isocyanate, room temperature.). [g] Determined by chiral HPLC (column: OD-H). [h] Absolute configuration was not determined.

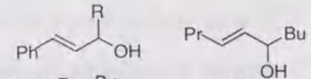


18 **19**



20

21 : R = Me
22 : = Bu



23 : R = Bu
24 : = 1-methylvinyl
25 : = vinyl

26

The present result is one of the successful applications of a Lewis acid-base complexation system to Grignard reagents that is generally useful for asymmetric alkylation of aldehydes.

Experimental Section

General Methods. All experiments were carried out under an atmosphere of dry argon. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF254 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel (E. Merck Art. 9385). Optical rotations were measured using a 3.5 mm x 0.5 dm Pyrex cell. Microanalyses were performed at the Faculty of Agriculture, Nagoya University. Phenol **3**, aniline **10**, and cinnamaldehyde (**17**) were obtained commercially. Aniline derivative **11**[14] and chiral secondary alcohols **18**,[15] **19**,[16] **20**,[15] **21**,[15] **22**,[17] **23**,[18] **25**,[19] and **26**[17] are all known compounds, and the spectral data, optical data, and analytical data of these compounds which we obtained agreed with those in the literature.

2,6-Dibromo-3,5-dimethylphenol (4). To a solution of *t*-$BuNH_2$ (84.0 mL, 800 mmol) in dry toluene (800 mL) was added Br_2 (20.6 mL, 400 mmol) at -20 °C from a dripping funnel over a period of 10 min. After the reaction mixture was cooled to -78 °C, 3,5-dimethylphenol (24.4 g, 200 mmol) in CH_2Cl_2 (80 mL) was added over 5 min. The mixture was allowed to warm to rt, and then stirred for 20 h. The reaction was quenched with 1M HCl, and the resulting mixture was extracted with Et_2O. The organic layer was dried over $MgSO_4$, and concentrated. The residue was recrystallized from Et_2O-hexane at rt to yield the product (33.9 g, yield 61%). **4**: IR (KBr) 3457, 1294, 1239, 1194, 1058 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.75 (s, 1H), 5.96 (s, 1H), 2.33 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.0, 137.4, 123.9, 109.3, 22.8; Anal. Calcd for $C_8H_8OBr_2$: C, 34.32; H, 2.88. Found: C, 34.21; H, 2.88.

2,6-Dibromo-3,5-dimethylanisole (5). A 200-mL, round-bottomed flask was charged with **4** (3.23 g, 11.5 mmol), MeOH (50 mL), and K_2CO_3 (4.77 g, 34.5 mmol). To this suspension was added MeI (2.15 mL, 34.5 mmol), and the reaction mixture was heated at reflux for 2 h, followed by the addition of MeI (2.15 mL, 34.5 mmol). After stirring during reflux for 10 h, the reaction mixture was cooled to rt, poured into aq.

NH_4Cl, and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated at reduced pressure using a rotary evaporator. The residue was purified by column chromatography on silica gel (Et_2O/hexane = 1/50 as the eluent) to give colorless solids (3.28 g, yield 97%). **5**: IR (KBr) 1456, 1437, 1312, 1075 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.93 (s, 1H), 3.86 (s, 3H), 2.33 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.9, 138.0, 127.8, 117.5, 60.1, 22.9; Anal. Calcd for $C_9H_{10}OBr_2$: C, 36.77; H, 3.43. Found: C, 36.77; H, 3.43.

***meso*- and *dl*-3,5-Dimethyl-2,6-bis(2-methylphenyl)anisole (*meso*- and *dl*-6).** A 300-mL, three-necked flask, equipped with a magnetic stirring bar, reflux condenser, and a rubber septum, was charged with tris(*o*-tolyl)phosphine (1.83 g, 6.0 mmol), $Pd(OAc)_2$ (673 mg, 3.0 mmol), *o*-tolylboronic acid (12.2 g, 90.0 mmol), $Ba(OH)_2•8H_2O$ (28.4 g, 90.0 mmol), methyl ether **5** (8.70 g, 29.6 mmol), DME (120 mL), and H_2O (24.0 mL). The mixture was degassed at reduced pressure *in vacuo* at -20 °C for ca. 20 min, and then heated at reflux for 3 h. After cooling at rt, the mixture was poured into aq. NH_4Cl and extracted with Et_2O. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (Et_2O/hexane = 1/200 to 1/10 as the eluent) to give a mixture of the diastereomers (8.80 g, yield 94%) as colorless solids. Recrystallization of the isomeric phenols from MeOH gave *meso*-**6** (4.2 g, yield 45%) as a colorless crystal after filtration and rinsing the cake with MeOH. The filtrate which included a 1 :10 (*meso*/*dl*) mixture of **6** was concentrated, and the residue was purified by column chromatography on silica gel (benzene/hexane = 1/25 as the eluent) to give *dl*-**6** (3.60 g, yield 38%) as colorless solids. *meso*-**6**: IR (KBr) 1454, 1393, 1308, 1287, 1271, 1073 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.29-7.18 (m, 8H), 7.01 (s, 1H), 3.01 (s, 3H), 2.08 (s, 6H), 2.02 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.0, 137.6, 136.8, 136.4, 132.6, 129.8, 129.7, 127.0 (two overlapped signals), 125.3, 60.4, 20.0, 19.8; Anal. Calcd for $C_{23}H_{24}O$: C, 87.30; H, 7.64. Found: C, 87.29; H, 7.75. *dl*-**6**: IR (KBr) 1453, 1393, 1285, 1269,

1111, 1075 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.28-7.13 (m, 8H), 6.98 (s, 1H), 2.96 (s, 3H), 2.14 (s, 6H), 2.00 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.8, 137.6, 136.4, 136.3, 132.5, 130.0, 129.7, 127.0, 126.7, 125.4, 59.7, 19.9, 19.7; Anal. Calcd for $C_{23}H_{24}O$: C, 87.30; H, 7.64. Found: C, 87.32; H, 7.71.

***dl*-3,5-Dimethyl-2,6-bis(2-methylphenyl)phenol (*dl*-1).** To a solution of *dl*-**6** (1.00 g, 3.16 mmol) in CH_2Cl_2 (13.0 mL) was added an excess of BBr_3 dropwise at 0 °C under argon, and the reaction mixture was stirred at 0 °C for 30 min. H_2O was added slowly and cautiously at the same temperature, followed by dropwise addition of aq. $NaHCO_3$ over a few minutes, during which time gas evolved vigorously. After the evolution of gas was complete, the mixture was extracted with CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (Et_2O/hexane = 1/9 as the eluent) to give colorless solids (944 mg, yield 99%). ^1H-NMR, ^{13}C-NMR, and elemental analysis data of *dl*-**1** were consistent with those of (+)-(*S*,*S*)-**1**. The Chiral HPLC analytical data (column: OD-H) of *dl*-**1**: retention times: t_R = 10.8 min for (*S*,*S*)-**1** and t_R = 13.8 min for (*R*,*R*)-**1** using *i*-PrOH/hexane (1/100) as the eluent at a flow rate of 0.5 mL/min.

(*S*,*S*)-3,5-Dimethyl-2,6-bis(2-methylphenyl)phenyl (+)-(*S*)-camphor-10-sulfonate [(*S*,*S*,*S*)-7]. To a suspension of NaH (60% in oil; 322 mg, 13.4 mmol) in THF (100 mL) was added *dl*-**1** (4.06 g, 13.4 mmol) portionwise at 0 °C, and the reaction mixture was stirred at rt under argon for 30 min. To the resulting solution was added (+)-camphor-10-sulfonyl chloride (3.36 g, 13.4 mmol) in one portion, and the mixture was stirred for 2 h at rt. After the mixture was cooled to 0 °C, H_2O was added, and the resulting mixture was poured into aq. NH_4Cl, extracted with Et_2O, dried, and concentrated. The residue was purified by column chromatography on silica gel (Et_2O/hexane = 1/4) to give (*S*,*S*,*S*)-**7** and (*R*,*R*,*S*)-**7** as colorless solids (5.17 g, yield 75%). Recrystallization of the diastereomixture **7** from Et_2O at rt with slow evaporation of the solvent gave one diastereomer (*S*,*S*,*S*)-**7** (1.17 g, yield 17%, based on

dl-**1**). HPLC analytical data (column: Finepak SIL) of (*R,R,S*)-**7** and (*S,S,S*)-**7**: t_R = 19.8 min for (*R,R,S*)-**7** and t_R = 20.7 min for (*S,S,S*)-**7** using EtOAc/hexane (1/10) as the eluent at a flow rate of 1.0 mL/min. (*S,S,S*)-**7**: IR (KBr) 1750, 1456, 1395, 1368, 1250, 1173, 1024 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.27-7.19 (m, 8H), 7.16 (s, 1H), 2.60 (d, 1H, *J* = 14.9 Hz), 2.27-1.71 (m, 5H), 2.16 (s, 6H), 2.05 (s, 6H), 1.67 (d, 1H, *J* = 14.9 Hz), 1.42-1.19 (m, 2H), 0.86 (s, 3H), 0.58 (s. 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 213.3, 145.8, 137.0, 136.9, 136.2, 133.2, 130.8, 130.0 (two overlapped signals), 127.9, 125.7, 57.6, 48.4, 47.6, 42.8, 42.3, 26.6, 25.0, 19.9, 19.7, 19.5 (two overlapped signals); Anal. Calcd for $C_{32}H_{36}O_4S$: C, 74.39; H, 7.02. Found: C, 74.40; H,7.20; $[\alpha]^{25}_D$ = +19.6° (*c* 1.00, $CHCl_3$).

(+)-(*S,S*)-3,5-Dimethyl-2,6-bis(2-methylphenyl)phenol [(+)-(*S,S*)-1]. An oven-dried, 25-mL, Schlenk tube was charged with naphthalene (497 mg, 3.88 mmol) and THF (5 mL). To this mixture was added small pieces of sodium (89 mg, 3.88 mmol) portionwise at rt under a gentle stream of argon, and the resulting dark purple suspension was stirred at rt for 2 h. After the mixture was cooled to -78 °C, optically active (*S,S,S*)-**7** (100 mg, 0.19 mmol) in THF (1 mL) was added, and the mixture was maintained at -78 °C with stirring for an additional 20 min. The reaction was quenched by dropwise addition of MeOH at -78 °C until the dark color disappeared. The mixture was poured into 1M HCl, extracted with Et_2O, dried over Na_2SO_4, and concentrated. The crude product was purified by column chromatography on silica gel (CH_2Cl_2/hexane = 1/2 as the eluent) to give colorless solids (40 mg, yield 68%). (+)-(*S,S*)-**1**: IR (KBr) 3497, 1449, 1402, 1291, 1233, 1152, 1049 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.30-7.16 (m, 8H), 6.82 (s, 1H), 4.42 (s, 1H), 2.12 (s, 6H), 2.00 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.4, 137.4, 135.8, 130.4, 130.3, 127.9, 126.2, 125.0, 123.1, 19.8, 19.6; Anal. Calcd for $C_{22}H_{22}O$: C, 87.38; H, 7.33. Found: C, 87.39; H, 7.61; $[\alpha]^{25}_D$ = +15.0° (*c* 1.00, $CHCl_3$).

2-Isopropyliodobenzene. The reaction was carried out as described in the

literature.[20] A 2-L, round-bottomed flask, equipped with a magnetic stirring bar, was charged with 2-isopropylaniline (84.9 mL, 600 mmol), H_2O (250 mL), and 12M HCl (250 mL, 3.0 mol). To the vigorously stirred mixture was added ice (500 g) and $NaNO_2$ (43.5 g, 630 mmol) in one portion. After 10 min, to the resulting brown mixture was added a H_2O (250 mL) solution of KI (100.3 g, 604 mmol), and the mixture was stirred at rt for 5 h, poured into H_2O (250 mL), and extracted with CH_2Cl_2. The organic layer was dried and concentrated, and the residue was filtered through a short-path column of silica gel (EtOAc/hexane = 1/100 as the eluent). Fractions were collected, concentrated, and the residual crude mixture was distilled through a 40-cm vigreux column to give 1-iodocumene (70.9 g, yield 47%) as a wine-red liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, 1H, *J* = 7.9 Hz), 7.38-7.18 (m, 2H), 6.87 (t, 1H, *J* = 7.6 Hz), 3.19 (heptet, 1H, *J* = 6.8 Hz), 1.23 (d, 6H, *J* = 6.8 Hz).

(2-Isopropylphenyl)boronic Acid. A 50-mL three-necked flask, equipped with a magnetic stirring bar, a reflux condenser and a rubber septum, was charged with magnesium (729 mg, 30.0 mmol), which was activated as usual with heat under reduced pressure, and furnished with an atmosphere of dry argon. THF (25 mL) and 1,2-dibromoethane (100 μL) were added to the flask, and to the resulting suspension was added 1-iodocumene (6.15 g, 25.0 mmol) dropwise with gentle heating. When the reaction started, heating was discontinued, and the reaction mixture was stirred as the remainder of the iodide was added dropwise at a rate such that gentle reflux was maintained. After the addition was complete, the mixture was stirred for an additional 30—60 min, and transferred *via* a steel cannula to a THF (25 mL) solution of trimethylborate (5.88 mL, 50.0 mmol) which was precooled to -78 °C under an argon atmosphere. The entire mixture was then allowed to warm to rt, and, after stirring for 1 h, was poured into 1M HCl, extracted with Et_2O, dried, and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane = 1/3 as the eluent) to give (2-isopropylphenyl)boronic acid (2.68 g, yield 65%) as colorless

solids.

***dl*-2,6-Bis(2-isopropylphenyl)-3,5-dimethylanisole (*dl*-8).** A 100-mL sealed tube equipped with a magnetic stirring bar was charged with tris(*o*-tolyl)phosphine (365 mg, 1.20 mmol), $Pd(OAc)_2$ (135 mg, 0.60 mmol), (2-isopropyl)phenylboronic acid (5.90 g, 36.0 mmol), K_3PO_4 (9.55 g, 45.0 mmol), **5** (4.4 g, 15.0 mmol), DME (60.0 mL), and H_2O (12.0 mL). The mixture was degassed at reduced pressure *in vacuo* at -20 °C for ca. 20 min, and heated at reflux for 5 h. After cooling to rt, the mixture was poured into aq. NH_4Cl and was extracted with Et_2O. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane = 1/300 to 1/50 as the eluent) to give colorless solids (yield 46%). ***dl*-8**: IR (KBr) 1605, 1306, 1283, 1084, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.39-7.10 (m, 8H), 6.96 (s, 1H), 3.00 (s, 3H), 2.79 (m, 2H), 2.02 (s, 6H), 1.17 (d, 6H, J = 6.8 Hz), 1.15 (d. 6H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.6, 147.1, 136.6, 136.4, 131.9, 130.5, 127.5, 126.3, 125.3, 125.2, 60.3, 30.0, 24.3, 23.9, 20.3; Anal. Calcd for $C_{27}H_{32}O$: C, 87.05; H, 8.66. Found: C, 87.04; H, 8.91. The procedure for demethylation of *dl*-**6** was followed except that *dl*-**8** (4.30 g, 11.6 mmol) was used to give *dl*-2,6-bis(2-isopropylphenyl)-3,5-dimethylphenol (*dl*-**2**) (3.80 g, yield 91%) as colorless solids. IR, ^1H-NMR, ^{13}C-NMR, and elemental analysis data of *dl*-**2** were consistent with those of (-)-(*R*,*R*)-**2**.

(*R*,*R*)- and (*S*,*S*)-2,6-Bis(2-isopropylphenyl)-3,5-dimethylphenyl (+)-(*S*)-camphor-10-sulfonate [(*R*,*R*,*S*)- and (*S*,*S*,*S*)-9]. To a solution of *dl*-phenol **2** (2.76 g, 7.70 mmol) in THF (50 mL) was added a 1.58 M hexane solution of *n*-BuLi (6.30 mL, 10.0 mmol) dropwise at 0 °C under an argon atmosphere. The mixture was stirred at 0 °C for 30 min, followed by the addition of (+)-(*S*)-camphor-10-sulfonyl chloride (3.86 g, 15.0 mmol) in one portion, and the resulting mixture was stirred at rt for 3 h. The reaction mixture was poured into aq. NH_4Cl and extracted with Et_2O. The organic layer was dried and concentrated. The residue was purified by column

chromatography on silica gel (EtOAc/hexane = 1/50 as the eluent) to give pure (*R*,*R*,*S*)-**9** (1.85 g, yield 42%) and a ca. 1 : 20 diastereomixture of (*R*,*R*,*S*)-**9** and (*S*,*S*,*S*)-**9** (yield 46%), which was recrystallized from EtOAc at rt to give pure (*S*,*S*,*S*)-**9** (1.68 g, yield 38%). (*R*,*R*,*S*)-**9**: IR (KBr) 1748, 1474, 1397, 1368, 1250, 1177, 1026 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.44-7.15 (m, 9H), 2.80-2.70 (m, 3H), 2.26-1.69 (m, 5H), 2.07 (s, 6H), 1.43 (d, 1H, J = 14.9 Hz), 1.37-1.12 (m, 2H), 1.26 (d, 6H, J = 6.8 Hz), 1.16 (d, 6H, J = 6.8 Hz), 0.88 (s, 3H), 0.60 (s. 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 213.4, 147.7, 146.1, 137.3, 134.7, 133.2, 130.8, 129.8, 128.3, 125.8, 125.4, 57.8, 48.6, 47.4, 42.9, 42.2, 30.2, 26.6, 25.0, 24.5, 23.8, 20.4, 19.6, 19.5; Anal. Calcd for $C_{36}H_{44}O_4S$: C, 75.49; H, 7.74. Found: C, 75.50; H, 8.07; $[\alpha]^{25}_D$ = -13.0° (*c* 1.00, $CHCl_3$). (*S*,*S*,*S*)-**9**: IR (KBr) 1748, 1474, 1395, 1372, 1250, 1173, 1026 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.42-7.15 (m, 9H), 2.74 (m, 2H), 2.24 (d, 1H, J = 14.8 Hz), 2.16-1.13 (m, 7H), 2.08 (s, 6H), 1.88 (d, 1H, J = 14.8 Hz), 1.25 (d, 6H, J = 6.8 Hz), 1.18 (d, 6H, J = 6.8 Hz), 0.80 (s, 3H), 0.58 (s. 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 213.0, 147.6, 146.5, 137.3, 134.7, 133.1, 131.1, 130.0, 128.3, 125.8, 125.5, 57.6, 48.9, 47.7, 42.9, 42.3, 30.1, 26.7, 25.2, 24.4, 24.1, 20.4, 19.6, 19.5; Anal. Calcd for $C_{36}H_{44}O_4S$: C, 75.49; H, 7.74. Found: C, 75.48; H, 8.01; $[\alpha]^{25}_D$ = +51.2° (*c* 1.00, $CHCl_3$).

(-)-(*R*,*R*)-2,6-Bis(2-isopropylphenyl)-3,5-dimethylphenol [(-)-(*R*,*R*)-2]. To a suspension of $LiAlH_4$ (53 mg, 1.40 mmol) in THF (17.5 mL) was added (*R*,*R*,*S*)-**9** (100 mg, 0.18 mmol) portionwise at rt. The mixture was immersed in an oil bath at 50 °C and maintained at this temperature for 9 h. After the reaction mixture was cooled to 0 °C, H_2O was added dropwise until no gas evolution was observed. The mixture was poured into 1M HCl, extracted with Et_2O, dried over Na_2SO_4, and concentrated. The residual crude product was purified by column chromatography on silica gel (EtOAc/hexane = 1/60 as the eluent) to give colorless solids (52 mg, yield 82%). (-)-(*R*,*R*)-**2**: IR (KBr) 3530, 1445, 1306, 1242, 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.45-7.10 (m, 8H), 6.81 (s, 1H), 4.38 (s, 1H), 2.76 (m, 2H, J = 6.9 Hz), 2.01 (s, 6H),

1.16 (d, 6H, J = 6.9 Hz), 1.11 (d, 6H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.2, 148.2, 136.1, 134.5, 130.4, 128.4, 126.2, 125.8, 124.9, 122.9, 30.2, 24.2, 23.7, 20.1; Anal. Calcd for $C_{26}H_{30}O$: C, 87.10; H, 8.43. Found: C, 87.10; H, 8.78. $[\alpha]^{25}_{D}$ = -58.1° (*c* 1.00, $CHCl_3$).

2,4,6-Tribromoiodobenzene (12). Prepared as described in the literature.[7] **12**: IR (KBr) 1375, 1337, 963 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.79 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.5, 130.4, 127.9, 110.8, 29.1; Anal. Calcd for $C_8H_6Br_3I$: C, 20.50; H, 1.29. Found: C, 20.60; H, 1.28.

***dl*- and *meso*-4-Bromo-2,6-bis(2-isopropylphenyl)-3,5-dimethylphenol (*dl*- and *meso*-13).**[8,9] To a THF solution of 2-isopropylphenylmagnesium iodide (3.5 mL, 1.5 mmol) was added **12** (236 mg, 0.5 mmol) in THF (7.0 mL) dropwise over 1h at rt under argon, and the mixture was stirred at rt for 3.5 h. The mixture was cooled to -78 °C, a 1.0 M THF solution of BH_3 (2.5 mL, 2.5 mmol) was added, and the resulting mixture was stirred at rt for 3 h. To this mixture was added sequentially a 3.0 M aqueous solution of NaOH (2.2 mL, 6.6 mmol) and 30 wt% aqueous H_2O_2 (2.2 mL, 20 mmol) at the same temperature. After 4 days of stirring, 4 g of K_2CO_3 was added. The entire mixture was then extracted twice with THF. The organic layer was dried, concentrated, and purified by column chromatography on silica gel (hexane only to EtOAc/hexane = 1/20 as the eluent) to give a mixture of *dl*- and *meso*-**13** (yield 28% and 14%, respectively). *dl*-**13:** IR (KBr) 3530, 1441, 1235, 1084 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45-7.07 (m, 8H), 4.38 (s, 1H), 2.73 (m, 2H), 2.15 (s, 6H), 1.15 (d, 6H, J = 6.9 Hz), 1.10 (d, 6H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.3, 148.0, 136.2, 134.5, 130.2, 128.7, 126.3, 126.0 (two overlapped signals), 119.4, 30.3, 24.1, 23.6, 21.9; Anal. Calcd for $C_{26}H_{29}OBr$: C, 71.39; H, 6.68. Found: C, 71.34; H, 6.59. *meso*-**13:** IR (KBr) 3528, 1445, 1283, 1232, 1157, 1057 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45-7.10 (m, 8H), 4.40 (s, 1H), 2.70 (m, 2H), 2.16 (s, 6H), 1.15 (d, 6H, J = 6.9 Hz), 1.08 (d, 6H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.3, 148.0, 136.2, 134.3,

130.2, 128.7, 126.3, 126.0, 125.5, 119.5, 30.2, 24.1, 23.7, 21.9; Anal. Calcd for $C_{26}H_{29}OBr$: C, 71.39; H, 6.68. Found: C, 71.33; H, 6.64.

Reduction of *dl*-13 and *meso*-13 with Bu_3SnH. A 2 : 1 mixture of *dl*-**13** and *meso*-**13** (39.5 mg, 0.09 mmol) in Bu_3SnH (500 μL) was heated at 140 °C for 3 h and purified by column chromatography on silica gel (hexane only to EtOAc/hexane = 1/30 as the eluent) to give *dl*-**2** and *meso*-**2** (22.6 mg, 0.063 mmol) in 70% yield in a ratio of 2 : 1. *meso*-**2:** IR (KBr) 3584, 1443, 1291, 1037 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45-7.15 (m, 8H), 6.83 (s, 1H), 4.41 (s, 1H), 2.75 (m, 2H), 2.02 (s, 6H), 1.16 (d, 6H, J = 6.9 Hz), 1.10 (d, 6H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.1, 148.1, 136.1, 134.2, 130.3, 128.4, 126.2, 125.8, 124.8, 123.0, 30.1, 24.2, 23.8, 20.1; Anal. Calcd for $C_{26}H_{30}O$: C, 87.10; H, 8.43. Found: C, 87.02; H, 8.59.

Preparation of (*R*)-15. To a toluene (4.0 mL) solution of phenol (*R,R*)-**1** (258 mg, 0.72 mmol; 2 equiv) was added a 1.0 M hexane solution of Me_3Al (0.36 mL, 0.36 mmol; 1 equiv) dropwise at 50 °C under argon with rigorous exclusion of air and moisture, and the mixture was stirred for 1 h. When CH_2Cl_2 was used as a solvent, the preparation was conducted at reflux for 1 h. (*R*)-**16** could be prepared similarly. Both the solutions of the reagents were used for the following alkylation experiments without further purification.

General Procedure for Enantioselective Alkylation of Aldehydes. To a CH_2Cl_2 (4.0 mL) solution of (*R*)-**16** (1.2 equiv) was added cinnamaldehyde (**17**) (38 μL, 0.3 mmol) at -78 °C under argon, and the mixture was stirred for ca. 10 min. To this solution was added a 1.86 M Et_2O solution of BuMgCl (0.32 mL, 0.6 mmol) dropwise at -78 °C, and the mixture was stirred for 0.5—1 h, quenched with 1 M HCl, and extracted with EtOAc. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane = 1/20 to Et_2O/hexane = 1/3 as the eluent) to give 1-phenyl-1-hepten-3-ol (**23**) (49 mg, yield 86%) as a colorless liquid.

Chiral HPLC analysis of 21—25. **21**: (column: OB-H); retention times: t_R = 13.0 min for (*R*)-**21** and t_R = 17.4 min for (*S*)-**21** using *i*-PrOH/hexane (1/9) as the eluent at a flow rate of 0.5 mL/min. **22**: (column: OB-H); retention times: t_R = 14.9 min for (*S*)-**22** and t_R = 18.0 min for (*R*)-**22** using *i*-PrOH/hexane (1/20) as the eluent at a flow rate of 0.5 mL/min. **23**: (column OB-H); retention times: t_R = 15.1 min for (*R*)-**23** and t_R = 18.2 min for (*S*)-**23** using *i*-PrOH/hexane (1/9) as eluent at a flow rate of 0.5 mL/min. **24**: (column: OD-H); retention times: t_R = 8.95 min and t_R = 12.61 min (the later peak for the major enantiomer when (*R*)-**16** was used) using *i*-PrOH/hexane (1/9) as the eluent at a flow rate of 1.0 mL/min. **25**: (column: OD-H); retention times: t_R = 10.6 min for (*R*)-**25** and t_R = 15.4 min for (*S*)-**25** using *i*-PrOH/hexane (1/9) as the eluent at a flow rate of 1.0 mL/min.

