J|A|C|S
ARTICLES
Published on Web 01/26/2002

An Improved Catalyst for the Asymmetric Arylation of Ketone Enolates

Takayuki Hamada,† André Chieffi, Jens Åhman, and Stephen L. Buchwald*

Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received May 4, 2001

Abstract: A new catalyst system for the enantioselective α-arylation of ketones is reported. This catalyst, prepared from $Pd_2(dba)_3$ and a bulky dialkylphosphino-binaphthyl ligand, is able to effect the asymmetric arylation of ketone enolates with aryl bromides utilizing NaO^{t}Bu as base. These new catalysts enjoy much higher reactivity than previous systems; arylation reactions could be effected at room temperature with only 2 mol % of the Pd catalyst. The coupling of α-alkyl-α′-protected cyclopentanones proceeded in high yield, and the resulting quaternary stereogenic center was installed in up to 94% ee.

Introduction

Several years ago, we reported a method for the synthesis of α-aryl ketones from ketones and aryl bromides using catalytic amounts of Pd and either BINAP or tol-BINAP.[1] This process represents an excellent complement to existing methods[2] to form α-aryl ketones since the advantages of this new method include experimental simplicity, good functional group tolerance, and high regioselectivity for ketones with two enolizable positions (arylation occurs preferentially at the least-hindered α-carbon). More recently, bulky, dialkylphosphinobiaryl ligands have been discovered which allow for the efficient generation of highly active catalysts for the α-arylation of ketones (Figure 1).[3] Aryl chlorides and bromides may be efficiently coupled with enolates, often with as little as 0.1 mol % Pd, and the anions of malonate esters, cyclic 1,3-diketones, nitroalkanes, and esters[4] can be used as nucleophilies under modified conditions. These commercially available[5] ligands are air stable as solids as well as in solution, and they can be prepared by a simple, one-pot procedure.[6]

Contemporaneously with our work, other groups have also developed Pd-catalysts for the formation of α-aryl ketones.[7−9] In particular, Hartwig reported the coupling of ketones and aryl bromides or iodobenzene with Pd/1,1′-bis (di-*o*-tolylphosphino)-ferrocene.[8a] More recently, the Yale group has disclosed that aryl chlorides, bromides, and in one case, an aryl tosylate could be coupled with ketone enolates or malonate esters using tri-(*tert*-butyl)phosphine, (1,1′-bis-(di-*tert*-butylphosphino)ferrocene), or 1-diphenylphosphino-2-(di-*tert*-butylphosphino)-ethylferrocene.[8b] Hartwig's group has also reported catalytic systems for the formation of α-aryl amides,[8c,d] α-arylcyanoacetates,[8e] esters,[8f] and α-amino esters.[8f] Additionally, Miura and co-workers have shown that $PdCl_2$ is an effective catalyst for the arylation of benzyl ketones.[9]

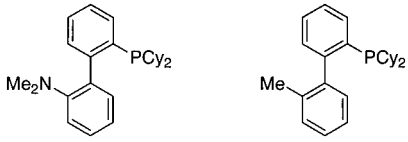


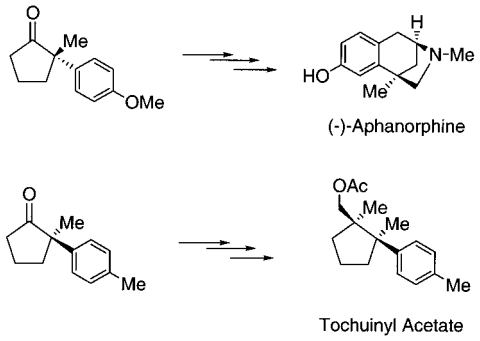
Figure 1. Bulky dialkylphosphino biaryl ligands.

The asymmetric arylation of enolates is an attractive means to prepare optically active carbonyl compounds that possess a quaternary asymmetric center α to the carbonyl group. Optically active 2-methyl-2-arylcyclopentanones are known to be important intermediates for natural product synthesis (Scheme 1). For example, Ogasawara and co-workers reported the total synthesis of (−)-Aphanorphine by using (*S*)-2-methyl-2-*p*-methoxyphenylcyclopentanone as a key intermediate.[10] Additionally, Srikrishna and Reddy used (*R*)-2-methyl-2-*p*-methylphenylcyclopentanone to synthesize tochiunyl acetate, a marine natural product.[11] The preparation of these chiral 2-methyl-2-arylcyclopentanones, however, were quite lengthy. For example, an enzymatic resolution was used to introduce optical activity in the synthesis of (−)-Aphanorphine. Thus, new catalytic, enantioselective

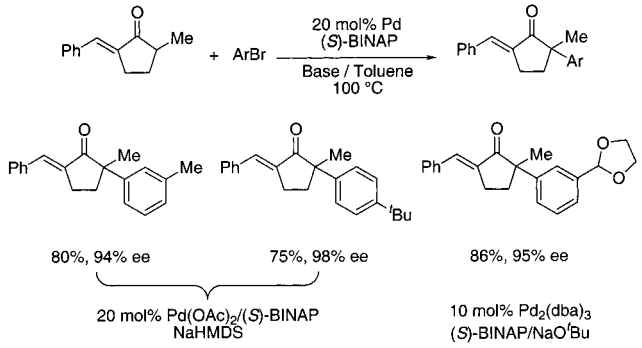
† Present address: AJINOMOTO Co., Inc. ALF-1, 1-1 Suzuki-cho, Kawasaki-shi, Kawasaki-ku, Kanagawa, Japan 210-8681. E-mail: takayuki_hamada@ajinomoto.com.

(1) Palucki, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 11108.
(2) For a survey of methods to prepare α-arylcarbonyl compounds, see references within ref 3.
(3) Fox, J. M.; Huang, X.; Chieffi, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 1360.
(4) Moradi, W. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7996.
(5) From Strem Chemicals, Inc.
(6) Tomori, H.; Fox, J. M.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 5334.
(7) For a related process for the intermolecular coupling of phenol with aryl halides to give biaryls, see: Hennings, D. D.; Iwasa, S.; Rawal, V. H. *J. Org. Chem.* **1997**, *62*, 2.
(8) (a) Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 12382. (b) Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 1473. (c) Shaughnessy, K. H.; Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1998**, *63*, 6546. (d) Lee, S.; Hartwig, J. F. *J. Org. Chem.* **2001**, *66*, 3402. (e) Stauffer, S. R.; Beare, N. A.; Stambuli, J. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 4641. (f) Lee, S.; Beare, N. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 8410.
(9) (a) Satoh, T.; Kawamura, Y.; Miura, M.; Nomura, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1740. (b) Satoh, T.; Inoh, J.; Kawamura, Y.; Kawamura, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2239.
(10) Takano, S.; Inomata, K.; Sato, T.; Takahashi, M.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1990**, 290.
(11) Srikrishna, A.; Reddy, T. J. *Tetrahedron* **1998**, *54*, 8133.

Scheme 1



Scheme 2



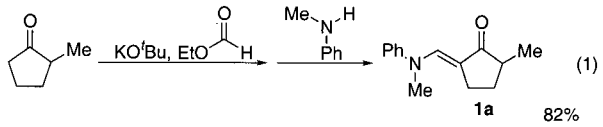
methods for the formation of quaternary stereocenters remain at the forefront of organic synthesis.[12]

A few years ago, we communicated that the asymmetric arylation of ketone enolates could be effected using a (*S*)-BINAP/Pd/catalyst[13] (Scheme 2), affording 2-aryl-2-methyl-5-benzylidenecyclopentanones in good yield and high enantiomeric excess. However, the reactions required high temperatures (100 °C) and catalyst loadings (10−20 mol % Pd/12−24 mol % (*S*)-BINAP). Additionally, it was not possible to remove the benzylidene blocking group from the products in good yield.

In this contribution, we report a significantly more active and general catalytic system for the asymmetric arylation of enolates. This new system allows the arylation reaction to proceed at room temperature and with much lower catalyst loadings (2 mol % Pd). In addition, we disclose a more efficient blocking-group strategy for the preparation of α-aryl-α-alkylcyclopentanones in high yield and with good-to-excellent levels of enantiomeric purity.

Results

To create a 2-aryl-2-alkylcyclopentanone using the Pd-catalyzed ketone arylation reaction, it is necessary to prevent arylation from occurring at the less substituted α-carbon of the 2-alkylcyclopentanone.[1,3,8b] Thus, we chose to install a 2-methyl-5-*N*-methyl-anilinomethylene moiety, a blocking group that can be easily installed in high yield.[14] Formylation of 2-methylcyclopentanone, followed by condensation with *N*-methylaniline, cleanly provided **1a** in 82% yield (eq 1).

