# Modular Synthesis of a New Class of Bis(amino-oxazoline) Using Palladium-Catalyzed Buchwald−Hartwig Amination Methodology

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The palladium-catalyzed Buchwald−Hartwig aryl amination between 2,2′-diaminobiphenyl and 2 equiv of 2-(2′-bromophenyl)oxazoline has been used to prepare a new class of tetradentate bis(amino-oxazoline). The reaction between 2,2′-diaminobiphenyl and 1 equiv of 2-(2′-bromophenyl)oxazoline is highly selective for monoarylation, and the resulting products have been reacted in a second arylation to afford unsymmetrically substituted bis(amino-oxazolines). These new diamido/donors belong to the *tropos* class of ligand and exist as an equilibrium mixture of *S*,a*S*,*S*- and *S*,a*R*,*S*-diastereoisomers, which interconvert by rotation about the biaryl axis. Variable-temperature $^1$H NMR studies and line-shape analysis of simulated spectra gave $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values of 51.5−57 kJ mol$^{-1}$ and −25.9 to −57.0 J mol$^{-1}$ K$^{-1}$, respectively, for diastereointerconversion. Interestingly, reaction of one of the symmetrical bis(amino-oxazoline) with [Cu(MeCN)$_4$][PF$_6$] results in dynamic resolution to afford diastereopure (*S*,a*S*,*S*)-[Cu(**L**)][PF$_6$], which has a highly unusual sawhorse geometry at copper with the two oxazolines occupying *trans* coordination sites and two weak interactions to the nitrogen atoms of the secondary amino groups. $^1$H and $^{13}$C NMR spectra of this copper complex are entirely consistent with a single $C_2$-symmetric diastereoisomer in solution that shows no sign of diastereointerconversion even after standing for one week.

## Introduction

Since its discovery, the palladium-catalyzed Buchwald−Hartwig amination of aromatic,[1] and more recently vinylic,[2] electrophiles has proven to be an immensely powerful transformation, since the resulting amines, enamines, or imines are either valuable products or highly versatile intermediates. Indeed this technique has been heralded as one of the most important modern cross-coupling processes and has been applied to the synthesis of a variety of important targets including (i) biologically active molecules such as *N*-arylpiperazines,[3] α-carboline natural product analogues,[4] and modified glycosylamines,[5] (ii) aryl- and alkylamine-based polymers,[6] oligomers,[7] and dendrimers,[8] (iii) small molecules that are useful as hole transport materials[9] and selective metal cation detection systems,[10] (iv) heterocyclic motifs such as 1-functionalized indoles,[11] and (v) aminations in solid-phase organic synthesis.[12] More recently, this methodology has been employed in the synthesis of nitrogen-based ligands[13] such as multidentate $C_1$- and $C_2$-symmetric monosulfoximes for copper-catalyzed Diels−Alder and hetero Diels−Alder reactions[14] as well as carbonyl-ene and Mukaiyama-type aldol reactions,[15] terdentate bis(oxazolines) for asymmetric transfer hydrogenation,[16] and nonracemic anisole and 2-pyridyl-functionalized tetradentate biaryls for zirconium-catalyzed polymerization.[17] The latter are rare examples of chiral nonracemic diamido/donors (Chart 1) that have been developed

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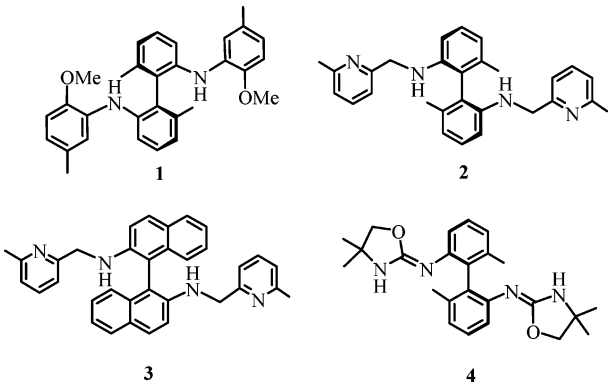
**Chart 1**

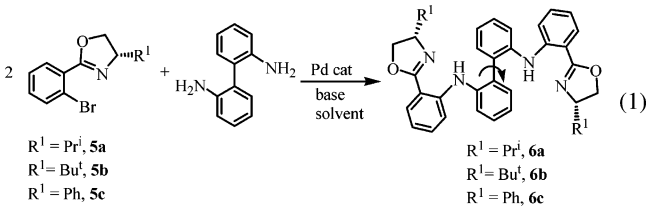


as potential alternatives to the *ansa*-$Cp_2$ unit for use in group 4 and lanthanide metal-catalyzed enantioselective reactions.[18] In this regard, Scott and co-workers have examined the efficiency of lanthanide complexes of diamido/donors such as **1** in enantioselective aminoalkene hydroamination/cyclization, although, despite the well-expressed chirality of the catalysts, the ee values obtained were at best modest (21−40%).[19] Brintzinger has reported that the closely related chiral biaryl-bridged diamido/donor **2** forms a zirconium complex that exhibits moderate activity for MAO-activated olefin polymerization; propene gives partly isotactic polypropene (55% *mmmm*).[20] In a closely related strategy, Schrock prepared the binaphthyl-based $C_2$-symmetric diamido/donor **3** and isolated cationic monoalkyl complexes of group 4 that were inactive toward 1-hexene polymerization.[21] The atropisomeric 6,6′-dimethylbiphenyl-bridged bis(iminooxazolidine) **4**, prepared by Scott and co-workers, formed $C_2$-symmetric dibenzyl complexes of group 4 that displayed low activity for ethene and 1-hexene polymerization, possibly due to formation of a tight ion pair between the active cation and the counteranion.[22]

Each of these ligands is chiral by virtue of restricted rotation about the biaryl axis; that is, they are atropisomeric and are prepared from the corresponding enantiopure 2,2′-diaminobiaryl, which either is relatively expensive to purchase or must be prepared in a multistep synthesis and resolved.[23] In this regard, we have been interested in examining alternative strategies for incorporating chirality into tetradentate biaryl-bridged diamido/donors and reasoned that this could be achieved by combining the readily available and inexpensive *tropos*[24] 2,2′-diaminobiphenyl with a chiral donor fragment such as an oxazoline to afford a new class of diamido/donor (**6**). Although the *tropos* biphenyl tether in these diamido/donors cannot be resolved, the combination of axial and central chirality could result in highly efficient asymmetric catalysis provided that coordination is highly diastereoselective or that the diastereoisomer with matched axial and central chirality is more active and/or selective than its mismatched counterpart. Since oxazoline-based ligands have proven to be extremely effective for stereocontrol in a variety of enantioselective metal-catalyzed reactions,[25] a multidentate ligand that combines a biaryl diamine and an oxazoline could find widespread use in early transition metal, main group, and lanthanide-based Lewis acid asymmetric catalysis. The escalating interest in chiral diamido ligands has prompted us to report our use of the palladium-catalyzed Buchwald−Hartwig aryl amination for the modular assembly of amino-oxazolines of type **6**.

## Results and Discussion

**Synthesis of Amino-Oxazolines.** Initially, the $C_2$-symmetric bis(amino-oxazolines) **6a**−**c** were targeted as potential nonracemic diamido/donors. The key step in the synthesis of this class of ligand involves a palladium-catalyzed Buchwald−Hartwig-type arylation between 2,2′-diaminobiphenyl and 2 equiv of the corresponding 2-(2′-bromophenyl)oxazoline, **5a**−**c**, according to eq 1. This is a particularly attractive strategy since both starting materials are readily available from inexpensive reagents. The 2,2′-diaminobiphenyl is conveniently prepared by reduction of 2,2′-dinitrobiphenyl in the presence of Pd/C,[23a] and the 2-(2′-bromophenyl)oxazoline is prepared in a single step via the zinc-catalyzed condensation between 2-bromobenzonitrile and an appropriate enantiopure amino alcohol, according to the procedure of Pfaltz and co-workers.[26]




(1)

Preliminary studies focused on the use of second-generation Buchwald−Hartwig catalysts based on $Pd_2(dba)_3$ and *rac*-BINAP [2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] since this combination has proven to be extremely effective for the amination of electron-rich, electron-poor, and electron-neutral aryl halides with a wide range of amines.[27] Moreover, both Schrock[28] and Scott[17] have previously used palladium catalysts based on *rac*-BINAP for the synthesis of diamido ligands. Thus, optimum conditions for the coupling of 2-(2′-bromophenyl)-oxazoline with 2,2′-diaminobiphenyl were identified (2 mol % $Pd_2(dba)_3$, 4 mol % *rac*-BINAP and $NaO^tBu$ in toluene at 95 °C for 16−20 h) and used to prepare bis(amino-oxazolines) **6a**−**c**, which were isolated in moderate to good yields after purification by column chromatography. In each case a minor amount of the corresponding monoarylation product **6d**−**f** (ca. 8−10%) was also isolated.

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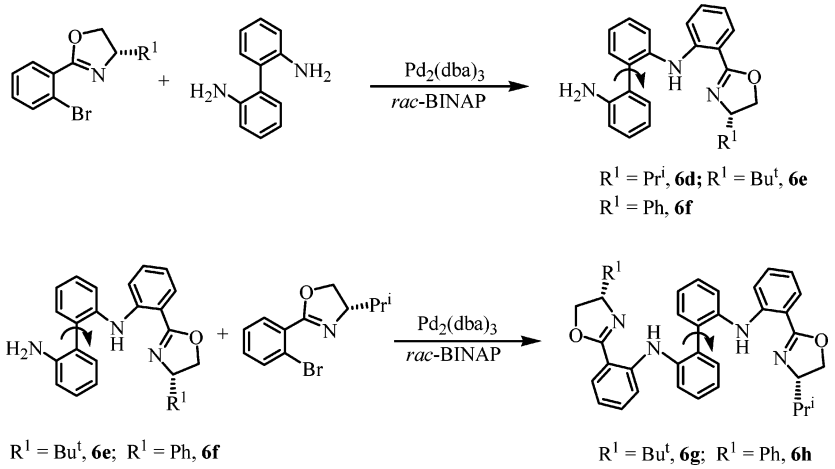
**Scheme 1. Synthesis of Monoarylation Products 6d−f and Unsymmetrically Substituted Bis(amino-oxazolines) 6g,h**[a]




[a] Reagents and conditions: (i) $Pd_2(dba)_3$ (2 mol %), *rac*-BINAP (4 mol %), NaO$^t$Bu, toluene, 90 °C, (ii) $Pd_2(dba)_2$ (2 mol %), *rac*-BINAP (4 mol %), NaO$^t$Bu, toluene, 95 °C.