4-Methyl-1-phenyl-1,4-penten-3-ol (24): IR (neat) 3083, 3029, 1449, 1094 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.40-7.21 (m, 5H), 6.63 (d, 1H, *J* = 15.9 Hz), 6.20 (dd, 1H, *J* = 15.9, 6.6 Hz), 5.10 (s, 1H), 4.91 (s, 1H), 4.71 (d, 1H, *J* = 6.6 Hz), 1.90 (bs, 1H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.2, 136.5, 131.1, 130.2, 128.5, 127.8, 126.4, 111.2, 76.3, 18.3; Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.40; H, 8.49. $[\alpha]^{25}_D$ = -11.0° (*c* 0.94, $CHCl_3$) for an 80% ee of **24**.

Preparation of Phenyl Carbamates from Alcohols for HPLC Analysis. To a pyridine solution of an alcohol was added phenyl isocyanate at rt, and the mixture was stirred for 0.5 h. Pyridine was removed under reduced pressure (1—3 mmHg). The residue was purified by column chromatography on silica gel.

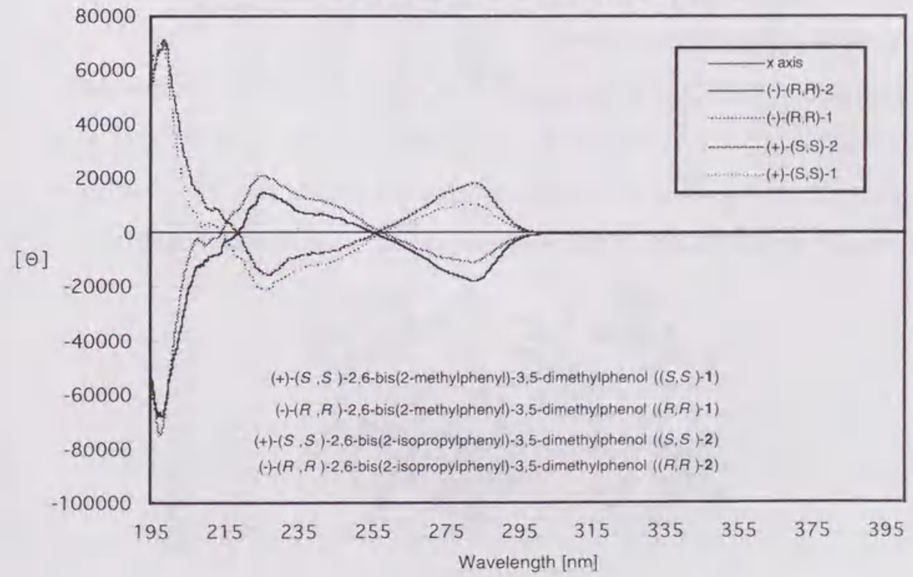
HPLC Analytical Data of Some Carbamates Using the Column OD-H. Phenyl carbamate from **18**: retention times: t_R = 16.5 min for (*S*)-**18** and t_R = 39.8 min for (*R*)-**18** using *i*-PrOH/hexane (1/9) as the eluent at a flow rate of 0.5 mL/min. Phenyl carbamate from **19**: retention times: t_R = 6.87 min for (*S*)-**19** and t_R = 14.3 min for (*E*)-**19** using *i*-PrOH/hexane (1/9) as the eluent at a flow rate of 1.0 mL/min. Phenyl carbamate from **20**: retention times: t_R = 13.7 min for (*S*)-**20** and t_R = 21.7 min for (*R*)-

20 using *i*-PrOH/hexane (1/20) as the eluent at a flow rate of 1.0 mL/min. Phenyl carbamate from **26**: retention times: t_R = 5.97 min for (*R*)-**26** and t_R = 7.65 min for (*S*)-**26** using *i*-PrOH/hexane (1/9) as the eluent at a flow rate of 0.5 mL/min.

CD Spectral Measurements. Circular dichroism (CD)-spectra were determined on a JASCO J-720WI. Solutions of (*R,R*)- and (*S,S*)-**1** and **2** in MeOH (1.2 mg/10 mL) were used for CD spectral analyses. Measurements were carried out at rt. CD curves were plotted using Microsoft Excel, version 5.0, and are attached at the end of this Supporting Information. Other measurement conditions were as follows:

Cell Length:	1.0 cm	Concentration:	0.0003968 M
Solvent:	MeOH	Temperature:	rt
Range:	400—195 nm	Band Width:	1.0 nm
Sensitivity:	50 mdeg	Resolution:	0.2 nm
Response:	2 sec	Accumulation:	3
		Speed:	50 nm/min

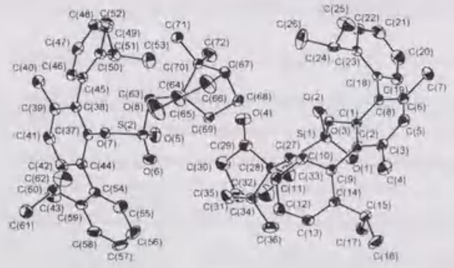
CD-spectra of (*S,S*)- and (*R,R*)-**1** and **2**



X-ray Crystallographic Determinations. A crystal of (*S,S,S*)-**9** was mounted with epoxy on the tip of a thin glass fiber. Diffraction data were obtained with graphite-monochromated Mo Kα radiation on a MAC Science DIP2020 diffractometer at 298 K. Intensity data were collected in the range $3 \leq 2\theta \leq 52.2°$ using oscillation photographs. Standard reflections for each data set showed no significant decrease in intensity throughout acquisition. All non-hydrogen atoms were located from the direct method, where the full-matrix was used for least-squares data. All non-hydrogen atoms were refined anisotropically. The hydrogens of all the methyl groups were refined from an initial idealized position (0.96 Å), and the other hydrogens were found by Fourier synthesis, using isotropic temperature factors. Crystallographic computations were performed on a Silicon Graphics INDY computer using the CRYSTAN program for data reduction, determining the structure, refining the structure, and molecular graphics. MAC DENZO software was used for cell refinement.

X-ray Crystal Analysis of (*S,S,S*)-9. Crystals of (*S,S,S*)-**9** suitable for X-ray diffraction were obtained by slow evaporation of a Et_2O solution at rt. 7254 collected reflections produced 7168 independent reflections. Crystallographic data and selected bond lengths and angles are as follows.

Crystal Data for (*S,S,S*)-9. $C_{36}H_{44}O_4S$, $Fw = 572.80$, monoclinic, space group $P2_1$, a = 15.170 (1)Å, b = 12,301 (1) Å, c = 17.964 (1) Å, β = 101.808 (2)°, V = 3281.257(1) Å^3, $Z = 4$, Dx = 1.160 Mg m^{-3}, Dm = 1.150 Mg m^{-3}, θ = 2—45°, μ = 0.1275 mm^{-1}, R_f = 4.7%, ωR = 5.7% (weighting scheme: $\omega = 1/(\sigma^2(F) + 0.001F^2)$).



FRACTIONAL ATOMIC COORDINATES & U(iso)

Atom	x/a	y/b	z/c	U(iso)
S(1)	0.37100(2)	0.19400	0.29102(2)	0.0534(2)
S(2)	0.20000(3)	0.33414(4)	0.66560(2)	0.0542(2)
O(1)	0.40377(9)	0.24060(14)	0.22984(8)	0.0810(8)
O(2)	0.42030(10)	0.10994(11)	0.33408(8)	0.0853(8)
O(3)	0.27128(7)	0.14929(8)	0.25859(5)	0.0488(4)
O(4)	0.38032(11)	0.18888(13)	0.49963(10)	0.0966(9)
O(5)	0.29165(10)	0.31547(15)	0.66690(8)	0.0892(9)
O(6)	0.15454(12)	0.41937(11)	0.62023(7)	0.0869(8)
O(7)	0.18780(6)	0.35645(8)	0.75055(5)	0.0466(4)
O(8)	-0.04290(14)	0.26648(21)	0.56646(14)	0.144(2)
C(1)	0.23177(10)	0.14209(12)	0.17994(7)	0.0475(6)
C(2)	0.17768(10)	0.22844(12)	0.14694(8)	0.0502(6)
C(3)	0.12678(11)	0.21110(15)	0.07305(8)	0.0598(8)
C(4)	0.06177(14)	0.29625(20)	0.03228(11)	0.082(1)
C(5)	0.13464(13)	0.11210(17)	0.03780(9)	0.0697(9)
C(6)	0.19060(13)	0.02992(14)	0.06997(9)	0.0643(8)
C(7)	0.19565(19)	-0.07598(19)	0.02729(12)	0.092(1)
C(8)	0.24163(11)	0.04441(13)	0.14405(8)	0.0534(7)
C(9)	0.16814(9)	0.32824(13)	0.19185(8)	0.0488(6)
C(10)	0.12393(10)	0.31515(14)	0.25266(9)	0.0575(7)
C(11)	0.11302(11)	0.40228(15)	0.29928(10)	0.0642(8)
C(12)	0.14573(12)	0.50270(15)	0.28522(11)	0.0680(9)
C(13)	0.18904(12)	0.51602(13)	0.22536(11)	0.0665(9)
C(14)	0.20117(10)	0.43057(13)	0.17750(9)	0.0533(7)
C(15)	0.25074(13)	0.45305(15)	0.11349(10)	0.0671(9)
C(16)	0.20473(19)	0.54231(23)	0.05968(14)	0.103(2)
C(17)	0.34927(15)	0.48624(20)	0.14571(14)	0.089(1)
C(18)	0.30320(11)	-0.04389(12)	0.18225(8)	0.0529(7)
C(19)	0.38606(14)	-0.05781(17)	0.16161(12)	0.077(1)
C(20)	0.44385(14)	-0.14096(20)	0.19051(15)	0.090(1)
C(21)	0.41954(14)	-0.21041(18)	0.24223(13)	0.082(1)
C(22)	0.33828(13)	-0.19705(15)	0.26421(11)	0.0685(9)
C(23)	0.27904(11)	-0.11391(12)	0.24639(9)	0.0539(7)
C(24)	0.19084(13)	-0.10118(13)	0.26222(11)	0.0671(8)
C(25)	0.11939(16)	-0.17935(23)	0.22247(20)	0.115(2)
C(26)	0.2034(2)	-0.1075(4)	0.3478(2)	0.142(3)
C(27)	0.34224(11)	0.29614(14)	0.35237(10)	0.0666(8)
C(28)	0.41787(9)	0.33270(13)	0.41753(8)	0.0523(7)
C(29)	0.41866(13)	0.27374(15)	0.49170(11)	0.0687(9)
C(30)	0.47431(17)	0.34370(21)	0.55454(12)	0.092(1)
C(31)	0.49467(17)	0.44230(20)	0.50972(13)	0.086(1)
C(32)	0.56745(16)	0.40475(27)	0.46787(18)	0.115(2)
C(33)	0.51576(12)	0.32744(22)	0.40748(13)	0.088(1)
C(34)	0.41039(13)	0.45248(13)	0.44565(10)	0.0633(8)
C(35)	0.32386(16)	0.47415(18)	0.47466(13)	0.088(1)
C(36)	0.4173(2)	0.5392(2)	0.3867(2)	0.105(2)
C(37)	0.26022(8)	0.36532(11)	0.81459(8)	0.0444(6)
C(38)	0.27597(9)	0.27697(12)	0.86363(8)	0.0470(6)

over

cont

H(17B)	0.378(3)	0.428(4)	0.177(3)	0.099(8)
H(17C)	0.3509(15)	0.5500(18)	0.1767(13)	0.14(4)
H(19)	0.4037(8)	-0.0077(11)	0.1263(7)	0.105(8)
H(20)	0.5052(18)	-0.1488(25)	0.1801(16)	0.164(7)
H(21)	0.4645(14)	-0.2610(19)	0.2685(13)	0.109(5)
H(22)	0.3137(14)	-0.2310(19)	0.3038(12)	0.13(1)
H(24)	0.1682(13)	-0.0289(17)	0.2512(11)	0.036(6)
H(25A)	0.0635(15)	-0.1713(18)	0.2491(14)	0.15(1)
H(25B)	0.1413(13)	-0.2521(15)	0.2330(10)	0.19(2)
H(25C)	0.1093(16)	-0.1667(20)	0.1687(13)	0.13(1)
H(26A)	0.1475(16)	-0.0994(23)	0.3644(14)	0.17(1)
H(26B)	0.2445(15)	-0.0517(22)	0.3704(14)	0.15(4)
H(26C)	0.22899	-0.17728	0.36344	0.17(2)
H(27A)	0.31004	0.34684	0.31537	0.107(7)
H(27B)	0.30834	0.24824	0.37967	0.14(1)
H(30A)	0.42441	0.36610	0.57624	0.11(2)
H(30B)	0.51031	0.29000	0.58564	0.14(2)
H(31)	0.51267	0.50880	0.53762	0.105(8)
H(32A)	0.61635	0.36855	0.50097	0.17(2)
H(32B)	0.59065	0.46605	0.44487	0.113(9)
H(33A)	0.51936	0.35094	0.35728	0.078(5)
H(33B)	0.53926	0.25494	0.41528	0.067(6)
H(35A)	0.31926	0.54715	0.49226	0.103(7)
H(35B)	0.32146	0.42505	0.51576	0.15(2)
H(35C)	0.27346	0.46025	0.43386	0.17(1)
H(36A)	0.41266	0.61219	0.40431	0.16(1)
H(36B)	0.37036	0.52779	0.34251	0.12(1)
H(36C)	0.47476	0.53079	0.37291	0.10(1)
H(40A)	0.39699	0.21588	1.00075	0.11(3)
H(40H)	0.37259	0.14128	0.97083	0.18(1)
H(40C)	0.29719	0.19258	1.00725	0.16(1)
H(41)	0.42508	0.39675	0.99508	0.083(6)
H(43A)	0.40217	0.64507	0.88021	0.12(2)
H(43H)	0.47707	0.57137	0.92421	0.14(3)
H(43C)	0.39787	0.60947	0.96151	0.18(3)
H(46)	0.10172	0.25070	0.85964	0.067(5)
H(47)	0.00761	0.10422	0.82147	0.071(5)
H(48)	0.06147	-0.05597	0.78559	0.087(6)
H(49)	0.22226	-0.07853	0.79652	0.081(6)
H(51)	0.38717	0.13258	0.85361	0.069(5)
H(52A)	0.45760	-0.05172	0.87954	0.101(7)
H(52H)	0.36190	-0.10502	0.85954	0.2(1)
H(52C)	0.38680	-0.03052	0.93024	0.11(1)
H(53A)	0.43799	0.03966	0.75142	0.17(1)
H(53B)	0.35519	0.11526	0.72142	0.110(9)
H(53C)	0.34209	-0.01064	0.72562	0.12(1)
H(55)	0.38947	0.53951	0.72565	0.101(8)
H(56)	0.35312	0.68037	0.63663	0.13(3)
H(57)	0.22744	0.78421	0.63143	0.107(8)
H(58)	0.12899	0.75006	0.71317	0.09(7)

over

cont

C(39)	0.33822(9)	0.29188(13)	0.93317(8)	0.0526(7)
C(40)	0.35429(12)	0.26568(18)	0.99383(10)	0.070(9)
C(41)	0.38278(10)	0.39115(15)	0.94578(9)	0.0613(8)
C(42)	0.36628(10)	0.47791(15)	0.89599(10)	0.0609(8)
C(43)	0.41347(14)	0.58507(19)	0.91511(14)	0.086(1)
C(44)	0.30247(9)	0.46361(12)	0.82742(9)	0.0505(6)
C(45)	0.22076(9)	0.17579(11)	0.84587(7)	0.0447(6)
C(46)	0.12862(10)	0.18460(13)	0.84284(8)	0.0529(7)
C(47)	0.07191(10)	0.09702(16)	0.82367(9)	0.0592(8)
C(48)	0.10677(11)	-0.00117(14)	0.80729(10)	0.0631(8)
C(49)	0.19776(12)	-0.01153(14)	0.81072(10)	0.0629(8)
C(50)	0.25729(10)	0.07598(12)	0.82983(8)	0.0511(6)
C(51)	0.35747(11)	0.05858(14)	0.83051(11)	0.0634(8)
C(52)	0.39480(16)	-0.04142(23)	0.87914(16)	0.099(1)
C(53)	0.37519(14)	0.04996(23)	0.75192(13)	0.096(1)
C(54)	0.27838(11)	0.55738(13)	0.77263(9)	0.0577(7)
C(55)	0.33587(17)	0.58171(21)	0.72375(15)	0.096(1)
C(56)	0.3156(3)	0.6659(3)	0.6723(2)	0.135(3)
C(57)	0.2387(3)	0.7282(2)	0.6708(2)	0.115(2)
C(58)	0.18369(17)	0.70616(16)	0.71988(12)	0.085(1)
C(59)	0.20163(12)	0.61926(12)	0.77193(9)	0.0596(7)
C(60)	0.13710(13)	0.59666(15)	0.82370(12)	0.072(1)
C(61)	0.1316(2)	0.6923(2)	0.8767(2)	0.112(2)
C(62)	0.04547(17)	0.56136(27)	0.77857(21)	0.121(2)
C(63)	0.11608(12)	0.21279(13)	0.64713(8)	0.0621(8)
C(64)	0.10252(10)	0.18355(12)	0.56437(7)	0.0510(6)
C(65)	0.00215(15)	0.20744(21)	0.53683(13)	0.091(1)
C(66)	-0.02850(19)	0.14088(27)	0.46528(16)	0.115(2)
C(67)	0.05497(14)	0.07831(15)	0.45975(9)	0.0695(9)
C(68)	0.1157(2)	0.1602(2)	0.4332(1)	0.107(1)
C(69)	0.14650(17)	0.23495(15)	0.50228(10)	0.081(1)
C(70)	0.10302(11)	0.06043(12)	0.54376(8)	0.0517(7)
C(71)	0.0483(2)	-0.0082(2)	0.5803(1)	0.100(1)
C(72)	0.19708(16)	0.01142(19)	0.55357(14)	0.090(1)
H(4A)	0.0271(16)	0.2844(22)	-0.0181(13)	0.15(1)
H(4H)	0.0966(16)	0.3609(22)	0.0299(15)	0.18(4)
H(4C)	0.019(2)	0.310(3)	0.064(2)	0.18(6)
H(5)	0.0982(17)	0.1010(22)	-0.0125(15)	0.080(6)
H(7A)	0.2349(11)	-0.1336(16)	0.0499(10)	0.15(2)
H(7B)	0.2138(13)	-0.0565(18)	-0.0191(11)	0.15(5)
H(7C)	0.136(2)	-0.106(3)	0.015(2)	0.16(3)
H(10)	0.1047(17)	0.2409(23)	0.2582(16)	0.069(5)
H(11)	0.0773(12)	0.3949(16)	0.3381(11)	0.095(7)
H(12)	0.138(4)	0.536(6)	0.332(4)	0.15(1)
H(13)	0.215(3)	0.581(4)	0.212(2)	0.067(5)
H(15)	0.266(5)	0.390(6)	0.087(4)	0.077(6)
H(16A)	0.236(2)	0.557(3)	0.019(2)	0.116(9)
H(16B)	0.204(3)	0.607(4)	0.089(3)	0.15(1)
H(16C)	0.144(3)	0.521(3)	0.038(2)	0.11(1)
H(17A)	0.381(2)	0.501(3)	0.105(2)	0.16(2)

over

cont

H(60)	0.16070	0.53256	0.85350	0.072(5)
H(61A)	0.09038	0.67762	0.90950	0.13(2)
H(61B)	0.11188	0.75592	0.84690	0.110(9)
H(61C)	0.19038	0.70562	0.90710	0.13(1)
H(62A)	0.00427	0.54686	0.81137	0.12(2)
H(62B)	0.05277	0.49678	0.75067	0.11(1)
H(62C)	0.02067	0.61786	0.74347	0.12(2)
H(63A)	0.08758	0.21649	0.67403	0.110(9)
H(63B)	0.16788	0.15209	0.67803	0.104(8)
H(66A)	-0.06650	0.15708	0.41618	0.18(3)
H(66B)	-0.05640	0.09748	0.49858	0.14(2)
H(67)	0.04587	0.00981	0.43435	0.074(6)
H(68A)	0.16357	0.12163	0.41488	0.14(1)
H(68B)	0.08967	0.19603	0.38488	0.108(8)
H(69A)	0.20760	0.26035	0.51238	0.13(2)
H(69B)	0.11250	0.30235	0.48918	0.11(2)
H(71A)	0.04872	-0.08411	0.57579	0.119(9)
H(71B)	-0.01268	0.01779	0.57709	0.12(1)
H(71C)	0.07252	0.00079	0.64169	0.17(1)
H(72A)	0.19748	-0.06448	0.54107	0.13(1)
H(721)	0.22818	0.02062	0.60537	0.16(1)
H(72C)	0.22878	0.05042	0.52087	0.15(4)

$T = \exp[2\pi^2(U_{11}h^2a^{*2} + \ldots + 2U_{12}hka^*b^* + \ldots)]$; $U = U_{iso}$ or $U_{eq} = U_{eq} = \frac{1}{3}\sum_{i=1}^{3}\sum_{j=1}^{3} U_{ij}a_i^*a_j^*\mathbf{a}_i\cdot\mathbf{a}_j$

ANISOTROPIC THERMAL PARAMETERS

atom	U11	U22	U33	U12	U13	U23
S(1)	0.0513(2)	0.0513(2)	0.0525(2)	0.0077(1)	-.0024(1)	-.0098(1)
S(2)	0.0789(2)	0.0467(2)	0.0412(2)	-.0096(2)	0.0057(2)	0.0008(1)
O(1)	0.0641(7)	0.1019(10)	0.0759(8)	-.0128(7)	0.0192(6)	-.0073(7)
O(2)	0.0919(9)	0.0699(8)	0.0807(9)	0.0360(7)	-.0270(7)	-.0156(7)
O(3)	0.0611(6)	0.0443(5)	0.0364(5)	-.0034(4)	-.0020(4)	0.0008(3)
O(4)	0.110(1)	0.065(1)	0.110(1)	-0.002(1)	0.020(1)	0.015(1)
O(5)	0.0813(9)	0.1119(12)	0.0709(8)	-.0202(8)	0.0294(7)	-.0217(8)
O(6)	0.145(1)	0.051(1)	0.034(1)	-0.004(1)	-0.010(1)	0.015(1)
O(7)	0.0468(5)	0.0485(5)	0.0408(5)	-.0009(4)	-.0033(4)	-.0041(3)
O(8)	0.104(1)	0.164(2)	0.155(2)	0.054(1)	0.001(1)	-0.068(2)
C(1)	0.0568(8)	0.0461(7)	0.0367(6)	-.0008(6)	0.0032(5)	0.0020(5)
C(2)	0.0517(8)	0.0548(8)	0.0417(7)	-.0061(6)	0.0046(6)	0.0054(5)
C(3)	0.0602(9)	0.0724(10)	0.0422(7)	-.0085(7)	0.0001(6)	0.0109(7)
C(4)	0.076(1)	0.099(1)	0.062(1)	0.004(1)	-0.010(1)	0.013(1)
C(5)	0.083(1)	0.081(1)	0.039(1)	-0.022(1)	-0.002(1)	0.008(1)
C(6)	0.085(1)	0.063(1)	0.041(1)	-0.018(1)	0.007(1)	-0.005(1)
C(7)	0.131(2)	0.079(1)	0.059(1)	-0.020(1)	0.009(1)	-0.025(1)
C(8)	0.0663(9)	0.0514(7)	0.0401(7)	-.0118(6)	0.0106(6)	-.0034(5)
C(9)	0.0419(7)	0.0568(8)	0.0454(7)	0.0052(6)	0.0065(5)	0.0059(6)
C(10)	0.0505(8)	0.0632(9)	0.0564(8)	0.0024(6)	0.0108(6)	0.0084(6)
C(11)	0.0577(9)	0.0740(10)	0.0607(9)	0.0170(7)	0.0232(7)	0.0094(7)
C(12)	0.070(1)	0.063(1)	0.068(1)	0.025(1)	0.019(1)	0.003(1)
C(13)	0.074(1)	0.048(1)	0.075(1)	0.016(1)	0.019(1)	-0.016(1)
C(14)	0.0529(8)	0.0517(8)	0.0521(8)	0.0078(6)	0.0093(6)	0.0117(6)
C(15)	0.078(1)	0.061(1)	0.061(1)	-0.001(1)	0.024(1)	-0.012(1)
C(16)	0.124(2)	0.097(2)	0.085(1)	0.008(1)	0.051(1)	0.042(1)
C(17)	0.082(1)	0.089(1)	0.096(2)	-0.015(1)	0.039(1)	0.004(1)
C(18)	0.0639(9)	0.0438(7)	0.0496(8)	-.0061(6)	0.0161(6)	-.0079(5)
C(19)	0.081(1)	0.069(1)	0.081(1)	-0.008(1)	0.035(1)	-0.006(1)
C(20)	0.070(1)	0.090(2)	0.110(2)	0.007(1)	0.032(1)	-0.016(1)
C(21)	0.078(1)	0.069(1)	0.096(1)	0.015(1)	0.015(1)	-0.021(1)
C(22)	0.080(1)	0.053(1)	0.069(1)	0.008(1)	0.017(1)	0.002(1)
C(23)	0.0639(9)	0.0435(7)	0.0522(8)	-.0033(6)	0.0149(6)	-.0055(5)
C(24)	0.076(1)	0.041(1)	0.084(1)	0.002(1)	0.035(1)	0.006(1)
C(25)	0.073(1)	0.087(2)	0.182(3)	-0.013(1)	0.040(2)	-0.027(2)
C(26)	0.134(2)	0.204(4)	0.091(2)	0.018(2)	0.068(2)	0.007(2)
C(27)	0.0539(8)	0.0573(8)	0.0651(9)	0.0044(6)	-.0020(7)	-.0178(7)
C(28)	0.0475(7)	0.0517(7)	0.0536(8)	-.0025(6)	0.0017(6)	-.0104(6)
C(29)	0.071(1)	0.053(1)	0.077(1)	0.007(1)	0.005(1)	0.005(1)
C(30)	0.111(2)	0.086(1)	0.067(1)	0.004(1)	-0.016(1)	0.002(1)
C(31)	0.089(1)	0.081(1)	0.078(1)	-0.019(1)	-0.009(1)	-0.025(1)
C(32)	0.067(1)	0.136(2)	0.132(2)	-0.034(1)	-0.007(1)	-0.046(2)
C(33)	0.0512(9)	0.1125(16)	0.0949(14)	-.0146(10)	0.0091(9)	-.0312(13)
C(34)	0.079(1)	0.048(1)	0.037(1)	-0.009(1)	0.002(1)	-0.007(1)
C(35)	0.102(2)	0.071(1)	0.086(1)	0.012(1)	0.015(1)	-0.026(1)
C(36)	0.140(2)	0.065(1)	0.102(2)	-0.033(1)	0.085(2)	0.018(1)
C(37)	0.0377(6)	0.0485(7)	0.0435(7)	-.0011(5)	0.0000(5)	-.0066(5)
C(38)	0.0411(7)	0.0501(7)	0.0462(7)	0.0047(5)	0.0015(5)	-.0029(5)