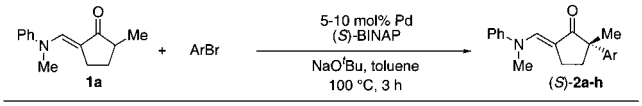


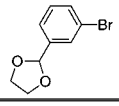
(1)

With the proper protecting-group strategy established, we set out to determine the effectiveness of the asymmetric arylation of ketone **1a** with 4-bromo-*tert*-butylbenzene using a number of commercially available chiral ligands such as BINAP, MOP, QUINAP, PFFA.[4,15] Among all these ligands, only BINAP gave good levels of enantioselectivity. We found that an excess of aryl bromide was necessary to ensure complete conversion of the ketone at 100 °C due to competitive aryl bromide homocoupling to yield 4,4′-di-*tert*-butylbiphenyl as well as reduction to form 4-*tert*-butylbenzene. A survey of different solvents and bases revealed that toluene and sodium *tert*-butoxide were most efficient in these reactions utilizing BINAP. There was only a slight difference in yield and enantioselectivity when the palladium source was changed from $Pd(OAc)_2$ to $Pd_2(dba)_3$. Under the best conditions, the arylation of **1a** with 4-bromo-*tert*-butylbenzene was complete within 3 h at 100 °C to furnish the desired product **2a** in 70% yield and 89% ee.

The (*S*)-BINAP/Pd catalyzed asymmetric arylation of **1a** with several aryl bromides is summarized in Table 1. The highest enantioselectivity in this reaction was observed in the coupling of **1a** and 4-bromo-*tert*-butylbenzene, which proceeded in 89% ee. Aryl bromides possessing electron-donating methoxy groups

Table 1. Asymmetric Ketone Arylation with a (*S*)-BINAP/Pd Catalyst[a]



entry	ArBr	Pd	2	yield(%)[b]	ee (%)[c]
1	(4-*t*Bu)-C_6H_4-Br	5 mol% $Pd_2(dba)_3$	**2a**	65	88
2	(4-*t*Bu)-C_6H_4-Br	10 mol% $Pd(OAc)_2$	**2a**	70	89
3	(2-Me)-C_6H_4-Br	2.5 mol% $Pd_2(dba)_3$	**2b**	45	8
4	(2-Me)-C_6H_4-Br	5 mol% $Pd(OAc)_2$	**2b**	52	10
5	(3-Me)-C_6H_4-Br	2.5 mol% $Pd_2(dba)_3$	**2c**	70	80
6	(4-Me)-C_6H_4-Br	5 mol% $Pd_2(dba)_3$	**2d**	65	63
7	(3-MeO)-C_6H_4-Br	5 mol% $Pd_2(dba)_3$	**2e**	87	85
8	(4-MeO)-C_6H_4-Br	5 mol% $Pd_2(dba)_3$	**2f**	74	57
9	(4-F_3C)-C_6H_4-Br	5 mol% $Pd_2(dba)_3$	**2g**	93	53
10		5 mol% $Pd_2(dba)_3$	**2h**	96	86

[a] Reaction conditions: 1.0 equiv ketone, 2.0 equiv ArBr, 2.0 equiv NaO^{t}Bu, 0.25 M toluene at 100 °C. Ligand/Pd = 1.25/1. [b] Isolated yield. [c] % ee determined by HPLC (Daicel CHIRALCEL OD).

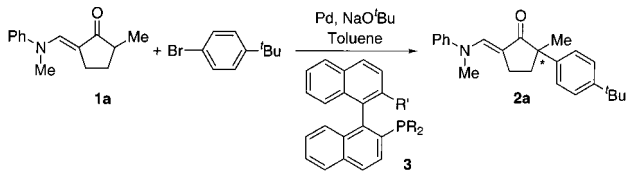
(12) Several elegant Pd-catalyzed methods for the enantioselective formation of quaternary centers have been reported. Allylation: (a) Trost, B. M.; Radinov, R.; Grenzer, E. M. *J. Am. Chem. Soc.* **1997**, *119*, 7879. (b) Trost, B. M.; Schroeder, G. M. *J. Am. Chem. Soc.* **1999**, *121*, 6759. (c) Trost, B. M.; Schroeder, G. M. *J. Org. Chem.* **2000**, *65*, 1569. (d) Hayashi, T.; Kanehira, K.; Hagihara, T.; Kumada, M. *J. Org. Chem.* **1988**, *53*, 113. Heck reaction: (e) Ashimori, A.; Bachand, B.; Calter, M. A.; Govek, S. P.; Overman, L. E. *J. Am. Chem. Soc.* **1998**, *120*, 6488. (f) Overman, L. E.; Poon, D. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 518. (g) Ashimori, A.; Matsuura, T.; Overman, L. E.; Poon, D. J. *J. Org. Chem.* **1993**, *58*, 6949.

(13) Åhman, J.; Wolfe, J. P.; Troutman, M. V.; Palucki, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 1918.

(14) (a) Birch, J.; Robinson. R. *J. Chem. Soc.* **1944**, 501. (b) Woodward, R. B.; Sondheimer, F.; Taub, D, Heusler, K.; McLamore, W. M. *J. Am. Chem. Soc.* **1947**, *74*, 4223. (c) Lin, C. H. *Handbook of Reagents for Organic Synthesis. Reagents, Auxiliaries and Catalysts for C−C bonds*; Coates, R. M., Denmark, S. E., Eds.; Wiley: New York, 1999; p. 509.

(15) For the details of these initial ligand screening experiments, consult the Supporting Information.

Table 2. Asymmetric Ketone Arylation Using Monodentate Ligands[a]



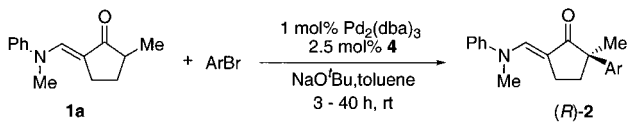
ligand	R	R′	Pd source	conditions	yield (%)[b]	ee (%)[c]
(*S*)-**3a**	Cy	NMe_2	2.5 mol % $Pd_2(dba)_3$	rt, 18 h	93	68 (*R*)
(*S*)-**3a**	Cy	NMe_2	2 mol % $Pd(OAc)_2$	rt, 18 h	99	67 (*R*)
(*R*)-**3b**	^{i}Pr	NMe_2	1 mol % $Pd_2(dba)_3$	rt, 18 h	80	70 (*S*)
(*R*)-**3c**	Cy	^{n}Bu	1 mol % $Pd_2(dba)_3$	rt, 3 h	78	60 (*S*)
(*R*)-**3d**	Cy	$SiMe_3$	1 mol % $Pd_2(dba)_3$	rt, 8 h	66	39 (*S*)
(*R*)-**3e**	Cy	PCy_2	1 mol % $Pd_2(dba)_3$	50 °C, 18 h	22	8 (*R*)

[a] Reaction conditions: 1.0 equiv ketone, 2.0 equiv ArBr, 2.0 equiv NaO^{t}Bu, 0.25 M toluene, **3**/Pd = 1.25/1. [b] Isolated yield. [c] % ee detemined by HPLC (Daicel Chiralcel OD).

were tolerated in the reaction to furnish the coupled product in moderate to good enantioselectivity. Although the reaction of 4-bromoanisole with **1a** proceeded in only 57% ee, the reaction of the 3-substituted isomer proceeded in 85% ee. Poor reactivity and enantioselectivity were observed in the reaction with 2-bromotoluene; coupled product **2b** was isolated in 52% yield and 10% ee.

We recently reported that(*S*)-2-(dimethylamino)-2′-*N*,*N*-dicyclohexylphosphino-1,1′-binaphthyl (**3a**) was an efficient ligand for the asymmetric vinylation of enolates[16] and the asymmetric Suzuki cross-coupling reaction.[17] The diphenyl analogue of **3a** has been independently developed and utilized by Kočovskoý, Lloyd-Jones, and co-workers,[18] by Mikami and co-workers[19] and by Noyori and co-workers.[20] After testing a variety of ligands and conditions, we found that the use of ligands such as **3a** allows for the reaction illustrated in Table 2 to be performed at room temperature and with smaller quantities of catalyst (2% Pd/**3a** vs 10% Pd/BINAP). Thus, the catalyst derived from electron-rich monophosphine ligand **3a** proceeded with faster rates than did those derived from BINAP.[21] As before, similar results were obtained when either $Pd(OAc)_2$ or $Pd_2(dba)_3$ was used as the palladium source. Toluene was the most suitable solvent for these arylation procedures, while the use of ethereal solvents either lowered reaction rates or enantioselectivities. Because of its structural similarity to both MOP and **3a**, (*S*)-2-dicyclohexylphosphino-2′-methoxy-1,1′-binaphthyl (**4a**) was prepared first and tested in the reaction of 3-bromotoluene with **1a**. The enantiomeric excess of the product (82% ee) was higher than that obtained when ligand (*S*)-**3a** was used (58% ee).[21] The groups on phosphorus and oxygen were then systematically varied, and the resulting ligands were

Table 3. Other Aryl Bromides in the Asymmetric Arylation Using Ligands **4**[a]