Isolation of **6d−f** from the reaction between 2,2′-diaminobiphenyl and 2 equiv of 2-(2′-bromophenyl)oxazoline strongly indicated that the first arylation was markedly faster than the second and that it should be possible achieve high selectivity for monoarylation by reducing the stoichiometric ratio of 2,2′-diaminobiphenyl to 2-(2′-bromophenyl)oxazoline. Indeed, the selective monoarylation of 2,2′-diaminobiphenyl with 1 equiv of **5a−c** was catalyzed by $Pd_2(dba)_3$/*rac*-BINAP in toluene to give good yields of the desired product, **6d−f** (Scheme 1). Spectroscopically and analytically pure samples of **6d−f** could only be obtained by flash column chromatography since the crude reaction mixture was always contaminated by minor quantities of **6a−c** (typically <5%). Slightly higher chemoselectivity for monoarylation could be obtained by increasing the stoichiometric ratio of diamine to oxazoline. The $Pd_2(dba)_3$/BINAP combination also proved to be a highly efficient catalyst for the monoarylation of **6e** and **6f** with **5a**, which afforded good to high yields of the unsymmetrically substituted bis(amino-oxazolines) **6g** and **6h**, respectively (Scheme 1). The most distinctive feature of the $^1$H NMR spectrum of **6g** is the presence of four low-field well-separated signals, which correspond to two pairs of nonequivalent secondary amines associated with an equilibrium mixture of two $C_1$-symmetric diastereoisomers, which interconvert slowly on the NMR time scale. Schrock and co-workers have previously prepared a tetradentate unsymmetrical chiral diamido/donor based on a *cis*-2,5-tetrahydrofuran via a stepwise reductive amination−substitution sequence,[29a] and Guiry and co-workers have prepared a series of unsymmetrical terdentate amido/bis(oxazolines) using Buchwald−Hartwig aryl amination methodology.[16] These latter amido/donors combine with chromium chloride to form highly efficient catalysts for the asymmetric Nozaki−Hiyama allylation and crotylation of aldehydes,[29b] while their symmetric counterparts have been applied to the zinc-catalyzed Friedel−Crafts alkylation of indole with nitroalkenes, the asymmetric Henry reaction of nitromethane with α-keto esters, and the asymmetric Michael addition of nitroalkanes to nitroalkenes.[29c−e]

**Solution NMR Studies.** Ligands based on a 2,2′-substituted biphenyl tether have been attracting considerable interest in recent years, and several noteworthy applications to the area of asymmetric catalysis have appeared.[30] Ligands of this type with only two *ortho* substituents typically exhibit *tropos* character; that is, the barrier to racemization of individual chiral skew conformations is not sufficiently high to allow resolution at room temperature. However, such *tropos* ligands have been successfully applied to asymmetric catalysis since coordination to a substitutionally inert metal increases the barrier to atropinterconversion and allows the enantiomeric conformations to be resolved.[31] Perhaps the best-documented of these ligands is BIPHEP (2,2′-bis(diphenylphosphino)biphenyl), **7**,[32] which has been successfully applied to palladium- and platinum-catalyzed Diels−Alder,[33] hetero-Diels−Alder,[34] and carbonyl-ene reactions,[35] the rhodium-catalyzed cycloisomerization of 1,6-enynes,[36] and the ruthenium-catalyzed asymmetric hydrogenation of ketones.[37]

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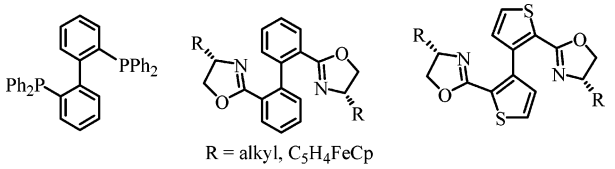
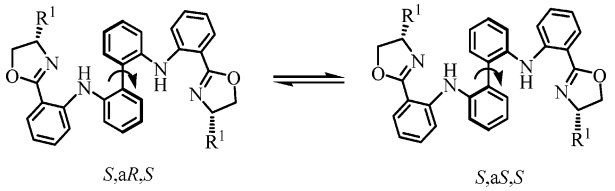
**Chart 2**




**7** **8** **9**

The biphenyl-bridged 2-(5-alkyl)- and 2-(5-ferrocenyl)bis(oxazolines), **8** (R = alkyl, $C_5H_4FeCp$), developed by Ikeda[38] and Patti,[39] respectively, also belong to the *tropos* class of ligand, as do the 3,3′-bithiophene-bridged analogues **9** recently introduced by Banaglia[40] (Chart 2). Even though **8** (R = alkyl) exists as an interconverting equilibrium mixture of two diastereoisomers, only one coordinates to copper(I), and the resulting complex catalyzes the highly enantio- and diastereoselective cyclopropanation of styrene with ethyl diazoacetate, giving ee values up to 84%.[38b] In marked contrast, their 2-(5-ferrocenyl) counterpart gave a much lower ee, even though its solution behavior and coordination properties paralleled its alkyl-substituted counterparts.[39] Similarly, the conformationally flexible 3,3′-bithiophene-bridged bis(oxazolines) **9** gave near-racemic mixtures in the copper-catalyzed cyclopropanation of styrene, although respectable ee's (66−67%) were obtained with their atropisomeric counterparts.[40] Since **6a**−**c** have only two *ortho* substituents on the biphenyl tether, they should also belong to the *tropos* class of ligand and exist as an equilibrium mixture of the *S*,a*R*,*S*- and *S*,a*S*,*S*-diastereoisomers, related by rotation about the biaryl axis (Chart 3).

**Chart 3**




*S*,a*R*,*S* *S*,a*S*,*S*

**Table 1. Minor:Major Diastereoisomeric Ratios for 6a−h at 293 and 213 K[a]**

| | 6a | 6b | 6c | 6d | 6e | 6f | 6g | 6h |
|---|---|---|---|---|---|---|---|---|
| 293 K | 45:55 | 41:59 | 45:55 | 48:52 | 49:51 | 46:54 | 45:55 | 45:55 |
| 213 K | 32:68 | 31:69 | 39:61 | 47:53 | 58:52 | 47:53 | 37:63 | 36:64 |

[a] Determined by $^1$H NMR spectroscopy (500 MHz) in $CD_2Cl_2$.

Solution $^1$H NMR studies revealed that **6a**−**h** exist as an equilibrium mixture of diastereoisomers, which interconvert slowly on the NMR time scale. The diastereoisomeric ratios listed in Table 1 show that the equilibrium is essentially independent of the oxazoline substituent but varies with temperature. A clear picture of the interconversion of the *S*,a*R*,*S*-**6b** and *S*,a*S*,*S*-**6b** diastereoisomeric pair was provided by a variable-temperature $^1$H NMR study. For comparison and to ensure consistency, the line-broadening behavior of the two low-field signals associated with the protons of the secondary amino groups (Figure 1a) and that of the two singlets belonging to the *tert*-butyl substituents of the oxazoline rings (Supporting Information) was monitored. In addition to the exchange process,

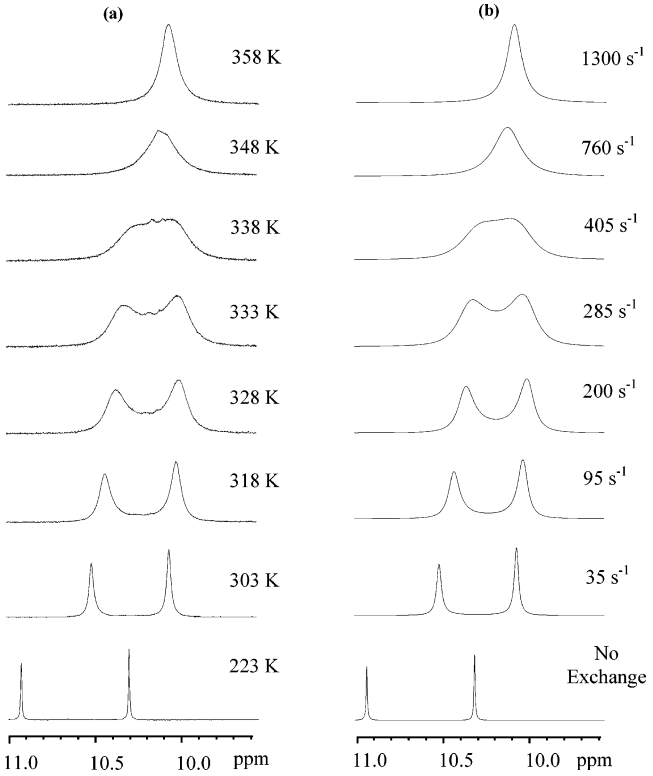



**Figure 1.** Observed (a) and simulated (b) variable-temperature $^1$H NMR spectra of **6b** showing exchange of the secondary amino protons as the *S*,a*S*,*S*- and *S*,a*R*,*S*-diastereoisomers interconvert. Spectra recorded in $d_8$-toluene.

**Table 2. Activation Parameters for the Atropinterconversion of 6b, 6e, and 6f**

| parameter | 6b[a] | 6b[b] | 6e | 6g |
|---|---|---|---|---|
| $\Delta H^{\ddagger}$, kJ mol$^{-1}$ | 57.5 ± 1 | 56.5 ± 1.5 | 51.5 ± 1.5 | 53.1 ± 1 |
| $\Delta S^{\ddagger}$, J mol$^{-1}$ K$^{-1}$ | −25.9 ± 4 | −30.0 ± 7 | −57.0 ± 7 | −39.3 ± 4 |

[a] Activation parameters determined from line-shape analysis of the N-H protons. [b] Activation parameters determined from line-shape analysis of the *tert*-butyl signals.