over -

- cont

C(39)	0.0395(7)	0.0625(8)	0.0514(8)	0.0062(6)	-.0021(6)	-.0075(6)
C(40)	0.066(1)	0.083(1)	0.054(1)	0.012(1)	-0.012(1)	0.004(1)
C(41)	0.0445(8)	0.0753(10)	0.0578(9)	0.0020(7)	-.0088(7)	-.0161(8)
C(42)	0.0393(7)	0.0689(10)	0.0695(10)	-.0069(6)	0.0003(7)	-.0211(8)
C(43)	0.071(1)	0.075(1)	0.102(2)	-0.025(1)	-0.010(1)	-0.018(1)
C(44)	0.0410(7)	0.0534(8)	0.0543(8)	-.0053(5)	0.0063(6)	-.0087(6)
C(45)	0.0413(7)	0.0500(7)	0.0391(6)	0.0013(5)	-.0012(5)	0.0033(5)
C(46)	0.0487(7)	0.0622(8)	0.0445(7)	0.0041(6)	0.0031(6)	0.0034(6)
C(47)	0.0451(8)	0.0781(10)	0.0505(8)	-.0067(7)	0.0009(6)	0.0101(7)
C(48)	0.0581(9)	0.0595(9)	0.0648(10)	-.0140(7)	-.0073(7)	0.0100(7)
C(49)	0.069(1)	0.047(1)	0.066(1)	-0.001(1)	-0.006(1)	0.001(1)
C(50)	0.0484(8)	0.0499(8)	0.0502(8)	-0.0046(6)	-.0028(6)	0.0014(6)
C(51)	0.0501(8)	0.0606(9)	0.0746(11)	-0.0104(7)	0.0018(7)	-.0070(8)
C(52)	0.072(1)	0.104(2)	0.114(2)	0.035(1)	0.003(1)	0.020(1)
C(53)	0.068(1)	0.112(2)	0.085(1)	0.015(1)	0.016(1)	-0.008(1)
C(54)	0.0600(9)	0.0500(8)	0.0601(9)	-.0174(6)	0.0101(7)	-.0063(6)
C(55)	0.097(2)	0.090(1)	0.102(2)	-0.034(1)	0.043(1)	-0.002(1)
C(56)	0.184(3)	0.116(3)	0.105(2)	-0.076(2)	0.068(2)	0.005(2)
C(57)	0.187(3)	0.066(1)	0.085(2)	-0.044(2)	0.016(2)	0.026(1)
C(58)	0.124(2)	0.051(1)	0.069(1)	-0.009(1)	-0.011(1)	0.010(1)
C(59)	0.077(1)	0.042(1)	0.058(1)	-0.006(1)	-0.002(1)	0.002(1)
C(60)	0.074(1)	0.059(1)	0.082(1)	0.019(1)	0.019(1)	0.013(1)
C(61)	0.162(2)	0.079(1)	0.095(2)	0.035(2)	0.047(2)	0.010(1)
C(62)	0.070(1)	0.108(2)	0.178(3)	0.006(1)	0.023(2)	-0.002(2)
C(63)	0.089(1)	0.052(1)	0.040(1)	-0.020(1)	0.002(1)	0.006(1)
C(64)	0.0666(9)	0.0465(7)	0.0366(6)	-.0030(6)	0.0056(6)	-.0003(5)
C(65)	0.082(1)	0.094(2)	0.089(1)	0.025(1)	-0.008(1)	-0.028(1)
C(66)	0.102(2)	0.130(2)	0.097(2)	0.025(2)	-0.046(1)	-0.040(2)
C(67)	0.094(1)	0.064(1)	0.044(1)	-0.012(1)	0.000(1)	-0.011(1)
C(68)	0.201(3)	0.073(1)	0.043(1)	-0.037(1)	0.032(1)	0.000(1)
C(69)	0.136(2)	0.057(1)	0.047(1)	-0.027(1)	0.025(1)	0.002(1)
C(70)	0.0648(9)	0.0459(7)	0.0417(7)	-.0060(6)	0.0097(6)	-.0002(5)
C(71)	0.158(2)	0.068(1)	0.074(1)	-0.033(1)	0.050(1)	-0.014(1)
C(72)	0.092(1)	0.075(1)	0.096(2)	0.022(1)	0.006(1)	-0.009(1)

$T=\exp[-2\pi^2(U_{11}h^2a^{*2}+U_{22}k^2b^{*2}+U_{33}l^2c^{*2}+2U_{12}hka^*b^*+2U_{23}klb^*c^*+2U_{13}hla^*c^*)]$

INTRAMOLECULAR BOND LENGTHS (H omitted)

Bond length limits based on covalent radii			
S(1)-O(1)	1.417(2)	S(1)-O(2)	1.411(2)
S(1)-O(3)	1.603(2)	S(1)-C(27)	1.783(2)
S(2)-O(5)	1.405(2)	S(2)-O(6)	1.417(2)
S(2)-O(7)	1.598(1)	S(2)-C(63)	1.774(2)
O(3)-C(1)	1.420(2)	O(4)-C(29)	1.217(3)
O(7)-C(37)	1.423(2)	O(8)-C(65)	1.194(4)
C(1)-C(2)	1.398(3)	C(1)-C(8)	1.386(3)
C(2)-C(3)	1.409(3)	C(2)-C(9)	1.492(3)
C(3)-C(4)	1.520(3)	C(3)-C(5)	1.389(3)
C(5)-C(6)	1.370(3)	C(6)-C(7)	1.521(3)
C(6)-C(8)	1.407(3)	C(8)-C(18)	1.504(3)
C(9)-C(10)	1.402(3)	C(9)-C(14)	1.398(3)
C(10)-C(11)	1.391(3)	C(11)-C(12)	1.374(3)
C(12)-C(13)	1.380(3)	C(13)-C(14)	1.394(3)
C(14)-C(15)	1.523(3)	C(15)-C(16)	1.533(4)
C(15)-C(17)	1.543(3)	C(18)-C(19)	1.392(3)
C(18)-C(23)	1.403(3)	C(19)-C(20)	1.378(4)
C(20)-C(21)	1.367(4)	C(21)-C(22)	1.379(3)
C(22)-C(23)	1.385(3)	C(23)-C(24)	1.511(3)
C(24)-C(25)	1.514(4)	C(24)-C(26)	1.513(4)
C(27)-C(28)	1.529(3)	C(28)-C(29)	1.515(3)
C(28)-C(33)	1.534(3)	C(28)-C(34)	1.569(3)
C(29)-C(30)	1.529(4)	C(30)-C(31)	1.522(4)
C(31)-C(32)	1.529(4)	C(31)-C(34)	1.540(4)
C(32)-C(33)	1.532(4)	C(34)-C(35)	1.532(4)
C(34)-C(36)	1.521(4)	C(37)-C(38)	1.389(2)
C(37)-C(44)	1.388(2)	C(38)-C(39)	1.418(2)
C(38)-C(45)	1.498(2)	C(39)-C(40)	1.502(3)
C(39)-C(41)	1.391(3)	C(41)-C(42)	1.383(3)
C(42)-C(43)	1.506(3)	C(42)-C(44)	1.409(3)
C(44)-C(54)	1.493(3)	C(45)-C(46)	1.392(2)
C(45)-C(50)	1.401(2)	C(46)-C(47)	1.378(3)
C(47)-C(48)	1.374(3)	C(48)-C(49)	1.375(3)
C(49)-C(50)	1.402(3)	C(50)-C(51)	1.532(3)
C(51)-C(52)	1.547(4)	C(51)-C(53)	1.510(3)
C(54)-C(55)	1.391(4)	C(54)-C(59)	1.389(3)
C(55)-C(56)	1.377(5)	C(56)-C(57)	1.391(6)
C(57)-C(58)	1.366(5)	C(58)-C(59)	1.410(3)
C(59)-C(60)	1.508(3)	C(60)-C(61)	1.527(4)
C(60)-C(62)	1.521(4)	C(63)-C(64)	1.513(2)
C(64)-C(65)	1.530(3)	C(64)-C(69)	1.547(3)
C(64)-C(70)	1.559(3)	C(65)-C(66)	1.515(4)
C(66)-C(67)	1.502(4)	C(67)-C(68)	1.507(4)
C(67)-C(70)	1.551(3)	C(68)-C(69)	1.538(3)
C(70)-C(71)	1.521(3)	C(70)-C(72)	1.526(3)

INTRAMOLECULAR BOND ANGLES (H omitted)

Bond length limits based on covalent radii			
O(1)-S(1)-O(2)	119.4(1)	O(1)-S(1)-O(3)	108.2(1)
O(1)-S(1)-C(27)	111.3(1)	O(2)-S(1)-O(3)	107.6(1)
O(2)-S(1)-C(27)	110.3(1)	O(3)-S(1)-C(27)	97.7(1)
O(5)-S(2)-O(6)	119.6(2)	O(5)-S(2)-O(7)	108.7(1)
O(5)-S(2)-C(63)	111.5(1)	O(6)-S(2)-O(7)	106.5(1)
O(6)-S(2)-C(63)	109.4(1)	O(7)-S(2)-C(63)	99.7(1)
S(1)-O(3)-C(1)	123.9(1)	S(2)-O(7)-C(37)	124.3(1)
O(3)-C(1)-C(2)	117.8(2)	O(3)-C(1)-C(8)	116.9(2)
C(2)-C(1)-C(8)	124.9(2)	C(1)-C(2)-C(3)	116.5(2)
C(1)-C(2)-C(9)	120.6(2)	C(3)-C(2)-C(9)	122.6(2)
C(2)-C(3)-C(4)	121.7(2)	C(2)-C(3)-C(5)	118.7(2)
C(4)-C(3)-C(5)	119.5(2)	C(3)-C(5)-C(6)	123.5(2)
C(5)-C(6)-C(7)	120.7(2)	C(5)-C(6)-C(8)	118.6(2)
C(7)-C(6)-C(8)	120.7(2)	C(1)-C(8)-C(6)	117.7(2)
C(1)-C(8)-C(18)	122.0(2)	C(6)-C(8)-C(18)	120.7(2)
C(2)-C(9)-C(10)	116.2(2)	C(2)-C(9)-C(14)	124.3(2)
C(10)-C(9)-C(14)	119.6(2)	C(9)-C(10)-C(11)	121.0(2)
C(10)-C(11)-C(12)	119.3(2)	C(11)-C(12)-C(13)	119.8(2)
C(12)-C(13)-C(14)	122.4(2)	C(9)-C(14)-C(13)	117.9(2)
C(9)-C(14)-C(15)	123.6(2)	C(13)-C(14)-C(15)	118.5(2)
C(14)-C(15)-C(16)	112.0(2)	C(14)-C(15)-C(17)	110.8(2)
C(16)-C(15)-C(17)	109.1(2)	C(8)-C(18)-C(19)	118.5(2)
C(8)-C(18)-C(23)	122.3(2)	C(19)-C(18)-C(23)	119.2(2)
C(18)-C(19)-C(20)	122.0(2)	C(19)-C(20)-C(21)	118.7(2)
C(20)-C(21)-C(22)	120.1(2)	C(21)-C(22)-C(23)	122.4(2)
C(18)-C(23)-C(22)	117.5(2)	C(18)-C(23)-C(24)	121.5(2)
C(22)-C(23)-C(24)	121.0(2)	C(23)-C(24)-C(25)	112.5(2)
C(23)-C(24)-C(26)	111.8(2)	C(25)-C(24)-C(26)	112.1(3)
S(1)-C(27)-C(28)	116.1(2)	C(27)-C(28)-C(29)	113.7(2)
C(27)-C(28)-C(33)	119.4(2)	C(27)-C(28)-C(34)	115.9(2)
C(29)-C(28)-C(33)	104.5(2)	C(29)-C(28)-C(34)	98.9(2)
C(33)-C(28)-C(34)	102.1(2)	O(4)-C(29)-C(28)	126.3(2)
O(4)-C(29)-C(30)	126.9(2)	C(28)-C(29)-C(30)	106.5(2)
C(29)-C(30)-C(31)	101.5(2)	C(30)-C(31)-C(32)	105.3(3)
C(30)-C(31)-C(34)	103.5(2)	C(32)-C(31)-C(34)	101.3(2)
C(31)-C(32)-C(33)	102.7(2)	C(28)-C(33)-C(32)	103.0(2)
C(28)-C(34)-C(31)	93.5(2)	C(28)-C(34)-C(35)	113.4(2)
C(28)-C(34)-C(36)	114.5(2)	C(31)-C(34)-C(35)	113.5(2)
C(31)-C(34)-C(36)	114.4(2)	C(35)-C(34)-C(36)	107.5(2)
O(7)-C(37)-C(38)	117.2(2)	O(7)-C(37)-C(44)	117.2(2)
C(38)-C(37)-C(44)	125.2(2)	C(37)-C(38)-C(39)	117.7(2)
C(37)-C(38)-C(45)	119.9(2)	C(39)-C(38)-C(45)	122.5(2)
C(38)-C(39)-C(40)	121.9(2)	C(38)-C(39)-C(41)	118.0(2)
C(40)-C(39)-C(41)	120.1(2)	C(39)-C(41)-C(42)	123.8(2)
C(41)-C(42)-C(43)	120.8(2)	C(41)-C(42)-C(44)	118.9(2)
C(43)-C(42)-C(44)	120.2(2)	C(37)-C(44)-C(42)	116.0(2)
C(37)-C(44)-C(54)	121.3(2)	C(42)-C(44)-C(54)	121.7(2)
C(38)-C(45)-C(46)	117.2(2)	C(38)-C(45)-C(50)	123.0(2)

over -

- cont

C(46)-C(45)-C(50)	119.8(2)	C(45)-C(46)-C(47)	121.3(2)
C(46)-C(47)-C(48)	119.5(2)	C(47)-C(48)-C(49)	119.9(2)
C(48)-C(49)-C(50)	122.0(2)	C(45)-C(50)-C(49)	117.5(2)
C(45)-C(50)-C(51)	123.7(2)	C(49)-C(50)-C(51)	118.9(2)
C(50)-C(51)-C(52)	111.3(2)	C(50)-C(51)-C(53)	111.7(2)
C(52)-C(51)-C(53)	111.3(2)	C(44)-C(54)-C(55)	118.6(2)
C(44)-C(54)-C(59)	120.8(2)	C(55)-C(54)-C(59)	120.6(2)
C(54)-C(55)-C(56)	120.0(3)	C(55)-C(56)-C(57)	120.0(4)
C(56)-C(57)-C(58)	119.9(3)	C(57)-C(58)-C(59)	121.4(3)
C(54)-C(59)-C(58)	118.0(2)	C(54)-C(59)-C(60)	122.8(2)
C(58)-C(59)-C(60)	119.2(2)	C(59)-C(60)-C(61)	111.6(2)
C(59)-C(60)-C(62)	111.2(2)	C(61)-C(60)-C(62)	113.0(3)
S(2)-C(63)-C(64)	116.4(2)	C(63)-C(64)-C(65)	112.6(2)
C(63)-C(64)-C(69)	120.2(2)	C(63)-C(64)-C(70)	116.6(2)
C(65)-C(64)-C(69)	103.7(2)	C(65)-C(64)-C(70)	99.4(2)
C(69)-C(64)-C(70)	101.7(2)	O(8)-C(65)-C(64)	126.5(3)
O(8)-C(65)-C(66)	127.0(3)	C(64)-C(65)-C(66)	106.4(2)
C(65)-C(66)-C(67)	102.5(2)	C(66)-C(67)-C(68)	104.8(2)
C(66)-C(67)-C(70)	104.1(2)	C(68)-C(67)-C(70)	101.9(2)
C(67)-C(68)-C(69)	104.4(2)	C(64)-C(69)-C(68)	103.5(2)
C(64)-C(70)-C(67)	94.0(2)	C(64)-C(70)-C(71)	112.6(2)
C(64)-C(70)-C(72)	114.0(2)	C(67)-C(70)-C(71)	113.1(2)
C(67)-C(70)-C(72)	114.2(2)	C(71)-C(70)-C(72)	108.5(2)

INTRAMOLECULAR TORSION ANGLES (H omitted)

Bond length limits based on covalent radii			
O(1)-S(1)-O(3)-C(1)	10.0(2)	O(1)-S(1)-C(27)-C(28)	-87.1(2)
O(2)-S(1)-O(3)-C(1)	120.3(2)	O(2)-S(1)-C(27)-C(28)	45.8(2)
C(27)-S(1)-O(3)-C(1)	125.5(2)	O(3)-S(1)-C(27)-C(28)	157.9(2)
O(5)-S(2)-O(7)-C(37)	5.3(2)	O(5)-S(2)-C(63)-C(64)	-86.4(2)
O(6)-S(2)-O(7)-C(37)	-124.8(2)	O(6)-S(2)-C(63)-C(64)	48.2(2)
C(63)-S(2)-O(7)-C(37)	121.7(2)	O(7)-S(2)-C(63)-C(64)	159.4(2)
S(1)-O(3)-C(1)-C(2)	-94.8(2)	S(1)-O(3)-C(1)-C(8)	92.8(2)
S(2)-O(7)-C(37)-C(38)	-103.8(2)	S(2)-O(7)-C(37)-C(44)	83.3(2)
O(3)-C(1)-C(2)-C(3)	-169.1(2)	O(3)-C(1)-C(2)-C(9)	4.7(2)
O(3)-C(1)-C(8)-C(6)	169.7(3)	O(3)-C(1)-C(8)-C(18)	-9.6(2)
C(8)-C(1)-C(2)-C(3)	3.2(2)	C(2)-C(1)-C(8)-C(6)	-2.6(2)
C(8)-C(1)-C(2)-C(9)	176.9(3)	C(2)-C(1)-C(8)-C(18)	178.2(3)
C(1)-C(2)-C(3)-C(4)	176.9(3)	C(1)-C(2)-C(3)-C(5)	-1.2(2)
C(1)-C(2)-C(9)-C(10)	-66.4(2)	C(1)-C(2)-C(9)-C(14)	112.7(3)
C(9)-C(2)-C(3)-C(4)	3.3(2)	C(9)-C(2)-C(3)-C(5)	-174.8(3)
C(3)-C(2)-C(9)-C(10)	107.0(2)	C(3)-C(2)-C(9)-C(14)	-73.9(2)
C(2)-C(3)-C(5)-C(6)	-1.3(2)	C(4)-C(3)-C(5)-C(6)	-179.4(3)
C(3)-C(5)-C(6)-C(7)	-179.6(3)	C(3)-C(5)-C(6)-C(8)	1.9(2)
C(5)-C(6)-C(8)-C(1)	0.6(2)	C(5)-C(6)-C(8)-C(18)	179.7(3)
C(7)-C(6)-C(8)-C(1)	-178.5(3)	C(7)-C(6)-C(8)-C(18)	0.8(2)
C(1)-C(8)-C(18)-C(19)	-102.9(3)	C(1)-C(8)-C(18)-C(23)	78.6(2)
C(6)-C(8)-C(18)-C(19)	77.8(2)	C(6)-C(8)-C(18)-C(23)	-100.6(3)
C(2)-C(9)-C(10)-C(11)	178.6(3)	C(2)-C(9)-C(14)-C(13)	-178.6(3)
C(2)-C(9)-C(14)-C(15)	0.4(2)	C(14)-C(9)-C(10)-C(11)	-0.5(2)
C(10)-C(9)-C(14)-C(13)	0.5(2)	C(10)-C(9)-C(14)-C(15)	179.5(3)
C(9)-C(10)-C(11)-C(12)	0.4(2)	C(10)-C(11)-C(12)-C(13)	-0.2(2)
C(11)-C(12)-C(13)-C(14)	0.1(2)	C(12)-C(13)-C(14)-C(9)	-0.3(2)
C(12)-C(13)-C(14)-C(15)	-179.3(3)	C(9)-C(14)-C(15)-C(16)	122.9(3)
C(9)-C(14)-C(15)-C(17)	-115.0(3)	C(13)-C(14)-C(15)-C(16)	-58.1(2)
C(13)-C(14)-C(15)-C(17)	64.0(2)	C(8)-C(18)-C(19)-C(20)	-176.0(3)
C(8)-C(18)-C(23)-C(22)	175.7(3)	C(8)-C(18)-C(23)-C(24)	-2.9(2)
C(23)-C(18)-C(19)-C(20)	2.6(2)	C(19)-C(18)-C(23)-C(22)	-2.7(2)
C(19)-C(18)-C(23)-C(24)	178.7(3)	C(18)-C(19)-C(20)-C(21)	-1.4(2)
C(19)-C(20)-C(21)-C(22)	0.4(3)	C(20)-C(21)-C(22)-C(23)	-0.7(2)
C(21)-C(22)-C(23)-C(18)	1.9(2)	C(21)-C(22)-C(23)-C(24)	-179.5(3)
C(18)-C(23)-C(24)-C(25)	99.2(3)	C(18)-C(23)-C(24)-C(26)	-133.6(3)
C(22)-C(23)-C(24)-C(25)	-79.3(3)	C(22)-C(23)-C(24)-C(26)	47.9(3)
S(1)-C(27)-C(28)-C(29)	-94.9(2)	S(1)-C(27)-C(28)-C(33)	29.1(2)
S(1)-C(27)-C(28)-C(34)	151.8(2)	C(27)-C(28)-C(29)-O(4)	17.0(2)
C(27)-C(28)-C(29)-C(30)	-161.2(2)	C(27)-C(28)-C(33)-C(32)	160.3(3)
C(27)-C(28)-C(34)-C(31)	177.0(2)	C(27)-C(28)-C(34)-C(35)	59.6(2)
C(27)-C(28)-C(34)-C(36)	-64.2(2)	C(33)-C(28)-C(29)-O(4)	-114.8(3)
C(33)-C(28)-C(29)-C(30)	67.1(2)	C(29)-C(28)-C(33)-C(32)	-71.2(2)
C(34)-C(28)-C(29)-O(4)	140.0(3)	C(34)-C(28)-C(29)-C(30)	-38.2(2)
C(29)-C(28)-C(34)-C(31)	55.3(2)	C(29)-C(28)-C(34)-C(35)	-62.1(2)
C(29)-C(28)-C(34)-C(36)	174.1(2)	C(33)-C(28)-C(34)-C(31)	-51.7(2)
C(34)-C(28)-C(33)-C(32)	31.4(2)	C(33)-C(28)-C(34)-C(35)	-169.2(2)
C(33)-C(28)-C(34)-C(36)	67.1(2)	O(4)-C(29)-C(30)-C(31)	-174.3(3)

