DOI: 10.1002/adsc.200800631

An *N*-Linked Bidentate Phosphoramidite Ligand (*N*-Me-BIPAM) for Rhodium-Catalyzed Asymmetric Addition of Arylboronic Acids to *N*-Sulfonylarylaldimines

Kazunori Kurihara,[a] Yasunori Yamamoto,[a,*] and Norio Miyaura[a,*]

[a] Division of Chemical Process Engineering, Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan
Fax: (+81)-11-706-6561; e-mail: yasuyama@eng.hokudai.ac.jp or miyaura@eng.hokudai.ac.jp

Received: October 14, 2008; Published online: December 29, 2008

Abstract: A chiral *N*-linked C_2-symmetric bidentate phosphoramidite (*N*-Me-BIPAM) was newly developed for the rhodium-catalyzed enantioselective addition of arylboronic acids to *N*-sulfonylimines. This ligand achieved high enantioselectivities in a range of 84–99% *ee* in additions of arylboronic acids to *N*-tosyl- and *N*-nosylarylaldimines.

Keywords: arylboronic acids; asymmetric catalysis; asymmetric synthesis; diarylamines; *N*-sulfonylaldimines

Introduction

Chiral diarylmethylamines are an important fragment involved in a variety of pharmacologiocally significant compounds.[1] For achieving a simple access to this versatile skeleton, rhodium-catalyzed enantioselective arylations of imines with arylboron,[2–8] -zinc,[9] -stannane[10] and -titanium compounds[11] have been developed. Among these extensive studies on catalytic addition of metallic and non-metallic compounds to aldimines, the use of arylboronic acids has attracted much attention due to their low toxicity, compatibility to a broad range of functional groups and high stability in water and air. The enantioselective rhodium-catalyzed arylation of aldimines with arylboroxines or arylboronic acids has been studied by Tomioka,[3] Zhou,[4] de Vries, Feringa and Minnerd,[5] Ellman,[6] Hayashi,[7] as well as Xu and Lin.[8] Amidophosphane (**1**), spiromonophosphite (**2**), bicyclo[2.2.2]octadiene (**6**), bicyclo[3.3.1]nonadiene (**7**) and tetrahydropentalene (**8**) were found to be effective as the chiral ligand for arylation of *N*-tosyl- (4-$MeC_6H_4SO_2$) and *N*-nosylimines (4-$NO_2C_6H_4SO_2$) (Figure 1). Phosphoramidite (**3**) was used for *N*-SO_2NMe_2 imines,[5] and deguphos [bis(diphenylphosphino)-1-benzylpyrrolidine] (**5**) gave high enantioselectivities for *N*-$P(=O)Ph_2$ imines and *N*-Boc imines.[6b] Thus, both monodentate and bidentate phosphorus ligands have been used successfully as chiral ligands, although the traditional BINAP (**4**) is less efficient in terms of chemical yields and enantioselectivities. The efficiency of Rh/chiral monodentate phosphine (MOP) and paracyclophane-based ketimine catalysts has been reported for analogous arylations of *N*-sulfonylimines and *N*-formylimines with arylstannanes[10] or arylzinc compounds.[9]

In the course of our study on bisphosphoroamidites as a chiral ligand for enantioselective bond-forming reactions,[13] we found a novel *N*-linked bidentate phosphoramidite (*N*-Me-BIPAM) that is effective for the arylation of both *N*-sulfonyl(aryl)imines (**9**–**11**)

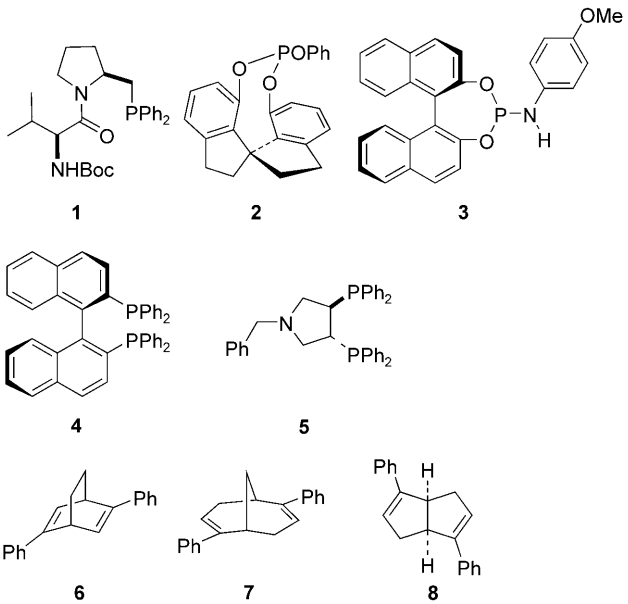
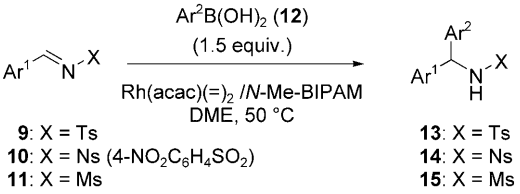


Figure 1. Chiral ligands reported for the arylation of imines.



Scheme 1. Arylation of imines.

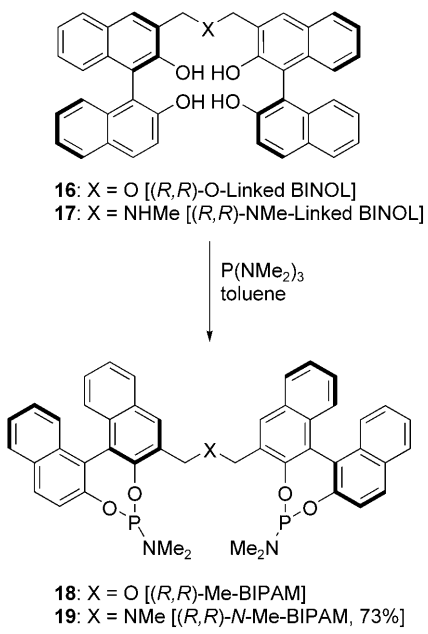
with arylboronic acids (Scheme 1). The reaction provided α-diarylmethylamines (**13**–**15**) with high yields and high enantioselectivities up to 99% *ee* in the presence of 1.5 equivalents of boronic acids.

Results and Discussion

Rhodium Catalyst

We previously reported that an *O*-linked bidentate phosphoramidite (**18**, Me-BIPAM) synthesized on the basis of Shibasaki's *O*-linked BINOL (**16**)[13] is an excellent ligand for rhodium-catalyzed 1,4-addition of arylboronic acids to α,β-unsaturated carbonyl compounds. The corresponding *N*-linked C_2-symmetric phosphoramidite (**19**, *N*-Me-BIPAM) was newly synthesized by treatment of **17**[12] with $P(NMe_2)_3$ (Scheme 2).

The ^{31}P NMR spectrum of the mixture of Rh(acac)-$(C_2H_4)_2$ and *N*-Me-BIPAM exhibited a single signal at 160.0 ppm (d, $J_{Rh,P} = 292.3$ Hz), thus suggesting the intramolecular complexation of two phosphorus atoms to a rhodium metal center. The formation of a 1:1 complex (Rh(acac)(*N*-Me-BIPAM) was also confirmed by HR-MS (ESI), calcd. for $C_{52}H_{49}N_3O_6P_2Rh$: 976.2152, found: 976.2148 (M+H).

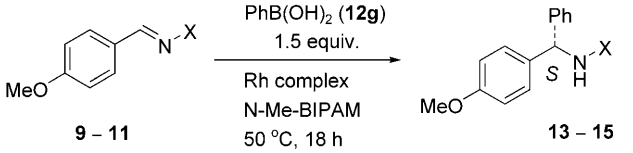


Scheme 2. Synthesis of *N*-Me-BIPAM.

Reaction Conditions

Several combinations of rhodium(I) precursors and solvents for *N*-Me-BIPAM (**19**) revealed the high efficiency of Rh(acac)$(C_2H_4)_2$ in DME for the addition of $PhB(OH)_2$ to 4-methoxybenzylaldehyde *N*-tosylimine (**9b**) (Table 1). The reaction took place smoothly at 50 °C in the presence of 1.5 equivalents of $PhB(OH)_2$ with 88% yield and 94% *ee* (entry 4). Thus, the reaction did not require the use of bases and a large excess of boronic acids or boroxines to achieve practical yields. On the other hand, the rhodium(I)-chloro complex previously used for 1,4-addition of arylboronic acid to α,β-unsaturated carbonyl compounds[13] unexpectedly did not catalyze the reaction even in the presence of a base (entries 6 and 7). It is also interesting that Me-BIPAM (**18**),[13] which achieved high enantioselectivities in the 1,4-addition of arylboronic acids to cyclic and acyclic enones, resulted in a significantly lower enantioselectivity than did *N*-Me-BIPAM (entry 8). Among the *N*-tosyl- (**9**, 4-$MeC_6H_4SO_2$), *N*-nosyl- (**10**, 4-$NO_2C_6H_4SO_2$), and *N*-mesylimines (**11**, $MeSO_2$) screened as substrates, *N*-tosyl- and *N*-nosylimines resulted in the best enantioselectivity (entries 4, 9 and 10).

Table 1. Reaction conditions.[a]



Entry	Imine	Rh complex	Solvent	Yield [%]	*ee* [%]
1	**9b**	Rh(acac)$(C_2H_4)_2$	toluene	66 (**13bg**)	77
2	**9b**	Rh(acac)$(C_2H_4)_2$	THF	86 (**13bg**)	64
3	**9b**	Rh(acac)$(C_2H_4)_2$	dioxane	70 (**13bg**)	87
4	**9b**	Rh(acac)$(C_2H_4)_2$	DME	88 (**13bg**)	94
5	**9b**	$[Rh(nbd)_2]BF_4$	DME	34 (**13bg**)	88
6	**9b**	$[Rh(nbd)Cl]_2$	DME	trace	–
7[b]	**9b**	$[Rh(nbd)Cl]_2$	DME	trace	–
8[c]	**9b**	Rh(acac)$(C_2H_4)_2$	DME	83 (**13bg**)	74
9	**10a**	Rh(acac)$(C_2H_4)_2$	DME	72 (**14ag**)	93
10	**11a**	Rh(acac)$(C_2H_4)_2$	DME	89 (**15ag**)	87

[a] A mixture of aldimine (0.5 mmol), $PhB(OH)_2$ (0.75 mmol), Rh complex (3 mol%) and *N*-Me-BIPAM (3.3 mol%) in solvent (2 mL) was stirred at 50 °C for 16 h.
[b] In the presence of aqueous KOH (20 mol%).
[c] Me-BIPAM was used instead of *N*-Me-BIPAM.

