Imidazolium-Based Frameworks: Imidazolium Salt–Oxazoline/Palladium(II) Acetate In Situ Catalyst Systems

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Abstract: New simple imidazolium-based bidentate ligand precursors were prepared by a three-step protocol and bis(oxazoline) ligands were prepared in two steps. A Suzuki–Miyaura reaction was utilized to ascertain the activity of a palladium(II) catalyst system generated in situ from an oxazolinyl-imidazolium cation, a bis(oxazoline), and palladium(II) acetate. Among them, two sterically hindered *N*-arylimidazolium cations demonstrated their efficiency with both aryl bromides and chlorides in low catalyst-system loading.

Key words: bidentate ligands, carbenes, cross-coupling, catalysis, N-heterocyclic carbenes

A broad array of imidazolium-based scaffolds have been rapidly developed with advances in both N-heterocyclic carbenes (NHCs)[1,2] and anion recognition chemistry,[3] as well as with room temperature ionic liquids (RILs).[4] N-Heterocyclic carbenes have emerged as a relevant family of ancillary ligands in organometallic chemistry due to their practical applications in both homogeneous and heterogeneous systems. In homogeneous catalysis, the catalytic potential of N-heterocyclic carbenes has been expanded by the inclusion of an ensemble of bidentate ligands. These incorporate an N-heterocyclic carbene moiety and a chiral donor subunit (e.g., oxazolinyl-imidazolylidene), with the aim of enhancing their catalytic activity in stereoselective transformations in organic synthesis.[2] Since the synthesis of the first type of oxazolinyl-N-heterocyclic carbene **A**, reported by Herrmann et al.,[5a] the new bidentate ligand prototypes **B**–**F**, among others, have been utilized as efficient chiral catalysts (Figure 1). Thus, Burgess and co-workers examined the asymmetric hydrogenation of alkenes using iridium(I) catalysts type **B**,[5b] Gade and co-workers reported type **C** ligands,[5c–e,6] Crudden and co-workers reported type **D** ligands,[5f] and Nanchen and Pfaltz reported type **A** and **E** ligands.[5g] Bolm et al. have described the type **F** ligands with a chiral paracyclophane linker.[5h]

The present study focuses on the oxazolinyl-imidazolium salts **1**–**5** and the corresponding bis(oxazoline) ligands **6** and **7** with a 2,4,6-trimethyl-1,3-phenylene interannular spacer. The oxazoline units contain (or not) a stereocenter at C4 and are combined with the *N*-methylimidazolium ring for **1** and **4** or sterically hindered *N*-arylimidazolium subunits for **2**, **3**, and **5** (Scheme 1). We have determined

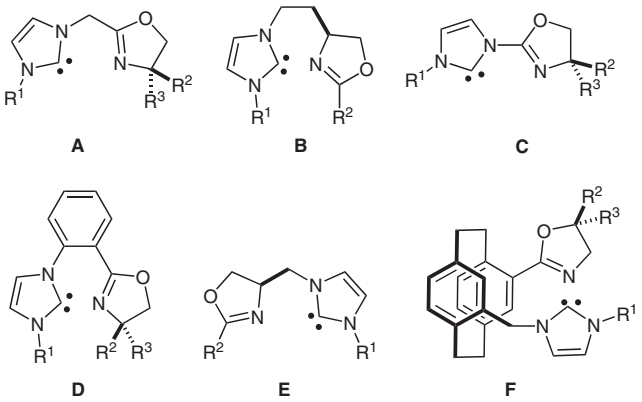

Figure 1 Different types of oxazolinyl-N-heterocyclic carbene bidentate ligands

a convenient multistep route, for the synthesis of cations **1**–**5**, which proceeds in three steps starting from intermediate **8**. In contrast, bis(oxazolines) **6** and **7** were directly obtained in two steps. To examine the catalytic potential of palladium(II)–bidentate ligands generated in situ from cations **1**–**3**, **5**, and bis(oxazoline) **6** and palladium(II) acetate, the classical Suzuki–Miyaura reaction was used to validate the catalytic efficiency. In this context, only one report describes a palladium(II)–bis(oxazoline) catalyst system generated in situ.[7]

Although different multistep routes could be applied for the synthesis of oxazolinyl-imidazolium ligand precursors **1**–**3**, (*S*)-**4**, and (*S*)-**5**, the coexistence of two different terminal heterocyclic moieties, joined through the spacer, implies the stepwise introduction of the two rings. A reasonable pathway to the target ligand precursors appeared to involve the incorporation of the imidazolium quaternary moiety in the last synthetic step. This route requires the preparation of [(hydroxymethyl)aryl]acetonitrile **8**, followed by sequential conversion into the title ligand precursors (Scheme 1). In accordance with the standard protocol, bis(oxazoline) ligands **6** and (*S*)-**7** were prepared from 2,4,6-trimethyl-1,3-phenylenediacetonitrile (**9**).