over

- cont

C(28)-C(29)-C(30)-C(31)	4.1(2)	C(29)-C(30)-C(31)-C(32)	-75.3(3)
C(29)-C(30)-C(31)-C(34)	32.8(2)	C(30)-C(31)-C(32)-C(33)	70.9(3)
C(30)-C(31)-C(34)-C(28)	-55.0(2)	C(30)-C(31)-C(34)-C(35)	62.3(2)
C(30)-C(31)-C(34)-C(36)	-173.9(3)	C(32)-C(31)-C(34)-C(28)	54.6(2)
C(34)-C(31)-C(32)-C(33)	-37.3(2)	C(32)-C(31)-C(34)-C(35)	171.9(3)
C(32)-C(31)-C(34)-C(36)	-64.3(3)	C(31)-C(32)-C(33)-C(28)	3.0(2)
O(7)-C(37)-C(38)-C(39)	-170.2(2)	O(7)-C(37)-C(38)-C(45)	3.1(2)
O(7)-C(37)-C(44)-C(42)	172.2(2)	O(7)-C(37)-C(44)-C(54)	-5.2(2)
C(44)-C(37)-C(38)-C(39)	2.0(2)	C(38)-C(37)-C(44)-C(42)	-0.1(2)
C(44)-C(37)-C(38)-C(45)	175.3(3)	C(38)-C(37)-C(44)-C(54)	-177.5(3)
C(37)-C(38)-C(39)-C(40)	174.3(3)	C(37)-C(38)-C(39)-C(41)	-3.7(2)
C(37)-C(38)-C(45)-C(46)	-62.6(2)	C(37)-C(38)-C(45)-C(50)	115.0(2)
C(45)-C(38)-C(39)-C(40)	1.2(2)	C(45)-C(38)-C(39)-C(41)	-176.8(3)
C(39)-C(38)-C(45)-C(46)	110.3(2)	C(39)-C(38)-C(45)-C(50)	-72.1(2)
C(38)-C(39)-C(41)-C(42)	3.6(2)	C(40)-C(39)-C(41)-C(42)	-174.4(3)
C(39)-C(41)-C(42)-C(43)	176.6(3)	C(39)-C(41)-C(42)-C(44)	-1.6(2)
C(41)-C(42)-C(44)-C(37)	-0.7(2)	C(41)-C(42)-C(44)-C(54)	177.2(3)
C(43)-C(42)-C(44)-C(37)	-178.5(3)	C(43)-C(42)-C(44)-C(54)	-1.0(2)
C(37)-C(44)-C(54)-C(55)	-102.8(3)	C(37)-C(44)-C(54)-C(59)	79.1(2)
C(42)-C(44)-C(54)-C(55)	79.9(3)	C(42)-C(44)-C(54)-C(59)	-98.2(3)
C(38)-C(45)-C(46)-C(47)	177.1(3)	C(38)-C(45)-C(50)-C(49)	-177.2(3)
C(38)-C(45)-C(50)-C(51)	1.5(2)	C(50)-C(45)-C(46)-C(47)	-0.6(2)
C(46)-C(45)-C(50)-C(49)	0.4(2)	C(46)-C(45)-C(50)-C(51)	179.1(3)
C(45)-C(46)-C(47)-C(48)	0.1(2)	C(46)-C(47)-C(48)-C(49)	0.5(2)
C(47)-C(48)-C(49)-C(50)	-0.7(2)	C(48)-C(49)-C(50)-C(45)	0.2(2)
C(48)-C(49)-C(50)-C(51)	-178.5(3)	C(45)-C(50)-C(51)-C(52)	129.5(3)
C(45)-C(50)-C(51)-C(53)	-105.4(3)	C(49)-C(50)-C(51)-C(52)	-51.8(2)
C(49)-C(50)-C(51)-C(53)	73.3(2)	C(44)-C(54)-C(55)-C(56)	-180.0(4)
C(44)-C(54)-C(59)-C(58)	178.7(3)	C(44)-C(54)-C(59)-C(60)	-1.8(2)
C(59)-C(54)-C(55)-C(56)	-1.9(3)	C(55)-C(54)-C(59)-C(58)	0.6(2)
C(55)-C(54)-C(59)-C(60)	-179.9(3)	C(54)-C(55)-C(56)-C(57)	1.5(3)
C(55)-C(56)-C(57)-C(58)	0.2(3)	C(56)-C(57)-C(58)-C(59)	-1.4(4)
C(57)-C(58)-C(59)-C(54)	1.0(3)	C(57)-C(58)-C(59)-C(60)	-178.9(4)
C(54)-C(59)-C(60)-C(61)	118.3(3)	C(54)-C(59)-C(60)-C(62)	-114.6(3)
C(58)-C(59)-C(60)-C(61)	-62.3(3)	C(58)-C(59)-C(60)-C(62)	64.5(3)
S(2)-C(63)-C(64)-C(65)	-103.8(2)	S(2)-C(63)-C(64)-C(69)	18.7(2)
S(2)-C(63)-C(64)-C(70)	142.3(2)	C(63)-C(64)-C(65)-O(8)	18.7(3)
C(63)-C(64)-C(65)-C(66)	-160.9(3)	C(63)-C(64)-C(69)-C(68)	162.9(3)
C(63)-C(64)-C(70)-C(67)	174.3(2)	C(63)-C(64)-C(70)-C(71)	57.2(2)
C(63)-C(64)-C(70)-C(72)	-67.0(2)	C(69)-C(64)-C(65)-O(8)	-112.8(3)
C(69)-C(64)-C(65)-C(66)	67.6(2)	C(65)-C(64)-C(69)-C(68)	-70.3(2)
C(70)-C(64)-C(65)-O(8)	142.7(3)	C(70)-C(64)-C(65)-C(66)	-36.9(2)
C(65)-C(64)-C(70)-C(67)	53.1(3)	C(65)-C(64)-C(70)-C(71)	-63.9(2)
C(65)-C(64)-C(70)-C(72)	171.9(2)	C(69)-C(64)-C(70)-C(67)	-53.1(2)
C(70)-C(64)-C(69)-C(68)	32.5(2)	C(69)-C(64)-C(70)-C(71)	-170.1(2)
C(69)-C(64)-C(70)-C(72)	65.7(2)	O(8)-C(65)-C(66)-C(67)	-176.1(4)
C(64)-C(65)-C(66)-C(67)	3.5(2)	C(65)-C(66)-C(67)-C(68)	-74.7(3)
C(65)-C(66)-C(67)-C(70)	32.0(2)	C(66)-C(67)-C(68)-C(69)	71.2(3)
C(66)-C(67)-C(70)-C(64)	-55.5(2)	C(66)-C(67)-C(70)-C(71)	63.1(2)
C(66)-C(67)-C(70)-C(72)	-172.1(3)	C(68)-C(67)-C(70)-C(64)	53.3(2)

over

- cont

C(70)-C(67)-C(68)-C(69)	-37.0(2)	C(68)-C(67)-C(70)-C(71)	172.0(3)
C(68)-C(67)-C(70)-C(72)	-63.3(2)	C(67)-C(68)-C(69)-C(64)	2.5(2)

INTERMOLECULAR NON-BONDED DISTANCES (H omitted)

non-bonded distance limits based on Van der Waal's radii

Atom(1)-Atom(2)	dist	e.s.d.	ns	np	Ta	Tb	Tc	x(2)	y(2)	z(2)
C(3)-C(40)	3.994	0.002	1	1	0	0	-1	0.35429	0.20568	-0.00617
C(4)-C(46)	3.989	0.002	1	1	0	0	-1	0.12862	0.18460	-0.15716
C(4)-C(61)	3.857	0.004	2	1	0	-1	1	-0.13158	0.19232	0.12330
C(5)-C(40)	3.759	0.003	1	1	0	0	-1	0.35429	0.20568	-0.00617
C(5)-C(46)	3.597	0.002	1	1	0	0	-1	0.12862	0.18460	-0.15716
C(5)-C(47)	3.773	0.002	1	1	0	0	-1	0.07191	0.09702	-0.17633
C(6)-C(40)	3.755	0.003	1	1	0	0	-1	0.35429	0.20568	-0.00617
C(7)-C(49)	3.977	0.003	1	1	0	0	-1	0.19776	-0.01153	-0.18928
C(7)-C(61)	3.913	0.004	1	1	0	-1	-1	0.13158	-0.30768	-0.12330
C(11)-C(47)	3.994	0.002	2	1	0	0	1	-0.07191	0.59702	0.17633
C(11)-C(48)	3.685	0.002	2	1	0	0	1	-0.10677	0.49883	0.19271
C(11)-C(71)	3.648	0.003	2	1	0	0	1	-0.04832	0.49179	0.41171
C(12)-C(47)	3.665	0.002	2	1	0	0	1	-0.07191	0.59702	0.17633
C(12)-C(48)	3.851	0.002	2	1	0	0	1	-0.10677	0.49883	0.19271
C(13)-C(25)	3.891	0.003	1	1	0	1	0	0.11939	0.82065	0.22247

over

- cont

Atom(1)-Atom(2)	dist	e.s.d.	ns	np	Ta	Tb	Tc	x(2)	y(2)	z(2)
C(16)-C(61)	3.735	0.004	1	1	0	0	-1	0.13158	0.69232	-0.12330
C(17)-C(41)	3.908	0.003	1	1	0	0	-1	0.38278	0.39115	-0.05422
C(19)-C(43)	3.994	0.003	2	1	1	-1	1	0.58653	0.08507	0.08489
C(20)-C(41)	3.963	0.003	2	1	1	-1	1	0.61722	-0.10885	0.05422
C(20)-C(42)	3.831	0.003	2	1	1	-1	1	0.63372	-0.02209	0.10410
C(21)-C(30)	3.736	0.003	2	1	1	-1	1	0.52569	-0.15630	0.44546
C(22)-C(30)	3.892	0.003	2	1	1	-1	1	0.52569	-0.15630	0.44546
C(22)-C(36)	3.966	0.003	1	1	0	-1	0	0.41726	-0.46081	0.38671
C(25)-C(47)	3.961	0.003	2	1	0	-1	1	-0.07191	-0.40298	0.17633
C(25)-C(62)	3.875	0.004	2	1	0	-1	1	-0.04547	0.06156	0.22143
C(32)-C(72)	3.898	0.003	2	1	1	0	1	0.80292	0.51142	0.44643
C(33)-C(56)	3.750	0.005	2	1	1	-1	1	0.68438	0.16587	0.32747
C(40)-C(43)	3.864	0.003	2	1	1	-1	2	0.58653	0.08507	1.08489
C(48)-C(61)	3.965	0.003	1	1	0	-1	0	0.13158	-0.30768	0.87670
C(49)-C(58)	3.824	0.003	1	1	0	-1	0	0.18369	-0.29384	0.71988
C(57)-C(66)	3.757	0.005	2	1	0	0	1	0.02850	0.64088	0.53472
C(58)-C(66)	3.748	0.004	2	1	0	0	1	0.02850	0.64088	0.53472

ns is the symmetry operator number - (* denotes inversion indicator)
np is the lattice point number
Ta,Tb & Tc are unit cell translations. The symmetry operations are:
1 + X, + Y, + Z
2 - X, 1/2 + Y, - Z

Acknowledgment: We gratefully acknowledge the financial support from the Ministry of Education, Science, and Culture of Japan. We also appreciate the assistance of A. Nakao (MAC Science Co., Ltd.) for the X-ray crystal analysis of sulfonate (*S*,*S*,*S*)-**9**, and A. Takakuwa (JASCO., Ltd.) for the CD-spectral analysis of (*R*,*R*)- and (*S*,*S*)-**1** and **2**.

References and Notes

(1) Methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD): (a) Maruoka, K.; Itoh, T.; Sakurai, M.; Nonoshita, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 3588. (b) Maruoka, K.; Saito, S.; Yamamoto, H. *ibid.* **1992**, *114*, 1089. Methylaluminum bis(4-bromo-2,6-di-*tert*-butylphenoxide) (MABR): (c) Maruoka, K.; Ooi, T; Yamamoto, H. *ibid.* **1989**, *111*, 6431. (d) Maruoka, K.; Ooi, T.; Yamamoto, H. *ibid.* **1990**, *112*, 9011. (e) Maruoka, K.; Sato, J.; Yamamoto, H.; *ibid.* **1993**, *113*, 5449 (f) Maruoka, K.; Nonoshita, K.; Banno, H.; Yamamoto, H. *ibid.* **1988**, *110*, 7922.

(2) (a) Maruoka, K.; Imoto, H.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 4131. (b) Maruoka, K.; Imoto, H.; Yamamoto, H. *ibid.* **1994**, *116*, 12115. ATPH for Claisen rearrangement: (c) Maruoka, K.; Saito, S.; Yamamoto, H. *ibid.* **1995**, *117*, 1165. (d) Maruoka, K.; Ito, M.; Yamamoto, H. *ibid.* **1995**, *117*, 9091. (e) Saito, S.; Ito, M.; Yamamoto, H. *ibid.* **1997**, *119*, 611.

(3) (a) Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314. (b) Oh-e, T.; Miyaura, N.; Suzuki, A. *J. Org. Chem.* **1993**, *58*, 2201.

(4) The optical purity was determined by chiral HPLC using a Daicel column OD-H.

(5) Otherwise, the yield of *dl*-**9** decreased significantly.

(6) See the Experimental Section.

(7) Hodgson, H. H.; Mahadevan, A. P. *J. Chem. Soc.* **1947**, 173.

(8) Du, C.-J. F., Hart, H.; Ng, K.-K. D. *J. Org. Chem.* **1986**, *51*, 3162.

(9) (a) Breuer, S. W.; Broster, F. A. *J. Organometal. Chem.* **1972**, *35*, C5. (b) Brown, H. C.; Zweifel, G. *Organic Reactions* **1963**, *13*, 1.

(10) The ^{1}H-NMR (300 MHz, $CDCl_3$) data of (*R*)-**15**: δ 7.20-5.60 (m, 16H), 6.66 (s, 2H), 1.92 (s, 12H), 1.89 (s, 12H), -2.13 (s, 3H, $AlCH_3$); (*R*)-**16**: δ 7.60-6.70 (m, 16H), 6.57 (s, 2H), 2.95-2.41 (b, 4H), 2.05-1.62 (b, 12H), 1.14 (bd, 12H, J = 6.1 Hz), 0.90-0.445 (b, 12H), -2.54 (s, 3H, $AlCH_3$).

(11) (a) Weber, B.; Seebach, D. *Tetrahedron*, **1994**, *50*, 7473. (b) Weber, B.; Seebach, D. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 84. (c) Greeves, N.; Pease, J. E. *Tetrahedron Lett.* **1996**, *37*, 5821. (d) Chibale, K.; Greeves, N.; Lyford, L.; Pease, J. E. *Tetrahedron: Asymmetry* **1993**, *4*, 2407. (e) Noyori, R.; Kitamura, M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 49. Dialkylzincs as alkylating agents: (f) Schmidt, B.; Seebach, D. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1321. (g) Nowotny, S.; Vettel, S.; Knochel, P. *Tetrahedron Lett.* **1994**, *35*, 4539. (h) Rozema, M. J.; Sidduri, A.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 1956. (i) Chaloner, P. A.; Langadianou, E. *Tetrahedron Lett.* **1990**, *31*, 5185. (j) Soai, K.; Niwa, S.; Hatanaka, T. *J. Chem. Soc., Chem. Commun.* **1990**, 709. (k) Zhang, H.; Xue, F.; Mak, T. C. W.; Chan, K. S. *J. Org. Chem.* **1996**, *61*, 8002.

(12) Optically active **15** and **16** were demonstrated to be more effective than methylaluminum (*R*)-3,3'-bis(tris(4-methylphenyl)silyl)-1,1'-bi-2 -naphthoxide [(*R*)-**27**]:[13] treatment of **17** with (*R*)-**27** (1.2 equiv) at -78 °C in toluene, followed by the addition of an ether solution of BuMgCl (2.0 equiv) gave, after 30 min, **23** in a yield of 89% with 5% ee.

(13) (a) Maruoka, K.; Itoh, T.; Araki, Y.; Shirasaka, T.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2975. (b) Maruoka, K.; Concepcion, A. B.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3501.

(14) (a) Kajigaeshi, S.; Kakinami, T.; Inoue, K.; Kondo, M.; Nakamura, H.; Fujikawa,

M.; Okamoto, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 597. (b) Jaeger, F.; Blanksma, J. *Rec. Trav. Chim. PaysBas*, **1906**, *25*, 253.

(15) Sada, K.; Kondo, T.; Miyata, M. *Tetrahedron: Asymmetry* **1995**, *6*, 2655,

(16) Terashima, S.; Tanno, N.; Koga, K. *Chem Lett*. **1980**, 981.

(17) Weber, B.; Seebach, D. *Tetrahedron* **1994**, *50*, 7473.

(18) Rozema, M. J.; Rajagopal, D.; Tucker, C. E.; Knochel, P. *J. Organomet. Chem.* **1992**, *438*, 11.

(19) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc*. **1991**, *113*, 6129.

(20) Bolton, R.; Sandall, J. P. B. *J. Chem. Soc., Perkin Trans. 2* **1977**, 278.

Chapter 3

Asymmetric Coupling of Phenols with Arylleads

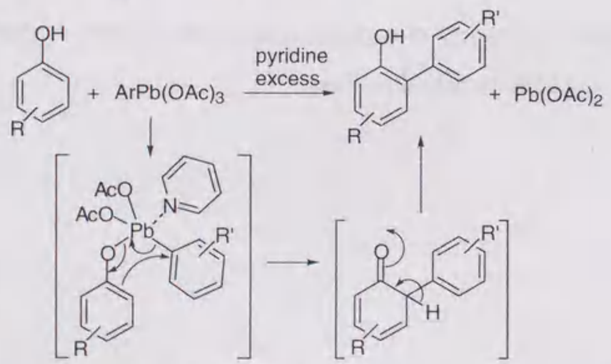
Abstract: The asymmetric coupling of various phenol derivatives with bulky aryllead triacetates was investigated for the first time using optically active amines including strychnine and brucine. We found that conformationally restricted tertiary amines, as well as the effect of lithium aryloxides and molecular sieves are essential for accelerating the rate of this coupling process. Consequently, the reaction can be carried out at a low temperature (-40 °C~-20 °C), giving a high degree of diastereo- and enantioselectivities. With this coupling method, a diverse set of di-, tri, and polyaryl compounds having axial chirality is easily obtainable, and will be convenient for the construction of a variety of aryl-aryl frameworks involved in metal ligands, natural products, and artificial helical polymers.

The optically pure biaryl axis has been the subject of increasing interest, due to its role as a pivotal element in a rapidly growing number of not only pharmacologically potent natural products[1], but also chiral metal catalysts[2] and artificial helical polymers.[3] Despite a broad spectrum of classical[4] and modern[5] procedures for the chemical connection of aromatic moieties, the development of efficient aryl-coupling methods that enable the directed construction of even highly sterically demanding bi- and polyaryls in optically active form[6-12] has become of great importance. We report here the first example of the diastereo- and enantioselective direct coupling of aryllead compounds with phenol derivatives.[16]

Result and Discussion

Amine Survey. Pinhey suggested that the coupling reaction of phenols with aryllead triacetates is facilitated by the participation of excess pyridine or analogous bases in $CHCl_3$ (Scheme 1).[14] Thereafter, Barton carefully optimized the reaction conditions, particularly for the use of aryllead compounds which incorporated electron rich aryl groups.[13] Our initial plan was guided by a reconsideration of an alternative base additive which could open the way to the future discovery of a chiral analogue, with a goal of the efficient asymmetric synthesis.

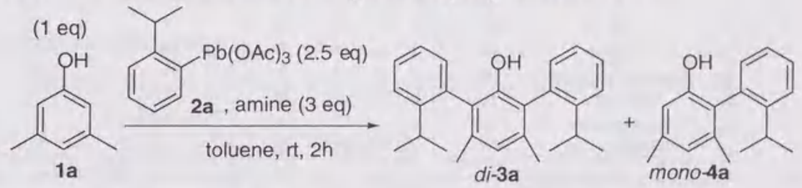
Scheme 1



The coupling reaction of 3,5-dimethylphenol (**1a**) with 2-isopropylphenyllead triacetate (**2a**)[17] was carried out in the presence of various amines (Table 1). The rate-

enhancing effect was moderate with a primary amine (entry 1) but less efficient with a secondary amine (entry 2) and tertiary amines, including *i*-Pr_2NEt andNEt_3 (entries 3 and 4). Surprisingly, this process using tertiary amines such as DABCO or quinuclidine exhibited good to excellent reactivity and high *dl*-selectivity (entries 5 and 6).[18,19] These results indicate that the conformationally restricted amines are necessary for the potential rate enhancement.

Table 1. Effect of Amine in the Ligand Coupling of **1a** with **2a**.



entry	amine	yield (%)[a]	*dl : meso*
1	*i*-$PrNH_2$	75 (7)	>99 : <1
2	$(i\text{-}Pr)_2NH$	0 (31)	-
3	$(i\text{-}Pr)_2Et$	0 (10)	-
4	Et_3N	0 (11)	-
5	DABCO	78	>99 : <1
6	quinuclidine	95	>99 : <1

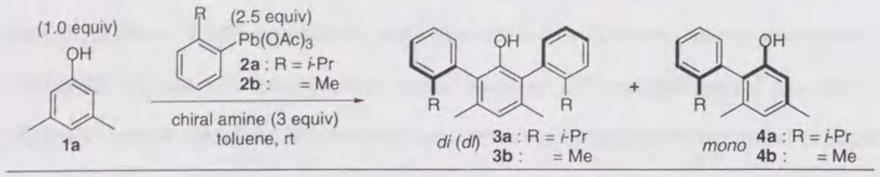
[a]Yields in parenthesis indicate the yields of monocoupling product.


DABCO


quinuclidine

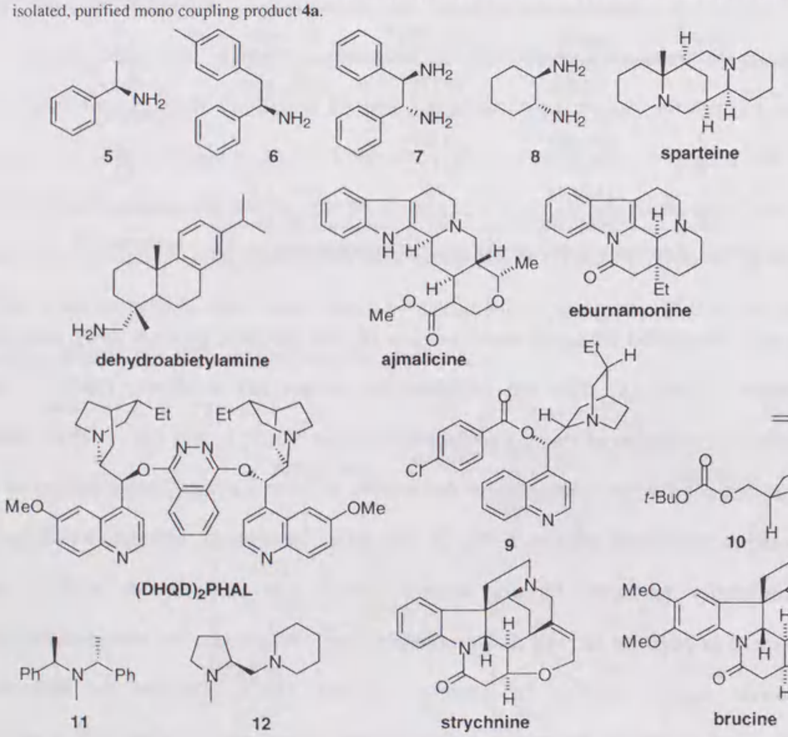
We next elucidated an asymmetric version of this potential process using optically active bases (Table 2). The use of bidentate amines led to slower reactions and incomplete consumption of starting phenol **1a** (entries 3-5, 7, 8, and 16). Poor yields were also obtained when quinuclidine derivatives with an oxygen functional group at the β-position were used (entries 9, 10, 13, and 14). In contrast, brucine, which had a conformationally restricted tertiary amine moiety, was essential to achieve rate enhancement in addition to high diastereoselectivity. Moreover, we obtained the best enantiomeric excess (ee) so far (entries 12 and 18).[20] Despite the structural resemblance of strychnine to brucine, the use of the former gave a lower yield as well as a lower ee (entry 17).

Table 2. Effect of Chiral Amine in the Asymmetric Coupling of **1a** with **2a** or **2b**.



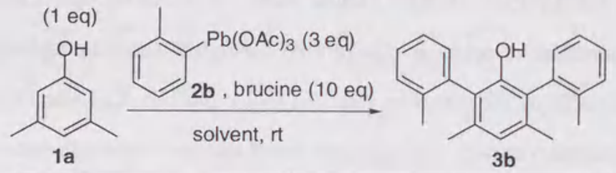
entry	aryllead	amine	yield(%)[a]	ee(%)[b]	entry	aryllead	amine	yield(%)[a]	ee(%)[b]
1	**2b**	**5**	99	0	10	**2b**	**9**	68	4
2	**2b**	**6**	48	0	11	**2b**	strychnine	99	15
3	**2b**	**7**	22	9	12	**2b**	brucine	99	14
4	**2b**	**8**	55	3	13	**2a**	**9**	14[c]	4
5	**2b**	sparteine	49	5	14	**2a**	**10**	16[c]	0
6	**2b**	dehydroabietylamine	99	6	15	**2a**	**11**	2[c]	6
7	**2b**	ajmalicine	16	0	16	**2a**	**12**	3[c]	0
8	**2b**	eburnamonine	36	0	17	**2a**	strychnine	32	20
9	**2b**	$(DHQD)_2PHAL$	55	3	18	**2a**	brucine	92	40

[a]Unless otherwise specified, of isolated purified dicoupling product **3a** or **3b**. [b]Determined by HPLC analysis. [c]Of isolated, purified mono coupling product **4a**.



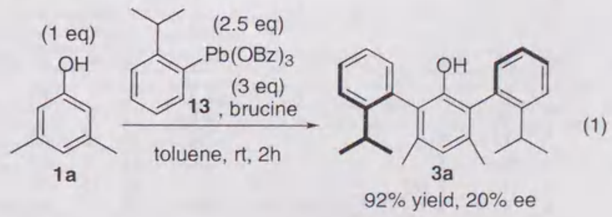
Optimization of Reaction Conditions. With the superior enantioselectivity exhibited by the combination of phenol **1a**, 2-methylphenyllead triacetate (**2b**) and brucine (Table 2, entry 18), a study was initiated to survey solvent effects for this reaction (Table 3). The use of solvents such as CH_2Cl_2, THF, and toluene gave comparable yields of 3,5-dimethyl-2,6-bis(2-methylphenyl)phenol[15] (**3b**) (entries 1 and 2), however, the reaction in hexane resulted in a lower yield presumably due to the poor solubility of brucine (entry 4). Among the solvents examined, the use of toluene gave the highest ee value (entry 3).

Table 3. Effect of Solvent in the Asymmetric Coupling of **1a** with **2b**.



entry	solvent	time (h)	yield (%)	*dl : meso*	ee(%)
1	CH_2Cl_2	2	99	8 : 1	14
2	THF	1	99	11 : 1	25
3	toluene	1	97	10 : 1	30
4	hexane	12	55	12 : 1	11

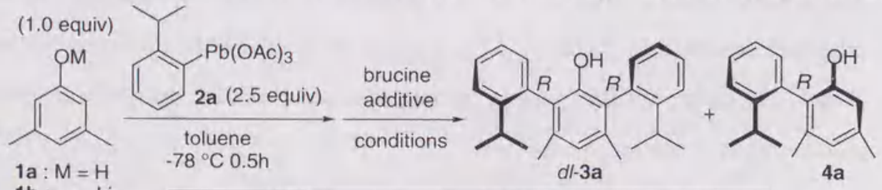
To investigate the effect of acetyl groups of arylleads on the enantioselectivity, 2-isopropylphenyllead tribenzoate (**13**) was prepared from lead tetrabenzoate[21] by the procedure described by Pinhey.[17c] The reaction between aryllead tribenzoate **13** and phenol **1a** using brucine gave a comparable yield of **3a** but with a lower enantioselectivity (eq 1).