Scope and Limitation

Results of the arylation of aromatic imines with arylboronic acids at 50 °C in DME in the presence of a $Rh(acac)(C_2H_4)_2$/*N*-Me-BIPAM catalyst (3 mol%) are summarized in Table 2. High enantioselectivities were achieved in most combinations of two aromatic rings having donating or withdrawing substituents at the *para*, *meta* or *ortho* carbons of imines and boronic acids. Thus, the performance of *N*-Me-BIPAM is comparable to or even higher than that of ligands previously reported for analogous arylations of imines.[3–8] However, this ligand may prefer some steric hindrance of substituents since the reaction often resulted in less than 90% *ee* when an unsubstituted phenyl group was used for either of the two aryl rings (entries 1, 2, 19, 21 28, 30 and 35). This is due to steric reasons rather than an electronic effect of substituents because high selectivities were easily achieved in all combinations of two aryl rings possessing substituents in both rings. The presence of an *ortho*-substituent in imines did not retard the reaction (entries 20–32), but 2-methyl- and 2-methoxyphenylboronic acids resulted

Table 2. Arylation of *N*-tosylimines (**9**, Scheme 1).[a]

Entry	Ar^1	Ar^2	Product	Yield [%]	*ee* [%]
1	C_6H_5 (**9a**)	4-$MeOC_6H_4$ (**12a**)	**13aa**	91	85 (*R*)
2	C_6H_5 (**9a**)	4-MeC_6H_4 (**12b**)	**13ab**	96	84 (*R*)
3	C_6H_5 (**9a**)	4-ClC_6H_4 (**12c**)	**13ac**	82	95 (*R*)
4	C_6H_5 (**9a**)	4-$CF_3C_6H_4$ (**12d**)	**13ad**	89	90 (*R*)
5	C_6H_5 (**9a**)	3-F-4-$MeOC_6H_3$ (**12e**)	**13ae**	96	97
6	C_6H_5 (**9a**)	1-naphthyl (**12f**)	**13af**	61	93 (*R*)
7	4-$MeOC_6H_4$ (**9b**)	C_6H_5 (**12g**)	**13bg**	88	94 (*S*)
8	4-MeC_6H_4 (**9c**)	4-$MeOC_6H_4$ (**12a**)	**13ca**	92	96 (*R*)
9	4-MeC_6H_4 (**9c**)	C_6H_5 (**12g**)	**13cg**	91	96 (*S*)
10	4-ClC_6H_4 (**9d**)	4-$MeOC_6H_4$ (**12a**)	**13da**	93	98 (*S*)
11	4-ClC_6H_4 (**9d**)	C_6H_5 (**12g**)	**13dg**	98	95 (*S*)
12	4-ClC_6H_4 (**9d**)	4-$CF_3C_6H_4$ (**12d**)	**13dd**	91	92
13	4-BrC_6H_4 (**9e**)	C_6H_5 (**12g**)	**13eg**	87	94 (*S*)
14	4-$CF_3C_6H_4$ (**9f**)	C_6H_5 (**12g**)	**13fg**	91	96 (*S*)
15	3-$MeOC_6H_4$ (**9g**)	C_6H_5 (**12g**)	**13gg**	95	99 (*S*)
16	3-ClC_6H_4 (**9h**)	C_6H_5 (**12g**)	**13hg**	92	97
17	3-Br-4-$MeOC_6H_3$ (**9i**)	C_6H_5 (**12g**)	**13ig**	98	92
18[b]	3,4-$(CH_2O_2)C_6H_3$ (**9j**)[c]	4-$MeOC_6H_4$ (**12a**)	**13ja**	99	97
19[b]	3,4-$(CH_2O_2)C_6H_3$ (**9j**)[c]	C_6H_5 (**12g**)	**13jg**	90	85
20[b]	2,3-$(C_2H_4O_2)C_6H_3$ (**9k**)[d]	C_6H_5 (**12g**)	**13kg**	93	99
21	2-$MeOC_6H_4$ (**9l**)	C_6H_5 (**12g**)	**13lg**	84	18 (*S*)
22	2-$MeOC_6H_4$ (**9l**)	4-$CF_3C_6H_4$ (**12d**)	**13ld**	74	98
23	2-MeC_6H_4 (**9m**)	4-$CF_3C_6H_4$ (**12d**)	**13md**	70	93
24	2-ClC_6H_4 (**9n**)	4-$MeOC_6H_4$ (**12a**)	**13na**	99	96 (*S*)
25	2-ClC_6H_4 (**9n**)	3-$MeOC_6H_4$ (**12h**)	**13nh**	92	93
26	2-ClC_6H_4 (**9n**)	4-$CF_3C_6H_4$ (**12d**)	**13nd**	99	96
27	2-$CF_3C_6H_4$ (**9o**)	4-$MeOC_6H_4$ (**12a**)	**13oa**	77	96
28	2-Me-4-$MeOC_6H_3$ (**9p**)	C_6H_5 (**12g**)	**13pg**	89	88
29	2,4-$Cl_2C_6H_3$ (**9q**)	4-$MeOC_6H_4$ (**12a**)	**13qa**	99	96
30	2,4-$Cl_2C_6H_3$ (**9q**)	C_6H_5 (**12g**)	**13qg**	95	85
31	2,4-$Cl_2C_6H_3$ (**9q**)	4-$CF_3C_6H_4$ (**12d**)	**13qd**	96	98
32	2-MeO-5-BrC_6H_3 (**9r**)	C_6H_5 (**12g**)	**13rg**	98	98
33	1-naphthyl (**9s**)	C_6H_5 (**12g**)	**13sg**	91	94 (*S*)
34	2-furyl (**9t**)	4-$MeOC_6H_4$ (**12a**)	**13ta**	93	99
35	2-furyl (**9t**)	C_6H_5 (**12g**)	**13tg**	89	75 (*S*)
36	2-furyl (**9t**)	3-$MeOC_6H_4$ (**12h**)	**13th**	99	95
37	2-furyl (**9t**)	4-$CF_3C_6H_4$ (**12d**)	**13td**	86	98
38	2-benzofuranyl (**9u**)	C_6H_5 (**12g**)	**13ug**	95	94

[a] A mixture of aldimine (0.5 mmol), $Ar^2B(OH)_2$ (0.75 mmol), Rh complex (3 mol%) and *N*-Me-BIPAM (3.3 mol%) in DME (2 mL) was stirred at 50 °C for 16 h.
[b] at 80 °C.
[c] 3,4-Methylenedioxyphenyl.
[d] 2,3-Dihydrobenzo[1,4]dioxine-6-yl.

Table 3. Arylation of *N*-nosylimines (**10**, Scheme 1).[a]

Entry	Ar^1	Ar^2	Product	Yield [%]	*ee* [%]
1	4-$MeOC_6H_4$ (**10a**)	C_6H_5 (**12g**)	**14ag**	72	93 (*S*)
2	4-ClC_6H_4 (**10b**)	4-$MeOC_6H_4$ (**12a**)	**14ba**	91	97
3	4-ClC_6H_4 (**10b**)	4-$CF_3C_6H_4$ (**12d**)	**14bd**	89	97
4	4-ClC_6H_4 (**10b**)	3-$MeOC_6H_4$ (**12h**)	**14bh**	97	97
5	4-ClC_6H_4 (**10b**)	4-Br-3-FC_6H_3 (**12i**)	**14bi**	99	97
6	3-ClC_6H_4 (**10c**)	4-$MeOC_6H_4$ (**12a**)	**14ca**	76	96
7	3-ClC_6H_4 (**10c**)	4-$CF_3C_6H_4$ (**12d**)	**14cd**	84	97
8	2-ClC_6H_4 (**10d**)	4-$CF_3C_6H_4$ (**12d**)	**14dd**	99	98
9	2-ClC_6H_4 (**10d**)	3-$MeOC_6H_4$ (**12h**)	**14dh**	88	98
10	2-$MeOC_6H_4$ (**10e**)	4-$CF_3C_6H_4$ (**12d**)	**14ed**	81	94
11	2-Me-4-$MeOC_6H_3$ (**10f**)	C_6H_5 (**12g**)	**14fg**	99	97
12	5-Br-2-$MeOC_6H_3$ (**10g**)	4-$CF_3C_6H_4$ (**12d**)	**14gd**	90	96

[a] A mixture of aldimine (0.5 mmol), $Ar^2B(OH)_2$ (0.75 mmol), Rh complex (3 mol%) and *N*-Me-BIPAM (3.3 mol%) in DME (2 mL) was stirred at 50 °C for 16 h.

in low conversion (*ca.* 30%) due to slow transmetalation to the catalyst.

The *N*-nosyl group (4-$NO_2C_6H_4SO_2$) is a alternative protecting group because of the mild conditions for its deprotection.[14] Although a retarding effect of a polar nitro group has been reported in an analogous rhodium-catalyzed arylation of aldehydes,[15] addition to *N*-nosylimines smoothly proceeded at 50 °C with high enantioselectivities in a range of 96–98% *ee*. The selectivities were comparable to those of *N*-tosylimines (Table 3).

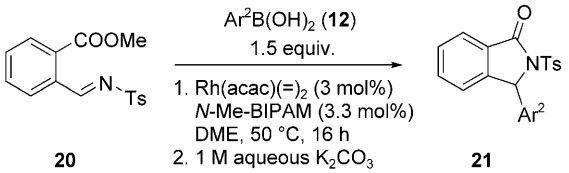
Synthetic Applications

Chiral isoindolinones (**21**) are valuable drug candidates that are difficult to access by the catalytic protocol.[16] An elegant synthesis of a chiral isoindolinone was first demonstrated by Lin *via* arylation of methyl 2-formylbenzoate *N*-tosylimine (**20**) with a chiral diene ligand followed by lactamization.[8]

This substrate possessing an *ortho*-ester group was found to be a suitable substrate for *N*-Me-BIPAM (Table 4). The representative arylboronic acids achieved quantitative yields and high enantioselectivities in the range of 97–99% *ee*.

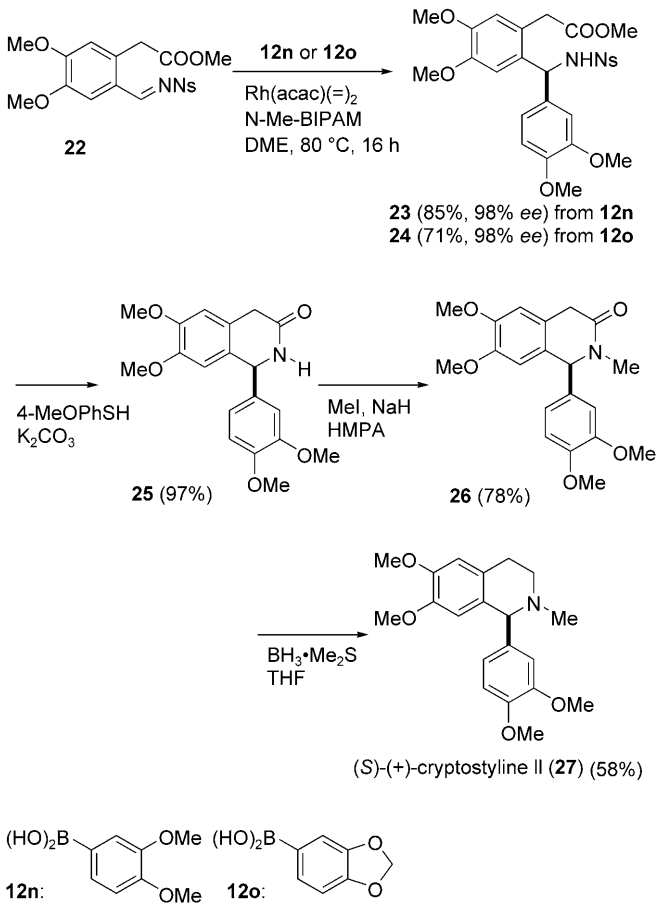
Numerous analogues of cryptostylines have been studied as pharmacological probes such as the D_1 dopamine receptor, an antagonist of substance P and a peptide neurotransmitter. The protocol shown in Table 4 readily provided a simple access to such enantiopure cryptostylines[17] (Scheme 3). A key intermediate (**23**) for synthesis of cryptostyline II was obtained by enantioselective arylation of **22**. The reaction at 50 °C was slow, but **23** was formed in good yield at 80 °C with 98% *ee*. In the same manner, **24** for synthesis of cryptostyline I was obtained by enantioselective arylation of **22** with **12o** (71%, 98% *ee*). Lactamization to **25** *via* deprotection of the nosyl group with