The synthesis of the key intermediate [3-(hydroxymethyl)-2,4,6-trimethylphenyl]acetonitrile (**8**) began with the transformation of commercially available bis(chloromethyl) derivative **10** into the known compound **11**,[8] which led to the cyanomethyl compound **8** upon treatment with calcium carbonate/water in dioxane (Scheme 2). Using calcium carbonate/water in dioxane,[9a] the hydrolysis

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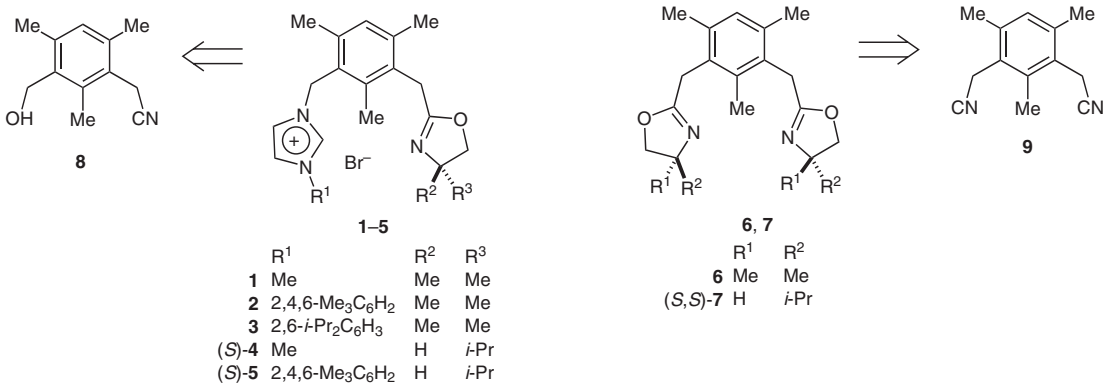
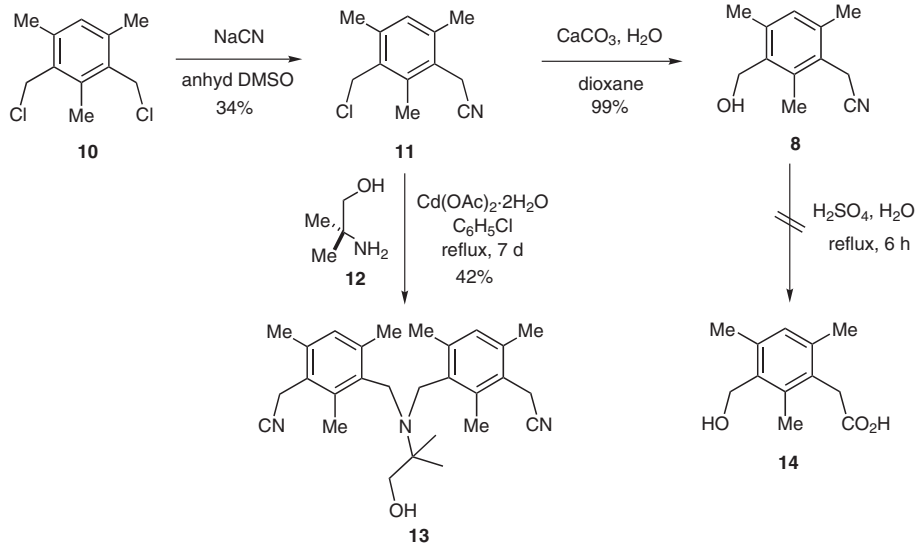