Figure 1a clearly shows that the chemical shift of one of the N-H protons is markedly more temperature-dependent than the other, which we tentatively attribute to a difference in the nature and extent of the intramolecular hydrogen-bonding interactions in the two diastereoisomers. Simulation of the variable-temperature $^1$H NMR spectra of **6b** (Figure 1b and Supporting Information) and Eyring analysis of the derived rate constants gave $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values of 57.5 ± 1 kJ mol$^{-1}$ and −25.9 ± 4 J K$^{-1}$ mol$^{-1}$, respectively, for the exchange process using the secondary amino protons and $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values of 56.5 ± 1.5 kJ mol$^{-1}$ and −30.0 ± 7 J K$^{-1}$ mol$^{-1}$, respectively, using the *tert*-butyl groups (Table 2). The $\Delta G^{\ddagger}$ value of 66.2 kJ mol$^{-1}$ calculated at 283 K is similar to that of 64.8 kJ mol$^{-1}$ determined by Ikeda[38] for interconversion of the *S*,a*R*,*S*- and *S*,a*S*,*S*-diastereoisomers of a series of 2,2′-biphenyl-bridged 2-(5-alkyl)-bis(oxazolines), **8**, and the estimated barrier of 68.2 kJ mol$^{-1}$ for the corresponding process in their 2-(5-ferrocenyl)-substituted derivative.[39] Since the activation barrier to axial torsion is relatively low and interconversion of the two diastereoisomers very fast (35 s$^{-1}$ at 303 K), it will not be possible to resolve these two diastereoisomers. The monoarylation product **6e** showed similar solution behavior, and line-shape analysis of the corresponding $^1$H NMR spectra gave $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values of 51.5 ± 1.5 kJ mol$^{-1}$ and −57.0 ± 7 J K$^{-1}$ mol$^{-1}$, respectively. In the case of **6g**, the low-temperature

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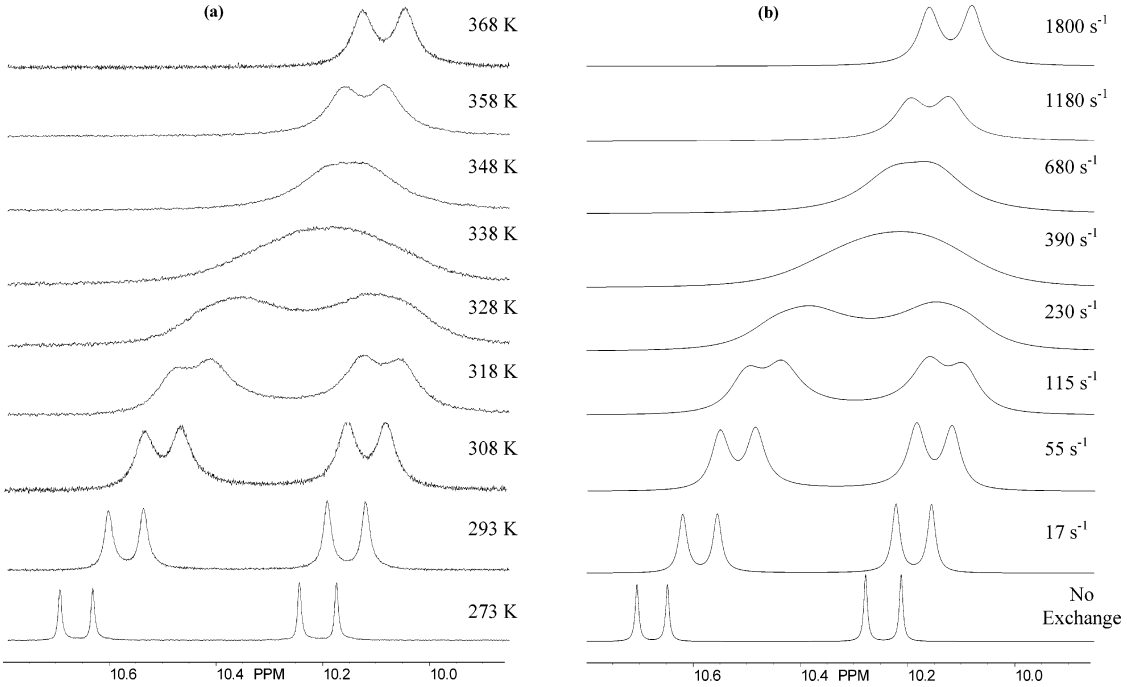


**Figure 2.** Observed (a) and simulated (b) variable-temperature $^1$H NMR spectra of **6g** to show the pairwise exchange of secondary amino protons as the *S*,a*S*,*S*- and *S*,a*R*,*S*-diastereoisomers interconvert. Spectra recorded in $d_8$-toluene.

limiting $^1$H NMR spectrum contains four well-separated signals associated with the N-H protons of the two possible $C_1$-symmetric diastereoisomers. The temperature dependence of these signals (Figure 2a) clearly shows that the two diastereoisomers interconvert, and line-shape analysis of these spectra (Figure 2b) gave $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values of 53.1 ± 1 kJ mol$^{-1}$ and −39.3 ± 4 J K$^{-1}$ mol$^{-1}$, respectively, which are entirely consistent with the corresponding activation parameters obtained for **6b** and **6e**.

**Single-Crystal X-ray Structures of 2,2′-Bis(2-(4-isopropyl-4,5-dihydro-oxazol-2-yl)phenylamino)-1,1′-biphenyl (6a), 2-(2-(4-isopropyl-4,5-dihydro-oxazol-2-yl)phenylamino)-2′-amino-1,1′-biphenyl (6d), and 2-(2-(4-*tert*-butyl-4,5-dihydro-oxazol-2-yl)phenylamino)-2′-(2-(4-isopropyl-4,5-dihydro-oxazol-2-yl)phenylamino)-1,1′-biphenyl (6h).** Crystals of a single diastereoisomer of **6a** suitable for X-ray structure determination were grown by slow diffusion of hexane into a concentrated dichloromethane solution at room temperature, and a perspective view of the molecular structure is shown in Figure 3. The molecule has a crystallographic $C_2$ axis. The structure reveals the presence of an intramolecular H-bonding interaction between the secondary amino N-H and the nitrogen atom of the proximal oxazoline ring [N(1)···N(2) = 2.700 Å and N(1)−H(1)- - -N(2) = 144°] as well as a weak $\pi-\pi$ interaction between the close and parallel phenyl ring attached to the oxazoline fragment. The two rings of the biaryl unit, which are related by 2-fold rotation symmetry, are close to perpendicular, with a dihedral angle of 72.5°, typical for a 2,2′-disubstituted biaryl. For example, the rings of the biaryl tether in 2,2′-bis(ferrocenylhydroxymethyl)-1,1′-biphenyl adopt a near-orthogonal arrangement according to Monte Carlo conformational searches.[41] A single-crystal X-ray structure of the monoarylated product **6d** has also been obtained, and in this case the crystal used for the data collection contained both diastereoisomers. The molecular structure of the *S*,a*R*-diastereoisomer, shown in Figure 4, reveals two types of intramolecular H-bonding interactions: one between the secondary amino N-H and the nitrogen atom of the oxazoline ring [N(2)···N(3) = 2.696 Å and N(2)−H(2A)···N(3) = 136°], essentially identical to the corresponding interaction described above for **6a**, and a weaker hydrogen bond between the primary amino N-H and the nitrogen atom of the secondary amine N(2) [N(1)···N(2) = 3.158 Å and N(1)−H(1A)···N(2) = 128°]. The dihedral angle between the two rings of the biaryl tether is 61.2°. The corresponding geometric parameters for the other diastereomer are similar. The structure of the unsymmetrical bis(amino-oxazoline) **6h** was also obtained for comparison with that of **6a**, and the crystals, grown by slow diffusion of a concentrated chloroform solution layered with methanol, contained a mixture of both diastereoisomers. The molecular structure of the *S*,a*R*,*R*-diastereoisomer (Figure 5) qualitatively

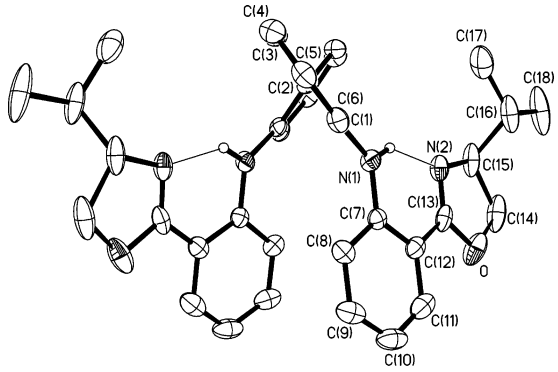


**Figure 3.** Molecular structure of **6a**, highlighting the *S*-stereochemistry about the biaryl tether and the intramolecular hydrogen-bonding interaction between N(1)-H and N(2). Hydrogen atoms except for H(1) and its symmetry equivalent have been omitted for clarity, and ellipsoids are at the 30% probability level. The unlabeled atoms are related to labeled atoms by a crystallographic $C_2$ axis running vertically down the page. Selected bond lengths (Å) and angles (deg): N(1)−C(1) 1.405(3), N(2)−C(13) 1.287(4), N(2)−C(15) 1.490(3), O−C(13) 1.361(3), O−C(14) 1.443(6) C(13)−N(2)−C(15) 108.0(3), C(13)−O−C(14) 105.8(3), C(1)−N(1)−C(7) 127.4(2), C(1)−N(1)−H(1), 120(2), C(7)−N(1)−H(1) 112(2).