(1)

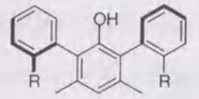
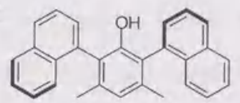
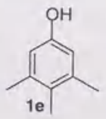
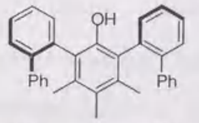
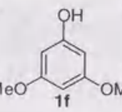
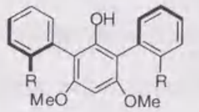
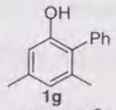
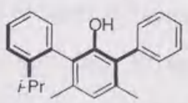
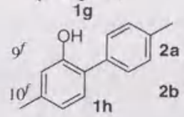
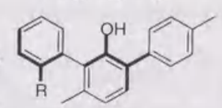
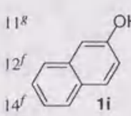
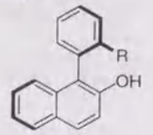
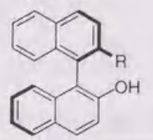
When the reaction was performed at a lower temperature (-20 °C), only mono-coupling product **4a** was obtained in a low yield but with slightly higher enantioselectivity (entry 2). In order to accelerate the reaction rate, we next examined the effect of metallation of phenol. With lithium phenoxide, prepared by treatment of phenol **1a** with *n*-BuLi at 0 °C in toluene, di-coupling product **3a** was obtained in a higher yield under similar conditions (entry 3). This may be due not only to higher reactivity of the metal phenoxide with aryllead triacetates but also to the decreased quantity of byproduct, acetic acid, which might concomitantly form the salt with brucine which subsequently retards reaction rates. Even more significant problem is that another equivalent of acetic acid is formed during the second coupling. Attempts to remove acetic acid by the inclusion effect of molecular sieves (4A or 13X) resulted in higher yields (entries 6 and 7). Finally, we found that the coupling reaction proceeded in a faster rate to completion using an excess (6 equiv) amount of brucine (entry 8). Despite lower conversions and slowed reaction rates, no diminution of enantioselectivity was achieved using smaller quantities of brucine (entries 9-11). These results indicate that a catalytic amount of brucine could facilitate the reaction, and in fact an improved turnover number (5.5) was realized by using 0.2 equiv of brucine.

Table 4. Effect of Metallation of **1a** and Additive in the Asymmetric Coupling with **2a**.

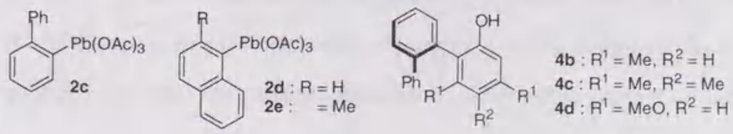


entry	M	brucine (equiv.)	additive	conditions (°C, h)	yield (%) 3a	4a	ee (%) 3a	4a
1	H	2	-	rt, 12	92	-	40	-
2	H	3	-	-20, 1	-	8	-	47
3	Li	3	-	-20, 2	22	25	60	52
4	Na	3	-	-20, 1	11	8	64	54
5	K	3	-	-20, 1	12	15	58	54
6	Li	3	MS 4A, 0.3g/mmol	-20, 16	64	8	63	56
7	Li	3	MS 13X, 0.3g/mmol	-20, 16	47	6	62	56
8	Li	6	MS 4A, 1.5g/mmol	-20, 24	99	-	61	-
9	Li	2	MS 4A, 1.5g/mmol	-20, 21	88	7	64	48
10	Li	1	MS 4A, 1.5g/mmol	-20, 21	75	20	66	58
11	Li	0.2	MS 4A, 1.5g/mmol	-20, 28	40	30	61	61

Table 5. Asymmetric ligand coupling with various arylleads.[a]

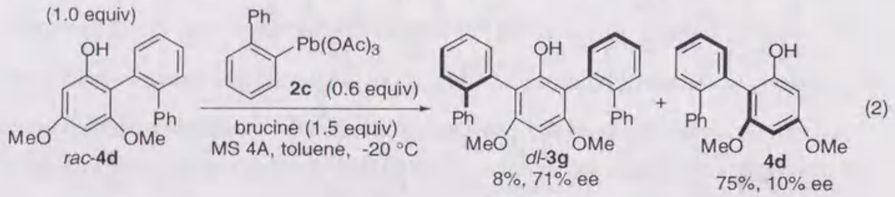
entry	phenol	aryllead	conditions[b] (°C, h)		major coupling product	yield (%)[c] (*dl*:*meso*)	ee (%)[d] (config)[e]
1	**1a**	**2a**	-20, 21	**3a** (R = *i*-Pr)		99 (>99:1)	61 (*R,R*)
2	**1a**	**2b**	-20, 28	**3b** (R = Me)		>99 (13:1)	49 (*R,R*)
3	**1a**	**2c**	-20, 52 0 , 12 rt, 24	**3c** (R = Ph)		68[h] (>99:1)	83
4	**1a**	**2d**	-20, 28	**3d**		>99 (2.0:1)	51
5	 **1e**	**2c**	-40, 120	**3e**		80[h] (>99:1)	87
6		**2a**	-40, 44 -20, 28	**3f** (R = *i*-Pr)		82 (>99:1)	54
7	MeO **1f** OMe	**2c**	-40, 35 -20, 28 0, 17 rt, 24	**3g** (R = Ph)		55[h] (6.9:1)	93
8[f]	 **1g**	**2a**	-40, 24	**3h**		86	46
9[f]	 **1h**	**2a**	-40, 72	**3i** (R = *i*-Pr)		99	85
10[f]		**2b**	-40, 24	**3j** (R = Me)		85	75
11[g]	 **1i**	**2a**	-40, 10	**3k** (R = *i*-Pr)		86	77
12[f]		**2c**	-40, 48	**3l** (R = Ph)		83	89 (*R*)
14[f]		**2d**	-40, 6	**3m** (R = H)		99	35
15[f]		**2e**	-40, 4	**3n** (R = Me)		99	20

[a] Unless otherwise specified, reactions were performed using lithiated phenol (1 eq), aryllead (2.5 eq), MS 4A (3 g/mmol), brucine (6 eq) in toluene. [b] All these reactants were mixed at -78 °C, and reacted under each reaction condition(s). For entries 3, 6 and 7, reaction temperature was gradually increased as specified. [c] Of isolated, purified major coupling product. [d] Enantiomeric excess of phenols, which was determined by chiral HPLC analysis. [e] The absolute configuration of the major enantiomer, which was determined in comparison with that in the literature. **3a-b**: ref. 10b; **3l**: ref. 18. Others are not assigned. [f] aryllead:brucine = 1.25:3 eq. [g] aryllead:brucine = 1:1 eq. [h] Mono-coupling products were also obtained (entry 3, **4b**, 26%, 38%ee; entry 5, **4c**, 16%, 70% ee; entry 7, **4d**, 25%, 29%ee).



Reaction Scope. The procedure described above was extended to the synthesis of various chiral phenols (Table 5). In general, the coupling of phenols with aryllead triacetates proceeded in high yields with moderate to high enantioselectivity, but with excellent diastereoselectivity. In particular, (2-phenyl)phenyllead triacetate (**2c**) was generally suitable in terms of high ee (entries 3, 5, 7, and 12). Moreover, enantiomerically pure phenols **3a**, **3c**, and **3e** were readily obtained by recrystallization from cyclohexane or hexane.

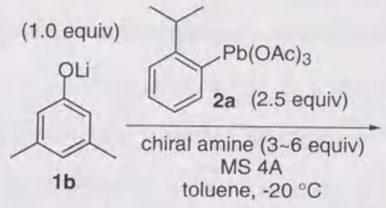
It should be noted that the kinetic resolution of mono-arylated phenols was observed in the second coupling to yield terphenols. For instance, the coupling of 3,5-dimethoxyphenol (**1f**) with aryllead **2c** afforded di-coupling product **3g** with high enantiomeric excess (93% ee), while providing mono-coupling product **4d** of 29% ee (entry 7). Further investigation indicated that the coupling of racemic mono-arylated phenol **4d** with aryllead **2c** gave 8% of di-coupling product **3g** with 71% ee, demonstrating the kinetic resolution despite the low conversion (eq 2).



Brucine Derivatives. Brucine is a structural analogue of strychnine which lacks methoxy substituents on the aromatic ring. Since the coupling reaction with strychnine displayed a lower enantioselectivity than that with brucine (Table 2, entries 17 and 18), we speculated that the methoxy group on the aromatic ring could affect enantioselectivity. Therefore, further studies aimed at the improvement of the enantioselectivity were undertaken using other brucine derivatives (Table 6). The enantioselectivity of the reaction between lithium phenoxide **1b** and aryllead **2a** was not influenced by the use of benzyloxy substituted brucine **14** (entry 2). In contrast, the

reaction with silyl-protected brucine **15** resulted in incomplete conversion of the staring substrate but increase in ee of mono-coupling product **4a** (entry 3).

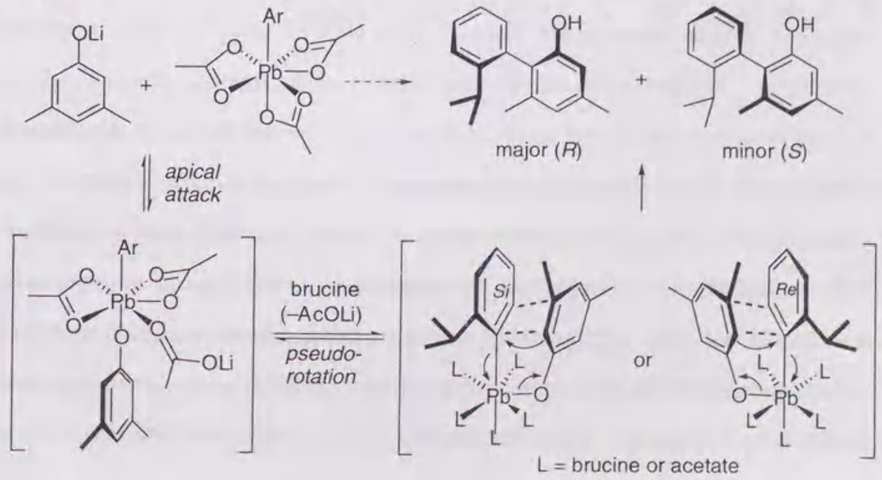
Table 6. Effect of Substituent on Brucine in the Asymmetric Coupling of **1a** with **2a**.



entry	brucine derivative	yield (%) 3a	yield (%) 4a	ee (%) 3a	ee (%) 4a
1	brucine	99	-	61	-
2	**14**	86	-	60	-
3	**15**	38	33	60	75

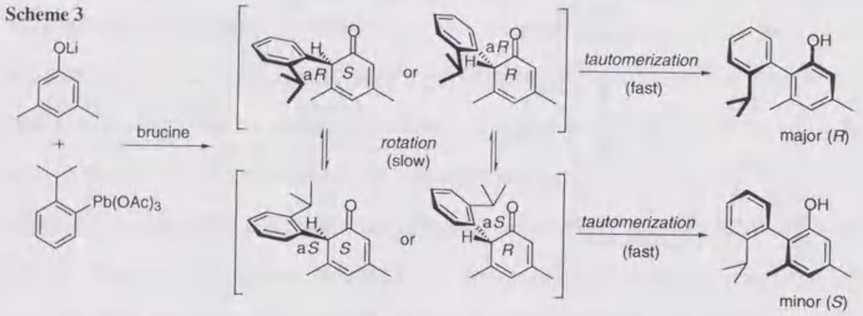
Plausible Mechanistic Model. Since brucine plays critical role for the high diastereo- and enantioselectivity, it presumably coordinates to the lead center to promote the ligand coupling. With this in mind and as suggested by Pinhey,[22] a plausible mechanism for the asymmetric ligand coupling was proposed (Scheme 2).

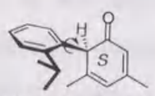
Scheme 2



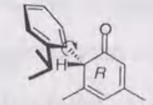
First, the lithium phenoxide coordinates to an apical position of lead, and the resulting lithium acetate might undergo ligand exchange with brucine. Subsequently, the configuration and conformation of this complex are supposed to be controlled by brucine during the pseudorotation. Finally, the oxidative coupling occurs to give (*R*)-**4a** as the major isomer.

Scheme 3

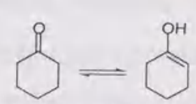




rotational barrier and rate constant:
AM1: ΔG = 17.7 kcal/mol (–Me)
: ΔG = 15.3 kcal/mol (–C=O)
: $k = 7.77 \times 10^{-1}$ s^{-1} (298 K) (–Me)
: $k = 4.2 \times 10^{1}$ s^{-1} (298 K) (–C=O)



rotational barrier and rate constant:
AM1: ΔG =16.5 kcal/mol (–Me)
: ΔG =11.2 kcal/mol (–C=O)
: k = 4.60 s^{-1} (298 K) (-Me)
: $k = 4.48 \times 10^{4}$ s^{-1} (298 K) (–C=O)



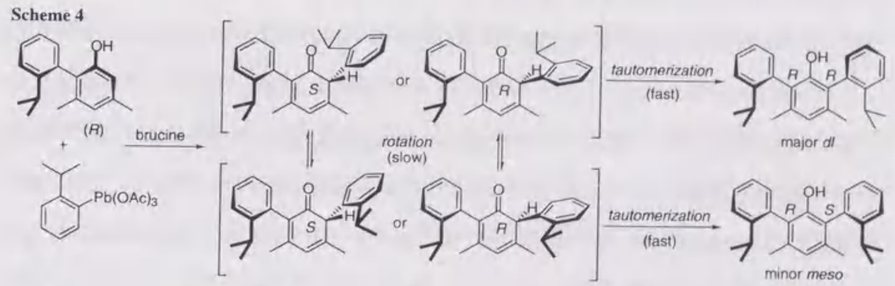
energy barrier and rate constant:
ΔG = 8.7 kcal/mol
$k = 3.10 \times 10^{6}$ s^{-1} (298 K)

The C-C bond formation between a phenol and an aryllead, as a phenonium cation equivalent, affords α-substituted dienones with a chiral center at their α-positions (Scheme 3). We envisioned that the axial chirality of the resulting phenol should not be transferred from this central chirality of the initially formed dienone, but rather arise from the chiral axis linking the dienone and its aryl group. The validity of this mechanism that involves the tautomerization of an axially chiral ketone to the phenol with no loss of axial chirality was demonstrated by comparison of several energy barriers. These were determined by molecular model calculations (AM1 and PM3) and measurement of the initial rate constant of the rotation, as well as some calculation results in the literatures.[23] Since the rotational barrier around the chiral axis at the α-

position of the ketone (the least value: >11.2 kcal/mol, rotation in the direction of C=O, see Scheme 3) is much higher than the energy barrier between cyclohexen-1-ol and cyclohexanone (8.7 kcal/mol), the tautomerism of dienone to phenol is likely much faster than the rotational isomerism. In this mechanism, whether initially formed central chirality is *S* or *R* is not important to induce the axial chirality. Rather a (pseudo-)axial chirality appended primarily on the sp^3 carbon should be translated accurately into a chiral axis on the sp^2 carbon, either a*S* or a*R*, although other possible chiral transfer pathways could not be ruled out.

On the basis of the above consideration and high diastereoselectivity (*dl* over *meso*) generally observed for di-coupling products, the second coupling might be intervened with steric constraints between *o*-substituents on arylleads and mono-arylated products to give *dl*-terphenols (Scheme 4). However, steric effect of brucine is nonnegligible in the second coupling as the kinetic resolution was observed.

Scheme 4



Conclusion

We have developed a method to prepare a variety of optically active biphenyls and terphenyls with axial chirality by the coupling of phenols with aryllead compounds. It was found that quinuclidine as a basic ligand for arylleads promotes the ligand coupling, and then the use of brucine, which had a conformationally restricted tertiary amine moiety, gave the desired axially chiral phenols with moderate to high enantioselectivity and excellent diastereoselectivity. This new method is applicable to the sterically

hindered substrates that could not be coupled by transition metal catalysts.

Experimental Section

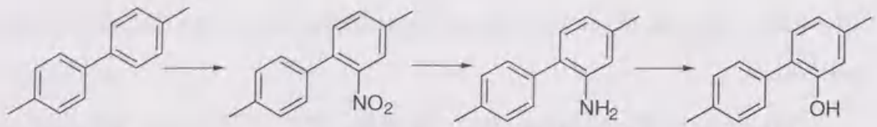
General. Infrared (IR) spectra were recorded on a Shimazu FTIR-8100 spectrometer. ^{1}H-NMR spectra were measured on Varian Gemini-300 (300 MHz) at ambient temperature. Data are recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (b = broad, s = singlet, d = doublet, t = triplet, and m = multiplet), coupling constant (Hz), integration, and assignment. ^{13}C-NMR spectra were recorded on Varian Gemini-300 (75 MHz) spectrometer at ambient temperature. Chemical shifts are recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.07 ppm). Chiral high-performance liquid chromatography (chiral HPLC) analyses were conducted using Shimazu LC-10AD coupled with diode array–detector SPD-MA10A-VP and the chiral column of CHIRALCEL OD-H (Daicel chemical industries, LTD.). All experiments were carried out under an atmosphere of dry argon. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF254 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel (E. Merck Art. 9385). Microanalysis was performed at the Faculty of Agriculture, Nagoya University. High-resolution mass spectra analyses were recorded at the Faculty of Technology, Nagoya University.

In experiments which required dry solvent toluene and CH_2Cl_2 were freshly distilled from calcium hydride, and tetrahydrofuran (THF) and hexane were freshly distilled from sodium metal using benzophenone ketyl as indicator. Organic substrates, phenol **1a**, **1e**, **1f**, **1g**, **1h**, and **1i**, and amine **5**, **6**, **7**, **8**, **9**, **12**, sparteine, dehydroabietylamine, eburnamonine, ajmalicine, $(DHQD)_2PHAL$, strychnine, and brucine were all commercially available, and were used without any purification. Lead compound **2d**,[17c] amines **10**,[24] and **11**,[25] and phenol **1g**[26] were prepared as described in the

literatures. Phenols (*R*)- and (*S*)-**3a**-**b**,[15c] *meso*-**3a**-**b**,[15c] **3m**,[11b] and **3n**[27] are all known compounds.

3,5-Dimethyl-2-phenylphenol (**1g**). IR (KBr) 3495, 1624, 1474, 1304, 1188 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.45 (m, 2H), 7.42-7.37 (m, 1H), 7.29-7.24 (m, 2H), 6.69 (s, 1H), 6.68 (s, 1H), 4.70 (s, 1H, OH), 2.32 (s, 3H, CH_3), 2.04 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 138.5, 136.9, 135.3, 130.4, 129.3, 128.0, 125.2, 122.8, 113.2. Anal. Calcd for C_14_H14O: C, 84.81, H, 7.12; Found: C, 84.82, **H**, 7.26.

3-Methyl-6-(4-methylphenyl)phenol (**1h**) IR (KBr) 3497, 1615, 1503, 1399, 1285, 1119 cm-1; 1H NMR (300 MHz, CDCl3) δ 7.34 (d, 2H, *J* = 8.4 Hz), 7.29 (d, 2H, *J* = 8.4 Hz), 7.12 (d, 1H, *J* = 7.8 Hz), 6.813 (s, 1H), 6.806 (d, 2H, *J* = 7.8 Hz), 5.16 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 139.0, 137.3, 134.0, 129.91, 129.85, 128.9, 125.2, 121.6, 116.2, 21.1 (two peaks are overlapped). Anal. Calcd for $C_{14}H_{14}O$: C, 84.81, H, 7.12; Found: C, 84.72, H, 7.18. This phenol **1h** was prepared from commercially available 4,4'-dimethylbiphenyl (**20**) according to the literature procedure [(1)-(2)][28] as follows: (1) Regioselective mono-nitration at the 2-position of **20** affording 2-nitro-4,4'-dimethylbiphenyl (**21**); (2) Reduction of the obtained mono-nitro compound **21** into 2-amino-4,4'-dimethylbiphenyl (**22**); (3) Sandmyer reaction to give the corresponding 4-diazo compound, followed by hydration with H_2O: To an aqueous H_2SO_4 (5.4 mL of H_2SO_4 in 15.0 mL of H_2O) solution of the amine (5.94 g, 30 mol) was added an aqueous solution of $NaNO_2$ (2.50 g, 36 mmol in 100 mL of H_2O) dropwise at 0 °C, followed by sequential treatment with urea (300 mg) and iced H_2O (ca. 30 g of ice + 30 mL of H_2O). This mixture was slowly warmed to 50 °C over 1h, stirred for 1h, and extracted with diethyl ether, and the organic layer was dried over Na_2SO_4. Evaporation of solvents and purification by column chromatography on silica gel gave the desirable phenol **19** (14.78 mmol, 49%) as a colorless solid



20 21 22 1h

General Procedure for the preparation of Aryllead Triacetate.[17c] The arylboronic acid (10.0 mmol) was added over 15 min to a stirred mixture of lead tetraacetate (4.43 g, 10.0 mmol) and mercury(II) acetate (0.5 mmol) in chloroform (15.2 ml) at 40 °C. The mixture was stirred at 40°C for 1h and then at room temperature overnight. The reaction mixture was filtered through Celite, which was then washed with chloroform (2 × 30 ml). The chloroform filtrate was washed with water (40 ml), and the aqueous layer was then extracted with chloroform (2 × 80 ml). The combined chloroform solution were filtered through Celite and then concentrated to a volume of 100 ml at 40 °C. Light petroleum (600 ml) was added and the mixture was kept at 0 °C overnight. Crystals of the aryllead triacetate were deposited and collected at the pump.

2-Isopropylphenyllead triacetate (**2a**). IR (KBr) 2967, 1572, 1374, 995 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, 1H, J = 8.4 Hz, ^{207}Pb satellites gave $J_{2\text{-}Pb}$ = 405 Hz), 7.89-7.09 (m, 3H), 3.03 (m, 1H), 2.10 (s, 9H, 3 x C=OCH_3), 1.34 (d, 6H, J = 6.6 Hz, 2 x CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.3, 162.9, 150.7, 132.1, 130.5, 129.4, 128.8, 37.0, 24.3, 20.4. Anal. Calcd for $C_{15}H_{20}O_6Pb$: C, 35.78, H, 4.00; Found: C, 35.78, H, 4.10.

2-Methylphenyllead triacetate (**2b**). IR (KBr) 3048, 1572, 1374, 994 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, 1H, J = 7.8 Hz, ^{207}Pb satellites gave $J_{2\text{-}Pb}$ = 405 Hz), 7.76-6.98 (m, 3H), 2.61 (s, 3H, C=CCH_3 ^{207}Pb satellites gave $J_{Me\text{-}Pb}$ = 33.3 Hz), 2.11 (s, 9H, 3 x C=OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.5, 163.2, 140.2, 132.8, 131.9, 130.8, 128.5, 21.9, 20.6. Anal. Calcd for $C_{13}H_{16}O_6Pb$: C, 32.84, H, 3.39; Found: C,

32.80, H, 3.44.

2-Phenylphenyllead triacetate (**2c**). IR (KBr) 3048, 1561, 1374, 994 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, 1H, J = 8.1 Hz, ^{207}Pb satellites gave $J_{2\text{-}Pb}$ = 403 Hz), 7.90-7.17 (m, 8H), 1.93 (s, 9H, 3 x C=OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.8, 164.9, 144.9 ,140.4, 131.7, 131.4, 130.0, 129.4, 128.8, 128.7, 128.6, 20.1. Anal. Calcd for $C_{18}H_{18}O_6Pb$: C, 40.22, H, 3.38; Found: C, 40.23, H, 3.32.

2-Methylnaphthyllead triacetate (**2e**). IR (KBr) 2977, 1759, 1547, 1427, 1264 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.35 (dd, 1H, J = 8.7, 4.5), 8.05-7.04 (m, 5H), 2.85 (s, 3H, ^{207}Pb satellites gave $J_{Me\text{-}Pb}$ = 21.3 Hz), 2.09 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.4, 164.2, 139.7, 134.5, 134.1, 131.9, 130.1, 128.5, 128.4, 126.4, s124.5, 22.5, 20.5. Anal. Calcd for $C_{17}H_{18}O_6Pb$: C, 38.85, H, 3.45; Found: C, 38.89, H, 3.43.

2-Isopropylphenyllead tribenzoate (**13**). IR (film) 2967, 1597, 1543, 1451, 1370, 1177 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (d, 6H, J = 7.2 Hz), 8.00-7.96 (m, 1H), 7.62-7.38 (m, 12H), 3.35-3.26 (m, 1H), 1.32 (d, 6H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 163.5, 150.9, 133.4, 132.1, 131.0, 130.8, 130.1, 129.5, 128.9, 128.2, 37.2, 24.5. HRMS (FAB+): Calcd for $C_{30}H_{26}O_6Pb$-$C_6H_5CO_2$: 569.1206; Found: 569.1238. This aryllead **13** was prepared according to the procedure described above, except for the use of lead tetrabenzoate[21] instead of lead tetraacetate.