Scheme 1

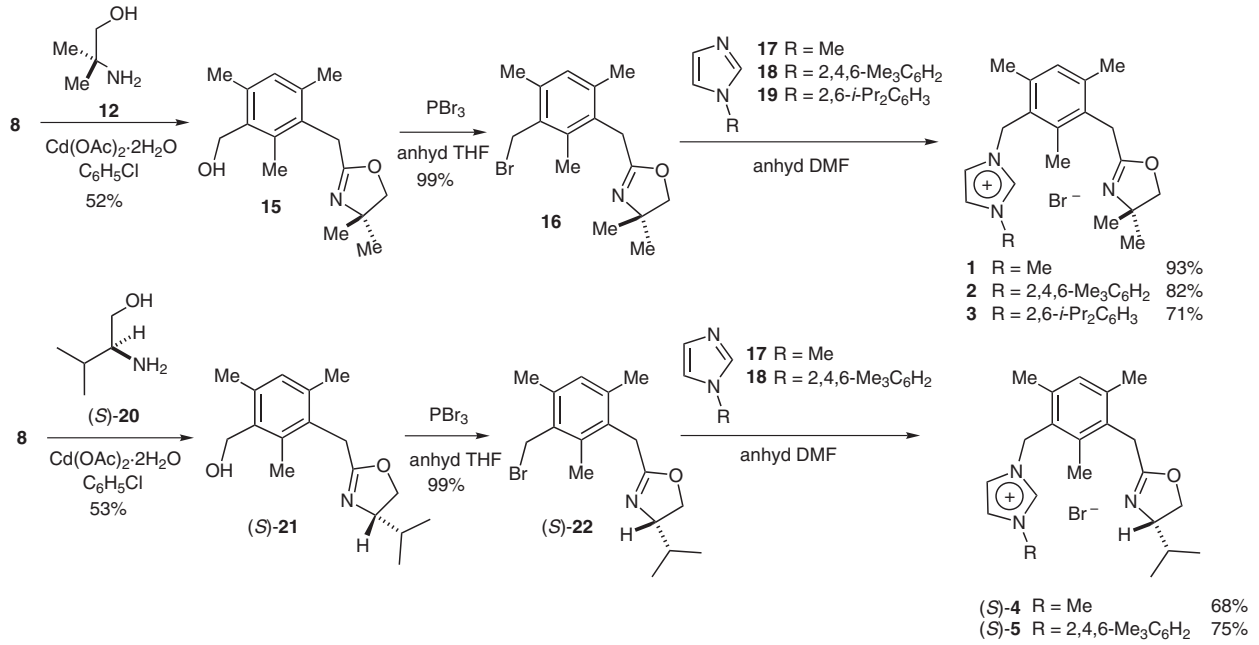
of compound **11** gave alcohol **8** in quantitative yield. However, an alternative and less efficient procedure has been applied to the related (cyanomethyl)benzyl alcohols.[9b] To shorten the sequential protocol leading to alcohol **8**, we attempted the conversion of [(chloromethyl)aryl]acetonitrile **11** into a 2-[3-(chloromethyl)-2,4,6-trimethylbenzyl]oxazoline. As this proved to be ineffective, resulting in the formation of compound **13**, we employed the standard transformation of arylacetonitrile **8** into arylacetic acid **14**, which, instead, produced polymerization products.

Oxazolinyl-imidazolium ligand precursors **1**–**3**, (*S*)-**4**, and (*S*)-**5** were prepared following a three-step sequence shown in Scheme 3, a synthetic strategy that relies on the formation of the imidazolium ring from suitable functionalized key intermediates **15** and (*S*)-**21**. Oxazoline ring formation was examined based on the condensation of arylacetonitrile **8** with amino alcohol **12** mediated by cadmium acetate hydrate. While we initially utilized similar conditions to those used in variety of oxazoline systems,[10,11] yields were low (≤25%). After examining various reaction conditions, the condensation proved most efficient in the presence of 50 mol% of cadmium acetate hydrate giving (oxazolinylmethyl)benzyl alcohol **15** in 52% yield, which was transformed into the bromomethyl derivative **16** by bromination with phosphorus tribromide in the absence of base. When the bromination was performed using phosphorus tribromide (1 equiv) and pyridine (either 1.5 or 1.0 equiv) and both the reaction temperature (0 °C to –20 °C) and time (12 h to 4 h) were varied, only decomposition products were observed. Finally, quaternization of *N*-alkylimidazoles **17**–**19** with [(bromomethyl)aryl]oxazoline **16** under neutral conditions yielded the corresponding targeted cations **1**–**3**. Following the same stepwise synthetic protocol, chiral cationic ligand precursors (*S*)-**4** and (*S*)-**5** were obtained starting from arylacetonitrile **8** and (+)-(*S*)-2-amino-3-methylbutan-1-ol [(*S*)-**20**] (Scheme 3).

Bis(oxazoline) ligands **6** and (*S*)-**7** were prepared from commercially available 2,4-bis(chloromethyl)-1,3,5-trimethylbenzene (**10**), which was transformed into give 2,4,6-trimethyl-1,3-phenylenediacetonitrile (**9**). The reaction of **9** with excess of 2-amino-2-methylpropan-1-ol (**12**) (3.75 equiv) and a catalytic amount of cadmium(II)