ArBr	(*S*)-**4b**	(*S*)-**4d**	(*S*)-**4e**
(2-Me)-C_6H_4-Br	40% [b] **42% ee** [c]	53% 23% ee	43% 22% ee
(3-Me)-C_6H_4-Br	72% 87% ee	82% 89% ee	85% **94% ee**
(4-Me)-C_6H_4-Br	70% 86% ee	83% 87% ee	84% **93% ee**
(3-MeO)-C_6H_4-Br	79% 80% ee	81% 84% ee	80% **89% ee**
(4-MeO)-C_6H_4-Br	77% 83% ee	82% 87% ee	80% **94% ee**
(4-*t*-Bu)-C_6H_4-Br	88% 86% ee	79% 88% ee	84% **93% ee**

[a] Reaction conditions: 1.0 equiv ketone, 2.0 equiv ArBr, 2.0 equiv NaO^{t}Bu, 0.25 M toluene, **3**/Pd = 1.25/1. [b] Isolated yield. [c] % ee detemined by HPLC (Daicel Chiralcel OD).

screened in the reaction displayed in Table 2. In general, it was found that replacing the cyclohexyl groups bound to phosphorus with isopropyl groups gave superior results, as did replacing the methyl ether of **4a** with an aryl methylene ether. Of the ligands reported here, (*R*)-2-(diisopropylphosphino)-2′-(1-naphthylmethoxy)-1,1′-binaphthyl (**4e**) consistently furnished desired products with the highest enantiomeric excesses. Ligand **4e** is an air stable, finely crystalline solid. For the reaction of **1a** with 3-bromotoluene, (*R*)-2-(diisopropylphosphino)-2′-(9-phenanthylmethoxy)-1,1′-binaphthyl (**4g**) gave a catalyst that was almost as selective as that derived from **4e**, but its use necessitated a much longer reaction time. In addition, (*R*)-2-(diisopropylphosphino)-1,1′-binaphthyl (**4h**) was prepared and tested in the arylation of **1a** with 3-bromotoluene. The desired product was produced in low yield (24%) and moderate enantiomeric excess (57% ee).

It should be noted that the preparation of 2-alkoxy-2′-dialkylphosphino-1,1′-binaphthyl ligands allowed substantial flexibility as well as increased modularity in their preparation since varying the dialkylphosphino and alkoxy groups were straightforward.[22] These phosphines bear an obvious structural resemblance to the MOP ligands prepared and studied in the elegant and seminal work of Hayashi,[23] except that the phosphines introduced here possess alkyl groups and are therefore more electron-rich. Thus, the series of new ligands **4a**−**4h** were prepared in analogy to Hayashi's method.[23] The desired ligands were obtained in up to 61% overall yield (Scheme 3).

Table 3 shows the results of the reactions of a series of aryl bromides with **1a** using phosphines **4b**, **4d**, or **4e**. In every coupling reaction involving meta- or para-substituted aryl bromides that was studied, the best enantiomeric excesses were observed using **4e**. Unfortunately, ortho-substituted aryl bro-

(16) Chieffi, A.; Kamikawa, K.; Åhman, J.; Fox, J. M.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 1897.
(17) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12501.
(18) (a) Vyskočil, S.; Smrčina, M.; Hanus V.; Polásek P.; Kočovský, P. *J. Org. Chem.* **1998**, *63*, 7738. (b) Kočovský, P.; Vyskočil, S.; Císařová, I.; Sejbal, J.; Tišlerová, I.; Smrčina, M.; Lloyd-Jones, G. C.; Stephen, S. C.; Butts, C. P.; Murray, M.; Langer, V. *J. Am. Chem. Soc.* **1999**, *121*, 7714. (c) Lloyd-Jones, G. C.; Stephen, S. C.; Murray, M.; Butts, C. P.; Vyskočil, S.; Kočovský, P. *Chem. Eur. J.* **2000**, *6*, 4348.
(19) Ding, K.; Wang, Y.; Yun, H.; Liu, J.; Wu, Y.; Terada, M.; Okubo, Y.; Mikami, K. *Chem. Eur. J.* **1999**, *5*, 1734.
(20) Sumi, K.; Ikariya, T.; Noyori, R. *Can. J. Chem.* **2000**, *78*, 697.
(21) For reactions between **1a** and other aryl halides using the **3a**/Pd catalyst, see the Supporting Information.
(22) For an elegant study applying a modular approach to ligand screening in the Pd-catalyzed allylation, see: Trost, B. M.; Van Vranken, D. L.; Bingel, C. *J. Am. Chem. Soc.* **1992**, *114*, 9327.
(23) (a) Uozumi, Y.; Suzuki, N.; Ogiwara, A.; Hayashi, T. *Tetrahedron* **1994**, *50*, 4293. (b) Hayashi, T.; Iwamura, H.; Naito, M.; Matsumoto, Y.; Uozumi, Y.; Miki, M.; Yanagi, K. *J. Am. Chem. Soc.* **1994**, *116*, 775. (c) Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354.

Scheme 3

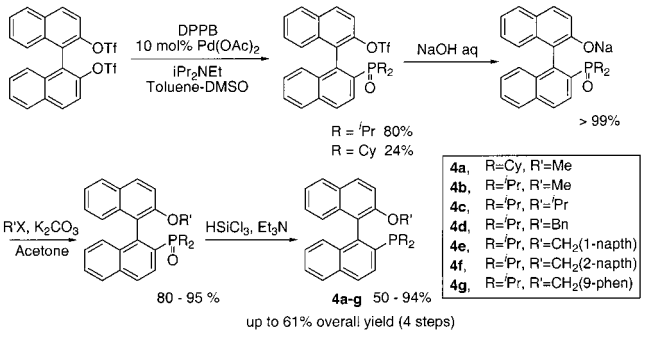
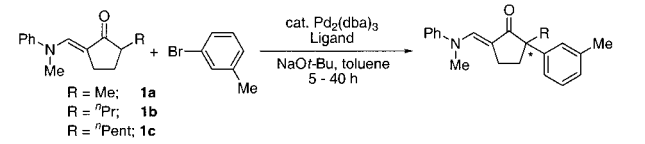


Table 4. Different Ketones in the Asymmetric Arylation: A Ligand Comparison[a]



Product / Ligand, Reaction Condtions	2c	2i	2j
(*S*)-**BINAP** 1-10 mol% Pd (100 °C)	70%[b,d] 80% ee[c] (*S*)	74%[b,d] 91% ee[c] (*S*)	75%[b,e] 93% ee[c] (*S*)
(*S*)-**4e** 2 mol% Pd (R.T.)	85%[b] 94% ee[c] (*R*)	85%[b] 88% ee[c] (*R*)	86%[b,d] 91% ee[c] (*R*)

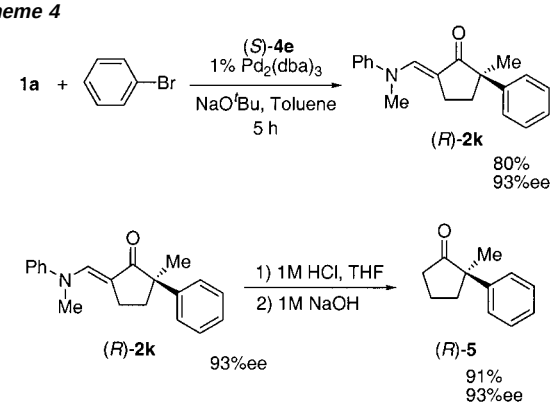
[a] Reaction conditions: 1.0 equiv ketone, 2.0 equiv aryl bromide, 2.0 equiv NaO^{t}Bu, 0.25 M toluene, ligand/$Pd_2(dba)_3$ = 2.5:1. [b] Isolated yield. [c] % ee was determined by HPLC (Daicel Chiralcel OD). [d] 2.5 mol % $Pd_2(dba)_3$ was used. [e] 10 mol % $Pd(OAc)_2$ was used.

mides such as 2-bromotoluene reacted with **1a** with low enantioselectivities (22−42% ee) and low yields with all three of the monodentate ligands studied.

The effect of the ketone α-substituent on the enantioselectivity was also examined (Table 4). The size of the α-substituent of the ketone was important for the enantioselectivity of the arylation reaction catalyzed by Pd/(*S*)-BINAP. The highest enantioselectivity was observed when the reaction was performed with the largest α-alkyl substituent (*n*-pentyl > *n*-propyl > methyl). For example, the coupling between *m*-bromotoluene and α-methyl-substituted ketone **1a** afforded the desired product in 80% ee. The same reaction with the α-*n*-propyl ketone **1b** gave the desired product in 91% ee. With the α-*n*-pentyl ketone **1c**, the product was afforded in 93% ee. The enantiomeric excesses observed were less sensitive to the size of the α-alkyl substituent of the ketone **1** when either ligand **4d** or **4e** was used. It should be noted that methyl-substituted **1a** was arylated with the highest enantiomeric excess with these new monodentate ligands (94% ee).

From the results given in Tables 3 and 4 it can be seen that a single ligand, **4e**, is highly effective for a wide variety of substrate combinations. This ligand, in combination with BINAP, provides a means to successfully generate quaternary stereogenic centers with high enantioselectivity. Despite the

Scheme 4



utility of these two catalyst systems, however, efficient arylation protocols capable of utilizing ortho-substituted aryl bromides have yet to be developed.