Table 4. Synthesis of 3-aryl-*N*-tosylphthalimidines.[a]



Entry	**12**, Ar^2	Product	Yield [%]	*ee* [%]
1	4-$MeOC_6H_4$ (**12a**)	**21a**	97	98 (*S*)
2	3-BrC_6H_4 (**12j**)	**21b**	98	97
3	3-$CF_3C_6H_4$ (**12k**)	**21c**	98	97
4	3-F-4-$MeOC_6H_3$ (**12l**)	**21d**	94	97
5	2,3-dihydrobenzo[1,4]dioxin-6-yl (**12m**)	**21e**	96	99

[a] A mixture of aldimine (0.5 mmol), $PhB(OH)_2$ (0.75 mmol), Rh complex (3 mol%) and *N*-Me-BIPAM (3.3 mol%) in DME (2 mL) was stirred at 50 °C for 16 h. The reaction mixture was then treated with aqueous K_2CO_3 (1 M, 2 mL) for 2 h at 50 °C.



Scheme 3. Synthesis of cryptostyline II.

K_2CO_3 resulted in a complex mixture of products, but quantitative yield was achieved when **23** was treated with 4-$MeOC_6H_4SH$ and K_2CO_3 at 50 °C in CH_3CN/DMSO (49/1) (97%).[18] Reduction of the carbonyl group with $BH_3{\cdot}Me_2S$ was followed by methylation of the N-H group with MeI and NaH to furnish (*S*)-(+)-cryptostyline II in 45% yield. The absolute configuration of the product thus obtained by (*R,R*)-*N*-Me-BIPAM ($[\alpha]_D$: +54.5, $CHCl_3$) was established to be *R* by the specific rotation reported for (*S*)-(+)-cryptostyline II ($[\alpha]_D$: +58.0, $CHCl_3$).[17a] Thus, the product was produced by the mode of face selection as for products shown in Table 2, Table 3, and Table 4.

Enantioselection Mechanism

The catalytic cycle involves (i) transmetalation of an arylboronic acid to an HO-[Rh] complex giving an Ar-[Rh] species, (ii) insertion of an imine C=N bond into the Ar–Rh bond and finally (iii) formation of a diarylamine *via* hydrolysis of the Rh-N intermediate with water.[2,5]

The absolute configuration and enantioselectivity are determined at the insertion step of imines into an arylrhodium(I)-phosphine intermediate. Thus, the *S* and *R* configurations in Tables and **23** and **24** in Scheme 3 obtained by (*R,R*)-*N*-Me-BIPAM are rationalized by the coordination of an imine with its *si*-face.

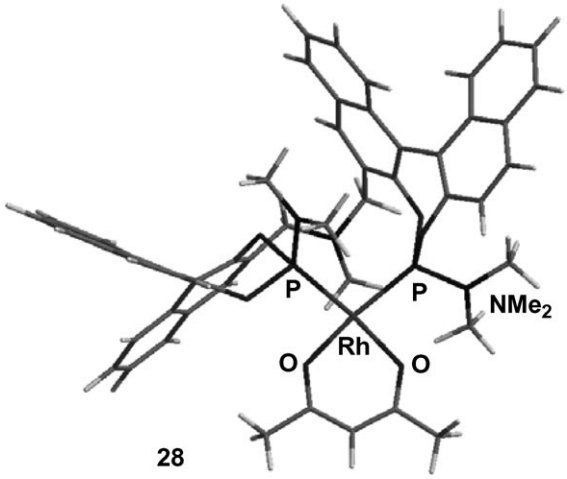


Figure 2. A top view of Rh(acac)(*N*-Me-BIPAM) obtained by DFT calculation.

No X-ray structure is yet available because of the difficulty in synthesizing a single crystal of Rh(acac)(*N*-Me-BIPAM). We therefore estimated this conformation by DFT computations on the B3LYP/6–31G//B3LYP/LANL2DZ level of theory. A top view of the stable complex (**28**) is shown in Figure 2. The stable conformation displays a slightly twisted square-planar coordination geometry for the rhodium(I) atom ligated with two phosphorus atoms of *N*-Me-BIPAM and two oxygen atoms of acetylacetone. The substituents on the left and right phosphorus atoms are not symmetrical. Although there is no large difference in steric hindrance between the upper and lower left areas, an equatorial NMe_2 group blocks the lower right area.

The stable conformation of the [Rh(Ph)(OH_2)((*R,R*)-*N*-Me-BIPAM)] intermediate generated by transmetalation of phenylboronic acid to Rh(OH)(OH_2)(*N*-Me-BIPAM) was calculated on the basis of theoretical modeling. A top view (**29**) is shown in Figure 3. There is a completely planar coordination space in the left area consisting of a phenyl group on the rhodium atom. A naphthyloxy group in the upper right occupies a pseudo-axial position in the chelate ring, whereas the lower right NMe_2 group is in a pseudo-equatorial position, thus suggesting that the space is accessible to reactants in the upper right quadrant and two quadrants in the left area.

On the basis of this calculation, a mode of coordination of the imine substrate to the current phenylrhodium(I) intermediate is proposed in **30**. The *si*-coordination of the substrate is preferred without signif-

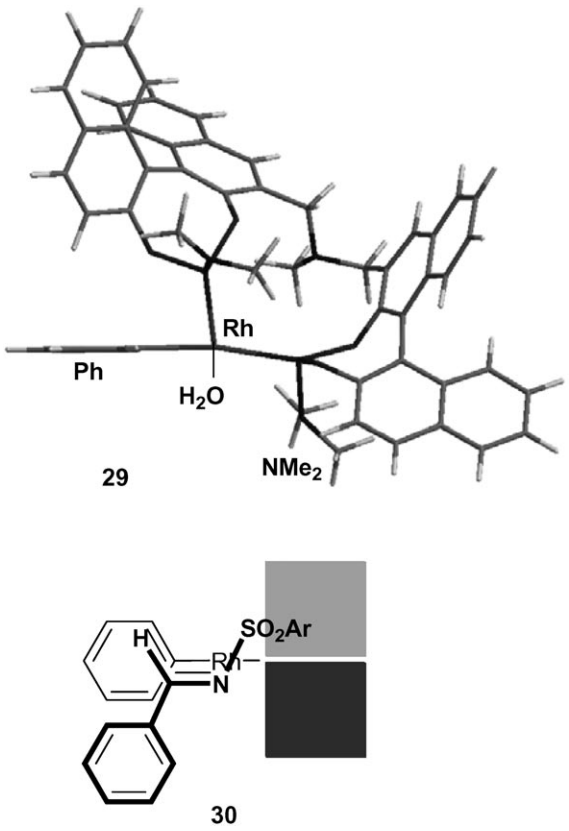


Figure 3. A top view of Rh(Ph)(OH_2)(N-Me-BIPAM) obtained by DFT calculation (29) and a proposed coordination mode.

icant steric interaction for giving the experimentally observed *S* enantiomer by parallel coordination of the C=N double bond to the Ph−Rh bond for the next insertion process. In mode **30**, the efficiency of *N*-Me-BIPAM for arylimines can be interpreted by parallel orientation or π-π stacking of the two aryl groups on the rhodium atom and imine substrate. On the other hand, the coordination of an imine from its opposite *re* face is being blocked by the equatorial NMe_2 group.

Conclusion

In conclusion, we have developed a new chiral bidentate phosphoramidite ligand (*N*-Me-BIPAM) that is highly efficient for asymmetric arylation of both *N*-tosyl and *N*-nosylarylimines with arylboronic acids. With this catalyst system, a broad range of enantiopure diarylmethylamines were easily prepared by using a minimum amount of arylboronic acid. Studies on further applications of *N*-Me-BIPAM to other C–C bond-forming reactions are in progress in our group.

Experimental Section

Synthesis of *N*-Me-BIPAM (19, Scheme 2)

(*R,R*)-3,3′-[Methyliminobis(methylene)]bis(1,1′-binaphthylene-2,2′-diol) (**19**,[12] 2.4 mmol) and $P(NMe_2)_3$ (6 mmol) in dry toluene were stirred for 2 days at 30 °C under nitrogen. The crude solid obtained by evaporation of the solvent was purified by column chromatography to give (*R,R*)-*N*-Me-BIPAM as a white solid. 73%; $[\alpha]_D^{22}$: −578.3 (*c* 0.56, $CHCl_3$); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.32 (s, 2H), 7.93 (q, *J* = 9.1 Hz, 6H), 7.36–7.41 (m, 4H), 7.18–7.29 (m, 8H), 4.09 (d, *J* = 15.4 Hz, 2H), 3.76 (d, *J* = 15.4 Hz, 2H), 2.58 (s, 3H), 2.32 (s, 6H), 2.30 (s, 6H); ^{13}C NMR (CD_2Cl_2): δ = 149.5, 149.4, 148.6, 132.9, 131.5, 130.9, 129.8, 129.3, 128.2, 127.6, 127.3, 126.9, 126.4, 125.5, 124.8, 124.0, 122.7, 122.6, 121.1, 57.3, 44.5, 36.1, 34.8; ^{31}P NMR (100 MHz, CD_2Cl_2): δ = 149.5; HR-MS (FAB): *m/z* = 774.2667, calcd. for $C_{47}H_{42}N_3O_4P_2$ (M+H): 774.2651.

General Procedure for Rhodium-Catalyzed Arylation of Aldimines with Arylboronic Acids (13 in Table 2 and 14 in Table 3)

A flask was charged with Rh(acac)(C_2H_4)$_2$ (0.015 mmol, 3 mol%) and *N*-Me-BIPAM (**19**, 0.0165 mmol, 3.3 mol%) under a nitrogen atmosphere. DME (2 mL) was added and the mixture then stirred at room temperature for 30 min. Arylboronic acid (0.75 mmol) and aldimine (**9** or **10**, 0.5 mmol) were added to this catalyst solution. After being stirred for 16 h at 50 °C, the product was extracted with ethyl acetate, washed with brine and dried over $MgSO_4$. Chromatography on silica gel with hexane/ethyl acetate gave the product as white or yellow solids.

Characterization data of known compounds are given below.