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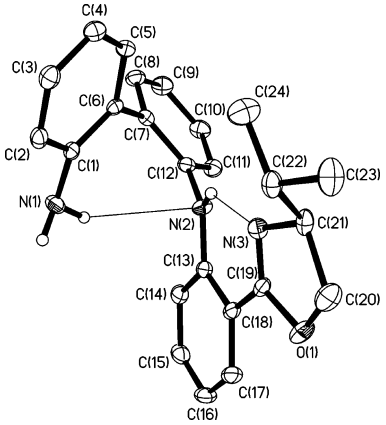


**Figure 4.** Molecular structure of the *S*,a*R*-diastereomer of the monoarylation product **6d**, illustrating the two sets of hydrogen-bonding interactions. Hydrogen atoms except for H(1A) and H(2A) have been omitted for clarity, and ellipsoids are at the 30% probability level. Selected bond lengths (Å) and angles (deg): N(1)−C(1) 1.404(4), N(2)−C(12) 1.420(4), N(2)−C(13) 1.378(3), N(3)−C(21), 1.484(3), N(3)−C(19) 1.273(3), O(1)−C(19) 1.367-(3), O(1)−C(20) 1.449(4), C(12)−N(2)−C(13) 125.4(3), C(19)−N(3)−C(21) 107.4(2), C(19)−O(1)−C(20) 105.4(2).

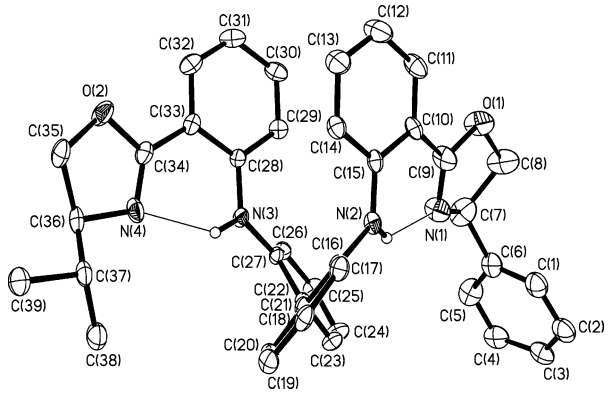


**Figure 5.** Molecular structure of the *S*,a*R*,*R*-diastereoisomer of the unsymmetrically substituted bis(amino-oxazoline) **6h** viewed along the biaryl axis to emphasize stereochemistry and showing the N(2)−H···N(1) and N(3)−H···N(4) hydrogen-bonding interactions. Hydrogen atoms except for H(2) and H(3) have been omitted for clarity, and ellipsoids are at the 30% probability level. Selected bond lengths (Å) and angles (deg): N(1)−C(7) 1.495(7), N(1)−C(9) 1.279(8), O(1)−C(9) 1.383(6), O(1)−C(8) 1.469(7), N(4)−C(34) 1.281(7), N(4)−C(36) 1.480(6), O(2)−C(35) 1.449(7), O(2)−C(34) 1.372(6), C(15)−N(2)−C(16) 127.4(4), C(27)−N(3)−C(28) 127.7(4), C(16)−N(2)−H(2) 114(3), C(15)−N(2)−H(2) 117(3), C(27)−N(3)−H(3) 119(3), C(28)−N(3)−H(3) 113(3).

resembles that of **6a** in that there are intramolecular H-bonding interactions between the secondary amine N-H and the nitrogen atoms of the oxazoline rings, respectively.

**Copper(I) Coordination Chemistry of 6b.** Since oxazoline ligands are most often used in combination with copper salts for asymmetric catalysis, the reaction between **6b** and [Cu-(MeCN)$_4$][PF$_6$] was investigated with the aim of establishing the nature of the metal−ligand bonding, the coordination geometry at the metal center, and whether one of the diastereoisomers coordinates preferentially. Addition of 1 equiv of **6b** to a dichloromethane solution of [Cu(MeCN)$_4$][PF$_6$] resulted in the gradual appearance of a pale green-yellow color, which became more intense with time. After stirring overnight the solution was filtered, concentrated, and layered with hexane to give colorless needlelike crystals of [Cu(**6b**)][PF$_6$] (**10**). The most striking feature of the $^1$H NMR spectrum of **10** is its simplicity, which is consistent with a single $C_2$-symmetric diastereoisomer. A single low-field resonance at $\delta$ 0.46 of intensity 18H, three doublets of doublets at $\delta$ 4.69, 4.33, and 3.46 associated with the protons attached to C4 and C5 of the oxazoline ring, and a broad singlet of intensity 2H at $\delta$ 5.96 belonging to the protons of the secondary amino group are all consistent with a $C_2$-symmetric environment. The $^{13}$C NMR spectrum supports this interpretation with one low-field signal at $\delta$ 168.8 for the carbon atom of the oxazoline imine, two signals at $\delta$ 75.0 and 70.5 for C4 and C5 of the oxazoline ring, and signals at $\delta$ 34.0 and 25.6 for the *tert*-butyl substituent, in addition to 12 distinct signals for the carbon atoms of the aromatic rings. A marked upfield shift of the N-H protons from $\delta$ 10.5 in **6b** to $\delta$ 5.96 in **10** and a characteristically large downfield coordination induced chemical shift, $\Delta\delta$, of −0.6 and −0.4 ($\Delta\delta = \delta \mathrm{H}i_{\mathrm{ligand}} - \delta\ \mathrm{H}i_{\mathrm{complex}}$, ppm) for the oxazoline ring C(5)-H signals[42] combined with a downfield shift of C1 of the oxazoline ring from $\delta$ 163.7 in **6b** to 167.3 in **10** suggest that **6b** coordinates in a $\kappa N,\kappa N,\kappa N,\kappa N$-tetradentate manner. In addition, the $^1$H NMR spectrum of a 1:1 mixture of **6b** and [Cu(MeCN)$_4$][PF$_6$] in $CD_2Cl_2$, recorded immediately after dissolution, also contained a single set of resonances, which suggests that the formation of **10** is both rapid and highly diastereoselective. Moreover, **10** appears to be stable with respect to diastereointerconversion since the $^1$H NMR spectrum showed no evidence for line-broadening between 213 and 308 K and no change after standing at room temperature for 1 week. Thus, it appears that the reaction between [Cu(MeCN)$_4$][PF$_6$] and an equilibrium mixture of **6b** results in dynamic resolution to afford a single $C_2$-symmetric diastereoisomer. However, the observed spectrum could also be accounted for by a rapidly interconverting mixture of two or more $C_2$-symmetric diastereoisomers. At this stage we favor the former explanation on the basis that the room-temperature $^1$H NMR spectrum of the uncoordinated ligand contains two sets of resonances associated with slow interconversion of the *S*,a*R*,*S*- and *S*,a*S*,*S*-diastereoisomers and that it is reasonable to assume that the rate of interconversion would not increase upon coordination compared with that of the free ligand. While coordination of *tropos* ligands often increases the barrier to diastereointerconversion,[30] there are examples in which metal coordination accelerates the rate of racemization.[43] In one instance, Rebek reported that coordination of a bipyridyl crown ether to palladium decreased $\Delta G^{\ddagger}$ for racemization by 11 kcal mol$^{-1}$ relative to the free ligand.[43a] However, such metal-accelerated racemization appears to be unique to bipyridyl and biisoquinoline ligands, the origin of which is poor overlap of the nitrogen lone-pair orbitals with those of the metal and the increase in M−N bond strength on going from the ground state to the transition state. Ikeda has recently investigated the coordination chemistry of a series of 2,2′-biaryl-bridged *tropos* 2-(5-alkyl)bis(oxazolines) and demonstrated that coordination to copper(I) occurs with high diastereoselectivity for all oxazolines examined, while the selectivity for other metal such as Ag(I), Pd(II), and Zn(II) depended on the oxazoline substituent.[38] Patti observed a similar level of selectivity for coordination of the *S*,a*S*,*S*-diastereoisomer of the 2-(5-ferrocenyl)-substituted **8** to zinc.[39] A related diastereoselective coordination has also been identified for a series

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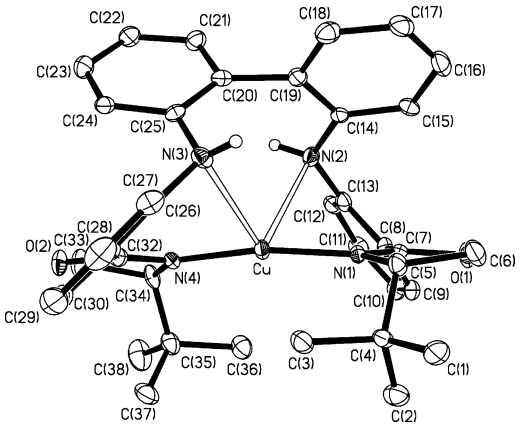


**Figure 6.** Structure of the cation of [Cu(**6b**)][$PF_6$] (**10**) showing the sawhorse geometry at copper and the approximate $C_2$-symmetry of the complex. Hydrogen atoms have been omitted for clarity, and ellipsoids are at the 30% probability level. Selected bond lengths (Å) and angles (deg): Cu(1)−N(1) 1.897(4), Cu(1)−N(2) 2.838(5), Cu(1)−N(3) 2.640(5), Cu(1)−N(4) 1.898(4), N(1)−C(5) 1.484(6), N(1)−C(7) 1.279(7), O(1)−C(7) 1.344(6), N(4)−C(32) 1.274(7), N(4)−C(34) 1.496(7), O(2)−C(32) 1.344(6), N(1)−Cu(1)−N(4) 169.12(18), N(2)−Cu(1)−N(3) 93.81(13), C(13)−N(2)−C(14) 125.4(4), C(13)−N(2)−H(2) 114(3), C(14)−N(2)−H(2) 117(3), C(25)−N(3)−C(26) 120.8(4), C(25)−N(3)−H(3) 118(4), C(26)−N(3)−H(3) 108(4).

of stereochemically dynamic 2,2′-bis(phospholes) linked by a chiral tether. Introduction of the chiral tether resulted in partial control of the central and axial chirality to afford an equilibrium mixture of diastereoisomers, which reacted with [$MCl_2(MeCN)_2$] (M = Pd, Pt) to afford diastereo- and enantiopure palladium and platinum complexes.[44]