Removing the Blocking Group and Determination of Absolute Configuration. The use of ethylformate and *N*-methyl aniline is a well-known method for blocking the α-position of a ketone.[14] After the arylation reaction, the blocking group could be removed by hydrolysis with aqueous HCl followed by a retro-Claisen reaction of the formylated ketone under basic conditions (Scheme 4). Removal of the blocking group afforded the arylated cyclopentanones in good yield and without loss of enantiopurity as determined by HPLC analysis. The absolute configuration of 2-methyl-2-phenylcyclopentanone **5** was determined by comparison of its optical rotation to the literature value.[24] Notably, the sense of asymmetric induction in the arylation reaction with (*S*)-**4e** was the same as that observed in the asymmetric vinylation reaction using ligands (*S*)-**3a-d**.

Discussion

The results described here for the asymmetric arylation of ketones increase the scope of our previously described methodology. The use of a protecting-group strategy provides access to α-aryl-α-alkylcyclopentanones in good yield and with high levels of enantiopurity. BINAP has an advantage in that it is commercially available and can induce high enantioselectivity for a limited range of substrate combinations. The preliminary indication is that BINAP is particularly effective when substrates of type **1b** or **1c** are used. However, the enantioselectivity is consistently higher for a wider range of aryl halides and ketones when **4e** is used in the ketone arylation reactions. Furthermore, palladium catalysts based on the monodentate dialkyl phosphines such as **3** and **4** are more active than Pd/BINAP systems in ketone arylations. These catalysts are effective at room temperature, in contrast to the Pd/BINAP catalyst, which requires heating to 100 °C. Moreover, it was possible to lower catalyst loadings when dialkylphosphinobinaphthyl ligands were used. This increase in catalyst activity correlates with our previous observations in ketone arylations,[3] Pd-catalyzed amination reactions,[25,26] Suzuki reactions,[27] and Pd-catalyzed diaryl ether-forming reactions using dialkylphosphinobiphenyl ligands.[28]

(24) Hoffman, T. D.; Cram, D. J. *J. Am. Chem. Soc.* **1969**, *91*, 1000.
(25) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1158.
(26) Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 2413.
(27) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550.
(28) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369.

Although ligands **3a,b** and **4a**−**g** could plausibly form P−N and P−O chelate structures, respectively, several experiments suggest that these modes of coordination are not important for the asymmetric arylation reaction. For the reaction displayed in Table 2, the product is obtained in only slightly lower ee (60% vs 68) when the dimethylamino group of **3a** was replaced by a hydrogen (**4h**). It should be noted that both ligands induce the same sense of asymmetry [(*R*)-ligand yields (*S*)-**2**]. For the bis-phosphine ligand BINAP, however, the correlation between the antipode of the binaphthyl moiety of the ligand and the absolute configuration of the product is reversed [(*S*)-BINAP furnished *(S)*-**2a**]. These observations suggest that the mechanism of asymmetric induction is significantly different when a bis-phosphine is used and are consistent with the proposal that BINAP chelates and that the amine and alkoxy functions of **3a,b** and **4a**−**g**, respectively, do not bind to Pd. Hence, reactions with chelating and monodentate ligands provide the products of opposite absolute configuration. We note that Overman and co-workers found in their elegant studies of the intramolecular asymmetric Heck reaction that reactions employing (*R*)-BINAP gave products that were enantiomeric to those formed when either (*R*)-*i*-PrO-MOP or (*R*)-2-(diphenylmethyl)-2′-diphenylphosphino-1,1′-binaphthyl were used as ligands. This finding was in accord with additional evidence that led the authors to conclude that BINAP forms a chelate structure in the step that determines the absolute stereochemistry.[12e,f,g] We also note that Kočovskoý and co-workers have crystallographically determined the structure of the complex (MOP)Pd(η^3-C_3H_5)$^+$ OTf$^-$, and found that the distal naphthyl ring (relative to P) binds to the Pd center.[18b] In our laboratories, η^2-binding of the distal aromatic ring of dialkylphosphinobiphenyl ligands has been characterized by X-ray crystallography for Pd(0) complexes.[29] While consideration should be given to Kočovskoý's comments on the possible significance of P−C coordination,[18b] the caveat remains that there is still no evidence that these modes of binding bear relevance to any catalytic process.

It is likely that the mechanism for the asymmetric processes reported here parallel those proposed in our previous studies.[3] With either BINAP or ligands **3** and **4a**−**h**, it is probable that the ratio of ligand:Pd is 1:1 for Pd(II) intermediates in the catalytic cycle; the reasoning has been discussed previously[3] and is supported by the observation that, with either BINAP or **4e**, the relationship between the ee of arylation product **2c** and the ee of the ligand is linear. As with the nonasymmetric ketone arylation reaction, it was found that the effectiveness of the catalyst was dramatically altered by subtle perturbations in the structure of the ligand.[30] Therefore, the development of the ligand synthesis illustrated in Scheme 3 is significant, since it provides a short and efficient means for the preparation of variety of 2-alkoxy-2′-phosphino-1,1′-binaphthyl ligands from an inexpensive, enantiomerically pure precursor. The coupling reaction of dialkylphosphines with BINOL-bis-triflate (Scheme 3) is noteworthy. Although numerous examples of Pd-catalyzed couplings of aryl triflates and halides with diarylphosphine oxides have been reported,[31] the analogous process with dialkylphosphine oxides is less studied. The C−P bond forming reaction between aryl bromides and dialkylphosphine oxide in the presence of $NaNH_2$ was reported by Raynal and co-workers.[32] Saá et al. described a similar reaction where diethylphosphine was presumably oxidized in situ by exogenous oxygen prior to the C−P bond forming reaction.[33] Additionally, several groups have utilized diaryl- and alkylarylphosphine boranes[34] as well as triaryl phosphines[35] in these Pd-catalyzed couplings. Direct access to triarylphosphines has also been achieved by Ni-catalyzed couplings using diarylphosphines[36] or chlorodiarylphosphines[37] and aryl bromides triflates. We anticipate that the small library of ligands introduced here, along with variants prepared by further alteration of the ether and phosphine substituents, should find excellent utility in the future development of catalytic asymmetric processes.

(29) Yin, J.; Rainka, M. P.; Zhang, X.-X.; Buchwald, S. L. Submitted for publication.

(30) Plausible intermediates for the asymmetric arylation reaction were modeled using molecular mechanics and the MacSpartan program. Unfortunately, our attempts to rationalize the enantioselectivity of the process were inconclusive.

Conclusions

A series of new ligands which are useful in the Pd-catalyzed asymmetric arylation reaction of enolates have been reported. (*R*)-2-(Diisopropylphosphino)-2′-(1-naphthylmethoxy)-1,1′-binaphthyl (**4e**) was the best of all ligands used in this study. Compared with our previous report, the catalyst derived from **4e** and $Pd_2(dba)_3$ not only delivers the desired products in higher enantioselectivity but also reacts under milder conditions.

Experimental Section

General Considerations. THF and Et_2O were distilled under argon from sodium/benzophenone ketyl, and toluene was distilled under nitrogen from molten sodium. Alternatively, these solvents were purchased from J.T. Baker in CYCLE-TAINER solvent-delivery kegs and vigorously purged with argon for 2 h. The solvents were further purified by passing them under argon pressure through two packed columns of neutral alumina (for Et_2O and THF) or through neutral alumina and copper (II) oxide (for toluene).[38] Aryl bromides and 2-methylcyclopentanone were purchased from Aldrich Chemical Co. Tris(dibenzylideneacetone) dipalladium (0), (*S*)-BINAP, (*R*)-QUINAP, (*S*)-MOP, (−)-PPFA, and (*rac*)-2,2′-dibromo-1,1′-binaphthyl were acquired from Strem Chemicals, Inc. (*R*)- and (*S*)-BINOL were purchased from Kankyo Kagaku Center Co., Ltd. Ookawa, Kanazawa-ku, Yokohama, Japan. NaO^{t}Bu was purchased from Aldrich; the bulk of this material was stored in an nitrogen-filled glovebox. Small portions (1−2 g) were removed from the glovebox in glass vials, stored in the air in desiccators filled with anhydrous calcium sulfate, and weighed in the air. All other reagents were available from commercial sources

(31) (a) Kurz, L.; Lee, G.; Morgans Jr., D.; Waldyke, M. J.; Ward, T. *Tetrahedron Lett.* **1990**, *31*, 6321. (b) Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945. (c) Horiuchi, T.; Ohta, T.; Stephan, M.; Takaya, H. *Tetrahedron: Asymmetry* **1994**, *5*, 325. (d) Doucet, H.; Brown, J. M. *Tetrahedron: Asymmetry* **1997**, *8*, 3775.

(32) Bergeret, W.; Gautier, J. C.; Raynal, S. *Phosphorus Sulfur* **1986**, *27*, 275.

(33) Martorell, G.; Garcías, X.; Janura, M.; Saá, J. M. *J. Org. Chem.* **1998**, *63*, 3463.