13aa: 85% *ee*, $[\alpha]_D^{25}$: +7.01 (*c* 0.38, $CHCl_3$);[7a] **13ab**: 84% *ee*, $[\alpha]_D^{25}$: +9.65 (*c* 0.41, $CHCl_3$);[4] **13ac** 95% *ee*, $[\alpha]_D^{25}$: +4.11 (*c* 0.32, CH_3Cl);[7a] **13ad**: 90% *ee*, $[\alpha]_D^{25}$: −6.11 (*c* 0.47, $CHCl_3$);[7a] **13af**: 93% *ee*, $[\alpha]_D^{22}$: +1.09 (*c* 0.13, $CHCl_3$);[4] **13bg**: 94% *ee*, $[\alpha]_D^{22}$: −6.34 (*c* 0.11, $CHCl_3$);[7a] **13ca**: 96% *ee*, $[\alpha]_D^{25}$: +4.08 (*c* 0.20, $CHCl_3$);[8] **13cg**: 96% *ee*, $[\alpha]_D^{25}$: −12.8 (*c* 0.34, CH_3Cl);[4] **13da**: 98% *ee*, $[\alpha]_D^{25}$: +10.2 (*c* 0.39, $CHCl_3$);[8] **13dg**: 95% *ee*, $[\alpha]_D^{22}$: −9.87 (*c* 0.29, $CHCl_3$);[8] **13eg**: 94% *ee*, $[\alpha]_D^{25}$: −11.5 (*c* 0.47, $CHCl_3$);[8] **13fg**: 96% *ee*, $[\alpha]_D^{25}$ −3.39 (*c* 0.14, $CHCl_3$);[7a] **13gg**: 99% *ee*, $[\alpha]_D^{25}$: +1.94 (*c* 0.38, $CHCl_3$);[4] **13lg**: 18% *ee*, $[\alpha]_D^{25}$: −6.77 (*c* 0.41, $CHCl_3$);[4] **13na** (96% *ee*, $[\alpha]_D^{24}$: +32.9 (*c* 0.28, $CHCl_3$);[8] **13sg**: 94% *ee*, $[\alpha]_D^{25}$: +4.25 (*c* 0.13, $CHCl_3$);[7a] **13tg**: 75% *ee*, $[\alpha]_D^{25}$: −10.8 (*c* 0.37, $CHCl_3$);[7a] **14ag**: 93% *ee*, $[\alpha]_D^{25}$: +13.8 (*c* 0.34, THF);[7b] **21a**: 98% *ee*, $[\alpha]_D^{25}$: +25.2 (*c* 0.48, $CHCl_3$).[8]

Characterization data of new compounds are given below.

13ae: $[\alpha]_D^{22}$: +2.47 (*c* 0.38, $CHCl_3$), 97% *ee* (Chiralcel OD-H, hexane/2-propanol = 4/1, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 19.6 and 27.1 min); ^{1}H NMR ($CDCl_3$): δ = 7.54 (d, *J* = 8.7 Hz, 2H), 7.22–7.18 (m, 3H), 7.14 (d, *J* = 8.2 Hz, 1H), 7.06–7.03 (m, 2H), 6.86–6.74 (m, 3H), 5.47 (d, *J* = 7.2 Hz, 1H), 5.14 (d, *J* = 7.2 Hz, 1H), 3.82 (s, 3H) 2.37 (s, 3H); ^{13}C NMR($CDCl_3$): δ = 153.3, 150.9, 147.1, 147.0, 143.4, 140.2, 137.2, 129.4, 128.7, 127.8, 127.2, 123.3, 115.4, 115.2, 113.2, 60.5, 56.3, 21.5; HR-MS (EI): *m/z* = 385.1155, calcd. for $C_{21}H_{20}FNO_3S$: 385.1148.

13dd: $[\alpha]_D^{25}$: −13.6 (*c* 0.56, $CHCl_3$), 92% *ee* (Chiralpak IB, hexane/ethanol = 95/5, flow = 0.8 mL min^{-1}, wavelength = 230 nm, t_R = 24.5 28.1 min); ^{1}H NMR ($CDCl_3$): δ = 7.52 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 4H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.99 (d, *J* = 8.6 Hz, 2H), 5.59 (d, 7.2 Hz, 1H), 4.98 (d, 7.2 Hz, 1H), 2.38 (s, 3H), 2.16 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 143.8, 138.2, 136.9, 134.1, 129.5, 129.0, 128.7, 127.7, 127.1, 125.6, 60.4, 21.5; HR-MS (ESI): *m/z* = 462.0515, calcd. for $C_{18}H_{17}ClF_3NO_2SNa$ (M + Na): 462.0518.

13hg: $[\alpha]_D^{24}$: +1.45 (*c* 0.42, $CHCl_3$), 97% *ee* (Chiralpak IB, hexane/ethanol = 99/1, flow = 0.8 mL min^{-1}, wavelength = 230 nm, t_R = 44.9 and 46.3 min); ^{1}H NMR ($CDCl_3$): δ = 7.54 (d, *J* = 8.2 Hz, 2H), 7.23–7.12 (m, 7H), 7.08–7.00 (m, , 4H), 5.52 (d, *J* = 6.8 Hz, 1H), 5.07 (d, *J* = 6.8 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 143.6, 142.4, 139.9, 137.1, 134.4, 129.8, 129.5, 128.8, 128.0, 127.7, 127.6, 128.8, 128.0, 127.7, 127.6, 127.3, 127.2, 125.6, 60.9, 21.6; HR-MS (ESI): *m/z* = 394.0634, calcd. for $C_{20}H_{18}ClNO_2SNa$ (M + Na): 394.0644.

13ig: $[\alpha]_D^{24}$: −16.41 (*c* 0.51, $CHCl_3$), 92%ee (Chiralpak IB, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 19.6 and 25.0 min); ^{1}H NMR ($CDCl_3$): δ = 7.53 (d, *J* = 8.6 Hz, 2H), 7.23–7.01 (m, 9H), 6.71 (d, *J* = 8.2 Hz, 1H), 6.61 (d, *J* = 2.7 Hz, 1H), 6.65 (dd, *J* = 8.2 Hz, 1H),5.47 (d, 9.1 Hz, 1H), 5.16 (d, *J* = 9.1 Hz, 1H), 3.82 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 155.3, 143.5, 140.2, 137.2, 134.0, 132.3, 129.5, 128.8, 127.9, 127.7, 127.3, 127.2, 111.7, 60.4, 56.3, 21.6; HR-MS (EI): *m/z* = 445.0338, calcd for $C_{21}H_{20}BrNO_2S$: 445.0347.

13ja: $[\alpha]_D^{24}$: −90.2 (*c* 0.52, $CHCl_3$), 97% *ee* (Chiralcel OB-H, hexane/2-propanol = 4/1, flow = 0.8 mL min^{-1}, wavelength = 230 nm, t_R = 21.6 and 35.7 min); ^{1}H NMR ($CDCl_3$): δ = 7.55 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 8.2 Hz, 9H), 6.98 (d, *J* = 8.6 Hz, 1H) 6.73 (dd, 2.2, 6.8 Hz, 2H), 6.63 (d, *J* = 7.7 Hz, 1H), 6.58–6.52 (m, 2H), 5.88 (dd, *J* = 1.4 and 5.0 Hz, 2H), 5.41 (d, *J* = 6.3 Hz, 1H), 4.83 (d, *J* = 6.3 Hz, 1H), 3.75 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 159.0, 147.8, 146.9, 143.2, 137.4, 134.8, 132.7, 129.4, 128.5, 127.3, 120.9, 113.9, 108.1, 107.9, 101.1, 60.5, 55.3, 21.6; HR-MS (EI): *m/z* = 411.1139, calcd. for $C_{22}H_{21}NO_5S$: 411.1140.

13jg: $[\alpha]_D^{24}$: −17.85 (*c* 0.54, $CHCl_3$), 85% *ee* (Chiralcel OD-H, hexane/2-propanol = 9/1, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 44.0 and 48.2 min); ^{1}H NMR ($CDCl_3$): δ = 7.55 (d, *J* = 8.1 Hz, 2H), 7.21–7.18 (m, 3H), 7.15 (d, *J* = 8.1 Hz, 2H) , 7.09 (dd, *J* = 2.3 and 7.3 Hz, 2H), 6.63 (d, 3.2 Hz, 1H), 6.57–6.52 (m, 2H), 5.88 (dd, *J* = 1.4 and 4.0 Hz, 2H), 5.46 (d, *J* = 6.8 Hz, 1H), 4.96 (d, *J* = 5.8 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 147.8, 147.1, 143.3, 140.5, 137.3, 134.5, 129.4, 128.6, 127.7, 127.3, 127.2, 121.0, 108.1, 107.9, 101.2, 61.2, 21.6; HR-MS (EI): *m/z* = 381.1035, calcd. for $C_{21}H_{19}NO_4S$: 381.1035.

13kg: $[\alpha]_D^{24}$: −18.7 (*c* 0.51, $CHCl_3$), 99% *ee* (Chiralpak IB, hexane/ethanol = 95/5, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 59.1 and 63.8 min); ^{1}H NMR ($CDCl_3$): δ = 7.55 (d, *J* = 8.2 Hz, 2H), 7.21–7.17 (m, 3H), 7.15 (d, *J* = 8.6 Hz, 1H), 7.10–7.08 (m, 2H), 6.68 (d, 8.6 Hz, 1H), 6.55 (dd, *J* = 2.3 and 7.7 Hz, 1H), 6.54 (s, 1H), 5.43 (d, *J* = 6.8 Hz, 1H), 4.95 (d, *J* = 6.8 Hz, 1H), 4.19–4.16 (m, 4H), 2.37 (s, 3H); ^{13}C NMR($CDCl_3$): δ = 143.4, 143.2, 143.0, 140.6, 137.4, 133.9, 129.4, 128.5, 127.6, 127.3, 120.5, 117.3, 116.5, 64.3, 60.9, 21.6; HR-MS (EI): *m/z* = 395.1207, calcd. for $C_{22}H_{21}NO_4S$: 395.1191.

13ld: $[\alpha]_D^{23}$: −29.99 (*c* 0.43, $CHCl_3$), 98% *ee* (Chiralpak IB, hexane/ethanol = 9/1, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 20.4 and 31.5 min); ^{1}H NMR ($CDCl_3$): δ = 7.50 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.17 (ddd, *J* = 1.4, 7.7 and 8.2 Hz, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 6.93 (d, *J* = 7.7 Hz, 1H), 7.77 (dd, *J* = 7.7 and 8.2 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 1H), 5.95 (d, *J* = 9.5 Hz, 1H), 5.65 (d, *J* = 9.5 Hz, 1H), 3.58 (s, 3H) 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 156.2, 144.7, 143.1, 137.3, 129.6, 129.5, 129.2, 127.2, 127.0, 125.1, 120.8, 111.2, 58.8, 55.3, 31.0, 21.5; HR-MS (EI): *m/z* = 435.1123, calcd. for $C_{22}H_{20}F_3NO_3S$: 435.1116.