The identity of **10** was unequivocally established by a single-crystal X-ray study (Figure 6), which provided precise details about the nature of the metal−ligand bonding, revealed a highly unusual geometry adopted by copper, and established the absolute stereochemistry of the coordinated bis(amino-oxazoline). A survey of the literature and the CSD[45] revealed that relatively few copper(I) complexes of bis(oxazolines) have been structurally characterized. The X-ray study confirmed that **10** crystallized as a single diastereoisomer, as anticipated from the solution $^1$H and $^{13}$C NMR spectra, and the configuration of the biaryl axis was established to be a*S*. At first site the copper appears to adopt a near-linear two-coordinate geometry with the two oxazolines in a *trans* arrangement with a N(4)−Cu(1)−N(1) angle of 169°. However, closer inspection reveals additional weak interactions between copper and the nitrogen atoms of the secondary amines, and although the Cu(1)−N(2) and Cu(1)−N(3) bond lengths of 2.838 and 2.640 Å, respectively, are significantly longer than a typical copper−nitrogen $\sigma$-bond, they are within the sum of the van der Waals radii of 2.90 Å. In fact, N(2) is close to planar and $sp^2$-hybridized (sum of angles at N(2) = 356.6°), which suggests that any interaction with copper is extremely weak. Thus, the coordination of copper is highly unusual, intermediate between square planar and tetrahedral, and can most aptly be described as a "sawhorse" geometry with the two secondary amino groups forming a N(2)−Cu(1)−N(3) angle of 93.81°. While **10** has $C_1$ symmetry in the solid state, it is clear from the projection shown in Figure 6 that only minor distortions are required to achieve the $C_2$-symmetric environment observed by solution NMR spectroscopy. The Cu(1)−N(1) and Cu(1)−N(4) bond lengths of 1.897(4) and 1.898(4) Å are similar to those in related copper(I) oxazoline complexes such as the 6,6′-dimethylbiphenyl-bridged 2,2′-bis(oxazoline) reported by Corey and used for the highly enantioselective synthesis of sirenin,[46] as are the C(7)−N(1) and C(32)−N(4) bond lengths of 1.279(7) and 1.274(7) Å, respectively. The dihedral angle between the two rings of the biaryl tether is 80.1°. Unfortunately, since a variable-temperature solution $^1$H NMR study of **10** showed no evidence for line-broadening between 213 and 208 K, it has not been possible to establish whether the resulting spectra are due to a time-averaged $C_2$-symmetric sawhorse geometry or a rapidly interconverting mixture of two- and four-coordinate complexes by virtue of N(amine)-dissociation and subsequent N-inversion. Similar behavior has recently been identified in a study of atropisomeric discrimination in new ruthenium(II) complexes of the $C_2$-symmetric bidentate chiral phenyl-bridged bis(oxazolines), 1,2-bis([4′-alkyl-4′,5′-dihydro-2′-oxazolyl]benzene.[47] Uncoordinated, these ligands exhibit free rotation about the C−C bond linking the aromatic tether and the oxazoline fragment, while coordination results in restricted rotation to afford a single diastereoisomer that shows no evidence for interconversion. DFT calculations gave an energy difference of 5.7 kcal mol$^{-1}$ in favor of the less sterically congested diastereoisomer and an energy barrier to diastereointerconversion of 26.0 kcal mol$^{-1}$, fully consistent with the formation of a single noninterconverting diastereoisomer.

## Conclusions

Palladium-catalyzed Buchwald−Hartwig arylation methodology has been used to prepare a new class of *tropos* tetradentate diamido/donor based on a 2,2′-biphenyl-bridged bis(amino-oxazoline). Previously, chiral diamido/donors have been based on an enantiopure atropisomeric biaryl-bridged tether such as binaphthyl or a 6,6′-substituted biphenyl. Here, we adopted an alternative strategy by incorporating central chirality, in the form of an oxazoline, into the donor fragment. Since the first arylation proceeds markedly faster than the second, the monoarylation products were isolated and used to prepare unsymmetrically substituted bis(amino-oxazolines) via a second palladium-catalyzed arylation. Variable-temperature $^1$H NMR studies showed that the bis(amino-oxazolines) and monoarylated products exist in solution as an equilibrium mixture of *S*,a*R*,*S*- and *S*,a*S*,*S*-diastereoisomers, which interconvert by rotation about the biaryl axis. Line-shape analysis of simulated spectra gave $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values of 51.5−57.0 kJ mol$^{-1}$ and −25.9 to −57.0 J mol$^{-1}$ K$^{-1}$, respectively. Coordination of **6b** to copper(I) results in a dynamic resolution to afford diastereopure (*S*,a*S*,*S*)-[Cu(**6b**)][$PF_6$], which shows no evidence for diastereointerconversion. The straightforward modular synthesis of these new diamido/donors, the combination of axial and central chirality, and the diastereoselective coordination will each be integral to the application of these ligands in asymmetric Lewis acid catalysis.

## Experimental Section

**General Comments.** All manipulations involving air-sensitive materials were carried out in an inert-atmosphere glovebox or using

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standard Schlenk line techniques under an atmosphere of nitrogen or argon in oven-dried glassware. Diethyl ether and hexane were distilled from sodium/potassium alloy, dichloromethane from calcium hydride, toluene from sodium, and THF from potassium under an atmosphere of nitrogen. Deuteriochloroform was predried with calcium hydride, vacuum-transferred, and stored over 4 Å molecular sieves. 2-Bromobenzonitrile, $Pd_2(dba)_3$, and sodium *tert*-butoxide were purchased from Aldrich Chemical Co., and *rac*-BINAP was purchased from Strem Chemical Co. Unless otherwise stated, commercially purchased materials were used without further purification. The 2-(2′-bromophenyl)oxazolines were prepared according to literature procedures.[26] $^1H$ and $^{13}C\{^1H\}$ NMR spectra were recorded on a JEOL LAMBDA 500 or a Bruker AMX 300 instrument. Thin-layer chromatography (TLC) was carried out on alumina sheets precoated with silica gel 60F 254, and column chromatography was performed using Merck Kieselgel 60.

**Synthesis of 2,2′-Bis(2-(4-isopropyl-4,5-dihydro-oxazol-2-yl)-phenylamino)-1,1′-biphenyl (6a).** An oven-dried Schlenk flask was loaded with $Pd_2(dba)_3$ (0.065 g, 0.07 mmol), *rac*-BINAP (0.087 g, 0.14 mmol), 2,2′-diaminobiphenyl (0.326 g, 1.78 mmol), 2-(2′-bromophenyl)oxazoline (0.954 g, 3.56 mmol), sodium *tert*-butoxide (0.512 g, 5.34 mmol), and dry degassed toluene (25 mL), and the mixture heated at 95 °C for 20 h, during which time the color of the solution turned from purple to a deep yellow-brown. The progress of the reaction was monitored by removing small aliquots, which were analyzed by TLC and $^1H$ NMR spectroscopy to determine when the 2-(2′-bromophenyl)oxazoline had been completely consumed. The toluene was removed in vacuo, the resulting residue extracted into diethyl ether (60 mL), and the resulting solution filtered through a short pad of silica gel. The ether was removed and the product purified by flash column chromatography (hexane−ethyl acetate, 50:3) to give **6a** as an off-white solid in 82% yield (0.81 g), present as an equilibrium mixture of two diastereoisomers (32:68). $^1H$ NMR (500.0 MHz, $CD_2Cl_2$, 218K, $\delta$): 10.51 (br s, NH), 9.82 (br s, NH), 7.58 (d, $J$ = 8.0 Hz, Ar-*H*), 7.51 (d, $J$ = 8.0 Hz, Ar-*H*), 7.32−7.41 (m, Ar-*H*), 7.24 (d, $J$ = 8.4 Hz, Ar-*H*), 7.20 (t, $J$ = 7.4 Hz, Ar-*H*), 7.15 (t, $J$ = 7.4 Hz, Ar-*H*), 7.06 (d, $J$ = 8.4 Hz, Ar-*H*), 7.03 (d, $J$ = 8.4 Hz, Ar-*H*), 6.84 (t, $J$ = 7.2 Hz, Ar-*H*), 6.54 (t, $J$ = 7.3 Hz, Ar-*H*), 6.44 (t, $J$ = 7.4 Hz, Ar-*H*), 4.3 (t, $J$ = 8.2 Hz, CH), 4.22 (t, $J$ = 9.0 Hz, oxazoline-C$H_2$O), 3.90 (m, oxazoline-C$H_2$O), 3.78 (m, oxazoline-C*H*N), 1.40 (sept, $J$ = 6.6 Hz, C*H*Me$_2$), 1.34 (sept, $J$ = 6.8 Hz, C*H*Me$_2$), 0.69 (d, $J$ = 6.8 Hz, CH*Me*$_2$), 0.64 (d, $J$ = 6.6 Hz, CH*Me*$_2$), 0.63 (d, $J$ = 6.6 Hz, CH*Me*$_2$), 0.48 (d, $J$ = 6.4 Hz, CH*Me*$_2$). $^{13}C\{^1H\}$ NMR (125.77 MHz, $CDCl_3$, 298 K, $\delta$): 163.5 (oxazoline-*C*═N), 145.9, 139.9, 139.8, 133.8, 133.0, 132.5, 131.5, 129.8, 129.6, 128.3, 128.2, 123.9, 123.3, 122.7, 116.5, 113.0, 112.5, 110.5, 73.2 (*C*H$_2$O), 68.9 (oxazoline-*C*HN), 33.3 (*C*HMe$_2$), 19.3 (*C*HMe$_2$), 19.0 (*C*HMe$_2$). Anal. Calcd for $C_{36}H_{38}N_4O_2$: C, 77.39; H, 6.86; N, 10.03. Found: C, 77.78; H, 7.01; N, 10.22. MS (70 eV, EI): $m/z$ 558 [$M^+$], 386, 355, 311, 269. $[\alpha]_D = +109.2$ ($c$ 1.0, $CH_2Cl_2$).