General Procedure for the Asymmetric Coupling of Phenols with Arylleads. *dl*-3,5-Dimethyl-2,6-bis(2-isopropylphenyl)phenol (*dl*-**3a**). To a solution of phenol **1a** (6.10 g, 50.0 mmol) in toluene (650 mL) was added a 1.59 M hexane solution of *n*-BuLi (31.4 mL) at 0 °C under argon, and the mixture was stirred for 15 min. After the mixture was cooled to -78 °C, brucine [39.4 g, 100 mmol; *Caution!* EXTREMELY POISONOUS (oral LD_{50} in rats = 1 mg kg^{-1}) Handle in well-ventilated hood only.], aryllead **2a** (50.4 g, 100 mmol; *Caution!* Poisonous. Handle in well-ventilated hood only.) and molecular sieves 4A powder (150 g) were added sequentially. The mixture

was stirred at -20 °C for 21h, and filtered through a celite pad. The obtained cake was washed with CH_2Cl_2, and the filtrate was concentrated. The residue was purified by column chromatography, where non-polar products initially came off the column (diethyl ether/hexane = 1/10 to 1/1 as the eluent) to give **3a** (15.6 g, 88%), **4a** (0.84 g, 7%), and **1a** (0.31 g, 5%), whereas brucine remained at almost the starting point of the column. The next eluent (Et_3N/MeOH = 1/10) allowed >90% recovery of brucine, which can be reused after being washed with 10% NH_4OH and subsequently with diethyl ether, and dried (100 °C for 12h at 3 mmHg). **3a**: mp 148-149 °C (**3a**, >99% ee)

2-(2-Isopropylphenyl)-3,5-dimethylphenol (**4a**). IR (KBr) 3495, 2963, 1624, 1570, 1302, 1183 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48-7.38 (m, 2H), 7.31-7.25 (m, 1H), 7.10 (d, 1H, J = 7.8 Hz), 6.68 (d, 2H, J = 4.8 Hz), 4.46 (s, 1H, OH), 2.68 (m, 1H), 2.33 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 1.12 (d, 3H, J = 6.9 Hz, CHCH_3), 1.11 (d, 3H, J = 6.9 Hz, CHCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 148.9, 138.3, 137.1, 132.9, 130.9, 129.0, 126.6, 126.3, 124.3, 122.7, 112.9, 30.0, 24.4, 23.6, 21.3, 20.2. Anal. Calcd for $C_{17}H_{20}O$: C, 84.96, H, 8.39; Found: C, 84.97, H, 8.44. HPLC analysis (column: OD-H): retention times of two enantiomers of **4a**: t_R = 11.4 (major) and 15.6 (minor) min using *i*-PrOH/hexane (1/400) as the eluent at a flow rate of 1.0 mL/min.

dl-3,5-Dimethyl-2,6-bis(2-phenylphenyl)phenol (*dl*-**3c**). mp 44 -45°C (**3c**, >99% ee); IR (KBr) 3544, 1448, 1291, 1225, 1150, 1051 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49-7.36 (m, 6H), 7.21 (s, 10H), 7.04-7.01 (m, 2H), 6.39 (s, 1H, MeC=CH-CMe), 4.58 (s, 1H, OH), 1.76 (s, 6H, 2 x CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 142.4, 141.2, 135.7, 134.8, 131.3, 130.3, 128.8, 128.1, 127.6 (two peaks are overlapped), 126.7, 124.9, 123.0, 20.0. Anal. Calcd for $C_{32}H_{26}O$: C, 90.11, H, 6.14; Found: C, 90.09, H, 6.39. HPLC analysis (column: OD-H): retention times of two enantiomers of *dl*-**3c**: t_R = 20.5 (major) and 25.3 (minor) min using *i*-PrOH/hexane (1/200) as the eluent at a flow rate

of 1.0 mL/min.

3,5-Dimethyl-2-(2-phenylphenyl)phenol (**4b**) (Table 5, entry 3). IR (KBr) 3438, 1622, 1570, 1302, 1188 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54-7.41 (m, 3H), 7.29-7.24 (m, 1H), 7.13-7.22 (m, 5H), 6.56 (s, 1H), 6.49 (s, 1H), 4.68 (s, 1H, OH), 2.24 (s, 3H, CH_3), 1.79 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 142.8, 140.6, 138.4, 136.8, 133.4, 131.5, 130.9, 128.7, 128.6, 128.1, 127.8, 126.9, 124.6, 122.7, 112.9, 21.2, 20.1. Anal. Calcd for $C_{20}H_{18}O$: C, 87.56, H, 6.61; Found: C, 87.55, H, 6.62. HPLC analysis (column: OD-H): retention times of two enantiomers of **4b**: t_R = 10.0 (major) and 12.4 (minor) min using *i*-PrOH/hexane (1/40) as the eluent at a flow rate of 1.0 mL/min.

dl- and *meso*-3,5-Dimethyl-2,6-bis(1-naphthyl)phenol (*dl*- and *meso*-**3d**). IR (KBr) 3546, 1509, 1389, 1289, 1238, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.91-7.87 (m, 4H), 7.68-7.42 (m, 10H), 6.96 (*dl*) (s, 1H, MeC=CH-CMe), 6.98 (*meso*) (s, 1H, MeC=CH-CMe), 4.49 (*dl*) (s, 1H, OH), 4.50 (*meso*) (s, 1H, OH), 2.02 (*dl*) (s, 6H, CH_3), 2.03 (*meso*) (s, 6H, 2 x CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) for *dl*-isomer: δ 151.0, 137.5, 134.1, 133.9, 132.3, 128.4, 128.2, 128.0, 126.4,126.0 (two peaks are overlapped), 125.7 (two peaks are overlapped), 125.6, 123.7, 123.3, 20.1. for *meso*-isomer: δ 151.0, 137.7, 134.0, 133.9, 132.3, 128.4, 128.3, 128.2, 126.4, 126.0 (two peaks are overlapped), 125.7 (two peaks are overlapped), 125.4, 123.6, 123.4, 20.1. Anal. Calcd for $C_{28}H_{22}O$: C, 89.81, H, 5.92; Found: C, 89.80, H, 6.03. HPLC analysis (column: OD-H): retention times of two enantiomers of *dl*-**3d**: t_R = 5.0 (minor) and 10.6 (major) min; *meso*-**3d**: t_R = 5.40 using *i*-PrOH/hexane (1/9) as the eluent at a flow rate of 1.0 mL/min.

3,4,5-Trimethyl-2,6-bis(2-phenylphenyl)phenol (**3e**). mp 44-45 °C (**3e**, >99% ee); IR (KBr) 3649, 1418, 1287, 1227, 1042 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48-7.35 (m, 6H), 7.20 (s, 10H), 7.02-6.99 (m, 2H), 4.41 (s, 1H, OH), 1.90 (s, 3H, CH_3), 1.72 (s, 6H, 2 x CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 142.6, 141.4, 135.8, 133.9, 131.4,

130.2, 128.8, 127.9, 127.6 (two peaks are overlapped), 126.5, 126.4, 125.0, 17.6, 15.8. Anal. Calcd for $C_{33}H_{28}O$: C, 89.96, H, 6.41; Found: C, 89.95, H, 6.69. HPLC analysis (column: OD-H): retention times of two enantiomers of *dl*-**3e**: t_R = 6.3 (minor) and 6.8 (major) min using *i*-PrOH/hexane (1/20) as the eluent at a flow rate of 1.0 mL/min.

3,4,5-Trimethyl-2-(2-phenylphenyl)phenol (**4c**) (Table 5, entry 5). IR (KBr) 3511, 1466, 1293, 1181, 1038 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53-7.43 (m, 3H), 7.27-7.24 (m, 1H), 7.20-7.12 (m, 5H), 6.58 (s, 1H), 4.52 (s, 1H, OH), 2.21 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 1.75 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 142.9, 140.7, 136.7, 134.9, 134.3, 131.7, 130.8, 128.6, 128.5, 128.0, 127.8, 126.8, 126.7, 125.2, 113.7, 20.8, 17.6, 15.2. Anal. Calcd for $C_{21}H_{20}O$: C, 87.46, H, 6.99; Found: C, 87.23, H,7.21. HPLC analysis (column: OD-H): retention times of two enantiomers of **4c**: t_R = 41.7 (major) and 66.1 (minor) min using *i*-PrOH/hexane (1/400) as the eluent at a flow rate of 1.0 mL/min.

2,6-Bis(2-isopropylphenyl)-3,5-dimethoxyphenol (**3f**). IR (KBr) 3532, 2961, 1624, 1337, 1206, 1109 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44-7.14 (m, 8H), 6.26 (s, 1H, MeOC=CH-COMe), 4.60 (s, 1H, OH), 3.77 (s, 6H, 2 x OCH_3), 2.84 (m, 2H), 1.19 (d, 6H, J = 6.9 Hz, $CH(CH_3)_2$), 1.12 (d, 6H, J = 6.9 Hz, $CH(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3, 151.8, 149.1, 131.5, 131.3, 128.4, 125.9, 125.6, 109.3, 87.4, 55.5, 30.4, 24.1, 23.7. Anal. Calcd for $C_{26}H_{30}O_3$: C, 79.97, H, 7.74; Found: C, 79.98, H, 7.87. HPLC analysis (column: OD-H): retention times of two enantiomers of *dl*-**3f**: t_R = 9.9 (minor) and 11.3 (major) min using *i*-PrOH/hexane (1/400) as the eluent at a flow rate of 1.0 mL/min.

3,5-Dimethoxy-2,6-bis(2-phenylphenyl)phenol (**3g**). IR (KBr) 3534, 1619, 1462, 1337, 1204, 1105 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) common peaks for *dl*- and *meso*-isomer: δ 7.46-7.32 (m, 6H), 7.24-7.03 (m, 12H), 5.77 (s, 1H), for *dl*-isomer: 4.77 (s,

1H, OH), 3.36 (s, 6H, 2 x OCH_3), for *meso*-isomer: 4.98 (s, 1H, OH), 3.31 (s, 6H, 2 x OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) for *dl*-isomer: δ 157.0, 151.1, 143.1, 141.7, 131.6, 129.9, 128.5, 127.9, 124.4, 127.3, 126.3, 109.6, 87.6, 55.2. for *meso*-isomer: δ 157.0, 151.0, 143.2, 141.8, 131.9, 131.4, 130.2, 128.5, 128.0, 127.4 (two peaks may be overlapped), 126.3, 109.6, 87.6, 55.1. Anal. Calcd for $C_{32}H_{26}O_3$: C, 83.82, H, 5.71; Found: C, 83.85, H, 5.75. HPLC analysis (column: OD-H): retention times of two enantiomers of *dl*-**3g**: t_R = 21.1 (major) and 28.4 (minor) min; *meso*-**3g**: t_R = 32.0 using *i*-PrOH/hexane (1/100) as the eluent at a flow rate of 1.0 mL/min.

3,5-Dimethoxy-2-(2-phenylphenyl)phenol (**4d**) (Table 5, entry 7). IR (KBr) 3534 ,1622, 1586, 1208, 1152, 1100 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52-7.41 (m, 3H), 7.37-7.31 (m, 1H), 7.24-7.13 (m, 5H), 6.09 (d, 1H, J = 2.4 Hz), 5.93 (d, 1H, J = 2.1 Hz), 4.93 (s, 1H, OH), 3.74 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8, 157.9, 154.1, 143.6, 141.1, 131.9, 130.6, 130.5, 128.6, 128.4, 128.0, 127.6, 126.7, 109.5, 92.3, 91.3, 55.3, 55.2. Anal. Calcd for $C_{20}H_{18}O_3$: C, 78.41, H, 5.92; Found: C, 78.41, H, 6.04. HPLC analysis (column: OD-H): retention times of two enantiomers of **4d**: t_R = 7.4 (major) and 8.3 (minor) min; using *i*-PrOH/hexane (1/9) as the eluent at a flow rate of 1.0 mL/min.

6-(2-Isoprpopylphenyl)-3,5-dimethyl-2-phenylphenol (**3h**). IR (KBr) 3544, 2961, 1458, 1401, 1291, 1051 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48-7.24 (m, 8H), 7.15-7.12 (m, 1H), 6.82 (s, 1H, MeC=CH-CMe), 4.55 (s, 1H, OH), 2.76 (m, 1H), 2.13 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 1.16 (d, 3H, J = 6.9 HZ, $CHCH_3$), 1.13 (d, 3H, J = 6.9 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 148.3, 136.6, 136.3, 136.0, 134.1, 130.5, 130.3, 128.7, 128.5, 127.3, 126.3, 125.9, 125.6, 125.1, 123.2, 30.2, 24.3, 23.7, 20.4, 20.1. Anal. Calcd for $C_{23}H_{24}O$: C, 87.30, H, 7.64; Found: C, 87.31, H, 7.92. HPLC analysis (column: OD-H): retention times of two enantiomers of **3h**: t_R = 9.0 (minor) and 10.6 (major) min using *i*-PrOH/hexane (1/400) as the eluent at a flow rate of 1.0

mL/min.

2-(2-Isopropylphenyl)-3-methyl-6-(4-methylphenyl)phenol (**3i**). IR (KBr) 3530, 2963, 1458, 1395, 1242, 1117 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49-7.40 (m, 4H), 7.33-7.15 (m, 5H), 6.92 (d, 1H, J = 7.8 Hz), 4.80 (s, 1H, OH), 2.73 (m, 1H), 2.38 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.15 (d, 3H, J = 6.9 Hz, $CHCH_3$), 1.14 (d, 3H, J = 6.9 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.7, 148.5, 136.74, 136.67, 135.2, 133.4, 130.5, 129.19, 129.16, 129.1, 128.9, 127.8, 126.6, 126.3, 125.4, 121.8, 30.1, 24.4, 23.7, 21.2, 20.3. Anal. Calcd for $C_{23}H_{24}O$: C, 87.30, H, 7.64; Found: C, 87.22, H, 7.94. HPLC analysis (column: OD-H): retention times of two enantiomers of **3i**: t_R = 12.2 (minor) and 21.6 (major) min using *i*-PrOH/hexane (1/400) as the eluent at a flow rate of 1.0 mL/min.

3-Methyl-2-(2-methylphenyl)-6-(4-methylphenyl)phenol (**3j**). IR (KBr) 3528, 1541, 1509, 1397, 1246 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (d, 2H, J = 8.1 Hz), 7.37-7.18 (m, 7H), 6.92 (d, 1H, J = 8.1 Hz), 4.82 (s, 1H, OH), 2.38 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.00 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.3, 137.6, 136.7, 136.4, 135.0, 134.9, 130.6, 130.3, 129.2 (two peaks are overlapped), 129.0, 128.4, 127.8, 126.6, 125.4, 121.9, 21.2, 19.9, 19.5. Anal. Calcd for $C_{21}H_{20}O$: C, 87.46, H, 6.99; Found: C, 87.46, H, 7.12. HPLC analysis (column: OD-H): retention times of two enantiomers of **3j**: t_R = 15.6 (minor) and 25.8 (major) min using *i*-PrOH/hexane (1/400) as the eluent at a flow rate of 1.0 mL/min.

1-(2-Isopropylphenyl)-2-naphthol (**3k**). IR (KBr) 3490, 2961, 1619, 1462, 1389, 1181 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85-7.79 (m, 2H), 7.58-7.48 (m, 2H), 7.39-7.16 (m, 6H), 4.89 (s, 1H, OH), 2.61 (m, 1H), 1.11 (d, 3H, J = 6.9 Hz, $CHCH_3$), 1.02 (d, 3H, J = 6.9 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.3, 149.8, 133.6, 131.6 (two peaks are overlapped), 129.4, 129.3, 128.8, 128.0, 126.8, 126.6., 126.4, 124.7, 123.3, 120.1, 117.2, 30.2, 24.3, 23.9. Anal. Calcd for $C_{19}H_{18}O$: C, 86.99, H, 6.92; Found: C,

86.98, H, 7.06. HPLC analysis (column: OD-H): retention times of two enantiomers of **3k**: t_R = 15.7 (major) and 18.3 (minor) min using *i*-PrOH/hexane (1/400) as the eluent at a flow rate of 1.0 mL/min.

1-(2-Phenylphenyl)-2-naphthol (**3l**). IR (KBr) 3507, 1620, 1540, 1389, 1181 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73-7.66 (m, 2H), 7.62-7.48 (m, 3H), 7.40-7.22 (m, 4H), 7.10-6.99 (m, 6H), 4.97 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 143.4, 140.2, 133.5, 132.7, 132.2, 131.0, 129.5, 129.2, 128.7, 128.4, 128.3, 128.0, 127.8, 127.1, 126.4, 124.7, 123.2, 120.4, 117.1. Anal. Calcd for $C_{22}H_{16}O$: C, 89.16, H, 5.44; Found: C, 89.13, H, 5.48. HPLC analysis (column: doubly-arrayed OD-H): retention times of two enantiomers of **3l**: t_R (*S*-**3l**: minor isomer) = 39.8 and t_R (*R*-**16**: major isomer) = 41.5 min using *i*-PrOH/hexane (1/20) as the eluent at a flow rate of 0.5 mL/min.

2-hydroxy-1,1'-Binaphthyl (**3m**). HPLC analysis (column: OD-H): retention times of two enantiomers of **3m**: t_R (*S*-**3m**: minor isomer) = 9.3 and t_R (*R*-**3m**: major isomer) = 15.5 min using *i*-PrOH/hexane (1/20) as the eluent at a flow rate of 1.0 mL/min.

2-hydroxy-2'-methoxy-1,1'-Binaphthyl (**3n**). HPLC analysis (column: triply-arrayed OD-H): retention times of two enantiomers of **3n**: t_R (*S*-**3n**: minor isomer) = 59.8 and t_R (*R*-**3n**: major isomer) = 62.3 min using *i*-PrOH/hexane (1/20) as the eluent at a flow rate of 0.5 mL/min.

10-Benzyloxy-11-methoxystrychnine (**14**). To a suspension of 10-hydroxy-11-methoxystrychnine[29] (1.6 g, 4.2 mmol) in DMSO (160 ml) at 80 °C was added NaH (110 mg, 4.6 mmol) under Ar. After 30 min, benzyl bromide (547 µl, 4.6 mmol) was added, and then the mixture was stirred at 80 °C for 1 h. The whole mixture was added CH_2Cl_2 (500 ml) and then washed with water (100 ml). The organic layer was dried over Na_2SO_4, and filtered, and the solvents were removed via rotary evaporation. The product was purified by flash chromatography (Methanol/Et_3N = 10/1 as the eluent) to give 395 mg (20%) of **14**. IR (film) 2861, 2361, 1665, 1497, 1451, 1401, 1283 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.42-7.28 (m, 5H), 6.64 (s, 1H), 5.89 (bs, 1H), 5.10 (s, 2H), 4.30-7.25 (m, 1H), 4.25-4.01 (m, 2H), 3.91 (s, 3H), 3.80 (d, 1H, J = 10.2 Hz), 3.74 (bs, 1H), 3.68 (d, 1H, J = 14.4 Hz), 3.19-3.06 (m, 3H), 2.86-2.77 (m, 1H), 2.71 (d, 1H, J = 15.0 Hz), 2.64 (dd, 1H, J = 17.7, 3.3 Hz), 2.31 (dt, 1H, J = 14.4, 4.2 Hz), 1.82-1.74 (m, 2H), 1.39 (d, 1H, J = 14.4 Hz), 1.28-1.22 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 150.3, 144.9, 140.3, 137.1, 136.6, 128.4, 127.8, 127.6, 127.5, 123.3, 109.6, 101.2, 77.7, 72.1, 64.5, 60.3, 59.9, 56.2, 52.6, 51.7, 50.1, 48.2, 42.4, 42.3, 31.5, 26.6. HRMS (FAB+): Calcd for $C_{29}H_{30}N_2O_4$+H$^+$: 471.2284; Found: 471.2270. $[\alpha]^{25}_D$ = -69.3° (*c* 1.63, $CHCl_3$).

10-*t*-Butyldiphenylsiloxy-11-methoxystrychnine (**15**). To a suspension of 10-hydroxy-11-methoxystrychnine[29] (380 mg, 1.0 mmol) in DMSO (20 ml) at 80 °C was added NaH (26 mg, 1.1 mmol) under Ar. After 30 min, *t*-Butylchlorodiphenylsilane (572 µl, 2.2 mmol) was added, and then the mixture was stirred at 60 °C for 5 h. The whole mixture was added CH_2Cl_2 (50 ml) and then washed with water (50 ml). The organic layer was dried over Na_2SO_4, and filtered, and the solvents were removed via rotary evaporation. The product was purified by flash chromatography (Methanol as the eluent) to give 62 mg (10%) of **15**. IR (film) 2857, 2361, 1665, 1497, 1449, 1401, 1287 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69-7.65 (m, 5H), 7.40-7.26 (m, 6H), 6.33 (s, 1H), 5.84 (bs, 1H), 4.26-4.21 (m, 1H), 4.16-3.98 (m, 2H), 3.70 (d, 1H, J = 10.8 Hz), 3.67 (s, 3H), 3.61 (bd, 1H, J = 15.0 Hz), 3.37 (bs, 1H), 3.11-3.02 (m, 3H), 2.77-2.56 (m, 3H), 2.18 (dt, 1H, J = 15.0, 6.0 Hz), 1.71-1.65 (m, 1H), 1.58-1.47 (m, 1H), 1.22-1.13 (m, 2H), 1.12 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 150.4, 141.8, 140.6, 136.1, 135.50, 135.45, 133.33, 133.30, 129.7, 129.6, 127.5, 127.4, 127.2, 123.3, 114.0, 101.2, 77.7, 64.5, 60.3, 59.7, 55.7, 52.5, 51.4, 50.1, 48.1, 42.3, 42.1, 31.4, 26.7, 26.5, 19.7. HRMS (FAB+): Calcd for $C_{38}H_{42}N_2O_4Si$+H$^+$: 619.2992; Found: 619.2964. $[\alpha]^{25}_D$ = -66.6° (*c* 0.56, $CHCl_3$).

Acknowledgment: We are grateful to Mr. S. Komai and H. Choshi (Nagoya University) for performing high resolution mass spectrometric analysis. T. K. also acknowledges a JSPS Fellowship for Japanese Junior Scientists.

Reference

(1) (a) Evans, D. A.; Wood, M. R.; Trotter, W.; Richardson, T. I.; Barrow, J. C.; Katz, J. L. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 2700. (b) Nicolaou, K. C.; Natarajan, S.; Li, H.; Jain, N. F.; Hughes, R.; Solomon, M.E.; Ramanjulu, J. M.; Boddy, C. N. C.; Takayanagi, M. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 2708. (c) Meyers, A. I.; Willemsen, J. J. *Chem. Commun.* **1997**, 1673. (d) Chau, P.; Czuba, I. R.; Rizzacasa, M. A.; Bringmann, G.; Gulden, K.-P.; Schäffer, M. *J. Org. Chem.* **1996**, *61*, 7101. (e) Tomioka, K; Ishiguro, T; Koga, K. *Tetrahedron Lett.* **1980**, *21*, 2973.

(2) (a) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. Eds. *Comprehensive Asymmetric Catalysis*; Springer-Verlag: Berlin Heidelderg, 1999. (b) Noyori, R. Ed. *Asymmetric Catalysis in Organic Synthesis*; John Wiley & Sons: New York, 1994.

(3) For recent examples: (a) Takata, T.; Furusho, Y.; Murakawa, K.; Endo, T.; Matsuoka, H.; Hirasa, T.; Matsuo, J.; Sisido, M. *J. Am. Chem. Soc.* **1998**, *120*, 4530. and references cited therein. (b) Nozaki, K.; Terakawa, T.; Takaya, H.; Hiyama, T. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 131. (c) Ito, Y.; Miyake, T.; Ghima, R.; Ohara, T.; Suginome, M. *J. Am. Chem. Soc.* **1998**, *120*, 11880.

(4) (a) Tamao, K.; Sumitani, K.; Kiso, Y.; Zembayashi, N.; Fujioka, A.; Kodama, S.; Nakajima, I.; Minato, A.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1958. (b) Stille, J. K. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 508.

(5) (a) Knochel, P.; Singer, R. *Chem. Rev.* **1993**, *93*, 2117. (b) Miyaura, A.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. For recent advances in this field, see: (c) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722. (d) Littke, A.

F.; Fu, G. C. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 3387.

(6) For recent reviews, see: (a) Bringmann, G.; Breuning, M.; Tasler, S. *Synthesis* **1999**, 525. (b) Bringmann, G.; Walter, R.; Weirich, R. In *Methods of Organic Chemistry (Houben Weyl)*, 4th ed.; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1995; Vol. E21a, p 567. (c) Bringmann, G.; Walter, R.; Weirich, R. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 977.

(7) (a) Miyano, S.; Fukushima, H.; Hanada, S.; Ito, H.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3249. (b) Lipshutz, B. H.; Kayser, F.; Liu, Z.-P. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1842. (c) Sugimura, T.; Yamada, H.; Inoue, S.; Tai, A. *Tetrahedron: Asymmetry* **1997**, *8*, 649. (d) Lin, G.-Q.; Zhong, M. *Tetrahedron: Asymmetry* **1997**, *8*, 1369.

(8) (a) Tomioka, K.; Ishiguro, T.; Iitaka, Y.; Koga, K. *Tetrahedron* **1984**, *40*, 1303. (b) Feldman, K. S.; Smith, R. S. *J. Org. Chem.* **1996**, *61*, 2606. (c) Arisawa, M.; Utsumi, S.; Nakajima, M.; Ramesh, N. G.; Tohma, H.; Kita, Y. *Chem. Commun.* **1999**, 469. (d) Feringa, B.; Wynberg, H. *J. Org. Chem.* **1981**, *46*, 2547. (e) Brussee, J.; Jansen, A. C. A. *Tetrahedron Lett.* **1983**, *24*, 3261. (f) Yamamoto, K.; Fukushima, H.; Nakazaki, M. *Chem. Commun.* **1984**, 1490. (g) Osa, T.; Kashiwagi, Y.; Yanagisawa, Y.; Bobbitt, M. *Chem. Commun.* **1994**, 2535. (h) Smrcina, M.; Poláková, J.; Vyskocil, S.; Kocovsky, P. *J. Org. Chem.* **1993**, *58*, 4534. (i) Nakajima, M.; Miyoshi, I.; Kanayama, K.; Hashimoto, S.; Noji, M.; Koga, K. *J. Org. Chem.* **1999**, *64*, 2264. (j) Irie, R.; Masutani, K.; Katsuki, T. *Synlett* **2000**, 1433.

(9) (a) Reuman, M.; Meyers, A. I. *Tetrahedron* **1985**, *41*, 837. (b) Gant, T. G.; Meyers, A. I. *Tetrahedron* **1994**, *50*, 2297. (c) Meyers, A. I.; Lutomski, K. A. *J. Am. Chem. Soc.* **1982**, *104*, 879. (d) Meyers, A. I.; Himmelsbach, R. J. *J. Am. Chem. Soc.* **1985**, *107*, 682. (e) Wilson, J. M.; Cram, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 881. (f) Hattori, T.; Hotta, H.; Suzuki, T.; Miyano, S. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 613. (g) Hattori, T.; Koike, N.; Miyano, S. *J. Chem. Soc. Perkin Trans. 1* **1994**, 2273. (h) Baker, R. W.; Pocock, G. R.; Sargent, M. V. *Chem. Commun.* **1993**, 1489. (i) Baker, R. W.; Pocock, G. R.; Sargent, M. V.; Twiss, E. *Tetrahedron: Asymmetry* **1993**, *4*, 2423.

(10) (a) Hayashi, T.; Hayashizaki, K.; Kiyoi, T.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8153. (b) Hayashi, T.; Hayashizaki, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 215. (c) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12051. (d) Cammidge, A. N.; Crépy, V. L. *Chem. Commun.* **2000**, 1723. (e) Uemura, M.; Kamikawa, K. *Synlett* **2000**, 938. (f) Kamikawa, K.; Watanabe, T.; Uemura, M. *J. Org. Chem.* **1996**, *61*, 1375. (g) Nelson, S. G.; Hilfiker, M. A. *Org. Lett.* **1999**, *1*, 1379.