Scheme 2

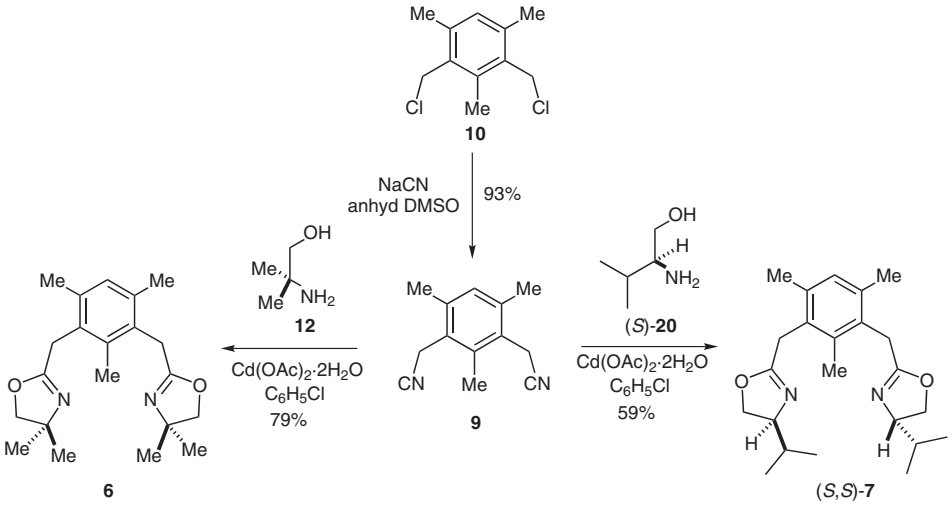


Scheme 3

acetate hydrate (0.05 equiv) gave bis(oxazoline) **6** in 79% yield, whereas condensation of dinitrile **9** with (*S*)-**20** led to chiral bis(oxazoline) (*S*)-**7** in 49% yield. Increasing the amount of cadmium acetate hydrate to 0.5 equivalents improved the yield of (*S*)-**7** to 59% (Scheme 4).

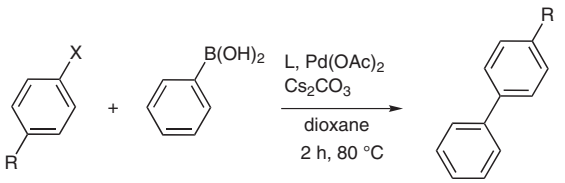
The cross-coupling reaction between aryl halides and arylboronic acids (Suzuki–Miyaura reaction) is the most versatile method for the synthesis of substituted biaryls. It is frequently utilized to show the efficiency of palladium(II) catalysts and efforts are currently directed towards obtaining improved results with deactivated substrates such as aryl chlorides at very low catalyst loadings.[12] Accordingly, the Suzuki–Miyaura reaction was selected to explore the catalytic efficiency of the new ligand precursors. To this end, the palladium(II) catalysts were generated in situ, thereby simplifying the reaction. However, the exact amount and chemical composition of the catalyst remain unknown.

Palladium(II) catalyst systems were produced in situ from palladium(II) acetate. Catalytic amounts of ligand precursor **1**–**3**, **5**, or **6** and palladium(II) acetate were stirred for two hours in the reaction medium (Cs_2CO_3, dioxane) at 80 °C before the aryl halide and phenylboronic acid were added. All experiments were stopped after two hours, and the reaction mixture was treated to isolate the coupling product (Table 1).



Scheme 4

Table 1 Suzuki–Miyaura Reactions between Aryl Halides and Phenylboronic Acid Using an In Situ Catalyst System[a]



Entry	R	X	Ligand	Catalyst (mol%)	Yield[b,c] (%)
1	OMe	Br	**1**	0.5	91
2		Br	**2**	0.5	93
3		Br	**3**	0.5	84
4		Br	**5**	0.5	36
5		Br	**6**	0.5	65
6		Br	**1**	0.1	12
7		Br	**2**	0.1	23
8		Br	**3**	0.1	25
9		Br	**5**	0.1	23
10	COMe	Br	**1**	0.5	93
11		Br	**2**	0.5	94
12		Br	**3**	0.5	99
13		Br	**5**	0.5	49
14		Br	**6**	0.5	90
15		Br	**1**	0.1	92
16		Br	**2**	0.1	97
17		Br	**3**	0.1	95
18		Br	**5**	0.1	19
19		Br	**6**	0.1	66
20	COMe	Cl	**1**	2.5	11
21		Cl	**2**	2.5	83
22		Cl	**3**	2.5	71
23		Cl	**5**	2.5	13
24		Cl	**6**	2.5	19
25		Cl	**1**	1	6
26		Cl	**2**	1	73
27		Cl	**3**	1	74
28		Cl	**5**	1	17
29	Me	Cl	**2**	2.5	77
30		Cl	**3**	2.5	71
31		Cl	**5**	2.5	8

[a] Reaction conditions: aryl halide (1 mmol), phenylboronic acid (1.5 mmol), Cs_2CO_3 (2 mmol), catalyst [ligand precursor/$Pd(OAc)_2$], dioxane (3 mL), 80 °C, 2 h.
[b] Yield after chromatographic purification.
[c] Average of two runs.

Initially, we examined the coupling of 4-bromoanisole (a deactivated bromoarene) and phenylboronic acid, using 0.5 mol% of oxazolinyl-imidazolium salts **1**–**3** and **5** or bis(oxazoline) **6** and palladium(II) acetate (Table 1, entries 1–5). The results showed excellent yields for imidazolium salts **1**–**3** and were comparable to those reported by Gade et al.,[5c] in which the reaction was carried out with 0.2 mol% isolated palladium–oxazolinyl-N-heterocyclic carbene complex. Moderate yields were, however, obtained for compounds **5** and **6**. When the catalyst loading was 0.1 mol%, the yield of 4-methoxybiphenyl decreased (Table 1, entries 6–9).