**2,2′-Bis(2-(4-*tert*-butyl-4,5-dihydro-oxazol-2-yl)phenylamino)-1,1′-biphenyl (6b)** was prepared according to the procedure described above for **6a** and isolated as an off-white solid in 67% yield, present as an equilibrium mixture of two diastereoisomers (46:54). $^1H$ NMR (500.0 MHz, $C_7D_8$, 253K, $\delta$): 10.92 (br s, N*H*), 10.32 (br s, N*H*), 7.49 (d, $J$ = 7.9 Hz Ar-*H*), 7.28−7.35 (m, Ar-*H*), 7.23 (t, $J$ = 7.9 Hz Ar-*H*), 7.18 (d, $J$ = 8.6 Hz, Ar-*H*), 7.11 (t, $J$ = 7.3 Hz, Ar-*H*), 7.06 (t, $J$ = 7.3 Hz, Ar-*H*), 6.98 (t, br, $J$ = 7.6 Hz, Ar-*H*), 6.84 (d, $J$ = 8.2 Hz, Ar-*H*), 6.66 (t, $J$ = 7.3 Hz, Ar-*H*), 6.43 (d, $J$ = 7.4 Hz, Ar-*H*), 6.30 (t, $J$ = 7.3 Hz, Ar-*H*), 4.13 (app t, $J$ = 9.2 Hz, oxazoline-C$H_2$O), 4.11 (app t, $J$ = 8.9 Hz, oxazoline-C$H_2$O), 3.94 (app t, $J$ = 8.6 Hz, oxazoline-C$H_2$O), 3.90 (app t, $J$ = 8.6 Hz, oxazoline-C$H_2$O), 3.79 (app t, $J$ = 9.15 Hz, oxazoline-CHN), 3.73 (app t, $J$ = 9.2 Hz, oxazoline-C*H*N), 0.64 (s, *tert*-Bu), 0.60 (s, *tert*-Bu). $^{13}C\{^1H\}$ NMR (125.77 MHz, $CDCl_3$, 298 K, $\delta$): 163.7 (oxazoline-*C*═N), 163.5 (oxazoline-*C*═N), 146.3, 146.2, 140.2, 139.9, 134.3, 133.3, 132.8, 132.7, 131.7, 13.0, 129.6, 128.6, 128.3, 124.5, 123.7, 123.4, 116.7, 116.6, 113.4, 113.3, 110.5, 110.4, 76.8 (oxazoline-$CH_2O$), 67.2 (oxazoline-*C*H$_2$N), 34.0 (*C*(CH$_3$)$_3$), 33.9 (*C*(CH$_3$)$_3$), 26.4 (C(*C*H$_3$)$_3$), 26.3 (C(*C*H$_3$)$_3$). Anal. Calcd for $C_{38}H_{42}N_4O_2$: C, 77.78; H, 7.21; N, 9.55. Found: C, 78.02; H, 7.31; N, 9.89. MS (70 eV, EI): $m/z$ 586 [$M^+$], 529, 429, 386, 369, 311, 269. $[\alpha]_D = +119.8$ ($c$ 1.0, $CH_2Cl_2$).

**2,2′-Bis(2-(4-phenyl-4,5-dihydro-oxazol-2-yl)phenylamino)-1,1′-biphenyl (6c)** was prepared according to the procedure described above for **6a** and isolated as a white solid in 58% yield, present as an equilibrium mixture of two diastereoisomers (45:55). $^1H$ NMR (500.0 MHz, $CD_2Cl_2$, 298K, $\delta$): 10.01 (br s, N-*H*), 9.87 (br s, N-*H*), 7.98 (t, $J$ = 9.0 Hz, Ar-H), 6.73−7.29 (m, Ar-*H*), 6.55 (t, $J$ = 8.6 Hz, Ar-H), 6.45 (t, $J$ = 8.6 Hz, Ar−H), 5.15 (dd, $J$ = 13.0, 19.0 Hz, oxazoline-C*H*$_2$O), 5.05 (dd, $J$ = 13.0, 19.0 Hz, oxazoline-C*H*$_2$O), 4.51 (dd, $J$ = 13.0, 16.0 Hz, oxazoline-C*H*$_2$O), 4.47 (dd, $J$ = 13.0, 16.0 Hz, oxazoline-C*H*$_2$O), 4.04 (dd, $J$ = 16.0, 19.0 Hz, oxazoline-C*H*N), 3.94 (dd, $J$ = 16.0, 19.0 Hz, oxazoline-C*H*N). $^{13}C\{^1H\}$ NMR (125.77 MHz, $CDCl_3$, 298 K, $\delta$): 164.9 (oxazoline-*C*═N), 164.8 (oxazoline-*C*═N), 146.2, 142.8, 139.8, 139.7, 133.1, 132.8, 132.1, 131.9, 130.2, 129.9, 128.9, 128.4, 128.2, 127.6, 123.3, 122.8, 122.2, 121.6, 116.9, 116.6, 113.8, 113.7, 110.6, 110.3, 73.4 (oxazoline-*C*H$_2$O), 73.1 (oxazoline-*C*H$_2$O), 70.4 (oxazoline-*C*HN), 70.2 (oxazoline-*C*HN). Anal. Calcd for $C_{38}H_{42}N_4O_2$: C, 80.49; H, 5.47; N, 8.94. Found: C, 80.79 H, 5.53; N, 9.09. MS (70 eV, EI): $m/z$ 626 [$M^+$], 506, 359, 331, 311, 285, 270, 255, 243. $[\alpha]_D = -278.2$ ($c$ 1.0, $CH_2Cl_2$).

**Synthesis of 2-(2-(4-Isopropyl-4,5-dihydro-oxazol-2-yl)phenylamino)-2′-amino-1,1′-biphenyl (6d).** An oven-dried Schlenk flask was loaded with $Pd_2(dba)_3$ (0.078 g, 0.085 mmol), *rac*-BINAP (0.105 g, 0.17 mmol), 2,2′-diaminobiphenyl (0.391 g, 2.13 mmol), isopropyl-substituted 2-(2′-bromophenyl)oxazoline (0.571 g, 2.13 mmol), sodium *tert*-butoxide (0.306 g, 3.19 mmol), and dry degassed toluene (15 mL), and the mixture heated at 90 °C for 16 h, during which time the solution turned from purple to deep yellow-brown. The reaction was monitored by removing small aliquots, which were analyzed by TLC and $^1H$ NMR spectroscopy to determine when the 2-(2′-bromophenyl)oxazoline had been completely consumed. The toluene was removed in vacuo, the residue extracted into diethyl ether (60 mL), and the resulting solution filtered through a short pad of silica. The ether was removed and the product purified by flash column chromatography (dichloromethane−hexane, 1:2, v/v) to give **6d** as a pale cream-colored solid, present as an equilibrium mixture of two diastereoisomers (48:52). $^1H$ NMR (500.0 MHz, $CD_2Cl_2$, 263 K, $\delta$): 10.18 (br s, N-*H*), 10.05 (br s, N-*H*), 7.66 (dd, $J$ = 1.5, 8.0 Hz, Ar-*H*), 7.62 (dd, $J$ = 1.5, 8.0 Hz, Ar-*H*), 7.58 (d, $J$ = 8.0 Hz, Ar-*H*), 7.55 (d, $J$ = 8.0 Hz, Ar-*H*), 7.44 (d, $J$ = 8.5 Hz, Ar-*H*), 7.42 (d, $J$ = 8.5 Hz, Ar-*H*), 7.22−7.33 (m, Ar-*H*), 7.04−7.13 (m, Ar-*H*), 6.64−6.7 (m, Ar-*H*), 3.70−4.20 (m, oxazoline C*H*N + C*H*$_2$O), 1.51 (sept, $J$ = 7.0 Hz, C*H*Me$_2$), 1.41 (sept, $J$ = 7.0 Hz, C*H*Me$_2$), 0.73 (d, $J$ = 7.0 Hz, CH*Me*$_2$), 0.69 (d, $J$ = 7.0 Hz, CH*Me*$_2$), 0.59 (d, $J$ = 7.0 Hz, CH*Me*$_2$), 0.58 (d, $J$ = 7.0 Hz, CH*Me*$_2$). $^{13}C\{^1H\}$ NMR (125.77 MHz, $CDCl_3$, 298 K, $\delta$): 162.9 (oxazoline-*C*═N), 162.8 (oxazoline-*C*═N), 145.4, 145.2, 144.2, 144.1, 139.6, 139.5, 132.4, 132.2, 132.0, 131.9, 131.7, 131.6, 130.0, 129.9, 128.5, 128.4, 128.0, 128.1, 125.1, 124.9, 123.3, 123.1, 121.8, 121.7, 118.6, 118.5, 117.1, 116.9, 115.5, 115.4, 112.9, 112.7, 111.1, 110.9, 72.6 (oxazoline-*C*HN), 72.6 (oxazoline-*C*HN), 68.4 (oxazoline-*C*H$_2$O), 68.2 (oxazoline-*C*H$_2$O), 32.6 (*C*HMe$_2$), 32.5 (*C*HMe$_2$), 18.9 (*C*HMe$_2$), 18.8 (*C*HMe$_2$), 18.3 (*C*HMe$_2$), 18.2 (*C*HMe$_2$). Anal. Calcd for $C_{24}H_{25}N_3O$: C, 77.60; H, 6.78; N, 11.31. Found: C, 77.91 H, 6.97; N, 11.37. MS (70 eV, EI): $m/z$ 371 [$M^+$], 354, 311, 296, 284, 269, 196, 168. $[\alpha]_D = +53.6$ ($c$ 1.0, $CH_2Cl_2$).