(34) (a) Oshiki, T.; Imamoto, T. *J. Am. Chem. Soc.* **1992**, *114*, 3975. (b) Imamoto, T. *Pure Appl. Chem.* **1993**, *65*, 655. (c) Gaumont, A.-C.; Hursthouse, M. B.; Coles, S. J.; Brown, J. M. *Chem. Commun.* **1999**, 63. (d) Lipshutz, B. H.; Buzard, D. J.; Yun, C. S. *Tetrahedron Lett.* **1999**, *40*, 201. (e) Al-Masum, M.; Kumaraswamy, G.; Livinghouse, T. *J. Org. Chem.* **2000**, *65*, 4776.

(35) (a) Kwong, F. Y.; Chan, K. S. *Organometallics* **2000**, *19*, 2058. (b) Kwong, F. Y.; Chan, K. S. *Organometallics* **2001**, *20*, 2570.

(36) (a) Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180. (b) Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *Organic Synthesis* **1999**, *76*, 6. (c) Sollewijn, A. E.; Kooijman, H.; Spek, A. L.; Hiemstra, H. *Chem. Eur. J.* **1999**, *5*, 2472.

(37) Ager, D. J.; East, M. B.; Eisenstadt, A.; Laneman, S. A. *Chem. Commun.* **1997**, 2359. (b) Kwong, F. Y.; Chan, A. S. C.; Chan, K. S. *Tetrahedron* **2000**, *56*, 8893.

(38) (a) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518. (b) Alaimo, P. J.; Peters, D. W.; Arnold, J.; Bergman, R. G. *J. Chem. Educ.* **2001**, *78*, 64.

and were used without further purification. Flash chromatography was performed on Silicycle ultrapure silica gel (230−400 mesh) unless otherwise noted. Yields refer to isolated yields of compounds of greater than 95% purity as estimated by capillary GC, ^{1}H NMR, and in most cases elemental analysis. Yields reported in this section refer to a single experiment, while those reported in the tables are an average of two or more runs, and therefore, the numbers may differ slightly. Elemental analyses were performed by Atlantic Microlab, Inc. Infrared (IR) spectra reported in this paper for neat solids were obtained by placing neat samples directly on the DiComp probe of an ASI Applied Systems React IR 1000 in situ IR instrument. Alternatively, IR spectra in this paper for several compounds were recorded on a Perkin-Elmer FT-IR 1600. Chiral HPLC analyses were performed on a Hewlett-Packard 1100 system with an HP 1100 diode array detector (monitoring at 254 nm) using a Chiralcel OD column (25 cm × 0.46 cm). Racemic compounds analogous to the enantiomerically enriched compounds described below were prepared by reaction with (*rac*)-BINAP. The HPLC retention times of the racemic products were the same as those of the enantiomerically enriched products. Optical rotations were recorded on a Perkin-Elmer 241 Polarimeter.

General Procedure for 2-Alkyl-5-(*N*-methyl-anilinomethylene)-cycloalkanones.[14,15] Ethylformate (10.0 mL) was added dropwise to a stirred solution of KO^{t}Bu (3.70 g, 33.0 mmol) in THF (25 mL) at 0 °C (CAUTION: gas evolution occurs.) The mixture was cooled to −10 °C, and the ketone (30.0 mmol) in ethylformate (20.0 mL) was added via cannula. The resulting mixture was stirred at −10 °C for 30 min, warmed to room temperature, and stirred for an additional 12 h. The mixture was transferred to a separatory funnel, acidified to pH = 1 with HCl (1 M), and extracted with Et_2O (3 × 100 mL). The combined organic extracts were dried with $MgSO_4$, filtered, and concentrated in vacuo to give the crude formylated ketone.

The crude formylated ketone was dissolved in benzene (60 mL), and *N*-methylaniline (4.20 mL, 39.0 mmol) was added. The flask was fitted with a Dean−Stark trap, and the mixture was refluxed for 3 h with azeotropic removal of water. The mixture was allowed to cool to room temperature and concentrated in vacuo. The excess *N*-methyl aniline was removed by distillation, and the resulting solid was purified by recrystallization from hexane.

2-Methyl-5-(*N*-methyl-anilinomethylene)cyclopentanone (1a). The general procedure gave 5.31 g (82% yield) of the title compound as a yellow solid: mp 88−90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (t, J = 1.8 Hz, 1 H), 7.37−7.31 (m, 2H), 7.15−7.10 (m, 3H), 3.49 (s, 3H), 2.52−2.07 (m, 4H), 1.43−1.30 (m, 1H), 1.12 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.3, 146.2, 141.3, 129.1, 124.4, 121.1, 108.9, 42.8, 40.0, 29.8, 26.2, 15.5; IR (neat, cm^{-1}) 2954, 2867, 1679, 1559, 1497, 1364, 1185; Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 78.36; H, 8.08.

2-Propyl-5-(*N*-methyl-anilinomethylene)cyclopentanone (1b). The general procedure gave 5.18 g (71% yield) of the title compound as a yellow solid: mp 78−79 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (t, J = 1.8 Hz, 1H), 7.36−7.31 (m, 2H), 7.15−7.10 (m, 3H), 3.48 (s, 3H), 2.58−2.37 (m, 2H), 2.27−2.05 (m, 2H), 1.87−1.76 (m, 1H), 1.48−1.16 (m, 4H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.1, 146.2, 141.3, 129.0, 124.4, 121.1, 109.3, 48.0, 40.0, 33.0, 27.5, 26.3, 20.9, 14.3; IR (neat, cm^{-1}) 2952, 2925, 2856, 1677, 1559, 1492, 1362, 1216, 1187; Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70. Found: C, 78.99; H, 8.72.

2-Pentyl-5-(*N*-methyl-anilinomethylene)cyclopentanone (1c). The general procedure gave 6.18 g (76% yield) of the title compound as a yellow solid: mp 72−73 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (t, J = 1.8 Hz, 1 H), 7.37−7.31 (m, 2H), 7.15−7.10 (m, 3H), 3.49 (s, 3H), 2.52−2.43 (m, 2H), 2.20−2.04 (m, 2H), 1.87−1.81 (m, 1H), 1.48−1.19 (m, 8H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.1, 146.2, 141.2, 129.1, 124.4, 121.1, 109.4, 48.2, 40.0, 32.1, 30.8, 27.5, 27.4, 26.5, 22.7, 14.2; IR (neat, cm^{-1}) 2927, 2858, 1679, 1559, 1493, 1268, 1212, 1181; Anal. Calcd for $C_{18}H_{25}NO$: C, 79.66; H, 9.28. Found: C, 79.84; H, 9.30.

Experimental Procedures for the Preparation of 2-(Dialkylphosphino)-2′-alkoxy-1,1′-binaphthyls.[23] To a mixture of (*S*)-2,2′-bis-((trifluoromethanesulfonyl)oxy)-1,1′-binaphthyl (2.75 g, 5.00 mmol), diisopropylphosphine oxide (1.34 g, 10.0 mmol), palladium diacetate (112 mg, 0.50 mmol), and 1,4-bis(diphenylphosphino)butane (dppb, 213 mg, 0.50 mmol) were added toluene (8 mL), dimethyl sulfoxide (15 mL), and diisopropylethylamine (3.50 mL, 20.0 mmol). The mixture was heated with stirring at 110 °C for 14 h. After cooling to room temperature, the solvent and excess amine were removed under reduced pressure (0.1−0.2 mmHg). The residue was diluted with EtOAc, washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with EtOAc) to give (*S*)-2-(diisopropylphosphinyl)-2′-[(trifluoromethanesulfonyl)oxy]-1,1′-binaphthyl as a white solid (2.14 g, 80%).

To a solution of (*S*)-2-(diisopropylphosphinyl)-2′-((trifluoromethanesulfonyl)oxy)-1,1′-binaphthyl (2.14 g, 4.00 mmol) in a 2:1 mixture of 1,4-dioxane and MeOH (30.0 mL) was added aqueous NaOH solution (3 M, 15.0 mL). The reaction mixture was stirred for 14 h at room temperature, acidified (pH = 1) with concentrated HCl, and extracted with EtOAc. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to give (*S*)-2-(diisopropylphosphinyl)-2′-hydroxy-1,1′-binaphthyl as a pale yellow solid, which was used in the next step without purification.

To a mixture of (*S*)-2-(diisopropylphosphinyl)-2′-hydroxy-1,1′-binaphthyl (502 mg, 1.25 mmol), obtained as described above, and K_2CO_3 (690 mg, 5.00 mmol) in acetone (6 mL) was added MeI (712 mg, 5.00 mmol). The mixture was stirred at 50 °C for 12 h. After cooling to room temperature, the mixture was filtered through Celite, and the solid was washed with Et_2O. The organic phases were combined and concentrated in vacuo. The residue was purified by silica gel chromatography (elution with EtOAc) to give 505 mg (97%) of (*S*)-2-(diisopropylphosphinyl)-2′-methoxy-1,1′-binaphthyl.

To a mixture of (*S*)-2-(diisopropylphosphinyl)-2′-methoxy-1,1′-binaphthyl (500 mg, 1.20 mmol) and Et_3N (5.60 mL, 40.0 mmol) in toluene (20 mL) was added Cl_3SiH (1.35 g, 10.0 mmol) at 0 °C. The reaction mixture was stirred at 110 °C for 12 h. After cooling to room temperature, the mixture was diluted with Et_2O (20 mL) and quenched with a small amount of saturated $NaHCO_3$ (2 mL). The resulting suspension was filtered through Celite and the solid washed with Et_2O. The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution: 10% EtOAc in hexane) to give **4b** as a white solid (340 mg, 71%).