(11) (a) Miyano, S.; Kawahara, K.; Inoue, Y.; Hashimoto, H. *Chem. Lett.* **1987**, 355. (b) Tamai, Y.; Nakano, T.; Koike, S.; Kawahara, K.; Miyano, S. *Chem. Lett.* **1989**, 1135.

(12) (a) T. Konegawa, T. Nakamura, T. Matsumoto, K. Suzuki, 76th National Meeting of the Chemical Society of Japan (1999). (b) Hayashi, T.; Niizuma, S.; Kamikawa, T.; Suzuki, N.; Uozumi, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9101.

(13) Barton, D. H. R.; Donnelly, D. M. X.; Guiry, P. J.; Finet, J.-P. *J. Chem. Soc. Perkin Trans. 1* **1994**, 2921.

(14) (a) Bell, H. C.; Pinhey, J. T.; Sternhell, S. *Aust. J. Chem.* **1979**, *32*, 1551. (b) Pinhey, J. T. *Aust. J. Chem.* **1991**, *44*, 1353. (c) Pinhey, J. T. *Pure Appl. Chem.* **1996**, *68*, 819.

(15) (a) Saito, S.; Hatanaka, K.; Kano, T.; Yamamoto, H. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 3378. (b) Saito, S.; Hatanaka, K.; Yamamoto, H. *Org. Lett.* **2000**, *2*, 1891. For preliminary preparation of **3a-b**, see: (c) Saito, S.; Kano, T.; Hatanaka, K.; Yamamoto, H. *J. Org. Chem.* **1997**, *62*, 5651.

(16) Saito, S.; Kano, T.; Muto, H.; Nakadai, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1999**, *121*, 8943.

(17) (a) Bell, H. C.; Kalman, J. R.; Pinhey, J. T. *Aust. J. Chem.* **1979**, *32*, 1521. (b) Kozyrod, R. P. Morgan, J.; Pinhey, J. T. *Aust. J. Chem.* **1985**, *38*, 1147. For the preparation of aryllead compounds **2a**-**e**, see: (c) Morgan, J.; Pinhey, J. T. *J. Chem. Soc. Perkin Trans. 1* **1990**, 715.

(18) The diastereoselectivity (*dl*:*meso*) was unambiguously ascertained by ^{1}H NMR and HPLC analysis. See reference 15c.

(19) 2,6-Dibromo-3,5-dimethylanisole (**23**) and boronic acids **24a**, **b** were subjected to Suzuki coupling to give the corresponding terphenyl adducts **25a**, **b** with moderate yields and diastereoselectivities. See reference 30.

(20) The ee % of each adduct was determined by chiral HPLC analysis.

(21) Hey, D. H.; Stirling, C. J. M.; Williams, G. H. *J. Chem. Soc.* **1954**, 2747.

(22) (a) Morgan, J.; Hambley, T. W. Pinhey, J. T. *J. Chem. Soc. Perkin Trans. 1* **1996**, 2173. A free radical process seems highly unlikely, see: (b) Hambley, T. W.; Holmes, R. J.; Parkinson, C. J.; Pinhey, J. T. *J. Chem. Soc. Perkin Trans. 1* **1992**, 1927. (c) Morgan, J.; Parkinson, C. J.; Pinhey, J. T. *J. Chem. Soc. Perkin Trans. 1* **1994**, 3361, and references cited therein.

(23) Energy barrier between cyclohexen-1-ol and cyclohexanone: Zhang, X.-M. *J. Org. Chem.* **1998**, *63*, 5314.

(24) Hoffmann, H. M. R.; Plessner, T.; von Riesen, C. *Synlett* **1996**, 690.

(25) The synthesis of (+)-bis[(*R*)-1-phenylethyl]amine: Marshall, J. A.; Lebreton, J. *J. Am. Chem. Soc.* **1988**, *110*, 2925. This procedure was followed by an usual reductive methylation by sequential treatment with formaldehyde and formic acid to give **11**. CAS Registry No. 210367-14-9.

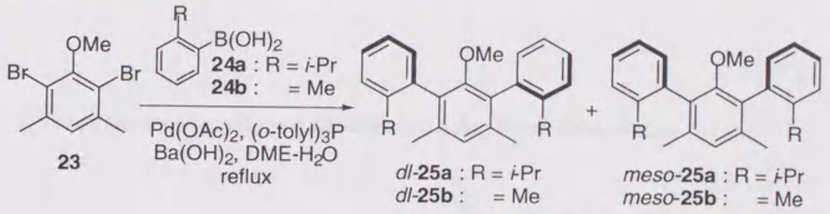
(26) Kaumi, T.; Murata , C.; Sasaki, Y.; Kitajima, H. *Synthesis*, **1980**, 634.

(27) Pirkle, W. H.; Schreiner, J. L. *J. Org. Chem.* **1981**, *46*, 4988.

(28) Whitesides, G. M.; Eisenhut, M.; Bunting, W. M.; *J. Am. Chem. Soc.* **1974**, *96*, 5398.

(29) Verpoorte, R.; van Beek, T. A.; Riegman, R. L. M. *Org. Magn. Reson.* **1984**, *22*, 345.

(30) Suzuki Coupling Reactions between bulky dibromophenyl methyl ether **23** and bulky boric acids (**24a**, **b**). The yield and the diastereoselectivity of each reaction were obtained as indicated below.[15c]



47% (*dl*-**25a** : *meso*-**25a** = 99 : 1)
95% (*dl*-**25b** : *meso*-**25b** = 49 : 51)

Chapter 4

Direct Coupling of Anilines with Aryllead Triacetates

Abstract: The aryl-aryl coupling of aryllead compounds at the *ortho*-position of anilines was achieved by simple magnesation of the aniline nitrogen.

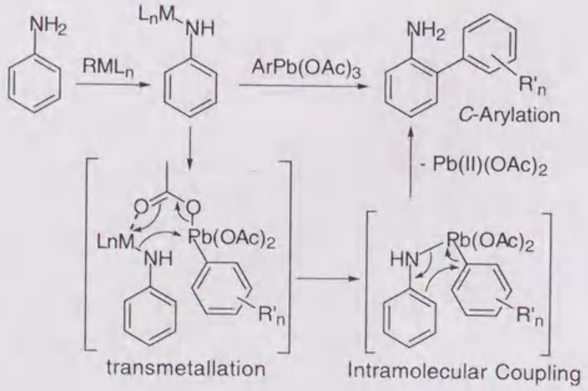
Metal catalysts ligated by aniline or diimine derivatives as well as aromatic tertiary amines with axial chirality are revolutionizing selective transformations.[1-8] In some potential catalyses and for the effective creation of a chiral axis, steric bulk is more significant than electronic contributions. Unfortunately, however, the lack of facile synthetic methods for the selective introduction of a bulky or asymmetric environment around the aniline nitrogen does not allow for a wide range of substitutions on the aromatic nucleus.[9-15] We report here the first example of the direct aryl-aryl coupling of anilines with aryllead compounds, which should lead to new opportunities for producing a vast array of aniline frameworks with axial chirality.[19]

Results and Discussion

Effect of Metallation

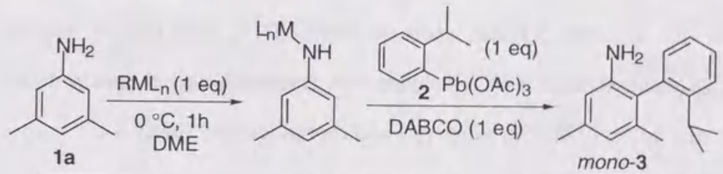
Barton pointed out that no reaction occurred between amines and organolead derivatives alone.[17,18] We speculated that anilines could not undergo ligand exchange with an acetoxy group of aryllead triacetates. Thus, our initial plan was to investigate the metalation of aniline nitrogen, which might promote effective ligand exchange and subsequent arylation with aryllead triacetate (Scheme 1, Table 1).

Scheme 1



Since we previously found that not only the lithiation of phenols, but also the use of DABCO or quinuclidine as a base facilitates aryl-aryl coupling of aryllead compounds with phenols,[20] we first tested the effect of lithiation on aniline coupling. The reaction of 2-isopropylphenyllead triacetate **2** with the lithium anilide, which was prepared from 3,5-dimethylaniline **1a** and *n*-BuLi, in the presence of DABCO in DME afforded only a small amount of the desired *ortho*-arylated product **3** (Table 1, entry 1). We next examined a magnesium anilide that would be expected to promote the ligand exchange by abstraction of an acetoxy group due to the greater Lewis acidity of magnesium. Treatment of magnesium anilide, prepared in situ by the reaction of aniline **1a** with *t*-BuMgCl, with aryllead **2** gave aniline **3** in 55-65% yield, along with di-arylated aniline **4** (entry 2). In contrast, metallating agents other than *t*-BuMgCl led to a significant decline in yield (entries 3-6).

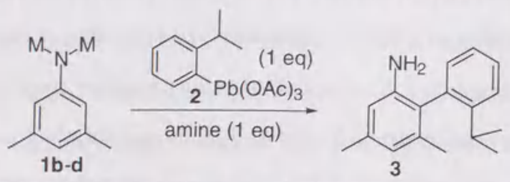
Table 1. Coupling Reactions of Aryllead with Metal Anilides



entry	RML_n	% yield *mono*	*di*
1	BuLi	10-20	-
2	*t*-BuMgCl	55-66	4-10
3	MeMgCl	24	2
4	MeMgBr	<5	-
5	MeMgI	<5	-
6	MeZnCl	<5	-

To achieve more efficient ligand exchange, the effect of more nucleophilic di-metallated anilines was examined (Table 2). Dimagnesium, dilithium, and disilyl anilides **1b-d** were prepared as described in the literature.[21,22] Disappointingly, this dimetallation strategy proved to be less effective, even though dimagnesium anilide **1d** was more suitable than the others (Table 2, entry 1).

Table 2. Coupling Reactions of Aryllead with Dimetal anilides



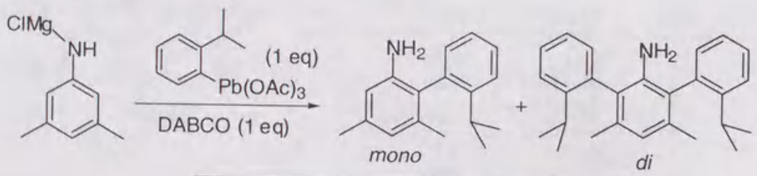
entry	dimetal anilide	M	amine	solvent	% yield[a]
1	**1b**	MgCl	quinuclidine	toluene-THF	28 (8)
2	**1c**	Li	brucine	THF	14
3	**1d**	TMS	quinuclidine	toluene	0

[a]Yields in parenthesis indicate the yields of monocoupling product.

Optimization

With the superior productivity exhibited by the combination of *t*-BuMgCl and aniline **1a**, we next examined the solvent effects for this reaction (Table 3). The use of Et_2O or dioxane gave somewhat lower yields (Table 3, entry 1, 43%; entry 2, 39%), while the use of other solvents such as DME, THF, *t*-BuOMe or toluene led to comparable yields (entries 3-6). Toluene was eventually chosen as a suitable solvent from the viewpoints of both productivity and reproducibility (entry 6).

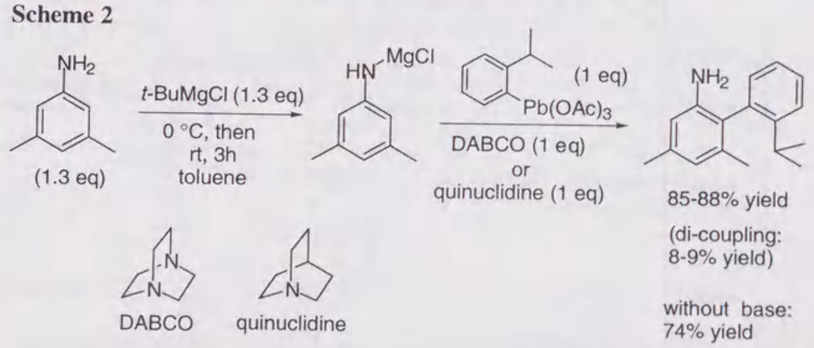
Table 3. Solvent Effect



entry	solvent	% yield *mono*	*di*
1	Et_2O	43	5
2	dioxane	39	4
3	DME	55-66	4-10
4	THF	55-56	2-10
5	*t*-BuOMe	50-70	9-12
6	toluene	52-62	2-10

Finally, we found that the mixing ratio of starting substrates (aryllead **2** : aniline **1a** : *t*-BuMgCl : DABCO = 1.0 : 1.3 : 1.3 : 1.0) was even more critical for high productivity. The mono-arylated product **3** was obtained in 85-88% yield based on the initial amount of Pb reagent under these optimal conditions. Quinuclidine, which has a structure analogous to DABCO, was also examined as a base to give **3** in a similar yield. Even more interesting, the reaction proceeded smoothly without a base to give **3** in 74 % yield. This result indicates that the reaction could be autocatalyzed by primary amines which were generated as the reaction proceeded (Scheme 2).

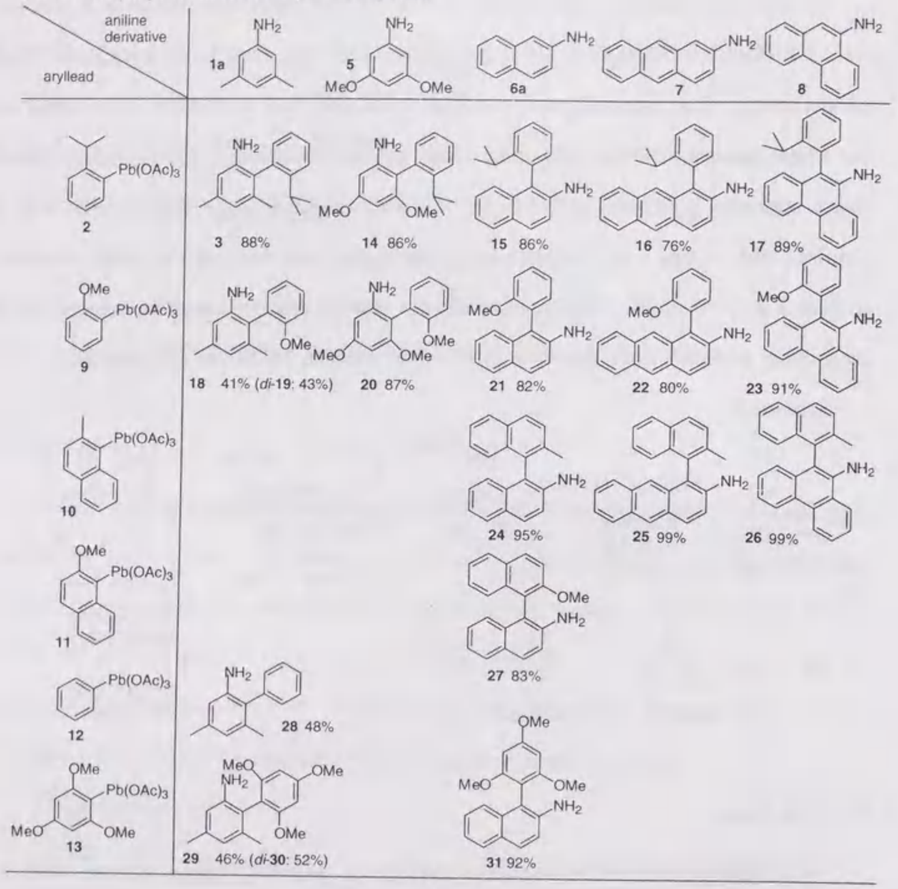
Scheme 2



Reaction Scope

As shown in Table 4, the reaction conditions described above can be used to synthesize a wide variety of *ortho*-arylanilines. This new reaction is characterized by several features: (1) Various aromatic amines were selectively arylated at the *ortho* position. (2) The reactive arylleads with electron-donating groups on the aromatic rings gave generally high yields. (3) *ortho*-Methoxyarylleads **9** and **13**[23] showed novel reactivity with **1a**, and the second *ortho*-arylation proceeded further to give significant amounts of the di-coupling products **19** and **30**, respectively. (4) In contrast, the reaction of phenyllead triacetate **12** was sluggish due to its poor reactivity resulting from the greater electron-deficient nature of the aromatic ring.[16]

Table 4. Coupling of Anilines with Aryllead Compounds

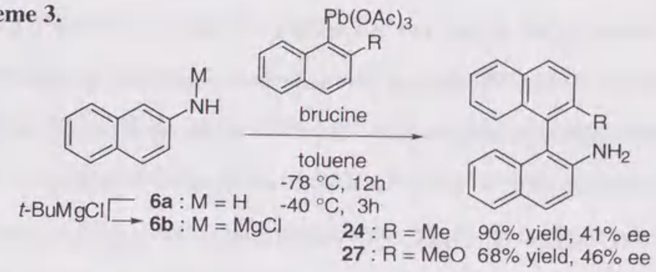


Asymmetric Coupling

Since biaryls bearing an axial chirality are readily obtained by this aryl-aryl coupling reaction, we again sought to realize an enantioselective version of this reaction. The use of brucine is essential for the asymmetric coupling reaction of phenols with aryllead compounds, and this method was applied to the synthesis of chiral aromatic amines (Scheme 3). When brucine was used instead of DABCO, the coupling reaction of β-naphthylamine **6a** with 2-methylnaphthyllead triacetate **10** or 2-

methoxynaphthyllead triacetate **11** proceeded even at a lower temperature (-78 °C~-40 °C) to give the desired axially chiral biaryls **24** in 41% ee and **27** in 46% ee, respectively. These results indicate that brucine participates in the process of C-C bond formation, and therefore the coordination of brucine to Pb may accelerate the rate of the reaction and induce asymmetry.[20] However, the enantioselectivity might be lowered by concomitant autocatalyzation with the primary amines that were generated as the reaction proceeded.

Scheme 3.



Conclusion

Magnesium anilides prepared from anilines with *t*-BuMgCl were found to be efficient for the *C*-arylation reaction of anilines using aryllead triacetates in the presence of tertiary amines such as DABCO and quinuclidine. In this reaction, a major product is a mono-arylated aniline at the *ortho* position, in contrast to the preferential *ortho*,*ortho*-di-arylation of phenols with aryllead derivatives. These results also indicate that the use of less than 1 equiv of *t*-BuMgCl is critical to produce mono-arylation, since mono-arylated anilines should not be effectively further metallated under these conditions, which would result in retardation of the second coupling. However, highly reactive lead reagents such as 2-methoxyphenyllead triacetate and 2,4,6-trimethoxyphenyllead triacetate sometimes give significant amounts of doubly-arylated products. This method is advantageous in that the *ortho*-mono-arylated anilines are directly accessible from various aromatic amines, although anilines are

inherently prone to electrophilic substitution at their *para*-position.

Experimental

General. Infrared (IR) spectra were recorded on a Shimazu FTIR-8100 spectrometer. ^{1}H-NMR spectra were measured on a Varian Gemini-300 (300 MHz) at ambient temperature. Data are recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (app. = apparent, b = broad, s = singlet, d = doublet, t = triplet, and m = multiplet), coupling constant (Hz), integration, and assignment. ^{13}C-NMR spectra were recorded on a Varian Gemini-300 (75 MHz) spectrometer at ambient temperature. Chemical shifts are recorded in ppm from the solvent resonance used as the internal standard (deuterochloroform at 77.07 ppm). Chiral high-performance liquid chromatography (chiral HPLC) analyses were conducted using a Shimazu LC-10AD coupled with a SPD-MA10A-VP detector and a chiral column of CHIRALCEL OD-H (Daicel Chemical Industries, LTD.). All experiments were carried out under an atmosphere of dry argon. For thin-layer chromatography (TLC) analysis, Merck precoated TLC plates (silica gel 60 GF254 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel (E. Merck Art. 9385). Microanalysis was performed at the Faculty of Agriculture, Nagoya University. High-resolution mass spectra analyses were recorded at the Faculty of Technology, Nagoya University.

In experiments that required dry solvent, toluene was freshly distilled from calcium hydride, and tetrahydrofuran (THF), 1,2-dimethoxyethane (DME), diethylether (Et_2O), dioxane, and *t*-butylmethylether (*t*-BuOMe) were freshly distilled from sodium metal using benzophenone ketyl as an indicator. With the following exceptions, the organic substrates **1a**, **5**, **6a**, **7**, **8**, and brucine were all obtained commercially and used without further purification. DABCO and quinuclidine were purified by recrystallization from

hexane before use. Lead compounds[24] **2**, **9**, **10**, **11**, **12**, and **13**, and dimetal anilides **1b**,[22] **1c**,[21] and **1d**[22] were prepared as described in the literature. Aniline **27**[25] is a known compound. Metal anilides were prepared by treating **1a** with BuLi (hexane solution, 0 °C, 0.5h), *t*-BuMgCl (THF solution, 0 °C, 1h), MeMgCl (THF solution, r.t., 1h), MeMgBr (ether solution, r.t., 1h), MeMgI (ether solution, r.t., 1h), or MeZnCl (THF solution, 70 °C, 1h).

2-Methylnaphthyllead triacetate 10. IR (KBr) 2977, 1759, 1547, 1427, 1264 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (dd, 1H, J = 8.7, 4.5), 8.05-7.04 (m, 5H), 2.85 (s, 3H, ^{207}Pb satellites gave $J_{Me\text{-}Pb}$ = 21.3 Hz), 2.09 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.4, 164.2, 139.7, 134.5, 134.1, 131.9, 130.1, 128.5, 128.4, 126.4, s124.5, 22.5, 20.5. Anal. Calcd for $C_{17}H_{18}O_6Pb$: C, 38.85, H, 3.45; Found: C, 38.89, H, 3.43.

2-Methoxynaphthyllead triacetate 11. IR (film) 3750, 1559, 1507, 1399, 1343, 1262 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, 1H, J = 8.4), 8.00 (d, 1H, J = 8.4, ^{207}Pb satellites gave $J_{H\text{-}Pb}$ = 18.6 Hz), 7.85 (dd, 1H, J = 8.4, 0.6, ^{207}Pb satellites gave $J_{H\text{-}Pb}$ = 43.5 Hz), 7.65 (td, 1H, J = 7.2, 1.5), 7.45 (td, 1H, J = 8.1, 1.2), 7.34 (d, 1H, J = 8.7, ^{207}Pb satellites gave $J_{H\text{-}Pb}$ = 105.0 Hz), 4.04 (s, 3H), 2.11 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0, 156.0, 147.5, 134.5, 134.3, 131.5, 128.9, 128.4, 125.0, 124.4, 113.0, 57.3, 20.2. HRMS (FAB+): Calcd for $C_{17}H_{18}O_7Pb$-CH_3CO_2: 483.0686; Found: 483.0733.

Typical Procedure for Coupling reaction of Magnesium Anilides with Aryllead Triacetates: Synthesis of Arylamine 3. To a solution of 3,5-dimethylaniline (162 μL, 1.3 mmol) in toluene (6.50 mL) was added a 1.0 M THF solution of *t*-BuMgCl (1.30 mL, 1.3 mmol) at 0 °C under argon. The mixture was stirred for 3h at room temperature. To a solution of 2-isopropylphenyllead triacetate (504 mg, 1.0 mmol) and DABCO (112 mg, 1.0 mmol) in toluene (20.0 mL) was added the above solution of the Mg-amide at room temperature. The mixture was stirred for 2h and subjected

directly to the column chromatography on silica gel (diethyl ether/hexane = 1/50 to 1/9 as the eluent) to give 2-(2-isopropylphenyl)-3,5-dimethylaniline **3** (211 mg, 88%) and 2,6-Bis(2-isopropylphenyl)-3,5-dimethylaniline **4** (14 mg, 8%). These yields are based on the initial amount of the Pb-reagent. Thus, 96% of the Pb species was converted into **3** and **4**.

Arylamine 3. IR (film) 3472, 3378, 1617, 1574, 1480, 1443, 1329 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, 1H, *J* = 7.5 Hz), 7.36 (t, 1H, *J* = 7.2 Hz), 7.24 (td, 1H, *J* = 7.2, 2.1 Hz), 7.06 (d, 1H, *J* = 7.5 Hz), 6.54 (s, 1H), 6.45 (s, 1H), 3.29 (s, 2H), 2.76-2.67 (m, 1H), 2.28 (s, 3H), 1.90 (s, 3H), 1.15 (d, 3H, *J* = 6.9 Hz), 1.11(d, 3H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1, 144.1, 137.4, 136.9, 136.1, 130.3, 128.0, 126.4, 125.9, 124.2, 120.7, 113.1, 29.9, 24.4, 23.9, 21.2, 20.4. Anal. Calcd for $C_{17}H_{19}N$: C, 85.30, H, 8.84, N, 5.95; Found: C, 85.31, H, 9.01, N, 5.95.

Arylamine 14. IR (film) 3478, 3382, 2959, 1611, 1204, 1157, 1082 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42-7.33 (m, 2H), 7.24(t, 1H, *J* = 7.2 Hz), 7.12 (d, 1H, *J* = 7.2 Hz), 6.01 (s, 1H), 5.99 (s, 1H), 3.81 (s, 3H), 3.65 (s, 3H), 3.44 (s, 2H), 2.81-2.71 (m, 1H), 1.12 (d, 6H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 158.5, 149.0, 145.7, 133.1, 131.1, 127.9, 126.0, 125.5, 108.4, 92.4, 88.7, 55.2, 55.0, 30.0, 24.1, 23.7. HRMS (EI+): Calcd for $C_{17}H_{21}NO_2$: 271.1573; Found: 271.1596.

Arylamine 15. IR (film) 3478, 3384, 2961, 1620, 1514, 1387, 1352 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.75-7.69 (m, 2H), 7.52(d, 1H, *J* = 7.8 Hz), 7.45 (t, 1H, *J* = 7.8 Hz), 7.33 (t, 1H, *J* = 7.5 Hz), 7.25-7.09 (m, 4H), 7.04 (d, 1H, *J* = 9.0 Hz), 3.60 (s, 2H), 2.71-2.57 (m, 1H), 1.14 (d, 3H, *J* = 6.9 Hz), 1.00 (d, 3H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.1, 141.2, 134.9, 134.0, 131.1, 128.5, 128.4, 127.8 (two peaks are overlapped), 126.6, 126.2, 126.1, 124.3, 122.0, 119.0, 117.9, 30.1, 24.2, 24.1. HRMS (EI+): Calcd for C19H19N: 261.1519; Found: 261.1559.