13md: $[\alpha]_D^{22}$: −8.46 (*c* 0.44, $CHCl_3$), 93% *ee* (Chiralpak IB, hexane/ethanol = 95/5, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 17.7 and 36.0 min); ^{1}H NMR ($CDCl_3$): δ = 7.51 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 7.7 Hz, 2H), 7.16–7.03 (m, 5H), 6.95 (d, *J* = 7.7 Hz, 1H), 5.84 (d, *J* = 6.8 Hz, 1H), 5.10 (d, *J* = 6.8 Hz, 1H), 2.36 (s, 3H), 2.19 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 144.0, 143.6, 137.6, 137.2, 135.7, 131.0, 129.4, 127.3, 127.1, 126.5, 125.5, 125.4, 57.7, 21.5, 19.4; HR-MS (EI): *m/z* = 418.1077, calcd. for $C_{22}H_{19}F_3NO_2S$ (M−H): 418.1089.

13nh: $[\alpha]_D^{24}$: −78.35 (*c* 0.51, $CHCl_3$), 96% *ee* (Chiralcel AS-H, hexane/2-propanol = 7/3, flow = 0.7 mL min^{-1}, wavelength = 230 nm, t_R = 39.5 and 46.5 min); ^{1}H NMR ($CDCl_3$): δ = 7.6 (d, *J* = 8.2 Hz, 2H), 7.33 (dd, *J* = 3.6, 5.4 Hz, 1H), 7.22–7.19 (m, 1H), 7.15–7.10 (m, 4H), 6.73 (dd, *J* = 1.8, 8.2 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 6.59 (d, *J* = 1.8 Hz, 1H), 5.87 (d, *J* = 7.7 Hz, 1H), 5.40 (d, *J* = 7.7 Hz, 1H), 3.67 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 159.7, 143.4, 140.9, 137.5, 137.0, 132.8, 129.9, 129.5, 129.3, 128.9, 127.3, 127.0, 119.5, 113.2, 113.1, 58.5, 55.2, 21.5; HR-MS (EI): *m/z* = 401.0866, calcd. for $C_{21}H_{20}ClNO_3S$: 401.0852.

13nd: $[\alpha]_D^{23}$: +2.03 (*c* 0.45, $CHCl_3$), 96% *ee* (Chiralcel OD-H, hexane/2-propanol = 9/1, flow = 0.8 mL min^{-1}, wavelength = 230 nm, t_R = 12.0 and 25.9 min); ^{1}H NMR ($CDCl_3$): δ = 7.57 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.25–7.12 (m, 8H), 5.95 (d, *J* = 7.2 Hz, 1H), 5.32 (d, *J* = 7.2 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 143.7, 143.3, 136.9, 136.8, 131.6, 130.2, 129.5, 129.4, 127.6, 129.4, 127.6, 127.3, 127.2, 125.6, 125.5, 58.4, 21.5; HR-MS (ESI): *m/z* = 462.0519, calcd. for $C_{21}H_{17}ClF_3NO_2SNa$ (M + Na): 462.0518.

13oa: $[\alpha]_D^{23}$: −78.61 (*c* 0.43, $CHCl_3$), 96% *ee* (Chiralpak IB, hexane/2-propanol = 9/1, flow = 0.8 mL min^{-1}, wavelength = 230 nm, t_R = 18.9 and 27.5 min); ^{1}H NMR ($CDCl_3$): δ = 7.65 (d, *J* = 8.1 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 8.1 Hz, 2H), 5.87 (d, *J* = 5.4 Hz, 1H), 4.96 (d, *J* = 5.4 Hz, 1H), 3.73 (s, 3H),2.40 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 159.2, 143.5, 138.9, 136.7, 132.1, 132.0, 129.4, 128.8, 127.6, 127.4, 114.0, 56.6, 55.3, 21.6; HR-MS (EI): *m/z* = 435.1121, calcd. for $C_{22}H_{20}F_3NO_3S$: 435.1116.

13pg: $[\alpha]_D^{22}$: −9.76 (*c* 0.56, $CHCl_3$); 88% *ee* (Chiralpak IB, hexane/ethanol = 95/5, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 28.3 and 32.5 min); ^{1}H NMR ($CDCl_3$): δ = 7.53 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.17–7.20 (m, 3H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.04–7.06 (m, 2H), 6.96 (d, *J* = 8.6 Hz, 1H), 6.61 (d, *J* = 2.8 Hz, 1H), 6.55 (dd, *J* = 2.8, 8.2 Hz, 1H), 5.72 (d, 6.8 Hz, 1H), 5.04 (d, 6.8 Hz, 1H), 3.73 (s, 3H), 2.36 (s, 3H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 155.8, 143.1, 140.4, 137.5, 137.1, 130.7, 129.4, 128.7, 128.5,

127.5, 127.2, 116.2, 111.2, 57.8, 55.2, 21.5, 19.6; HR-MS (EI): $m/z = 381.1396$, calcd. for $C_{22}H_{23}NO_3S$: 381.1399.

13qa: $[\alpha]_D^{23}$: −75.11 (*c* 0.46, $CHCl_3$), 96% *ee* (Chiralpak IB, hexane/2-propanol = 9/1, flow = 0.8 mL min^{-1}, wavelength = 230 nm, t_R = 19.5 and 28.7 min); ^{1}H NMR ($CDCl_3$): $\delta = 7.59$ (d, $J = 8.6$ Hz, 2H), 7.34 (d, $J = 8.2$ Hz, 1H), 7.22 (d, $J = 2.3$ Hz, 1H), 7.18 (d, $J = 8.6$ Hz, 2H), 7.11 (dd, $J = 2.3$ and 8.6 Hz 1H), 6.90 (d, $J = 8.6$ Hz, 2H), 6.73 (d, $J = 8.6$ Hz, 2H), 5.77 (d, 6.8 Hz, 1H), 5.33 (d, 6.8 Hz, 1H), 3.72 (s, 3H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 159.3$, 143.8, 136.8, 136.5, 133.9, 133.4, 130.8, 130.0, 129.6, 128.6, 127.3, 114.2, 57.7, 55.3, 21.6; HR-MS (EI): $m/z = 435.0467$, calcd. for $C_{21}H_{19}Cl_2NO_2S$: 435.0463.

13qg: $[\alpha]_D^{22}$: +3.88 (*c* 0.43, $CHCl_3$), 85% *ee* (Chiralpak IB, hexane/ethanol = 95/5, flow = 0.8 mL min^{-1}, wavelength = 230 nm, t_R = 14.4 and 15.7 min); ^{1}H NMR ($CDCl_3$): $\delta = 7.60$ (d, $J = 8.2$ Hz, 2H), 7.32 (d, $J = 8.6$ Hz, 1H), 7.21–7.25 (m, 4H), 7.18 (d, $J = 8.2$ Hz, 2H), 7.13 (dd, $J = 2.8$, 8.2 Hz 1H), 7.00–7.03 (m, 2H), 5.83 (d, 6.8 Hz, 1H), 5.20 (d, 6.8 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 143.8$, 138.8, 136.7, 136.3, 134.1, 133.5, 130.3, 129.6, 128.9, 128.2, 127.3, 58.2, 21.6; HR-MS (ESI): $m/z = 428.0239$, calcd. for $C_{20}H_{17}Cl_2NO_2SNa$ (M + Na): 428.0255.

13qd: $[\alpha]_D^{23}$: −100.84 (*c* 0.50, $CHCl_3$), 98% *ee* (Chiralpak IB, hexane/2-propanol = 9/1, flow = 0.8 mL min^{-1}, wavelength = 230 nm, t_R = 18.0 and 20.0 min); ^{1}H NMR ($CDCl_3$): $\delta = 7.57$ (d, $J = 8.1$ Hz, 2H), 7.48 (d, $J = 8.1$ Hz, 1H), 7.26–7.13 (m, 8H), 7.18 (d, $J = 8.6$ Hz, 2H), 5.89 (d, 7.2 Hz, 1H), 5.33 (m, 1H), 2.39 (s, 3H); ^{13}C NMR($CDCl_3$): $\delta = 144.0$, 142.7, 136.6, 135.5, 135.4, 134.7, 133.5, 130.2, 129.9, 129.6, 128.7, 128.5, 128.3, 128.1, 127.6, 127.2, 125.7, 57.9, 21.6; HR-MS (ESI): $m/z = 496.0128$, calcd. for $C_{21}H_{16}Cl_2F_3NO_2SNa$ (M + Na): 496.0129.

13rg: $[\alpha]_D^{24}$: +1.26 (*c* 0.42, $CHCl_3$), 98% *ee* (Chiralpak IB, hexane/ethanol = 95/5, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 27.6 and 33.6 min); ^{1}H NMR ($CDCl_3$): $\delta = 7.50$ (d, $J = 8.2$ Hz, 2H), 7.25–7.14 (m, 6H), 7.08 (d, $J = 8.2$ Hz, 2H), 6.97 (d, $J = 2.3$ Hz, 1H), 6.54 (j, $J = 8.6$ Hz, 1H) 5.64 (d, 9.1 Hz, 1H), 5.51 (d, $J = 9.1$ Hz, 1H), 3.58 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 155.5$, 143.3, 139.7, 137.1, 132.2, 131.4, 129.7, 129.3, 128.36, 127.4, 127.1, 126.7, 113.0, 112.8, 58.4, 55.7, 21.6; HR-MS (EI): $m/z = 445.0354$, calcd. for $C_{21}H_{20}BrNO_2S$: 445.0347.

13ug: $[\alpha]_D^{23}$: −49.6 (*c* 0.45, $CHCl_3$), 94% *ee* (Chiralpak IB, hexane/ethanol = 95/5, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 28.5 and 29.9 min); ^{1}H NMR ($CDCl_3$): $\delta = 7.56$ (d, $J = 8.6$ Hz, 2H), 7.40 (dd, $J = 1.3$ and 6.8 Hz, 1H), 7.28–7.13 (m, 8H), 6.99 (d, $J = 8.1$ Hz, 2H), 6.40 (s, 1H), 5.73 (d, $J = 8.2$ Hz, 1H), 5.37 (d, $J = 8.2$ Hz, 1H), 2.22 (s, 3H), ^{13}C NMR ($CDCl_3$): $\delta = 157.9$, 157.3, 143.3, 137.6, 137.0, 129.2, 128.8, 128.4, 127.7, 127.3, 127.1, 124.4, 122.9, 121.1, 111.2, 105.6, 55.9, 21.4; HR-MS (EI): $m/z = 377.1091$, calcd. for $C_{22}H_{19}NO_3S$: 377.1086.

13ta: $[\alpha]_D^{22}$: +2.79 (*c* 0.45, $CHCl_3$), 99% *ee* (Chiralcel OD-H, hexane/2-propanol = 4/1, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 21.6 and 23.8 min); ^{1}H NMR ($CDCl_3$): $\delta = 7.56$ (d, $J = 8.2$ Hz, 2H), 7.20 (s, 1H), 7.15 (d, $J = 8.2$ Hz, 2H), 7.07 (d, $J = 8.6$ Hz, 2H), 6.75 (d, $J = 8.6$ Hz, 2H), 6.27–6.08 (m, 1H), 5.98 (d, $J = 3.2$ Hz, 1H), 5.54 (d, $J = 7.3$ Hz, 1H), 5.23 (d, $J = 7.3$ Hz, 1H), 3.89 (s, 3H), 2.53 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 159.3$, 152.5, 143.2, 142.5, 137.4, 130.4, 129.4, 128.5, 127.2, 113.9, 110.2, 108.2, 55.3, 55.1, 21.6; HR-MS (EI): $m/z = 357.1024$, calcd. for $C_{19}H_{19}NO_4S$: 357.1035.