Better results were obtained when the reaction was carried out with an activated bromoarene like 4-bromoacetophenone. When using 0.5 mol% or 0.1 mol% of oxazolinyl-imidazolium salt **1**–**3** and palladium(II) acetate, the coupling reaction produced similarly satisfactory isolated yields (>90%) (Table 1, entries 10–12, 15–17). This confirms the catalytic efficiency of the in situ palladium(II)/oxazolinyl-N-heterocyclic carbene system even at low concentrations. Compounds **5** and **6** demonstrated their efficiency when using 0.5 mol% of the catalyst system. However, yields decreased when catalyst system loading was lowered to 0.1 mol% (Table 1, entries 13, 14 vs. 18, 19).

Bearing in mind that the Suzuki–Miyaura reaction involving chloroarenes requires higher catalyst loading (2.5–3 mol%),[12] we examined cross-coupling with 4-chloroacetophenone using 2.5 mol% of either **1**–**3**, **5**, or **6** and palladium(II) acetate. Among these, oxazolinyl-*N*-arylimidazolium ligand precursors **2** and **3** provided the best results; moreover, when the in situ catalyst system was decreased to 1 mol% the isolated yield was maintained (Table 1, entries 21, 22 vs. 26, 27). Going further, this coupling was carried out using 4-chlorotoluene in the presence of 2.5 mol% of ligand precursor **2** or **3** and palladium(II) acetate and the diaryl product was formed in 71% or 77% isolated yield, respectively (Table 1, entries 29, 30). Notably, catalysis with oxazolinyl-N-heterocyclic carbene ligand precursor **2** showed that coupling with either 4-chlorotoluene or the activated 4-chloroacetophenone resulted in similar isolated yields for the diaryl product as shown in Table 1, when comparing yields given in entries 29 to 21 and 29 to 26.

In summary, new simple imidazolium-based bidentate ligand precursors **1**–**3**, (*S*)-**4**, and (*S*)-**5** and bis(oxazoline) ligands **6** and (*S*,*S*)-**7** were prepared using an efficient multistep sequence. A Suzuki–Miyaura reaction was used to illustrate the activity of the palladium(II) catalyst system produced in situ from oxazolinyl-imidazolium cations **1**–**3** and (*S*)-**5** or bis(oxazoline) **6** and palladium(II) acetate. Of these, sterically hindered *N*-arylimidazolium cations **2** and **3** demonstrated their efficiency with both aryl bromides and aryl chlorides using low catalyst system loading. The synthetic protocol applied to these simple cationic ligand precursors could be adapted to a variety of oxazolinyl-N-heterocyclic carbene chiral frameworks, thereby developing their catalytic performance in asymmetric reactions.

Melting point: CTP-MP 300 hot-plate apparatus with ASTM 2C thermometer. IR (NaCl or KBr disks): Nicolet 205 FT spectrophotometer. Optical rotations $[\alpha]_D^{20}$: Perkin-Elmer 241 polarimeter using a 589 nm Na light. ^{1}H NMR: Varian Gemini 200 (200 MHz), Varian Gemini 300 (300 MHz), and Mercury 400 (400 MHz) spectrometers at 298 K with chemical shifts were referenced relative to TMS for $CDCl_3$. ^{13}C NMR: Varian Gemini 200 (50.3 MHz), Varian Gemini 300 (75.4 MHz), and Mercury 400 (100.6 MHz) spectrometers at 298 K. Chemical shifts were referenced relative to the central peak $CDCl_3$ (δ = 77.0). MS were obtained using CI or EI at 70 eV in a Hewlett-Packard spectrometer (HP-5989A model). ESI+ MS was carried out using a Waters ZQ spectrometer (Micromass Instruments). TLC: Merck precoated silica gel 60 F254 plates or Merck neutral alumina 60 F254 plates using UV light (254 nm) as a visualizing agent and/or 3% aq H_2PtCl_2–10% aq KI (1:1) or $KMnO_4$ in EtOH soln. Column chromatography: silica gel 60 ACC (Merck) or neutral alumina 90 activity II–III (Merck). Microanalyses were performed on a Carlo Erba 1106 analyzer.

2,4-Bis(chloromethyl)-1,3,5-trimethylbenzene (**10**), 2-amino-2-methylpropan-1-ol (**12**), 1-methyl-1*H*-imidazole (**17**), (*S*)-2-amino-3-methylbutan-1-ol [(*S*)-**20**], 4-bromoanisole, 4-bromoacetophenone, 4-chloroacetophenone, 4-chlorotoluene, and phenylboronic acid were purchased from commercial sources. 2,4,6-Trimethyl-1,3-phenylenediacetonitrile (**9**),[8] [3-(chloromethyl)-2,4,6-trimethylphenyl]acetonitrile (**11**),[8] 1-mesityl-1*H*-imidazole (**18**),[13] and 1-(2,6-diisopropylphenyl)-1*H*-imidazole (**19**),[13] were prepared as previously described.