**2-(2-(4-*tert*-Butyl-4,5-dihydro-oxazol-2-yl)phenylamino)-2′-amino-1,1′-biphenyl (6e)** was prepared according to the procedure described above for **6d** and isolated as a pale yellow solid in 73% yield, present as an equilibrium mixture of two diastereoisomers (48:52). $^1$H NMR (500.0 MHz, $CD_2Cl_2$, 213 K, $\delta$): 10.09 (br s, N*H*), 9.93 (br s, N-*H*), 7.67 (dd, $J$ = 1.5, 8.0 Hz, Ar-*H*), 7.64 (dd, $J$ = 1.5, 8.0 Hz, Ar-*H*), 7.58 (d, $J$ = 8.0 Hz, Ar-*H*), 7.54 (d, $J$ = 8.0 Hz, Ar-*H*), 7.41 (d, $J$ = 8.5 Hz, Ar-*H*), 7.39 (d, $J$ = 8.5 Hz, Ar-*H*), 7.32 (t, $J$ = 7.5 Hz, Ar-*H*), 7.29 (t, $J$ = 8.0 Hz, Ar-*H*), 7.27 (dd, $J$ = 1.5, 7.5 Hz, Ar-*H*), 7.24 (t, $J$ = 7.0 Hz, Ar-*H*), 7.14 (t, $J$ = 7.0 Hz, Ar-*H*), 7.11 (t, $J$ = 7.5 Hz, Ar-*H*), 7.07 (t, $J$ = 8.0 Hz, Ar-*H*), 7.05 (d, $J$ = 8.90 Hz, Ar-*H*), 7.03 (d, $J$ = 7.5 Hz, Ar-*H*), 6.29−6.74 (m, Ar-*H*), 4.15 (dd, $J$ = 9.5 Hz, oxazoline-C$H_2$O), 4.11 (dd, $J$ = 10.0 Hz, oxazoline-C$H_2$), 3.95 (dd, $J$ = 8.0 Hz, oxazoline-C$H_2$O), 3.89 (dd, $J$ = 9.0 Hz, oxazoline-C$H_2$O), 3.80 (dd, $J$ = 9.0 Hz, oxazoline-C*H*N), 3.74 (dd, $J$ = 8.0, 10.0 Hz, oxazoline-C*H*N), 3.64 (br s, N$H_2$), 3.60 (br s, N$H_2$), 0.62 (s, *tert*-Bu), 0.52 (s, *tert*-Bu). $^{13}$C{$^1$H} NMR (125.77 MHz, $CDCl_3$, 298 K, $\delta$): 163.6 (oxazoline-*C*═N), 163.4 (oxazoline-*C*═N), 146.4, 146.3, 144.8, 144.6, 140.1, 139.9, 133.6, 133.2, 132.9, 132.5, 132.4, 132.3, 131.8, 131.7, 130.6, 130.5, 129.2, 129.1, 128.6, 128.5, 125.7, 125.3, 124.4, 124.1, 123.4, 123.3, 119.5, 119.1, 117.5, 117.4.116.3, 116.2, 113.3, 113.1, 111.5, 111.4, 76.9 (oxazoline-*C*HN), 76.8 (oxazoline-*C*HN), 67.4 (oxazoline-*C*$H_2$O), 67.3 (oxazoline-*C*$H_2$O), 34.1 (*C*(CH$_3$)$_3$), 33.9 (*C*(CH$_3$)$_3$), 26.4 (C(*C*H$_3$)$_3$), 26.2 (C(*C*H$_3$)$_3$). Anal. Calcd for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N, 10.90. Found: C, 78.11, H, 6.89; N, 11.01. MS (70 eV, EI): *m*/*z* 385 [M$^+$], 368, 328, 285, 256. $[\alpha]_D$ = +42.9 (*c* 1.0, $CH_2Cl_2$).

**2-(2-(4-Phenyl-4,5-dihydro-oxazol-2-yl)phenylamino)-2′-amino-1,1′-biphenyl (6f)** was prepared according to the procedure described above for **6d** and isolated as a red oil in 79% yield, present as an equilibrium mixture of two diastereoisomers (47:53). $^1$H NMR (500.0 MHz, $CD_2Cl_2$, 298 K, $\delta$): 10.18 (br s, N-*H*), 10.16, br s, N-*H*), 7.69 (t, $J$ = 6.0 Hz, Ar-*H*), 7.53 (t, $J$ = 8.6 Hz, Ar-*H*), 7.40 (d, $J$ = 8.5 Hz, Ar-*H*), 7.30 (d, $J$ = 8.5 Hz Ar-*H*), 7.12−7.26 (m, Ar-*H*), 7.01 (t, $J$ = 6.6 Hz, Ar-*H*), 6.97 (t, $J$ = 7.4 Hz, Ar-*H*), 6.91 (dd, $J$ = 1.2, 7.5 Hz, Ar-*H*), 6.87 (t, $J$ = 7.6 Hz, Ar-*H*), 6.83 (t, $J$ = 7.1 Hz, Ar-*H*), 6.65 (t, $J$ = 7.5 Hz Ar-*H*), 6.63 (t, $J$ = 7.5 Hz, Ar-*H*), 6.47 (t, $J$ = 7.4 Hz, Ar-*H*), 6.43 (t, $J$ = 7.8 Hz, Ar-*H*), 6.33 (d, $J$ = 7.8 Hz, Ar-*H*), 6.32 (d, $J$ = 7.9 Hz, Ar-*H*), 5.08 (app t, $J$ = 9.6 Hz, oxazoline-C$H_2$O), 5.06 (app t, $J$ = 9.6 Hz, oxazoline-C$H_2$O), 4.47 (app t, $J$ = 9.6 Hz, oxazoline-C$H_2$O), 4.46 (app t, $J$ = 9.6 Hz, oxazoline-C$H_2$O), 3.90 (app t, $J$ = 9.6 Hz, oxazoline-C*H*N), 3.89 (app t, $J$ = 9.4 Hz, oxazoline-C*H*N), 3.31 (br s, N$H_2$), 3.14 (br s, N$H_2$). $^{13}$C{$^1$H} NMR (125.77 MHz, $CDCl_3$, 298 K, $\delta$): 164.8 (oxazoline-*C*═N), 164.7 (oxazoline-*C*═N), 146.1, 145.7, 144.8, 144.4, 142.8, 142.7, 140.1, 140.0, 132.5, 132.4, 132.3, 132.2, 132.0, 131.9, 129.0, 128.9, 128.7, 128.6, 128.5, 127.8, 127.7, 127.2, 127.1, 125.3, 125.2, 123.5, 123.1, 121.9, 120.4, 118.9, 118.8, 117.7, 117.5, 115.9, 115.8, 114.0, 113.8, 114.0, 113.7, 111.4, 111.2, 71.9 (oxazoline-*C*HN), 71.8 (oxazoline-*C*HN), 69.0 (oxazoline-*C*$H_2$O), 68.8 (oxazoline-*C*$H_2$O). Anal. Calcd for $C_{27}H_{23}N_3O$: C, 79.97; H, 5.72; N, 10.36. Found: C, 80.10, H, 5.89; N, 10.52. MS (70 eV, EI): *m*/*z* 405 [M$^+$], 388, 374, 357, 284, 270, 256. $[\alpha]_D$ = −99.4 (*c* 0.85, $CH_2Cl_2$).

**Synthesis of 2-(2-(4-*tert*-Butyl-4,5-dihydro-oxazol-2-yl)phenylamino)-2′-(2-(4-isopropyl-4,5-dihydro-oxazol-2-yl)phenylamino)-1,1′-biphenyl (6g).** An oven-dried Schlenk flask was loaded with $Pd_2(dba)_3$ (0.016 g, 0.017 mmol), *rac*-BINAP (0.0205 g, 0.033 mmol), **6b** (0.160 g, 0.42 mmol), isopropyl-substituted 2-(2′-bromophenyl)oxazoline (0.111 g, 0.41 mmol), sodium *tert*-butoxide (0.06 g, 0.63 mmol), and dry degassed toluene (5 mL), and the mixture heated at 100 °C for ca. 20 h, during which time the color of the solution turned from purple to a blood red. The progress of the reaction was monitored by removing small aliquots, which were analyzed by TLC to determine when the starting materials had been completely consumed. The toluene was removed in vacuo, the resulting residue extracted into diethyl ether (2 × 30 mL), and the resulting solution filtered through a short pad of silica. The ether was removed and the product purified by flash column chromatography (hexane−dichloromethane, 2:1) to give **6g** as an off-white solid in 84% yield (0.20 g). An analytically pure sample was obtained by slow diffusion of a chloroform solution layered with methanol. The product is present as an equilibrium mixture of two diastereoisomers (32:68). $^1$H NMR (500.0 MHz, $C_7D_8$, 273K, $\delta$): 10.70 (br s, N-H), 10.63 (br s, N-H), 10.25 (br s, N-*H*), 10.17 (br s, N-*H*), 7.78 (t, $J$ = 9.4 Hz, Ar-*H*), 7.50 (t, $J$ = 7.8 Hz, Ar-*H*), 7.45 (t, $J$ = 8.5 Hz, Ar-*H*), 7.39 (dd, $J$ = 7.6, 1.5 Hz, Ar-*H*), 7.38 (dd, $J$ = 7.9, 1.5 Hz, Ar-*H*), 7.33 (d, $J$ = 8.55 Hz, Ar-*H*), 7.30 (d, $J$ = 8.5 Hz, Ar-*H*), 7.26 (t, $J$ = 8.9 Hz, Ar-*H*), 7.20 (d, $J$ = 8.6 Hz, Ar-*H*), 7.16 (d, $J$ = 8.6 Hz, Ar-*H*), 6.9−7.14 (m, Ar-*H*), 6.83 (t, $J$ = 7.4 Hz, Ar-*H*), 6.79 (t, $J$ = 7.6 Hz, Ar-*H*), 6.54 (t, $J$ = 7.0 Hz, Ar-*H*), 6.52 (t, $J$ = 7.0 Hz, Ar-*H*), 6.47 (t, $J$ = 6.7 Hz Ar-*H*), 3.44−3.77 (m, oxazoline-C$H_2$O + C*H*N), 1.33 (sept, $J$ = 6.7 Hz, C*H*Me$_2$), 1.24 (sept, $J$ = 6.7 Hz, C*H*Me$_2$), 0.71 (d, $J$ = 6.7 Hz, CH*Me*$_2$), 0.67 (d, $J$ = 6.7 Hz, CH*Me*$_2$), 0.65 (d, $J$ = 6.7 Hz, CHMe$_2$), 0.63 (s, *tert-Bu*), 0.61 (s, *tert-Bu*), 0.60 (d, $J$ = 6.7 Hz, CH*Me*$_2$). Anal. Calcd for $C_{37}H_{40}N_4O_2$: C, 77.49; H, 7.04; N, 9.78. Found: C, 77.78, H, 7.19; N, 10.04. MS (70 eV, EI): *m*/*z* 572 [M$^+$], 515, 429, 386, 369, 355, 311. $[\alpha]_D$ = +98.8 (*c* 1.0, $CH_2Cl_2$).