13th: $[\alpha]_D^{24}$: −150.71 (*c* 0.32, $CHCl_3$), 95% *ee* (Chiralcel AD-H, hexane/2-propanol = 4/1, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 32.5 and 34.5 min); ^{1}H NMR ($CDCl_3$): $\delta = 7.56$ (d, $J = 8.6$ Hz, 2H), 7.20 (d, $J = 1.8$ Hz, 1H), 7.18–7.09 (m, 3H), 6.74 (d, $J = 8.2$ Hz, 2H), 6.68 (d, $J = 1.8$ Hz, 1H), 6.16 (dd, $J = 1.8$ and 3.2 Hz, 1H), 6.00 (d, $J = 3.2$ Hz, 1H), 5.57 (d, $J = 7.7$ Hz, 1H), 5.46 (d, $J = 7.7$ Hz, 1H), 3.68 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 159.8$, 152.1, 143.2, 142.6, 139.7, 137.3, 129.7, 127.2, 119.6, 113.7, 112.7, 110.3, 108.4, 55.5, 55.2, 21.5; HR-MS (EI): $m/z = 357.1020$, calcd. for $C_{19}H_{19}NO_4S$: 357.1035.

13td: $[\alpha]_D^{23}$: −10.95 (*c* 0.56, $CHCl_3$), 98% *ee* (Chiralcel AD-H, hexane/2-propanol = 4/1, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 16.5 and 17.2 min); ^{1}H NMR ($CDCl_3$): $\delta = 7.53$ (d, $J = 8.6$ Hz, 2H), 7.45 (d, $J = 8.2$ Hz, 2H), 7.30 (d, $J = 8.2$ Hz, 2H), 7.12 (d, $J = 8.6$ Hz, 2H), 6.20 (dd, $J = 1.8$ and 3.2 Hz, 1H), 5.97 (d, $J = 3.2$ Hz, 1H), 5.65 (d, $J = 7.3$ Hz, 1H), 5.49 (d, $J = 7.3$ Hz, 1H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 151.2$, 143.6, 143.0, 142.0, 137.0, 129.5, 127.8, 127.1, 125.5, 125.4, 110.4, 108.8, 55.2, 21.5; HR-MS (EI): $m/z = 395.0806$, calcd. for $C_{19}H_{16}F_3NO_3S$: 395.0803.

14ba: $[\alpha]_D^{23}$: +12.04 (*c* 0.56, THF), 97% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 37.0 and 41.4 min); ^{1}H NMR ($CDCl_3$): $\delta = 8.14$ (d, $J = 8.6$ Hz, 2H), 7.76 (d, $J = 9.1$ Hz, 2H), 7.19 (d, $J = 8.6$ Hz, 2H), 7.07 (d, $J = 8.6$ Hz, 2H), 6.92 (d, $J = 8.6$ Hz, 2H), 6.71 (d, $J = 9.1$ Hz, 2H), 5.62 (d, $J = 7.3$ Hz, 1H), 5.28 (d, $J = 7.3$ Hz, 1H), 3.72 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 159.7$, 149.8, 146.2, 138.4, 134.0, 131.1, 128.9, 128.7, 128.6, 128.4, 124.0, 114.2, 60.6, 55.4; HR-MS (EI): $m/z = 432.0546$, calcd. for $C_{20}H_{17}ClN_2O_5S$: 432.0547.

14bd: $[\alpha]_D^{23}$: −8.34 (*c* 0.59, THF), 97% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 26.9 and 39.1 min); ^{1}H NMR ([D_6]acetone): $\delta = 8.43$–8.13 (m, 2H), 8.07–7.78 (m, 2H), 7.62 (d, $J = 8.2$ Hz, 2H), 7.41 (d, $J = 8.2$ Hz, 2H), 7.38–7.32 (m, 2H), 7.26–7.15 (m, 2H), 7.04 (s, 1H), 5.83 (s, 1H); ^{13}C NMR(acetone-d_6): $\delta = 150.0$, 146.3, 255.5, 138.6, 133.4, 129.4, 129.3, 129.1, 128.8, 128.5, 128.2, 125.6, 124.3, 122.9, 60.3; HR-MS (ESI): $m/z = 469.0222$, calcd. for $C_{20}H_{13}ClF_3N_2O_4S$ (M−H): 469.0237.

14bh: $[\alpha]_D^{22}$: +4.88 (*c* 0.54, $CHCl_3$), 97% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 22.7 and 45.9 min); ^{1}H NMR ($CDCl_3$): $\delta = 8.12$ (d, $J = 9.1$ Hz, 2H), 7.76 (d, $J = 9.1$ Hz, 2H), 7.19 (d, $J = 8.6$ Hz, 2H), 7.15–7.04 (m, 3H), 6.71 (dd, $J = 2.3$ and 8.2 Hz, 1H), 6.60 (d, $J = 7.7$ Hz, 1H), 6.49 (t, $J = 1.8$ Hz, 1H), 5.61 (d, $J = 7.7$ Hz, 1H), 5.43 (d, $J = 7.7$ Hz, 1H), 3.66 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 159.9$, 149.8, 146.1, 140.4, 138.0, 134.1, 130.1, 128.9, 128.8, 128.3, 123.9, 119.5, 113.6, 112.9, 61.0, 55.2; HR-MS (EI): $m/z = 432.0527$, calcd. for $C_{20}H_{17}ClN_2O_5S$: 432.0547.

14bi: $[\alpha]_D^{23}$: −2.28 (*c* 0.55, THF), 97% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 0.7 mL min^{-1}, wavelength = 230 nm, t_R = 49.0 and 52.2 min); ^{1}H NMR (acetone-d_6): $\delta = 8.26$ (d, $J = 8.6$ Hz, 2H), 7.91 (d, $J = 8.6$ Hz, 2H), 7.56 (t, $J = 8.2$ Hz, 2H), 7.34 (d, $J = 8.6$ Hz, 2H), 7.19 (d, 8.6 Hz, 2H), 7.10–7.07 (m, 1H), 6.99–6.96 (m, 2H), 5.72 (s, 1H); ^{13}C NMR (acetone-d_6): $\delta = 160.0$, 157.6, 150.0, 146.2, 142.5, 142.4, 138.4, 133.9, 133.5, 129.2, 128.8, 128.5, 124.9, 124.3,

115.8, 115.5, 107.8, 59.8; HR-MS (ESI): m/z = 496.9362, calcd. for $C_{19}H_{12}BrClFN_2O_4S$ (M−H): 496.9374.

14ca: $[\alpha]_D^{22}$: +17.99 (*c* 0.55, $CHCl_3$), 96% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 34.7 and 65.1 min); ^{1}H NMR ($CDCl_3$): δ = 8.13 (d, J = 9.1 Hz, 2H), 7.74 (d, J = 9.1 Hz, 2H), 7.19–7.11 (m, 2H), 7.02 (s, 1H), 6.96 (d, J = 8.7 Hz, 2H), 6.72 (d, J = 8.7 Hz, 1H), 5.62 (d, J = 6.8 Hz, 1H), 5.40 (d, J = 6.8 Hz, 1H), 3.73 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 159.6, 146.1, 141.6, 134.7, 130.9, 130.0, 128.7, 128.3, 128.1, 127.4, 125.6, 123.9, 114.3, 60.8, 55.4; HR-MS (EI): m/z = 432.0525, calcd. for $C_{20}H_{17}ClN_2O_5S$: 432.0547.

14cd: $[\alpha]_D^{22}$: −3.07 (*c* 0.52, THF), 97% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 18.7 and 59.1 min); ^{1}H NMR ($CDCl_3$): δ = 8.16 (d, J = 9.1 Hz, 2H), 7.78 (d, J = 8.6 Hz, 2H), 7.51 (d, J = 8.6 Hz, 2H), 7.26 (d, J = 9.1 Hz, 2H), 7.23–7.15 (m, 2H), 6.98–6.95 (m, 2H), 5.72 (d, J = 7.3 Hz, 1H) , 5.49 (d, J = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 150.0, 145.7, 142.8, 140.5, 135.1, 128.7, 128.3, 127.8, 127.5, 125.9, 125.6, 124.1, 60.8; HR-MS (ESI): m/z = 469.0224, calcd. for $C_{20}H_{13}ClF_3N_2O_4S$ (M−H): 469.0237.

14dd: $[\alpha]_D^{21}$: −0.90 (*c* 0.43, $CHCl_3$), 98% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 12.4 and 37.9 min); ^{1}H NMR ($CDCl_3$): δ = 8.13 (d, J = 8.6 Hz, 2H), 7.82 (d, J = 9.1 Hz, 2H), 7.53 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 7.26–7.07 (m, 4H), 6.07 (d, J = 8.6 Hz, 1H), 5.77 (d, J = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 149.9, 145.6, 142.4, 135.8, 132.9, 130.5, 130.3, 129.4, 128.4, 127.2, 123.9, 119.4, 113.4, 113.0, 58.9, 55.3; HR-MS (ESI): m/z = 469.0221, calcd. for $C_{20}H_{13}ClF_3N_2O_4S$ (M−H): 469.0237.

14dh: $[\alpha]_D^{23}$: +6.69 (*c* 0.42, $CHCl_3$), 98% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 16.3 and 24.4 min); ^{1}H NMR ($CDCl_3$): δ = 8.12 (d, J = 8.6 Hz, 2H), 7.81 (d, J = 8.6 Hz, 2H), 7.24–7.06 (m, 5H), 6.76 (dd, J = 2.3, 8.2 Hz, 1H), 6.68 (d, J = 7.7 Hz, 1H), 6.64 (s, 1H), 6.01 (d, J = 7.7 Hz, 1H), 5.62 (d, J = 7.7 Hz, 1H), 3.73 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 159.8, 149.8, 145.9, 139.9, 136.5, 133.0, 130.2, 129.9, 129.5, 129.4, 128.4, 127.2, 123.9, 119.4, 113.4, 113.0, 58.9, 55.3; HR-MS (EI): m/z = 432.0532, calcd. for $C_{20}H_{17}ClN_2O_5S$: 432.0547.

14ed: $[\alpha]_D^{23}$: −39.92 (*c* 0.50, $CHCl_3$), 94% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 14.0 and 41.0 min); ^{1}H NMR ($CDCl_3$): δ = 8.05 (d, J = 8.8 Hz, 2H), 7.76 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 7.17 (ddd, J = 1.9, 7.7 and 8.2 Hz, 2H), 6.93 (d, J = 7.3 Hz, 1H), 6.78 (ddd, J = 1.9, 7.3 and 7.7 Hz, 1H), 6.65 (d, J = 8.2 Hz, 1H), 6.11 (t, J = 9.5 Hz, 1H), 5.7 (d, J = 9.5 Hz, 1H), 3.59 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 156.2, 149.7, 146.0, 130.1, 129.9, 128.1, 127.0, 125.8, 125.3, 123.7, 121.0, 111.5, 59.5; HR-MS (EI): m/z = 466.0819, calcd. for $C_{21}H_{17}F_3N_2O_5S$: 466.0810.