[3-(Hydroxymethyl)-2,4,6-trimethylphenyl]acetonitrile (8)

To a stirred soln of **11** (0.69 g, 3.30 mmol) in anhyd dioxane (20 mL) was added a suspension of $CaCO_3$ (1.70 g, 17.01 mmol) in H_2O (20 mL); the mixture was heated to reflux temperature for 12 h. The resulting white suspension was cooled to r.t., acidified with 5 M HCl, and extracted with EtOAc (3 × 100 mL). The organic layer was washed with sat. aq Na_2CO_3 (3 × 100 mL) and dried (anhyd Na_2SO_4) and the solvent was evaporated to dryness to produce **8** (0.62 g, 99%) as a yellow solid; mp 120–122 °C.

IR (KBr): 3297, 2249, 995 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.34 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.43 (s, 3 H, CH_3), 3.63 (s, 2 H, CH_2CN), 4.69 (s, 2 H, CH_2OH), 6.93 (s, 1 H).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.6 (CH_3), 18.0 (CH_2CN), 19.5 (CH_3), 20.1 (CH_3), 59.2 (CH_2OH), 117.4 (CN), 125.7, 130.5 (CH), 135.2, 136.2, 136.3, 137.2.

MS (EI): *m*/*z* (%) = 189 [M$^+$] (24), 171 [M$^+$ – 18] (100).

Anal. Calcd for $C_{12}H_{15}NO$·0.1 EtOAc: C, 74.89; H, 8.06; N, 6.97. Found: C, 74.90; H, 8.06; N, 6.86.

(3-{[(3-Cyanomethyl-2,4,6-trimethylbenzyl)(2-hydroxy-1,1-dimethylethyl)amino]methyl}-2,4,6-trimethylphenyl)acetonitrile (13)

A soln of $Cd(OAc)_2$·2 H_2O (0.08 g, 0.30 mmol), **11** (1.25 g, 6.02 mmol), and 2-amino-2-methylpropan-1-ol (**12**, 1.08 mL, 11.29 mmol) in chlorobenzene (25 mL) was stirred at reflux temperature under an argon atmosphere for 7 d. The resulting soln was evaporated to dryness. The resulting orange oil was purified by column chromatography (silica gel, EtOAc–MeOH mixtures of increasing polarity) to provide **13** (1.08 g, 42%) as a yellow oil.

IR (KBr): 3161, 2252 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.22 [s, 6 H, $C(CH_3)_2$], 2.34 (s, 6 H, CH_3), 2.36 (s, 6 H, CH_3), 2.42 (s, 6 H, CH_3), 3.39 (s, 2 H, CH_2OH), 3.64 (s, 4 H, NCH_2), 3.77 (s, 4 H, CH_2CN), 6.93 (s, 2 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 15.7 (CH_3), 18.2 (CH_2CN), 19.6 (CH_3), 20.1 (CH_3), 23.4 (CH_3), 40.3 (NCH_2), 54.7, 68.7 (CH_2OH), 117.4 (CN), 125.8, 130.7 (CH), 134.2, 135.6, 135.9, 137.1.

MS (CI): *m*/*z* (%) = 432 [M^+ + 1] (100).

Attempted Preparation of [3-(Hydroxymethyl)-2,4,6-trimethylphenyl]acetic Acid (14)

A mixture of **8** (0.59 g, 3.12 mmol), H_2SO_4 (2.93 mL, 95–98% w/w), and H_2O (3.51 mL) was stirred and heated at reflux temperature for 6 h. The mixture was cooled to r.t. and poured into ice. The resulting brownish solid was filtered, washed with cold H_2O, and dried under vacuum, generating an unidentified product.

{3-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)methyl]-2,4,6-trimethylphenyl}methanol (15)

A soln of $Cd(OAc)_2{\cdot}2\ H_2O$ (0.60 g, 2.25 mmol), **8** (0.85 g, 4.49 mmol), and 2-amino-2-methylpropan-1-ol (**12**, 0.81 mL, 8.53 mmol) in chlorobenzene (80 mL) was stirred at reflux temperature under an argon atmosphere for 7 d. The resulting soln was evaporated to dryness. The resulting orange oil was purified by column chromatography (silica gel, hexanes–EtOAc mixtures of increasing polarity) to provide **15** (0.61 g, 52%) as a yellow oil.

IR ($CHCl_3$): 3345, 1658 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.21 [s, 6 H, $C(CH_3)_2$], 2.31 (s, 3 H, CH_3), 2.34 (s, 3 H, CH_3), 2.39 (s, 3 H, CH_3), 3.61 (s, 2 H, CH_2-oxazoline), 3.86 (s, 2 H, OCH_2), 4.66 (s, 2 H, CH_2OH), 6.87 (s, 1 H).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.6 (CH_3), 19.6 (CH_3), 20.4 (CH_3), 28.2 (CH_3), 29.2 (CH_2-oxazoline), 59.3 (CH_2OH), 66.7, 79.1 (OCH_2), 130.1 (CH), 130.4, 135.7, 136.8, 136.9, 163.9.

MS (EI): *m*/*z* (%) = 261 [M^+] (60), 242 [M^+ – 19] (100).

Anal. Calcd for $C_{16}H_{23}NO_2{\cdot}0.21$ EtOAc: C, 72.29; H, 8.89; N, 5.01. Found: C, 72.23; H, 8.98; N, 5.32.