Arylamine 16. IR (film) 3384, 2961, 1624, 1460, 1408, 1343 cm-1; 1H NMR

(300 MHz, CDCl3) δ 8.31 (s, 1H), 7.93-7.87 (m, 2H), 7.71-7.68(m, 1H), 7.58-7.48 (m, 3H), 7.40-7.35 (m, 1H), 7.33-7.29 (m, 2H), 7.24-7.21 (m, 1H), 7.08 (d, 1H, *J* = 9.0 Hz), 3.67 (s, 2H), 2.73-2.64 (m, 1H), 1.14 (d, 3H, *J* = 6.9 Hz), 0.99 (d, 3H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.3, 140.2, 135.0, 132.8, 132.3, 131.4, 129.3, 129.0, 128.4, 127.94, 127.86, 127.6, 126.8, 126.4, 126.3, 125.1, 123.9, 121.6, 119.7, 116.5, 30.1, 24.3, 24.1. HRMS (EI+): Calcd for $C_{23}H_{21}N$: 311.1675; Found: 311.1657.

Arylamine 17. IR (film) 3384, 2963, 1622, 1496, 1435, 1399, 1266 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.75 (d, 1H, *J* = 7.8 Hz), 8.62 (d, 1H, *J* = 8.1 Hz), 7.94-7.93 (d, 1H, *J* = 6.9 Hz), 7.69-7.60 (m, 2H), 7.56-7.32 (m, 5H), 7.20 (d, 1H, *J* = 6.9 Hz), 3.91 (s, 2H), 2.73-2.64 (m, 1H), 1.11 (d, 3H, *J* = 6.9 Hz), 0.99 (d, 3H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.3, 136.7, 135.4, 133.2, 131.3, 130.6, 128.5, 126.73, 126.69, 126.5 (two peaks are overlapped), 126.3, 125.7, 125.1, 125.0, 123.3, 123.1, 122.3, 121.5, 117.1, 30.1, 24.4, 24.0. HRMS (EI+): Calcd for $C_{23}H_{21}N$: 311.1675; Found: 311.1701.

Arylamine 18. IR (film) 3374, 2942, 1617, 1574, 1482, 1460, 1258 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 (td, 1H, *J* = 7.8, 2.1 Hz), 7.14 (dd, 1H, *J* = 7.5, 1.8 Hz), 7.05-6.99 (m, 2H), 6.55 (s, 1H), 6.47 (s, 1H), 3.76 (s, 3H), 3.38 (s, 2H), 2.27 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 144.1, 137.7, 137.5, 131.7, 128.9, 126.4, 121.4, 121.1, 120.9, 113.5, 111.3, 55.6, 21.3, 20.1. HRMS (FAB+): Calcd for $C_{15}H_{17}NO$: 227.1311; Found: 227.1334.

Arylamine 19 (dl or meso). IR (film) 2923, 1601, 1507, 1478, 1266, 1252 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (td, 2H, *J* = 7.8, 1.8 Hz), 7.20 (dd, 2H, *J* = 7.5, 1.8 Hz), 7.05-6.99 (m, 4H), 6.68 (s, 1H), 3.79 (s, 6H), 3.24 (s, 2H), 1.99 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3, 142.1, 136.2, 131.9, 128.8, 126.9, 121.6, 121.1, 121.0, 111.2, 55.6, 20.2. HRMS (FAB+): Calcd for $C_{22}H_{23}NO_2$+H^+: 334.1808; Found: 334.1793.

Arylamine 19 (meso or dl). IR (film) 2923, 1601, 1491, 1456, 1435, 1267, 1244 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (td, 2H, J = 7.8, 1.8 Hz), 7.20 (dd, 2H, J =

7.5, 1.8 Hz), 7.04 (d, 2H, J = 6.9 Hz), 7.00 (d, 2H, J = 7.8 Hz), 6.68(s, 1H), 3.77 (s, 6H), 3.25 (s, 2H), 2.00 (s, 6H); 13C NMR (75 MHz, CDCl3) δ 157.3, 142.1, 136.2, 131.9, 128.9, 126.9, 121.7, 121.12, 121.06, 111.4, 55.5, 20.3. HRMS (FAB+): Calcd for C22H23NO2: 333.1730; Found: 333.1719.

Arylamine 20. IR (film) 3378, 3002, 1622, 1458, 1242, 1204, 1154 cm-1; 1H NMR (300 MHz, CDCl3) δ 7.37-7.32 (m, 1H), 7.26-7.21 (m, 1H), 7.05-6.99 (m, 2H), 6.04 (d, 1H, J = 2.4 Hz), 6.00 (d, 1H, J = 2.1 Hz), 3.80 (s, 3H), 3.78 (s, 3H), 3.68 (s, 3H), 3.56 (s, 2H); 13C NMR (75 MHz, CDCl3) δ 160.5, 158.8, 157.6, 145.9, 132.7, 128.8, 123.5, 120.9, 111.5, 106.0, 92.9, 89.5, 55.8, 55.7, 55.1. HRMS (EI+): Calcd for C15H17NO3: 259.1209; Found: 259.1214.

Arylamine 21. IR (film) 3380, 3056, 1622, 1493, 1431, 1242 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74-7.67 (m, 2H), 7.46-7.41 (m, 1H), 7.26-7.19 (m, 4H), 7.14-7.02 (m, 3H), 3.69 (s, 3H), 3.62 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 141.4, 133.8, 132.7, 129.3, 128.7, 128.0, 127.9, 126.1, 125.3, 124.2, 122.0, 121.4, 118.1, 116.6, 111.7, 55.7. HRMS (EI+): Calcd for $C_{17}H_{15}NO$: 249.1155; Found: 249.1169.

Arylamine 22. IR (film) 3382, 2928, 1624, 1491, 1462, 1244 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.93-7.88 (m, 2H), 7.73-7.68 (m, 2H), 7.51 (td, 1H, *J* = 7.8, 1.8 Hz), 7.34-7.28 (m, 3H), 7.20-7.09 (m, 3H), 3.78 (s, 2H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 140.3, 133.0, 132.5, 132.2, 129.4, 129.3, 129.2, 128.0, 127.9, 127.8, 126.4, 125.5, 125.0, 123.8, 121.5 (two peaks are overlapped), 120.0, 114.1, 112.0, 55.9. HRMS (FAB+): Calcd for $C_{21}H_{17}NO$: 299.1311; Found: 299.1307.

Arylamine 23. IR (film) 2834, 1619, 1489, 1433, 1399, 1254 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.72 (dd, 1H, *J* = 8.7, 1.2 Hz), 8.60 (dd, 1H, *J* = 8.4, 2.1 Hz), 7.91 (dd, 1H, *J* = 8.7, 1.2 Hz), 7.66-7.55 (m, 2H), 7.48-7.32 (m, 3H), 7.28-7.18 (m, 2H), 7.13 (d, 1H, *J* = 7.2 Hz), 7.08 (d, 1H, *J* = 8.4 Hz) 3.98 (s, 2H), 3.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 136.9, 132.9, 132.8, 130.7, 129.5, 126.6, 126.4, 126.3, 125.8

(two peaks are overlapped), 125.2, 124.9, 123.2, 123.0, 122.3, 121.6, 121.5, 114.7, 111.8, 55.7. HRMS (FAB+): Calcd for $C_{21}H_{17}NO+H^{+}$: 300.1389; Found: 300.1361.

Arylamine 25. IR (film) 3384, 3050, 1624, 1429, 1343, 1266 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.96-7.88 (m, 4H), 7.57 (d, 1H, *J* = 8.1 Hz), 7.52 (d, 1H, *J* = 7.8 Hz), 7.42-7.37 (m, 2H), 7.31-7.18 (m, 4H), 7.12 (d, 1H, *J* = 9.3 Hz), 3.53 (s, 2H), 2.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5, 136.2, 132.8, 132.7, 132.4, 132.2, 132.1, 129.4, 129.2, 128.04, 127.99, 127.94, 127.85, 127.83, 126.594, 126.587, 126.4, 125.6, 125.2, 125.1, 123.9, 121.2, 119.8, 113.7, 20.0. HRMS (FAB+): Calcd for $C_{25}H_{19}N$: 333.1519; Found: 333.1479.

Arylamine 26. IR (film) 3056, 1622, 1541, 1509, 1404, 1267 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, 1H, *J* = 7.8 Hz), 8.67 (d, 1H, *J* = 8.4 Hz), 7.96-7.89 (m, 3H), 7.74-7.62 (m, 2H), 7.55 (d, 1H, *J* = 8.1 Hz), 7.42-7.37 (m, 2H), 7.32-7.17 (m, 3H), 6.92 (d, 1H, *J* = 8.1 Hz), 3.85 (s, 2H), 2.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.1, 136.3, 132.7, 132.6 (two peaks are overlapped), 132.4, 130.9, 129.1, 128.1, 128.0, 127.1, 126.6, 126.5 (two peaks are overlapped), 125.9, 125.6, 125.2, 125.1, 124.7, 123.4, 123.2, 122.5, 121.6, 114.3, 20.0. Anal. Calcd for $C_{25}H_{19}N$: C, 90.06, H, 5.74, N, 4.20; Found: C, 89.91, H, 5.96, N, 4.23.

Arylamine 28. IR (film) 3376, 2921, 1617, 1482, 1458, 1329 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (app.t, 2H, *J* = 7.5 Hz), 7.34 (app.t, 1H, *J* = 7.5 Hz), 7.24 (d, 2H, *J* = 7.5 Hz), 6.54 (s, 1H), 6.47 (s, 1H), 3.40 (s, 2H), 2.27 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 138.2, 137.7, 136.8, 130.1, 129.0, 127.1, 125.1, 120.9, 113.4, 21.2, 20.5. HRMS (EI+): Calcd for $C_{14}H_{15}N$: 197.1206; Found: 197.1247.

Arylamine 29. IR (film) 3007, 1609, 1456, 1418, 1266, 1127 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.54 (s, 1H), 6.46 (s, 1H), 6.24 (s, 2H), 3.86 (s, 3H), 3.71 (s, 6H), 3.37 (s, 2H), 2.26 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 158.7, 144.6, 138.3, 137.4, 120.9, 117.2, 113.5, 106.89, 90.9, 55.9, 55.3, 21.4, 19.9. HRMS

(EI+): Calcd for $C_{17}H_{21}NO_3$: 287.1522; Found: 287.1510.

Arylamine 30. IR (film) 2938, 1509, 1458, 1339, 1225, 1125 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.67 (s, 1H), 6.23 (s, 4H), 3.85 (s, 6H), 3.72 (s, 12H), 3.61 (s, 2H), 1.96 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8, 158.9, 136.8 (two peaks are overlapped), 121.2, 117.3, 108.0, 91.2, 56.0, 55.3, 20.2. HRMS (FAB+): Calcd for $C_{26}H_{33}NO_6$: 453.2152; Found: 453.2192.

Arylamine 31. IR (film) 3370, 1605, 1462, 1221, 1156, 1127 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.72-7.66 (m, 2H), 7.27-7.15 (m, 3H), 7.05 (d, 1H, J = 9.0 Hz), 6.32 (s, 2H), 3.90 (s, 3H), 3.66 (s, 2H), 3.63 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 159.5, 142.0, 134.2, 128.5, 128.1, 127.9, 125.8, 124.2, 121.8, 118.1, 112.7, 105.7, 91.3, 56.0, 55.4. Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77, H, 6.19, N, 4.53; Found: C, 73.63, H, 6.37, N, 4.56.

Typical Procedure for Asymmetric Coupling reaction of Magnesium Anilides with Aryllead Triacetates: Synthesis of Arylamine 24. To a solution of _-naphthylamine (186 mg, 1.3 mmol) in toluene (6.50 mL) was added a 1.0 M THF solution of *t*-BuMgCl (1.30 mL, 1.3 mmol) at 0 °C under argon. The mixture was stirred for 3h at room temperature. To a solution of 2-methylnaphthyllead triacetate (526 mg, 1.0 mmol) and brucine (395 mg, 1.0 mmol) in toluene (20.0 mL) was added the above solution of the Mg-amide at –78 °C. The mixture was stirred for 14h at –78 °C and for 3h at –40 °C, and subjected directly to the column chromatography on silica gel (diethyl ether/hexane = 1/5 to 1/1 as the eluent) to give 2-amino-2'-methylbinaphthyl **24** (255 mg, 90%). These yields are based on the initial amount of the Pb-reagent: IR (film) 3384, 3054, 1619, 1509, 1381, 1266 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.88 (app. d, 2H, J = 8.1 Hz), 7.78 (app. d, 2H, J = 8.4 Hz), 7.53 (d, 1H, J = 8.4 Hz), 7.43-7.37 (m, 1H), 7.24-7.09 (m, 5H), 6.88 (d, 1H, J = 8.1 Hz), 3.48 (s, 2H), 2.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5, 136.0, 133.7, 132.7, 132.6, 132.0, 129.1, 128.9, 128.1, 128.01, 127.99, 127.9, 126.5, 126.4, 125.5, 125.1, 124.0, 122.2, 118.0, 116.2, 20.0. HRMS (EI+): Calcd for $C_{21}H_{17}N$: 283.1362; Found: 283.1363. HPLC analysis (column: OD-H): retention times of two enantiomers of **24**: t_R=6.6 (major) and 7.4 (minor) min using *i*-PrOH/hexane (1/9) as the eluent at a flow rate of 1.0 mL/min.

Arylamine 27. HPLC analysis (column: OD-H): retention times of two enantiomers of **27**: t_R=23.8 (major) and 29.3 (minor) min using *i*-PrOH/hexane (1/50) as the eluent at a flow rate of 1.0 mL/min.

Acknowledgment: We are grateful to Mr. S. Komai and H. Choshi (Nagoya University) for performing high resolution mass spectrometric analysis. T. K. also acknowledges a JSPS Fellowship for Japanese Junior Scientists.

References

(1) (a) B. L. Small, M. Brookhart, and A. M. A. Bennett, *J. Am. Chem. Soc.*, **120**, 4049 (1998). (b) B. L. Small and M. Brookhart, *J. Am. Chem. Soc.*, **120**, 7143 (1998). c) G. J. P. Britovsek, V. C. Gibson, B. S. Kimberley, P. J. Maddox, S. J. McTavish, G. A. Solan, A. J. P. White, and D. J. Williams, *Chem. Commun.*, 849 (1998)

(2) Polyolefin: (a) L. K. Johnson, C. M. Killian, M., and M. Brookhart, *J. Am. Chem. Soc.*, **117**, 6414 (1995). (b) L. K. Johnson, S. Mecking, and M. Brookhart, *J. Am. Chem. Soc.*, **118**, 267 (1996). (c) C. M. Killian, D. J. Tempel, L. K. Johnson, and M. Brookhart, *J. Am. Chem. Soc.*, **118**, 11664 (1996). (d) S. Mecking, L. K. Johnson, L. Wang, and M. Brookhart, *J. Am. Chem. Soc.*, **129**, 888 (1998). Polycarbonate: (e) M. Cheng, E. B. Lobkovsky, and G. W. Coates, *J. Am. Chem. Soc.*, **120**, 11018 (1998). Polyester: (f) M. Cheng, A. B. Attygalle, E. B. Lobkovsky, and G. W. Coates, *J. Am. Chem. Soc.*, **121**, 11583 (1999).

(3) T. R. Younkin, E. F. Connor, J. I. Henderson, S. K. Friedrich, R. H. Grubbs, and D.

A. Bansleben, *Science*, **287**, 467 (2000).

(4) (a) M. Scholl, S. Ding, C. W. Lee, and R. H. Grubbs, *Org. Lett.*, **1**, 953 (1999). (b) A. K. Chatterjee and R. H. Grubbs, *Org. Lett.*, **1**, 1751 (1999). (c) A. K. Chatterjee, J. P. Morgan, M. Scholl, and R. H. Grubbs, *J. Am. Chem. Soc.*, **122**, 3783 (2000).

(5) (a) O. Fujimura and R. H. Grubbs, *J. Am. Chem. Soc.*, **118**, 2499 (1996) and references therein. (b) J. B. Alexander, D. S. La, D. R. Cefalo, A. H. Hoveyda, and R. R. Schrock, *J. Am. Chem. Soc.*, **120**, 4041 (1998). (c) D. S. La, J. B. Alexander, D. R. Cefalo, D. D. Graf, A. H. Hoveyda, and R. R. Schrock, *J. Am. Chem. Soc.*, **120**, 9720 (1998). (d) S. S. Zhu, D. R. Cefalo, D. S. La, J. Y. Jamieson, W. M. Davis, A. H. Hoveyda, and R. R. Schrock, *J. Am. Chem. Soc.*, **121**, 8251 (1999). (e) D. S. La, J. G. Ford, E. S. Sattely, P. J. Bonitatebus, R. R. Schrock, and A. H. Hoveyda, *J. Am. Chem. Soc.*, **121**, 11603 (1999). (f) G. S. Weatherhead, J. G. Ford, E. J. Alexanian, R. R. Schrock, and A. H. Hoveyda, *J. Am. Chem. Soc.*, **122**, 1828 (2000).

(6) Kumada coupling: (a) J. Huang and S. P. Nolan, *J. Am. Chem. Soc.*, **121**, 9889 (1999). (b) V. P. W. Böhm, T. Weskamp, C. W. K. Gstöttmayr, and W. A. Herrmann, *Angew. Chem. Int. Ed. Engl.*, **39**, 1602 (2000). Suzuki coupling: (c) C. Zhang, J. Huang, M. L. Trudell, and S. P. Nolan, *J. Org. Chem.*, **64**, 3804 (1999).

(7) (a) M. T. Reetz, E. Bohres, and R. Goddard, *Chem. Commun.*, 935 (1998). (b) C. J. Sanders, K. M. Gillespie, D. Bell, and P. Scott, *J. Am. Chem. Soc.*, **122**, 7132 (2000). (c) E. Vedejs, A. W. Kruger, N. Lee, S. T. Sakata, M. Stec, and E. Suna, *J. Am. Chem. Soc.*, **122**, 4602 (2000) and references therein.

(8) (a) M. Fujita, O. Kitagawa, Y. Yamada, H. Izawa, H. Hasegawa, and T. Taguchi, *J. Org. Chem.*, **65**, 1108 (2000). (b) D. P. Curran, H. Qi, S. J. Geib, and N. C. DeMello, *J. Am. Chem. Soc.*, **116**, 3131 (1994). (c) D. P. Curran, W. Liu, and C. H.-T. Chen, *J. Am. Chem. Soc.*, **121**, 11012 (1999). (d) K. Kondo, H. Fujita, T. Suzuki, and Y. Murakami, *Tetrahedron Lett.*, **40**, 5577 (1999). (e) T. Bach, J.

Schröder, and K. Harms, *Tetrahedron Lett.*, **40**, 9003 (1999). (f) A. D. Hughes and N. S. Simpkins, *Synlett*, 967 (1998). (g) C. R. A. Godfrey, N. S. Simpkins, and D. Walker, *Synlett*, 388 (2000).

(9) J. March, "Advanced Organic Chemistry," Wiley, New York (1992), p. 1216.

(10) Review: A. J. Belfield, G. R. Brown, A. J. Foubister, *Tetrahedron*, **55**, 11399 (1999)

(11) Review: (a) J. Hartwig, *Synlett*, 329 (1997). (b) J. Hartwig, *Angew. Chem. Int. Ed. Engl.*, **37**, 2046 (1998). (c) J. P. Wolfe, S. Wagaw, J.-F. Marcoux, and S. J. Buchwald, *Acc. Chem. Res.*, **31**, 805 (1998). (d) B. H. Yang and S. L. Buchwald, *J. Organomet. Chem.*, **576**, 125 (1999).

(12) S. Gervat, E. Léonel, J.-Y. Barraud, and V. Ratovelomanana, *Tetrahedron Lett.*, **34**, 2115 (1993) and references therein.

(13) (a) W. Fuhrer and H. W. Gschwend, *J. Org. Chem.*, **44**, 1133 (1979). (b) J. M. Muchowski and M. C. Venuti, *J. Org. Chem.*, **45**, 4798 (1980).

(14) (a) T. Sugasawa, T. Toyoda, M. Adachi, and K. Sasakura, *J. Am. Chem. Soc.*, **100**, 4842 (1978). (b) P. D. Johnson and P. A. Aristoff, *J. Org. Chem.*, **55**, 1374 (1990).

(15) (a) J. A. Aeschlimann, N. D. Lees, N. P. McCleland, and G. N. Nicklin, *J. Chem. Soc.*, **127**, 66 (1925). (b) Q.-Y. Chen and Z.-T. Li, *J. Org. Chem.*, **58**, 2599 (1993). (c) Q.-Y. Chen and Z.-T. Li, *J. Chem. Soc., Perkin Trans. 1*, 1705 (1993). (d) A. B. Pierini, M. T. Baumgartner, and R. A. Rossi, *Tetrahedron Lett.*, **28**, 4653 (1987). (e) A. B. Pierini, M. T. Baumgartner, and R. A. Rossi, *J. Org. Chem.*, **56**, 580 (1991).

(16) Review: (a) J. T. Pinhey, *Aust. J. Chem.*, **44**, 1353 (1991). (b) J. T. Pinhey, *Pure Appl. Chem.*, **68**, 819 (1996).

(17) J. T. Pinhey, "Comprehensive Organometallic Chemistry II," ed by E. W. Abel, F. G. A. Stone, and G. Wilkinson, Pergamon, Oxford (1995), Vol. 11, p. 461.

(18) (a) D. H. R. Barton, N. Yadav-Bhanagar, J.-P. Finet, and J. Khamsi, *Tetrahedron*

Lett., 28, 3111 (1987). (b) D. H. R. Barton, D. M. X. Donnelly, J.-P. Finet, and P. J. Guiry, *J. Chem. Soc., Perkin Trans. 1*, 2095 (1991).

(19) S. Saito, T. Kano, Y. Ohyabu, and H. Yamamoto, *Synlett*, 1676 (2000).

(20) S. Saito, T. Kano, H. Muto, M. Nakadai, and H. Yamamoto, *J. Am. Chem. Soc.*, **121**, 8943 (1999).

(21) Li: T. Ooi, E. Tayama, M. Yamada, and K. Maruoka, *Synlett*, 729 (1999).

(22) E. W. Abel and G. R. Willey, *J. Chem. Soc.*, 1528 (1964).

(23) D. H. R. Barton, D. M. X. Donnelly, P. J. Guiry, and J.-P. Finet, *J. Chem. Soc. Perkin Trans. 1*, 2921 (1994).

(24) For the preparation of aryllead triacetates, see: (a) J. Morgan, J. T. Pinhey, *J. Chem. Soc., Perkin Trans. 1*, 715 (1990). (b) R. P. Kozyrod, J. Morgan, J. T. Pinhey, *Aust. J. Chem.*, **38**, 1147 (1985).

(25) J. M. Wilson and D. J. Cram, *J. Org. Chem.*, **49**, 4930 (1984).

Publication List

I. Parts of the present thesis have been, or to be published in the following Journals

Chapter 2 2,6-Bis(2-alkylphenyl)-3,5-dimethylphenol as a New Chiral Phenol with C_2-Symmtery. Application to the Asymmetric Alkylation of Aldehydes

Susumu Saito, Taichi Kano, Keiko Hatanaka, and Hisashi Yamamoto

J. Org. Chem., **62**, 5651 (1997)

Chapter 3 Asymmetric Coupling of Phenols with Arylleads

Susumu Saito, Taichi Kano, Hiroo Muto, Masakazu Nakadai, and Hisashi Yamamoto

J. Am. Chem. Soc., **121**, 8943 (1999)

Asymmetric Coupling of Phenols with Arylleads

Taichi Kano, Susumu Saito, and Hisashi Yamamoto

Submitted for publication.

Chapter 4 Direct Coupling of Anilines with Aryllead Triacetates

Susumu Saito, Taichi Kano, Yuki Ohyabu, Hisashi Yamamoto

Synlett, 1676 (2000)

Direct Coupling of Anilines with Arylleads

Taichi Kano, Yuki Ohyabu, Susumu Saito, and Hisashi Yamamoto

Submitted for publication.

II. Following publications are not included in this thesis.

1. Diastereoselective Aldol Reaction with an Acetate Enolate: 2,6-Bis(2-isopropylphenyl)-3,5-dimethylphenol as an Extremely Effective Chiral Auxiliary

Susumu Saito, Keiko Hatanaka, Taichi Kano, and Hisashi Yamamoto

Angew. Chem. Int. Ed Engl., **37**, 3378 (1998)

2. Enantioselective Total Synthesis of Nicandrenones

Brian M. Stoltz, Taichi Kano, and E. J. Corey

J. Am. Chem. Soc., **122**, 9045 (2000)

Acknowledgment

The author would like to express his grateful acknowledgment to his supervisor, Professor Hisashi Yamamoto whose encouragement and helpful suggestions have been indispensable to the completion of the present thesis. Grateful acknowledgement is also made to Dr. Susumu Saito for his practical guidance, encouragement, pertinent and tolerant advice, and helpful discussions. He is indebted to Drs. Akira Yanagisawa and Kazuaki Ishihara for practical and fruitful discussions. It is great pleasure to express his appreciation to the colleagues, especially, Dr. Noriaki Murase, Messrs. Itsuro Shimada, Yoichi Tozaki, Masahiro Ito, Masakazu Nakadai, Mss. Keiko Hatanaka, and Yuki Ohyabu for valuable contribution.

He wish to express special acknowledgment to Professor E. J. Corey who kindly gave him an opportunity to study at the Department of Chemistry, Harvard University, Cambridge, U. S. A. for a period of June to September. 1999. He is also indebted to colleagues at Harvard University, especially Drs. Manabu Horikawa, Hiroshi Danjo and Brian M. Stoltz for the warm hospitality and friendship they had extended to him during his stay.

He is very grateful to the Fellowship of the Japan Society for the Promotion of Science for Japanese Junior Scientist.

Finally, he would like to express special thanks to Professors Kazukiyo Kobayashi and Takashi Yamane for serving on his Dissertation committee.