14fg: $[\alpha]_D^{23}$: −10.06 (*c* 0.47, THF), 97% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 16.3 and 24.4 min); ^{1}H NMR ($CDCl_3$): δ = 8.08 (d, J = 8.3 Hz, 2H), 7.71 (d, J = 8.3 Hz, 2H), 7.19 (t, J = 3.2 Hz, 3H), 7.13–7.03 (m, 2H), 6.08 (d, J = 8.6 Hz, 2H), 6.63 (d, J = 2.8 Hz, 1H), 6.48 (dd, J = 2.8 and 8.6 Hz, 1H), 5.90 (d, J = 7.3 Hz, 1H), 5.13 (d, J = 7.3 Hz, 1H), 3.71 (s, 3H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 159.1, 149.6, 146.4, 139.2, 137.5, 129.5, 128.7, 128.6, 128.2, 127.9, 127.5, 123.8, 116.4, 111.2, 58.1, 55.2, 19.7; HR-MS (EI): m/z = 412.1085, calcd. for $C_{21}H_{20}N_2O_5S$: 412.1093.

14gd: $[\alpha]_D^{22}$: −12.14 (c 0.47, $CHCl_3$), 96% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 17.4 and 48.5 min); ^{1}H NMR ($CDCl_3$): δ = 8.13 (d, J = 8.6 Hz, 2H), 7.78 (d, J = 8.6 Hz, 2H), 7.51 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 7.27–7.24 (m, 1H), 6.95 (d, J = 2.8 Hz, 1H), 6.57 (d, J = 8.6 Hz, 1H), 5.97 (d, J = 9.5 Hz, 1H), 5.64 (d, J = 9.5 Hz, 1H), 3.60 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 155.3, 149.9, 145.8, 142.9, 132.5, 132.3, 128.2, 128.0, 126.9, 125.5, 123.9, 113.2, 58.6, 55.9; HR-MS (EI): m/z = 543.9889, calcd. for $C_{21}H_{16}BrF_3N_2O_5S$: 543.9915.

15ag: $[\alpha]_D^{25}$: −12.5 (c 0.31, $CHCl_3$), 87% *ee* (Chiralcel OD-H, hexane/ethanol = 9/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, t_R = 17.4 and 48.5 min); ^{1}H NMR ($CDCl_3$): δ = 7.37–7.21 (m, 5H), 7.22 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.70 (d, J = 7.1 Hz, 1H), 5.05 (d, J = 7.1 Hz, 1H), 3.78 (s, 3H), 2.64 (s, 3H), ^{13}C NMR ($CDCl_3$): δ = 159.3, 140.9, 132.7, 128.9, 128.7, 128.0, 127.4, 114.3, 60.8, 55.4, 42.0; HR-MS (EI): m/z = 291.0929, calcd. for $C_{21}H_{16}BrF_3N_2O_5S$: 291.0929.

General Procedure for Synthesis of Isoindolinones (21, Table 4):

A flask was charged with $Rh(acac)(C_2H_4)_2$ (0.015 mmol, 3 mol%) and *N*-Me-BIPAM (**19**, 0.0165 mmol, 3.3 mol%) under a nitrogen atmosphere. DME (2 mL) was added and the mixture then stirred at room temperature for 30 min. Arylboronic acid (0.75 mmol) and aldimine (**20**, 0.5 mmol) were added to this catalyst solution. After being stirred for 16 h at 50 °C, the mixture was cooled to room temperature. A solution of K_2CO_3 (2 mmol, 1 M in H_2O) was then added, and the resulting mixture was stirred for 2 h at room temperature. The product was extracted with ethyl acetate, washed with brine and dried over $MgSO_4$. Chromatography on silica gel with hexane/ethyl acetate gave the product as a white or yellow solids.

21a: Spectral data of **21a** were as previously reported.[8]

21b: $[\alpha]_D^{22}$: −42.35 (*c* 0.54, $CHCl_3$), 97% *ee* (AD-H, hexane/2-propanol = 7/3, flow = 0.7 mL min^{-1}, wavelength = 230 nm, t_R = 15.7 and 17.5 min); ^{1}H NMR ($CDCl_3$): δ = 7.86 (d, J = 7.7 Hz, 1H), 7.59–7.46 (m, 4H), 7.43 (dt, J = 1.8, 7.3 Hz, 1H), 7.21–7.15 (m, 5H), 6.96 (s, 1H), 6.14 (s, 1H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 166.3, 145.7, 145.2, 139.2, 135.8, 134.6, 131.9, 130.5, 130.4, 129.5, 129.4, 128.8, 128.0, 127.0, 125.0, 123.7, 122.9, 64.9, 21.8; HR-MS (ESI): m/z = 463.9930, calcd. for $C_{21}H_{16}BrNO_3SNa$ (M+Na): 463.9932.

21c: $[\alpha]_D^{23}$: +102.85 (*c* 0.50, $CHCl_3$), 97% *ee* (AD-H, hexane/ethanol = 99/1, flow = 0.5 mL min^{-1}, wavelength = 230 nm, t_R = 80.9 and 88.3 min); ^{1}H NMR ($CDCl_3$): δ = 7.88 (d, J = 7.2 Hz, 1H), 7.59–7.40 (m, 7H), 7.13 (d, J = 7.7 Hz, 4H), 6.25 (s, 1H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 166.3, 145.5, 145.2, 138.2, 135.7, 134.6, 131.8, 129.5, 129.4, 128.8, 125.6, 125.1, 124.2, 123.7, 77.3, 64.9, 21.5; HR-MS (ESI): m/z = 454.0698, calcd. for $C_{22}H_{16}F_3NO_3S$ (M+Na): 454.0701.

21d: $[\alpha]_D^{22}$: −24.03 (*c* 0.51, $CHCl_3$), 97% *ee* (Chiralcel AD-H, hexane/2-propanol = 7/3, flow = 0.7 mL min^{-1}, wavelength = 230 nm, t_R = 19.5 and 25.4 min); ^{1}H NMR ($CDCl_3$): δ = 7.84 (d, J = 7.7 Hz, 1H), 7.58–7.54 (m, 3H), 7.47 (dd, J =

7.4, 7.6 Hz, 1H), 7.16 (dd, $J=7.7$, 8.6 Hz, 3H), 7.00 (d, $J=$ 8.2 Hz, 1H), 6.89 (dd, $J=8.2$ Hz, 8.6 Hz, 1H), 6.57 (dd, $J=$ 1.8, 10.3 Hz, 1H), 3.89 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta=166.3$, 153.5, 151.0, 148.1, 146.0, 145.0, 135.9, 134.5, 129.7, 129.3, 129.2, 128.8, 128.1, 124.9, 124.6, 123.7, 115.4, 115.2, 113.2, 64.8, 56.3, 21.7; HR-MS (EI): $m/z=$ 411.0929, calcd. for $C_{22}H_{18}FNO_4S$: 411.0941.

21e: $[\alpha]_D^{23}$: −26.22 (*c* 0.42, $CHCl_3$), 99% *ee* (AD-H, hexane/2-propanol = 7/3, flow = 0.7 mL min^{-1}, wavelength = 230 nm, $t_R=42.0$ and 53.0 min); ^{1}H NMR ($CDCl_3$): $\delta=7.82$ (d, $J=7.7$ Hz, 1H), 7.62–7.49 (m, 3H), 7.44 (dd, $J=7.3$, 7.7 Hz, 1H), 7.16 (dd, $J=7.3$, 7.7 Hz, 3H), 6.73 (d, $J=$ 8.2 Hz, 1H), 6.58 (dd, $J=2.3$, 8.2 Hz, 1H), 6.48 (d, $J=2.3$, 1H) 6.09 (s, 1H), 4.24–4.17 (m, 4H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$); $\delta=166.4$, 146.5, 144.7, 143.9, 143.6, 136.0, 134.4, 129.9, 129.2, 129.0, 128.8, 128.2, 128.1, 124.7, 123.7, 121.2, 117.4, 116.9, 65.3, 64.4, 64.3, 21.7; HR-MS (EI): $m/z=$ 421.0973, calcd. for $C_{23}H_{19}NO_5S$: 421.0984.

Synthesis of 23 and 24 (Scheme 3)

A flask was charged with $Rh(acac)(C_2H_4)_2$ (0.015 mmol, 3 mol%) and *N*-Me-BIPAM (**19**, 0.0165 mmol, 3.3 mol%) under a nitrogen atmosphere. DME (2 mL) was added and the mixture then stirred at room temperature for 30 min. Arylboronic acid (**12n** or **12o**, 0.75 mmol) and aldimine (**22**, 0.5 mmol) were added to this catalyst solution. After being stirred for 16 h at 80 °C, the product was extracted with ethyl acetate, washed with brine and dried over $MgSO_4$. Chromatography on silica gel with hexane/ethyl acetate gave the product.

23: $[\alpha]_D^{22}$: −13.98 (*c* 0.50, $CHCl_3$), 98% *ee* (Chiralpak IB, hexane/2-propanol = 2/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, $t_R=18.0$ and 20.6 min); ^{1}H NMR ($CDCl_3$): $\delta=8.11$ (d, $J=8.6$ Hz, 2H), 7.78 (d, $J=9.0$ Hz, 2H), 6.75–6.52 (m, 4H),6.35 (s, 1H), 6.30 (d, $J=7.7$ Hz, 1H), 5.78 (d, $J=$ 7.7 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.73 (s, 3H), 3.68 (s, 3H) ,3.56 (s, 3H) 3.49 (d, $J=15.4$ Hz, 1H), 3.43 (d, $J=$ 15.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): $\delta=173.0$, 149.6, 149.1, 148.7, 148.0, 146.6, 131.7, 130.5, 128.4, 124.7, 123.7, 119.4, 114.3, 112.1, 110.7, 110.4, 59.0, 56.1, 56.0, 55.9, 52.6, 37.9; HR-MS (EI): m/z = 560.1476, calcd. for $C_{26}H_{28}N_2O_{10}S$: 560.1465.

24: $[\alpha]_D^{23}$: −17.2 (c 0.55, $CHCl_3$), 98% *ee* (Chiralcel IB column, hexane/2-propanol = 2/1, flow = 1.0 mL min^{-1}, wavelength = 230 nm, $t_R=32.4$ min and 36.1 min); ^{1}H NMR ($CDCl_3$): $\delta=8.13$ (d, $J=8.6$ Hz, 2H), 7.80 (d, $J=9.1$ Hz, 2H), 6.65–6.56 (m, 4H), 6.36 (s, 1H), 6.28 (d, $J=7.7$ Hz, 1H), 5.90 (d, $J=1.3$ Hz, 1H), 5.87 (d, $J=1.3$, 1H) 5.74 (d, $J=7.7$ Hz, 1H), 3.83 (s, 3H), 3.71 (s, 3H), 3.59 (s, 3H), 3.49 (d, $J=15.4$ Hz, 1H) , 3.49 (d, $J=15.4$ Hz, 1H); ^{13}C NMR-($CDCl_3$): $\delta=172.9$, 149.7, 148.8, 148.1, 147.3, 146.5, 133.2, 130.5, 128.4, 124.6, 123.7, 120.7, 114.5, 112.1, 108.2, 107.7, 101.4, 59.1, 56.0, 55.8, 52.7, 37.9; HR-MS (EI): $m/z=$ 544.1152, calcd. for $C_{25}H_{24}N_2O_{10}S$: 544.1152.