2-[3-(Bromomethyl)-2,4,6-trimethylbenzyl]-4,4-dimethyl-4,5-dihydrooxazole (16)

To a soln of **15** (0.55 g, 1.94 mmol) in anhyd THF (30 mL) was added PBr_3 (0.18 mL, 1.94 mmol) at –20 °C under an argon atmosphere and the mixture was stirred for 1 h. It was then washed with an ice-cold sat. aq $NaHCO_3$ (30 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were dried (anhyd Na_2SO_4), filtered, and evaporated under reduced pressure to yield **16** (0.62 g, 99%) as a yellow oil, which was subjected to the next step without further purification.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.25 [s, 6 H, $C(CH_3)_2$], 2.34 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 2.40 (s, 3 H, CH_3), 3.64 (s, 2 H, CH_2-oxazoline), 3.87 (s, 2 H, OCH_2), 4.59 (s, 2 H, CH_2Br), 6.89 (s, 1 H).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.4 (CH_3), 19.2 (CH_3), 20.5 (CH_3), 28.2 (CH_3), 29.3 (CH_2-oxazoline), 30.4 (CH_2Br), 66.7, 79.1 (OCH_2), 130.2 (CH), 130.6, 131.8, 135.9, 136.8, 137.8, 163.5.

MS (EI): *m*/*z* (%) = 324 [M^+] (4), 245 [M^+ – 79] (19), 244 [M^+ – 80] (100).

(3-{[(4*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl]methyl}-2,4,6-trimethylphenyl)methanol [(*S*)-21]

A soln of $Cd(OAc)_2{\cdot}2\ H_2O$ (0.70 g, 2.64 mmol), **8** (1 g, 5.28 mmol), and (+)-(*S*)-2-amino-3-methylbutan-1-ol [(*S*)-**20**, 1.04 g, 10.04 mmol) in chlorobenzene (25 mL) was stirred at reflux temperature under an argon atmosphere for 7 d. The resulting soln was evaporated to dryness. The resulting orange oil was purified by column chromatography (neutral alumina, hexanes–EtOAc mixtures of increasing polarity) to give (*S*)-**21** (0.77 g, 53%) as a white solid; mp 112–114 °C.

$[\alpha]_D^{20}$ –36.0 (*c* 1.0, MeOH).

IR (KBr): 3191, 1651 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (d, *J* = 6.8 Hz, 3 H, *i*-Pr), 0.91 (d, *J* = 6.8 Hz, 3 H, *i*-Pr), 1.67–1.79 (m, 1 H, *i*-Pr), 2.33 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 3.66 (s, 2 H, CH_2-oxazoline), 3.81–3.92 (m, 2 H, OCH_2), 4.10–4.19 (m, 1 H, NCH), 4.70 (s, 2 H, CH_2OH), 6.89 (s, 1 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 15.7 (CH_3), 17.7 (CH_3), 18.8 (CH_3), 19.5 (CH_3), 20.4 (CH_3), 29.1 (CH_2-oxazoline), 32.2 (CH), 59.6 (CH_2OH), 66.7 (OCH_2), 71.7 (NCH), 130.2 (CH), 130.7, 134.8, 135.8, 137.0, 137.1, 165.3.

MS (EI): *m*/*z* (%) = 275 [M^+] (69), 256 [M^+ – 19] (100).

Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.12; H, 9.15; N, 5.09. Found: C, 74.19; H, 9.26; N, 5.24.

(4*S*)-2-[3-(Bromomethyl)-2,4,6-trimethylbenzyl]-4-isopropyl-4,5-dihydrooxazole [(*S*)-22]

To a soln of (*S*)-**21** (0.45 g, 1.62 mmol) in anhyd THF (25 mL) was added PBr_3 (0.15 mL, 1.62 mmol) at –20 °C under an argon atmosphere and the mixture was stirred for 1 h. It was then was washed with ice-cold sat. aq $NaHCO_3$ (30 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were dried (anhyd Na_2SO_4), filtered, and evaporated under reduced pressure to give (*S*)-**22** (0.54 g, 99%) as a yellow oil, which was subjected to the next step without further purification.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.8 Hz, 3 H, *i*-Pr), 0.92 (d, *J* = 6.8 Hz, 3 H, *i*-Pr), 1.67–1.84 (m, 1 H, *i*-Pr), 2.35 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 3.67 (s, 2 H, CH_2-oxazoline), 3.86–3.95 (m, 2 H, OCH_2), 4.10–4.22 (m, 1 H, NCH), 4.59 (s, 2 H, CH_2Br), 6.89 (s, 1 H).

Oxazolinyl-imidazolium Salts 1–5; General Procedure

[(Bromomethyl)aryl]oxazoline **16** or (*S*)-**22** (1 equiv) and N-substituted imidazoles **17**, **18**, or **19** (1.1–1.5 equiv) were dissolved in anhyd DMF and heated to 80 °C under an argon atmosphere for 12 h, and the solvent was then removed under vacuum. The white solids obtained were washed several times with Et_2O and used without further purification. The yields were not optimized.