4a−**4g** were prepared using the method above.

(*R*)-(+)-2-(Dicyclohexylphosphino)-2′-methoxy-1,1′-binaphthyl (4a). Prepared as above in 17% overall yield as a white solid which was judged to be 95% pure by ^{31}P NMR; mp 177−179 °C dec; ^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.04−7.78 (m, 5H), 7.49−7.43 (m, 2H), 7.33−7.09 (m, 4H), 6.89 (d, J = 8.4 Hz, 1H), 3.78 (s, 3H), 1.95−0.84 (m, 22H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 154.7, 134.4, 134.3, 133.7, 133.4, 133.3, 129.56, 129.53, 128.7, 128.0, 127.9, 126.9, 126.8, 126.5, 126.1, 123.4, 123.4, 112.5, 55.7, 36.0, 35.7, 34.5, 34.3, 31.1, 31.0, 30.8, 30.7, 30.5, 30.3, 28.1, 28.0, 27.9, 27.8, 27.6, 27.5, 27.4, 26.9, 26.7 (observed complexity due to P−C splitting); ^{31}P NMR (121 MHz, CD_2Cl_2) δ −8.90; IR (neat, cm^{-1}) 2950, 1594, 1509, 1463, 1272, 1248, 1084, 814, 746; $[\alpha]^{20}_{Na}$ +65.7 (*c* 2.5, CH CH_2Cl_2); HRMS (+)FAB, *m*/*z* 481 $[M + H]^+$; HRMS calcd for $[M + H]^+$: +481.2655, Found$[M + H]^+$: +481.2636.

(*S*)-(−)-2-(Diisopropylphosphino)-2′-methoxy-1,1′-binaphthyl (4b). Prepared as above in 55% overall yield as a white solid; mp 133−134 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05−7.78 (m, 5H), 7.49−7.42 (m, 2H), 7.32−7.14 (m, 4H), 6.96 (d, J = 8.4 Hz, 1H), 3.76 (s, 3H), 2.11−2.07 (m, 2H), 1.14−0.98 (m, 6H), 0.93−0.83 (m, 6H);^{13}C NMR (75

MHz, $CDCl_3$) δ 154.6, 143.5, 134.4, 133.9, 133.4, 129.6, 129.23, 129.19, 128.1, 128.0, 127.2, 126.9, 126.8, 126.2, 126.1, 123.4, 122.6, 122.5, 112.6, 55.7, 26.2, 26.0, 24.9, 24.7, 20.9, 20.7, 20.63, 20.57, 20.45, 20.41, 20.3 (observed complexity due to P−C splitting);^{31}P NMR (121 MHz, $CDCl_3$) δ −0.80; IR (neat, cm^{-1}) 2966, 2950, 1594, 1574, 1495, 1208, 885, 748; $[\alpha]^{20}_{Na}$ −81.9 (*c* 3.5, $CHCl_3$); MS (+)FAB, *m*/*z* 401 $[M + H]^+$; Anal. Calcd for $C_{27}H_{29}OP$: C, 80.97; H, 7.30. Found; C, 80.94; H, 7.34.

(*S*)-(−)-2-(Diisopropylphosphino)-2′-isopropoxy-1,1′-binaphthyl (4c). Prepared as above in 24% overall yield as a white solid; mp 48−49 °C;^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.01−7.78 (m, 5H), 7.50−7.42 (m, 2H), 7.33−7.11 (m, 4H), 6.90 (d, J = 8.4 Hz, 1H), 3.76 (s, 3H), 2.11−2.07 (m, 2H), 1.14−0.98 (m, 6H), 0.93−0.83 (m, 6H);^{13}C NMR (75 MHz, CD_2Cl_2) δ 150.7, 147.4, 129.9, 129.6, 129.0, 128.7, 127.8, 127.1, 126.2, 125.9, 123.4, 121.7, 120.1 115.4, 22.6, 22.2, 20.7, 20.6, 17.7, 17.2, 15.6, 15.4, 14.0 (observed complexity due to P−C splitting);^{31}P NMR (121 MHz, CD_2Cl_2) δ −0.75; IR (neat, cm^{-1}) 2966, 2950, 1594; $[\alpha]^{20}_{Na}$ −134.5 (*c* 1.0, CH_2Cl_2); MS (+)ESI, *m*/*z* 429 $[M + H]^+$; Anal. Calcd for $C_{29}H_{33}OP$: C, 81.28; H, 7.76. Found; C, 81.00; H, 7.85.

(*S*)-(−)-2-(Diisopropylphosphino)-2′-benzyloxy-1,1′-binaphthyl (4d). Prepared as above in 61% overall yield as a white solid; mp 123 °C (dec); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92−7.77 (m, 5H), 7.47−6.90 (m, 11H), 5.04 (s, 2H), 2.07−2.00 (m, 2H), 1.04−0.98 (m, 6H), 0.92−0.81 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6, 137.6, 136.0, 134.4, 133.7, 133.3, 133.2, 128.8, 128.2, 128.0, 127.9, 127.2, 127.0, 126.4, 126.0, 123.4, 114.4, 70.1, 25.9, 25.7, 25.0, 24.8, 20.9, 20.7, 20.6, 20.5, 20.3 (observed complexity due to P−C splitting); ^{31}P NMR (121 MHz, $CDCl_3$) δ −0.88; IR (neat, cm^{-1}) 2966, 2950, 1594, 1509, 1465, 1270, 814, 742; MS (+)FAB, *m*/*z* 477 $[M + H]^+$; $[\alpha]^{20}_{Na}$ −65.9 (c 1.67, $CHCl_3$) Anal. Calcd for $C_{33}H_{33}OP$: C, 83.16; H, 6.98. Found; C, 82.92; H, 7.00.

(*S*)-(−)-2-(Diisopropylphosphino)-2′-(1-naphthylmethoxy)-1,1′-binaphthyl (4e). Prepared as above in 61% overall yield as a white solid; mp 94 °C (dec); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96−7.81 (m, 4H), 7.72−7.40 (m, 6H), 7.72−7.40 (m, 6H), 5.45 (m, 2H), 2.02−1.96 (m, 2H), 1.02−0.70 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6, 143.4, 143.0, 136.2, 134.5, 133.7, 133.5, 133.4, 132.7, 130.8, 129.7, 129.0, 128.9, 128.4, 128.2, 128.0, 127.8, 127.1, 126.5, 126.3, 126.0, 125.9, 125.4, 125.2, 123.6, 123.6, 123.4, 114.6, 69.2, 25.9, 25.8, 25.2, 25.1, 21.0, 20.7, 20.6, 20.5, 20.4, 20.3 (observed complexity due to P−C splitting); ^{31}P NMR (121 MHz, $CDCl_3$) δ −0.67; IR (neat, cm^{-1}) 3054, 2948, 2865, 1509, 1465, 1455, 1270, 814, 744; $[\alpha]^{20}_{Na}$ −6.78 (*c* 6.0, $CHCl_3$); MS (+)FAB, *m*/*z* 527 $[M + H]^+$; Anal. Calcd for $C_{37}H_{35}OP$: C, 84.38; H, 6.70. Found; C, 84.15; H, 6.69.

(*R*)-(−)-2-(Diisopropylphosphino)-2′-(2-naphthylmethoxy)-1,1′-binaphthyl (4f). Prepared as above in 49% overall yield as a white solid; mp 74−76 °C (dec); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96−7.00 (m, 19H), 5.19 (s, 2H), 2.07−2.00 (m, 2H), 1.04−0.82 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.5, 135.1, 134.4, 133.8, 133.4, 133.3, 133.2, 132.7, 129.6, 129.1, 128.8, 128.0, 127.9, 127.8, 127.2, 127.1, 126.5, 126.4, 126.1, 126.05, 126.0, 125.8, 125.2, 124.4, 123.6, 114.6, 70.1, 26.0, 25.8, 25.0, 24.8, 20.7, 20.6, 20.4, 20.2 (observed complexity due to P−C splitting); ^{31}P NMR (121 MHz, $CDCl_3$) δ −1.81; IR (neat, cm^{-1}) 1509, 1463, 1270, 812, 744; $[\alpha]^{20}_{Na}$ −9.08 (*c* 4.0, $CHCl_3$); MS (+)FAB, *m*/*z* 527 $[M + H]^+$; Anal. Calcd for $C_{37}H_{35}OP$: C, 84.38; H, 6.70. Found; C, 84.08; H, 6.72.