Synthesis of 25 (Scheme 3)

A flask was charged with **23** (459 mg, 0.82 mmol), *p*-methoxybenzenethiol (0.3 mL, 2.46 mmol), CH_3CN (4.9 mL) and DMSO (0.1 mL) in an nitrogen atmosphere. Then K_2CO_3 (566 mg, 4.1 mmol) was added and the mixture stirred for 16 h at 50 °C. The reaction mixture was extracted with CH_2Cl_2 and washed with NH_3Claq and brine, dried over $MgSO_4$. After concentration chromatography on silica gel with hexane/ethyl acetate gave the cyclic product **25** as a yellow solid; yield: 273 mg (97%). ^{1}H NMR ($CDCl_3$): $\delta=$ 6.84 (s, 2H), 6.70 (s, 1H), 6.64 (s, 1H), 6.33 (s, 1H), 6.19 (brs, 1H), 5.52 (d, $J=1.7$ Hz, 1H), 3.88 (s, 3H) 3.87 (s, 3H), 3.81 (s, 3H), 3.68 (s, 3H) , 3.64 (s, 2H); ^{13}C NMR ($CDCl_3$): $\delta=170.6$, 149.6, 149.2, 147.9, 134.1, 126.4, 123.1, 120.1, 111.1, 109.6, 60.0, 56.0, 35.8

Synthesis of Cryptostyline II (27, Scheme 3)

A flask was charged with NaH (60% in oil, 70 mg, 1.75 mmol) and THF (5 mL). Then hexamethylphosphoric acid amide (1.75 mmol) and **25** (400 mg, 1.17 mmol) in DMF (5 mL) were added and then the mixture was stirred for 15 min at 0 °C. MeI (93 μL, 1.52 mmol) was then added at 0 °C, and the resulting mixture was stirred for 2 h at room temperature. The product was treated with saturated NH_3Cl solution and extracted with CH_2Cl_2. The organic layer was washed with brine and dried over $MgSO_4$. After concentration, chromatography on silica gel with hexane/ethyl acetate gave the *N*-methyl compound **26** as yellow oil; yield: 325 mg (78%). ^{1}H NMR ($CDCl_3$): $\delta=6.80$ (s, 1H), 6.79 (d, $J=$ 1.9 Hz, 1H), 6.61 (d, $J=1.9$ Hz, 1H), 6.59 (s, 1H), 6.53 (s, 1H), 5.29 (s, 1H), 3.85 (s, 3H) 3.84 (s, 3H), 3.80 (s, 3H), 3.7 (s, 3H), 3.77 (d, $J=20.4$, 1H) , 3.74 (d, $J=20.4$, 1H) , 2.98 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta=168.5$, 149.6, 148.9, 148.7, 148.0, 133.9, 126.5, 122.5, 119.2, 111.2, 109.9, 109.5, 109.2, 67.5, 56.0, 35.7, 33.3

To a solution of **26** (260 mg, 0.727 mmol) in THF (7 mL), $BH_3{\cdot}Me_2S$ (0.7 mL, 7.27 mmol) was added under nitrogen atmosphere. The reaction mixture was refluxed for 1 h. The reaction mixture was cooled to room temperature, and then the solvent and dimethyl sulfide were evaporated. After an addition of 6N HCl (7.27 mL) to the residue, the solution was heated at 100 °C for 1 h and then cooled to room temperature. The mixture was neutralized with 4N NaOH and extracted with CH_2Cl_2. The organic layer was washes with brine and dried over $MgSO_4$. After concentration, the product (cryptostyline II, **27**) was isolated by chromatography on basic alumina with hexane/ethyl acetate; yield: 146 mg (58%); $[\alpha]_D^{23}$: +54.5 (*c* 0.26, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=$ 6.82–6.97 (m, 2H), 6.73 (s, 1H), 6.58 (s, 1H), 6.11 (s, 1H), 4.08 (s, 1H), 3.88 (s, 3H), 3.84 (s, 3H), 3.80 (s, 3H), 3.20–3.07 (m, 2H), 2.74–2.55 (m, 2H), 2.22 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta=149.3$, 148.3, 147.4, 147.0, 136.3, 130.5, 126.4, 122.1, 111.8, 111.3, 110.6, 110.3, 71.1, 55.9, 55.8, 52.6, 44.2, 28.7; HR-MS (EI): $m/z=357.1952$, calcd. for $C_{21}H_{27}NO_4$ $[M+Me]^+$: 357.1940.

Computational Details

All calculations were performed by means of the density functional theory method, the hybrid Becke3LYP functional with a hybrid Becke exchange functional, and a Lee–Yang–Parr correlation functional as implemented in Gaussian 03.[19] The LanL2DZ basis set, with relativistic effective core potentials, was used for the Rh atoms.[20] The basis set used for the remaining atoms was the standard 6–31G.

Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research in Priority Areas (No. 18064001, Synergy of Elements) and the Global COE Program (No. B01, Catalysis as the Basis for Innovation in Materials Science) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

References

[1] For examples of such pharmacophores, see: a) N. Plobeck, D. Delorme, Z. Y. Wei, H. Yang, F. Zhou, P. Schwarz, L. Gawell, H. Gagnon, B. Pelcman, R. Schmidt, S. Y. Sue, C. Walpole, W. Brown, E. Zhou, M. Labarre, K. Payza, S. St-Onge, A. Kamassah, P. E. Morin, D. Projean, *J. Med. Chem.* **2000**, *43*, 3878–3894; b) C. J. Opalka, T. E. D′Ambra, J. J. Faccone, G. Bodxon, E. Cossement. *Synthesis* **1995**, 766–768; c) D. Ferraris. *Tetrahedron* **2007**, 63, 9581–9597.

[2] a) M. Ueda, N. Miyaura, *J. Organomet. Chem.* **2000**, *595*, 31–35; b) M. Ueda, A. Saito, N. Miyaura, *Synlett* **2000**, 1637–1639.

[3] M. Kuriyama, T. Soeta, X. Hao, Q. Chen, K. Tomioka, *J. Am. Chem. Soc.* **2004**, *126*, 8128–8129.

[4] H. F. Duan, Y. X. Jia, L. X. Wang, Q. L. Zhou, *Org. Lett.* **2006**. *8*. 2567–2569.

[5] R. B. C. Jagt, P. Y. Toullec, D. Geerdink, J. G. de Vries, B. L. Feringa, A. J. Minnaard, *Angew. Chem.* **2006**, *118*, 2855–2857; *Angew. Chem. Int. Ed.* **2006**, *45*, 2789–2791.

[6] a) D. J. Weix, Y. L. Shi, J. A. Ellman, *J. Am. Chem. Soc.* **2005**, *127*, 1092–1093; b) H. Nakagawa, J. C. Rech, R. W. Sindelar, J. A. Ellman, *Org. Lett.* **2007**, *9*, 5155–5157.

[7] a) N. Tokunaga, Y. Otomaru, K. Okamoto, K. Ueyama, R. Shintani, T. Hayashi, *J. Am. Chem. Soc.* **2004**, *126*, 13584–13585; b) Y. Otomaru, N. Tokunaga, R. Shintani, T. Hayashi, *Org. Lett.* **2005**, *7*, 307–310.

[8] A. Q. Wang, C. G. Feng, M. H. Xu, G. Q. Lin, *J. Am. Chem. Soc.* **2007**, *129*, 5336–5337.

[9] N. Hermanns, S. Dahmen, C. Bolm. S. Bräse, *Angew. Chem.* **2002**, *114*, 3844–3846; *Angew. Chem. Int. Ed.* **2002**, *41*, 3692–3694.

[10] a) T. Hayashi, M. Ishigedani, *J. Am. Chem. Soc.* **2000**, *122*, 976–977; b) T. Hayashi, M. Ishigedani, *Tetrahedron* **2001**, *57*, 2589–2595.

[11] T. Hayashi, M. Kawai, N. Tokunaga, *Angew. Chem.* **2004**, *116*, 6251–6254; *Angew. Chem. Int. Ed.* **2004**, *43*, 6125–6128.

[12] K. Majima, R. Takita, A. Okada, T. Ohshima, M. Shibasaki, *J. Am. Chem. Soc.* **2003**, *125*, 15837–15845.

[13] a) Y. Yamamoto, K. Kurihara, N. Sugishita, K. Oshita, D. Piao, N. Miyaura, *Chem. Lett.* **2005**, *34*, 1224–1225; b) K. Kurihara, N. Sugishita, K. Oshita, D. Piao, Y. Yamamoto, N. Miyaura, *J. Organomet. Chem.* **2007**, *692*, 428–435.

[14] a) T. Fukuyama, C. K. Jow, M. Cheung, *Tetrahedron Lett.* **1995**, *36*, 6373–6374; b) T. Kan, T. Fukuyama, *Chem. Commun.* **2004**, 353–359; c) T. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 3rd edn.; Wiley, New York, **1999**, pp 860–861.

[15] M. Sakai, M. Ueda, M. Miyaura, *Angew. Chem.* **1998**, *110*, 3475–3477; *Angew. Chem. Int. Ed.* **1998**, *37*, 3279–3281.

[16] a) E. Deneau, D. Enders, A. Couture, P. Grandclaudon, *Teteahedron Asymmetry* **2003**, *14*, 2253–2258; b) D. L. Comins, S. Cchilling, Y. Zhang, *Org. Lett.* **2005**, *7*, 95–98.

[17] a) K. Leander, B. Luning, E. Ruusa, *Acta Chem. Scand.* **1969**, *23*, 244–248; b) M. Yamato, K. Hashigaki, N. Qais, S. Ishikawa, *Tetrahedron* **1990**, *46*, 5909–5920; c) B. T. Cho, C. K. Han, *Bull. Korean Chem. Soc.* **1990**, *11*, 81–82; d) D. L. Minor, S. D. Wyrich, P. S. Charifson, V. J. Watts, D. E. Nichols, R. B. Mailman, *J. Med. Chem.* **1994**, *37*, 4317–4328; e) M. J. Munchhof, A. I. Meyers, *J. Org. Chem.* **1995**, *60*, 7086–7087; f) R. Gitto, R. Ficarra, R. Stancanelli, M. Guardo, L. D. Luca, M. L. Barreca, B. Pagano, A. Rotondo, G. Bruno, E. Russo, G. D. Sarro, A. Chimirri, *Bio. Med. Chem.* **2007**, *15*, 5417–5423.

[18] R. S. Narayan, M. S. VanNieuwenhzn, *Org. Lett.* **2005**, *7*, 2655–2685.

[19] a) C. Lee, R. G. Parr, W. Yang, *Phys. Rev. B* **1988**, *37*, 785–789; b) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652; c) P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. J. Frisch, *J. Phys. Chem.* **1994**, *98*, 11623–11627.

[20] a) W. R. Wadt, P. J. Hay, *J. Chem. Phys.* **1985**, *82*, 284–298; b) P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299–310.