**2-(2-(4-Phenyl-4,5-dihydro-oxazol-2-yl)phenylamino)-2′-(2-(4-isopropyl-4,5-dihydro-oxazol-2-yl)phenylamino)-1,1′-biphenyl (6h)** was prepared according to the procedure described above for **6g** and isolated as colorless crystals in 77% yield by slow diffusion of a chloroform solution layered with methanol at room temperature. The product is present as a rapidly interconverting mixture of two diastereoisomers. $^1$H NMR (500.0 MHz, $C_7D_8$, 343 K, $\delta$): 10.35 (br s, N-*H*), 10.20 (br s, N-*H*), 7.80 (d, $J$ = 7.7 Hz, Ar-*H*), 7.70 (d, $J$ = 7.8 Hz, Ar-*H*), 7.4 (d, $J$ = 8.0 Hz, Ar-*H*), 7.31 (d, $J$ = 8.0 Hz, Ar-*H*), 7.28 (br d, $J$ = 7.3 Hz, Ar-*H*), 7.18 (d, $J$ = 7.6 Hz, Ar-*H*), 6.9−7.1 (m, Ar-H), 6.8 (t, $J$ = 7.4 Hz, Ar-*H*), 6.7 (t, $J$ = 7.4 Hz, Ar-*H*), 6.51 (t, $J$ = 7.6 Hz, Ar-*H*), 6.45 (t, $J$ = 7.0 Hz, Ar-*H*), 4.88 (br app t, $J$ = 8.5 Hz, oxazoline-C$H_2$O), 4.08 (app t, $J$ = 14.0 Hz, oxazoline-C$H_2$O), 3.76 (app t, $J$ = 7.6 Hz, oxazoline-C$H_2$O), 3.66 (app t, $J$ = 8.3 Hz, oxazoline-C$H_2$O), 3.54−3.60 (m, oxazoline-C$H_2$O + C*H*N), 1.40 (br sept, $J$ = 6.7 Hz, C*H*Me$_2$), 0.70 (d, $J$ = 6.7 Hz, CH*Me*$_2$), 0.62 (d, $J$ = 6.7 Hz, CH*Me*$_2$). Anal. Calcd for $C_{39}H_{36}N_4O_2$: C, 79.03; H, 6.12; N, 9.45. Found: C, 79.45, H, 6.34; N, 9.89. MS (70 eV, EI): *m*/*z* 592 [M$^+$], 429, 388, 355, 3111, 270. $[\alpha]_D$ = −65.0 (*c* 1.0, $CH_2Cl_2$).

**Synthesis of [Cu(6b)][PF$_6$] (10).** A solution of **6b** (0.070 g, 0.12 mmol) in dichloromethane (5 mL) was transferred via cannula to a dichloromethane solution of [Cu(MeCN)$_4$][PF$_6$] (0.045 g, 0.12 mmol). After stirring overnight the resulting solution was filtered, concentrated, layered with *n*-hexane, and left to diffuse at room temperature to afford colorless needlelike crystals of **10** in 88% yield (0.083 g). $^1$H NMR (500.0 MHz, $CDCl_3$, 298 K, $\delta$): 6.8 (t, $J$ = 7.4 Hz, 2H, Ar-*H*), 7.50 (d, $J$ = 7.7 Hz, 2H, Ar-*H*), 7.32 (d, $J$ = 7.9 Hz, 4H, Ar-*H*), 7.25 (t, $J$ = 6.7 Hz, Ar-*H*), 7.19 (t, $J$ = 7.0 Hz, 4H, Ar-*H*), 6.82 (d, $J$ = 7.9 Hz, 2H, Ar-*H*), 5.94 (br s, 2H, N−H), 4.40 (app t, $J$ = 9.3, 6.4 Hz, 2H, oxazoline-C$H_2$O), 4.32 (app t, $J$ = 8.5 Hz, oxazoline-C$H_2$O), 3.58 (dd, $J$ = 9.8, 6.4 Hz, oxazoline-C*H*N), 0.54 (s, 18H, *tert-Bu*). $^{13}$C{$^1$H} NMR (125.77 MHz, $CDCl_3$, 298 K, $\delta$): 168.7 (oxazoline-*C*═N), 142.6 (*Ar*), 140.1 (*Ar*), 135.1 (*Ar*), 132.0 (*Ar*), 129.9 (Ar), 129.3 (*Ar*), 127.3 (*Ar*), 125.4 (*Ar*), 125.3 (*Ar*), 124.2 (*Ar*), 120.9 (*Ar*), 113.1(*Ar*), 74.9 (oxazoline-*C*HN), 70.5 (oxazoline-*C*$H_2$O), 33.9 (*C*(CH$_3$)$_3$), 25.6 (C(*C*H$_3$)$_3$). Anal. Calcd for $C_{39}H_{44}CuCl_2F_6N_4O_2P$: C, 53.22; H, 5.04; N, 6.37. Found: C, 53.31, H, 5.29; N, 6.63. MS (70 eV, EI) *m*/*z* 649 [M$^+$].

**Crystal Structure Determinations of 6a, 6d 6h, and 10.** Data were collected on Nonius KappaCCD and Bruker SMART diffractometers with graphite-monochromated Mo Kα radiation ($\lambda$ =

**Table 3. Summary of Crystal Data and Structure Determination for Compounds 6a, 6d, 6h, and 10**

| | 6a | 6d | 6h | 10 |
|---|---|---|---|---|
| formula | $C_{36}H_{38}N_4O_2$ | $C_{24}H_{25}N_3O$ | $C_{39}H_{36}N_4O_2$ | $C_{38}H_{42}Cu\ N_4O_2^+ \cdot PF_6^- \cdot CH_2Cl_2$ |
| $M_r$ | 558.7 | 371.5 | 592.7 | 880.2 |
| cryst size, mm | 0.48 × 0.44 × 0.42 | 0.40 × 0.30 × 0.30 | 0.15 × 0.15 × 0.05 | 0.33 × 0.25 × 0.22 |
| temperature, K | 150(2) | 150(2) | 120(2) | 150(2) |
| cryst syst | monoclinic | monoclinic | triclinic | tetragonal |
| space group | *C*2 | $P2_1$ | *P*1 | $P4_1$ |
| *a*, Å | 16.5149(16) | 11.8347(11) | 9.9081(15) | 10.6787(3) |
| *b*, Å | 9.3288(7) | 11.6956(15) | 11.1339(17) | 10.6787(3) |
| *c*, Å | 10.5748(10) | 14.5993(16) | 14.528(2) | 34.894(2) |
| α, deg | 90 | 90 | 96.546(2) | 90 |
| *β*, deg | 109.120(8) | 102.316(10) | 102.257(2) | 90 |
| *γ*, deg | 90 | 90 | 90.104(2) | 90 |
| *V*, Å$^3$ | 1539.3(2) | 1974.2(4) | 1553.8(4) | 3979.1(3) |
| *Z* | 2 | 4 | 2 | 4 |
| $D_{calc}$, g cm$^{-3}$ | 1.205 | 1.250 | 1.267 | 1.469 |
| $\mu$(Mo Kα), mm$^{-1}$ | 0.076 | 0.078 | 0.079 | 0.792 |
| $\theta_{max}$, deg | 26.4 | 27.5 | 31.0 | 25.0 |
| no. of reflns measd | 14 339 | 30 409 | 10 537 | 28 949 |
| no. of unique reflns | 1662 | 4722 | 5652 | 6999 |
| $R_{int}$ (on $F^2$) | 0.0402 | 0.0431 | 0.0478 | 0.0423 |
| no. of params | 197 | 534 | 831 | 510 |
| $R^a$ [$F^2 > 2\sigma(F^2)$] | 0.0552 | 0.0427 | 0.0625 | 0.0546 |
| $R_w{}^b$ (all data) | 0.1361 | 0.1019 | 0.1682 | 0.1422 |
| GOF$^c$ (*S*) | 1.187 | 1.102 | 1.016 | 1.078 |
| max., min. diff map, e Å$^{-3}$ | 0.34, −0.45 | 0.26, −0.31 | 0.67, −0.27 | 0.97, −0.43 |

[a] Conventional $R = \sum||F_o| - |F_c||/\sum|F_o|$ for "observed" reflections having $F_o^2 > 2\sigma(F_o^2)$. [b] $R_w = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$ for all data. [c] GOF = $[\sum w(F_o^2 - F_c^2)^2/(\text{no. of unique reflns} - \text{no. of params})]^{1/2}$.

0.71073Å) for **6a**, **6d**, and **10** and on a Bruker APEX2 diffractometer with synchrotron radiation ($\lambda = 0.8462$ Å) for **6h**.[48] Selected crystal data are given in Table 3. Semiempirical absorption corrections were applied, based on symmetry-equivalent and repeated reflections. The structures were solved using direct methods and refined with the SHELXTL program package, and the non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included at idealized positions, and a riding model was used for subsequent refinement.[49] All the structures are fully ordered. The absolute configuration was assumed from the known *S* configuration of the isopropyl-substituted oxazoline starting material, enabling the axial configuration to be established for each structure; for the ligands, Friedel pairs were merged because of the absence of significant anomalous scattering effects, but for the copper complex **10**, anomalous scattering could be used to confirm the absolute configuration (and the correct choice of the chiral space group $P4_1$ rather than $P4_3$) by refinement of the enantiopole parameter to a value of 0.009(17).[50]

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**Supporting Information Available:** Full details of experimental procedures and characterization data, variable-temperature NMR, simulations, and Eyring analysis for compounds **6b**, **6e**, and **6f** and, for **6a**, **6d**, **6h**, and **10**, details of crystal data, structure solution and refinement, atomic coordinates, bond distances, bond angles, and anisotropic parameters in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org. Observed and calculated structure factor tables are available from the authors upon request.

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