(*R*)-(+)-2-(Diisopropylphosphino)-2′-(9-phenanthylmethoxy)-1,1′-binaphthyl (4 g). Prepared as above in 38% overall yield as a white solid; mp 113−116 °C (dec); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.66 (t, J = 9.3 Hz, 2H), 7.94−6.99 (m, 19H), 5.46 (s, 2H), 2.00 (m, 2H), 1.13−1.01 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.5, 143.0, 136.2, 135.9, 134.4, 133.7, 133.6, 133.5, 133.2, 131.5, 131.3, 130.8, 130.3, 130.2, 130.1, 129.8, 129.7, 128.9, 128.7, 128.5, 128.0, 127.9, 127.7, 127.1, 126.8, 126.5, 126.4, 126.3, 126.1, 126.0, 125.8, 125.7, 123.9, 123.6, 123.0, 122.8, 122.7, 122.4, 122.0, 114.8, 114.5, 69.5, 68.9, 31,8, 25.9, 25.8, 25.6, 25.2, 24.9, 22.9, 21.0, 20.8, 20.7, 20.6, 20.44, 20.37, 20.29, 14.5 (observed complexity due to P−C splitting); ^{31}P NMR (121 MHz, $CDCl_3$) δ −0.73, −0.64, IR (neat, cm^{-1}) 2948, 2863, 1509, 1463, 1268, 1223, 814, 744; $[\alpha]^{20}_{Na}$ +17.5 (*c* 1.0, $CHCl_3$); HRMS (+)FAB calcd for $[M + H]^+$: +577.2660 Found$[M + H]^+$: +577.2674.

(*R*)-(−)-2-(Diisopropylphosphino)-1,1′-binaphthyl (4h). Prepared as above in 55% overall yield from (*S*)-2-(trifluoromethanesulfonyl)-oxy-1,1′-binaphthyl[21] as a white solid; mp 128−130 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (q, J = 8.7 Hz, 3H), 7.75 (dd, J = 8.7 Hz, 1.5 Hz, 1H), 7.55 (dd, J = 8.1 Hz, 6.9 Hz, 1H), 7.46−7.33 (m,3H), 7.20 (t, J = 6.9 Hz, 2H), 7.12(d, 2H), 2.17−1.97(m, 2H), 1.08−0.78 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 146.6, 138.4, 134.9, 133.6, 133.5, 133.4, 133.3, 129.41, 129.37, 128.7, 128.4, 128.0, 127.8, 127.6, 127.3, 127.1, 126.5, 126.2, 125.7, 124.9, 26.6, 26.4, 24.7, 24.5, 21.3, 21.1, 20.9, 20.8, 20.7, 20.5, 20.2, 20.1 (observed complexity due to P−C splitting); ^{31}P NMR (121 MHz, $CDCl_3$) δ −2.09; IR (neat, cm^{-1}) 3053, 2948, 2863, 1505, 1462, 1360, 816, 780, 747; $[\alpha]^{20}_{Na}$ δ −291.4 (*c* 7.0, $CHCl_3$); MS (+)FAB, *m*/*z* 371 $[M + H]^+$; HRMS (+)FAB calcd for $[M + H]^+$: +371.1923 Found$[M + H]^+$: +371.1920.

General procedure for asymmetric arylation using (*S*)-BINAP.[13,16] An oven-dried Schlenk tube equipped with a rubber septum was evacuated and backfilled with argon. The tube was charged with palladium acetate (0.05 mmol), (*S*)-BINAP (0.12 mmol) and ketone **1** (0.50 mmol). The tube was evacuated and backfilled with argon (repeated three times). Toluene (2 mL) was added and the mixture was stirred for 15 min at room temperature. The corresponding aryl halide (1.00 mmol) and NaO^{t}Bu (96 mg, 1.00 mmol) were added to the tube. The tube was capped with a septum, purged with argon, and additional toluene (4 mL) was added via syringe. The mixture was stirred at 100 °C until the starting ketone had been completely consumed as judged by GC analysis (2−3 h). The reaction mixture was quenched with saturated aqueous ammonium chloride (10 mL) and diluted with ether (20 mL). The mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was extracted with ether (20 mL) and the combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude materials were purified by silica gel chromatography (elution: 10%-20% EtOAc in hexane).

General procedure for asymmetric arylation using ligands 3 and 4.[16] An oven-dried Schlenk tube equipped with a rubber septum was evacuated and backfilled with argon. The tube was charged with tris-(dibenzylideneacetone)dipalladium (0.005 mmol), ligand **3** or **4** (0.0125 mmol) and the ketone **1** (0.50 mmol). The tube was evacuated and backilled with argon (repeated three times). Toluene (2 mL) was added and the mixture was stirred for 15 min at room temperature. The corresponding aryl halide (1.00 mmol) and sodium *t*-butoxide (96 mg, 1.00 mmol) were added to the tube. The tube was capped with a septum, purged with argon, and additional toluene (1 mL) was added through the septum. The mixture was stirred at room temperature until the starting ketone had been completely consumed as judged by GC analysis. The reaction mixture was quenched with saturated aqueous ammonium chloride (10 mL) and diluted with ether (20 mL). The mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was extracted with ether (20 mL) and the combined organic layers were washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated in vacuo. The crude materials were purified by silica gel chromatography (elution: 10%-20% EtOAc in hexane). See Tables 3 and 4 and the Supporting Information for yields.

(*R*)-(+)-2-Methyl-2-(*p*-*tert*-butylphenyl)-5-(*N*-methylanilinomethylene)cyclopentanone (2a).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (t, J = 1.5 Hz, 1H), 7.33−7.27 (m, 5H), 7.13−7.07 (m, 4H), 3.45 (s, 3H), 2.57−2.36 (m, 3H), 1.91−1.81 (m, 1H), 1.43 (s, 3H), 1.28 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.6, 148.7, 146.2, 142.8, 141.1, 129.1, 126.1, 125.2, 124.6, 121.1, 108.2, 52.1, 40.1, 36.7, 34.3, 31.5, 25.2, 25.0; IR (neat, cm^{-1}) 2960, 2927, 2867, 1684, 1605, 920, 841, 752,

737, 694; $[\alpha]^{20}_{Na}$ +5.39 (*c* 10.0, $CHCl_3$); MS(EI), *m*/*z* 347[M]$^+$; Anal. Calcd for $C_{23}H_{25}NO$: C, 82.95; H, 8.41. Found; C, 82.73; H, 8.54.

(*R*)-(+)-2-Methyl-2-(*o*-tolyl)-5-(*N*-methylanilinomethylene)cyclopentanone (2b). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (t, J = 1.5 Hz, 1H), 7.38−7.32 (m, 3 H), 7.17−7.12 (m, 6H), 3.53 (s, 3H), 2.63−2.55 (m, 2H), 2.26 (s, 3H), 2.25−2.16 (m, 1H), 1.85−1.76 (m, 1H), 1.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.6, 146.3, 143.0, 136.5, 132.1, 129.3, 129.1, 127.6, 126.7, 125.7, 124.9, 121.7, 107.7, 53.5, 40.7, 36.5, 25.1, 23.8, 22.5; IR(neat, cm^{-1}) 2964, 1684, 1567, $[\alpha]^{20}_{Na}$ +29.3 (*c* 1.2, $CHCl_3$); MS(EI), *m*/*z* 305[M]$^+$, Anal. Calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59. Found; C, 82.53; H, 7.68.

(*R*)-(+)-2-Methyl-2-(*m*-tolyl)-5-(*N*-methylanilinomethylene)cyclopentanone (2c). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (t, J = 1.5 Hz, 1H), 7.34−7.29 (m, 2H), 7.19−7.09 (m, 6H), 7.02−6.98 (m, 1H), 3.47 (s, 3H), 2.51−2.33 (m, 3H), 2.32 (s, 3H), 1.90−1.81 (m, 1H), 1.43 (s, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ 207.6, 146.2, 144.2, 142.6, 137.8, 129.2, 128.2, 127.3, 127.0, 124.7, 123.4, 121.3, 108.3, 52.7, 40.2, 36.9, 25.4, 25.1, 21.9; IR (neat, cm^{-1}) 2960, 2932, 2863, 1686, 1563, 920, 787, 754, 696; $[\alpha]^{20}_{Na}$ +9.37 (*c* 10.0, $CHCl_3$); MS(EI), *m*/*z* 305[M]$^+$; Anal. Calcd for C21H23NO: C, 82.58; H, 7.59. Found; C, 82.40; H, 7.70.

(*R*)-(+)-2-Methyl-2-(*p*-tolyl)-5-(*N*-methyl-anilinomethylene)cyclopentanone (2d). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (t, J = 1.5 Hz, 1H), 7.34−7.24 (m, 4H), 7.14−7.08 (m, 5H), 3.47 (s, 3H), 2.51−2.34 (m, 3H), 2.30 (s, 3H), 1.90−1.80 (m, 1H), 1.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.6, 146.2, 142.5, 141.2, 135.8, 129.2, 129.1, 126.5, 124.7, 121.3, 108.3, 52.4, 40.2, 36.7, 25.4, 25.0, 21.2; IR (neat, cm^{-1}) 2958, 2923, 2863, 1688, 1605, 1563, 920, 818, 802, 754, 694; $[\alpha]^{20}_{Na}$ +5.41 (*c* 10.0, $CHCl_3$); MS(EI), *m*/*z* 305[M]$^+$; Anal. Calcd for $C_{23}H_{25}NO_3$: C, 82.95; H, 8.41. Found; C, 82.73; H, 8.54, Anal. Calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59. Found; C, 82.56; H, 7.58.

(*R*)-(+)-2-Methyl-2-(*m*-anisyl)-5-(*N*-methyl-anilinomethylene)cyclopentanone (2e). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.34−6.95 (m, 8H), 6.75−6.71 (m, 1H), 3.78 (s, 3H), 3.45 (s, 3H), 2.49−2.34 (m, 3H), 1.90−1.81 (m, 1H), 1.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2, 159.5, 146.1, 145.9, 142.6, 129.2, 129.1, 124.7, 121.3, 118.9, 112.8, 111.3, 108.1, 55.3, 52.7, 40.2, 36.8, 25.3, 25.0; IR (neat, cm^{-1}) 2960, 2863, 1686, 1561, 920, 895, 781, 739, 694; $[\alpha]^{20}_{Na}$ +0.30 (*c* 10.0, $CHCl_3$); MS(EI), *m*/*z* 321[M]$^+$; Anal. Calcd for $C_{21}H_{23}NO_2$: C, 78.47; H, 7.21. Found; C, 78.22; H, 7.22.

(*R*)-(+)-2-Methyl-2-(*p*-anisyl)-5-(*N*-methyl-anilinomethylene)cyclopentanone (2f). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (t, J = 1.5 Hz, 1H), 7.33−7.29 (m, 4 H), 7.13−7.08 (m, 3H), 6.85−6.80 (m, 2H), 3.75 (s, 3H), 3.45 (s, 3H), 2.56−2.32 (m, 3H), 1.89−1.79 (m, 1H), 1.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.5, 157.8, 146.1, 142.4, 136.1, 129.1, 127.4, 124.6, 121.1, 113.6, 108.0, 55.3, 51.9, 40.1, 36.6, 25.4, 24.9; IR (neat, cm^{-1}) 2960, 2836, 1684, 1561 920, 860, 802, 729, 694; $[\alpha]^{20}_{Na}$ +1.53 (*c* 10.0, $CHCl_3$); MS(EI), *m*/*z* 321[M]$^+$; Anal. Calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59. Found; C, 82.53; H, 7.68.

(*R*)-(+)-2-Methyl-2-(*p*-trifluoromethanephenyl)-5-(*N*-methyl-anilinomethylene)cyclopentanone (2 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.55−7.49 (m, 4H), 7.35−7.30 (m, 2H), 7.16−7.10 (m, 3H), 3.48 (s, 3H), 2.56−2.30 (m, 3H), 1.97−1.87 (m, 1H), 1.45 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.4, 148.7, 145.9, 143.3, 128.2, 128.5, 128.1, 127.0, 126.1, 125.2, 125.1, 125.0, 122.5, 121.6, 107.3, 52.7, 40.5, 36.7, 25.0, 24.8; IR(neat, cm^{-1}) 2964, 1686, 1565; $[\alpha]^{20}_{Na}$ +7.7 (*c* 10.0, $CHCl_3$); MS(EI), *m*/*z* 359[M]$^+$, Anal. Calcd for $C_{21}H_{20}NOF_3$: C, 70.18; H, 5.61. Found; C, 69.89, H, 5.47.

(*R*)-(+)-2-(3-[1,3]Dioxolan-2-yl-phenyl)-2-methyl-5-(*N*-methyl-anilinomethylene)cyclopentanone (2h). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.49 (s, 1H), 7.42−7.27 (m, 4H), 7.14−7.08 (m, 3H), 5.78 (s, 1H), 4.14−3.98 (m, 3H), 3.46 (s, 3H), 2.55−2.37 (m, 3H), 1.92−1.83 (m, 1H), 1.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 146.1, 144.4, 142.7, 141.2, 137.6, 129.3, 129.1, 128.4, 127.6, 124.8, 124.7, 121.4, 108.1, 104.0, 65.4, 52.4, 40.3, 36.7, 25.4, 25.0; IR (neat, cm^{-1}) 2960, 2927, 2887, 1684, 1605, 1565, 920, 802, 756, 696; $[\alpha]^{20}_{Na}$ +22.9 (*c* 10.0, $CHCl_3$); MS(EI), *m*/*z* 363[M]$^+$; Anal. Calcd for $C_{23}H_{25}NO_3$: C, 82.95; H, 8.41. Found; C, 82.73; H, 8.54.

(*R*)-(+)-2-Propyl-2-(*m*-tolyl)-5-(*N*-methyl-anilinomethylene)cyclopentanone (2i). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.33−6.99 (m, 9H), 3.43 (s, 3H), 2.56−2.37 (m, 3H), 2.33 (s, 3H), 2.01−1.82 (m, 2H), 1.67−1.57 (m, 1H), 1.21−1.03 (m, 2H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.7, 146.3, 142.2, 141,5, 137.7, 129.1, 128.1, 127.7, 127.1, 124.6, 123.8, 121.1, 108.6, 56.3, 41.8, 40.0, 32.5, 25.2, 21.9, 18.4, 14.9; IR (neat, cm^{-1}) 2956, 2931, 2871, 1686, 1567, 885, 773, 731; $[\alpha]^{20}_{Na}$ +28.4 (*c* 10.0, $CHCl_3$); MS-(EI), *m*/*z* 333[M]$^+$, Anal. Calcd for $C_{23}H_{27}NO$: C, 82.84; H, 8.16. Found; C, 82.91; H, 8.30.

(*R*)-(+)-2-Pentyl-2-(*m*-tolyl)-5-(*N*-methyl-anilinomethylene)cyclopentanone (2j). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.31−6.98 (m, 9H), 3.44 (s, 3H), 2.56−2.43 (m, 3H), 2.32 (s, 3H), 2.02−1.83 (m, 2H), 1.70−1.60 (m, 1H), 1.20−1.02 (m, 6H), 0.81 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.6, 146.2, 142.1, 141.5, 137.6, 129.1, 128.0, 127.6, 127.0, 124.5, 123.7, 121.0, 108.6, 56.2, 39.9, 39.4, 32.6, 32.6, 25.1, 24.6, 22.7, 21.9, 14.3; IR(neat) 2954, 2931, 2858, 1686, 1567, 908, 754, 710; $[\alpha]^{25}_{Na}$ +35.4 (*c* 10.0, $CHCl_3$); MS-(EI), *m*/*z* 361[M]$^+$, Anal. Calcd for $C_{25}H_{31}NO$: C, 83.06; H, 8.64. Found; C, 82.81; H, 8.66.

(*R*)-(+)-2-Methyl-2-phenyl-5-(*N*-methyl-anilinomethylene)cyclopentanone (2k). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (t, J = 1.5 Hz, 1H), 7.40−7.09 (m, 10H), 3.47 (s, 3H), 2.52−2.37 (m, 3H), 1.93−1.82 (m, 1H), 1.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.6, 146.2, 144.3, 142.8, 129.2, 128.4, 126.5, 126.3, 124.9, 121.4, 108.2, 52.7, 40.4, 36.9, 25.3, 25.0; IR (neat, cm^{-1}) 2957, 2862, 1683, 1602, 1569, 923, 756, 697; $[\alpha]^{20}_{Na}$ +20.0 (*c* 5.83, $CHCl_3$); MS(EI), *m*/*z* 291[M]$^+$; Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26. Found; C, 82.20; H, 7.24.

Procedure for Removing the Blocking Group.[16] Ketone **2k** (84 mg, 0.29 mmol) was dissolved in THF (8.0 mL) in a round-bottomed flask. Aqueous HCl (1 M, 6.0 mL) was added and the mixture stirred at room temperature until **2k** had been completely consumed, as judged by GC analysis (ca. 3 h). The mixture was diluted with water (10 mL) and ether (10 mL) and was poured into a separatory funnel; the layers were then separated. The aqueous layer was extracted with ether (10 mL), and the organic layers were combined and concentrated in vacuo. The residual oil was dissolved in aqueous NaOH solution (1 M, 8 mL) in a round-bottomed flask equipped with a reflux condenser, and the resulting solution was stirred at 90 °C for 2 h. The mixture was cooled to room temperature, neutralized with aqueous HCl (1 M), and diluted with ether (20 mL). The mixture was poured into a separatory funnel, and the layers were separated. The aqueous layer was extracted with ether (10 mL), and the combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to give (*R*)-(+)-2-methyl-2-phenylcyclopentanone **5**[22] (46.0 mg, 91%, $[\alpha]^{20}_{Na}$ +76.6 (*c* 3.4, EtOH), 93% ee) as a colorless oil.

Acknowledgment. This research was funded by the National Institutes of Health (GM46059) with additional support from Ajinomoto Co., Inc. We are grateful to Drs. Joseph M. Fox and Alex R. Muci for helpful discussions as well as assistance in the preparation of the manuscript.

Supporting Information Available: ^{1}H and ^{31}P NMR spectra of **4a** and **4h**, and additional results in the arylation of **1a** with other commercially available ligands and reactions with different aryl halides using **3**/Pd-based catalysts (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA011122+