1-{3-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)methyl]-2,4,6-trimethylbenzyl}-3-methylimidazolium Bromide (1)

The above procedure was followed using oxazoline **16** (0.50 g, 1.54 mmol), 1-methyl-1*H*-imidazole (**17**, 0.18 mL, 2.31 mmol), and anhyd DMF (5 mL). The product was obtained as a hygroscopic solid; yield: 93%.

IR (NaCl): 2967, 1733 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 [s, 6 H, $C(CH_3)_2$], 2.24 (s, 6 H, CH_3), 2.31 (s, 3 H, CH_3), 3.58 (s, 2 H, CH_2-oxazoline), 3.84 (s, 2 H, OCH_2), 4.07 (s, 3 H, CH_3-Im), 5.53 (s, 2 H, CH_2-Im), 6.94 (s, 1 H), 6.98 (s, 1 H, Im), 7.54 (s, 1 H, Im), 10.05 (s, 1 H, Im).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 16.2 (CH_3), 20.0 (CH_3), 20.4 (CH_3), 28.2 (CH_3), 29.2 (CH_2-oxazoline), 36.9 (CH_3-Im), 48.4 (CH_2-Im), 66.9, 79.1 (OCH_2), 120.8 (Im), 123.5 (Im), 126.0, 131.0 (CH), 131.7, 136.7, 136.8, 137.5 (Im), 139.4, 163.2.

MS (ESI+): *m*/*z* (%) = 326 [M]$^+$ (100), 731 [2 M + Br]$^+$ (2).

Anal. Calcd for $C_{20}H_{28}BrN_3O{\cdot}1.5\ H_2O$: C, 55.43; H, 7.21; N, 9.70. Found: C, 55.83; H, 7.18; N, 9.30.

1-{3-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)methyl]-2,4,6-trimethylbenzyl}-3-3-(2,4,6-trimethylphenyl)imidazolium Bromide (2)

The above procedure was followed using oxazoline **16** (0.73 g, 2.24 mmol), 1-mesityl-1*H*-imidazole (**18**, 0.46 g, 2.46 mmol), and anhyd DMF (6 mL). The product was obtained as a white solid; yield: 82%; mp 148–150 °C.

IR (KBr): 2967, 1734 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.21 [s, 6 H, $C(CH_3)_2$], 2.07 (s, 6 H, CH_3), 2.34–2.37 (m, 12 H, CH_3), 3.64 (s, 2 H, CH_2-oxazoline), 3.88 (s, 2 H, OCH_2), 6.02 (s, 2 H, CH_2-Im), 6.97 (s, 1 H), 7.00 (s, 2 H), 7.12 (s, 1 H, Im), 7.34 (s, 1 H, Im), 10.38 (s, 1 H, Im).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.2 (CH_3), 17.6 (CH_3), 20.1 (CH_3), 20.5 (CH_3), 21.0 (CH_3), 28.2 (CH_3), 29.3 (CH_2-oxazoline), 49.3 (CH_2-Im), 66.9, 79.2 (OCH_2), 121.9 (Im), 122.9 (Im), 126.8, 129.9 (CH), 130.6, 131.1 (CH), 131.9, 134.1, 136.8, 137.7 (Im), 137.7, 139.3, 141.4, 163.4.

MS (ESI+): *m*/*z* (%) = 430 $[M]^+$ (100), 941 $[2\ M + Br]^+$ (1).

Anal. Calcd for $C_{28}H_{36}BrN_3O{\cdot}1.7\ H_2O$: C, 62.23; H, 7.33; N, 7.78. Found: C, 62.27; H, 7.27; N, 7.42.

1-{3-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)methyl]-2,4,6-trimethylbenzyl}-3-(2,6-diisopropylphenyl)imidazolium Bromide (3)

The above procedure was followed using oxazoline **16** (0.59 g, 1.81 mmol), 1-(2,6-diisopropylphenyl)-1*H*-imidazole (**19**, 0.46 g, 1.99 mmol), and anhyd DMF (5 mL). The product was obtained as a white solid; yield: 71%; mp 132–134 °C.

IR (KBr): 2965, 1735 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.15 (d, *J* = 6.8 Hz, 6 H, *i*-Pr), 1.21 [s, 6 H, $C(CH_3)_2$], 1.23 (d, *J* = 6.8 Hz, 6 H, *i*-Pr), 2.20–2.40 (m, 11 H), 3.64 (s, 2 H, CH_2-oxazoline), 3.87 (s, 2 H, OCH_2), 6.10 (s, 2 H, CH_2-Im), 7.00 (s, 1 H), 7.13 (s, 1 H), 7.29 (s, 1 H), 7.31 (s, 1 H), 7.51–7.57 (m, 2 H, Im), 10.33 (s, 1 H, Im).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.1 (CH_3), 20.0 (CH_3), 20.5 (CH_3), 24.0 (CH_3), 24.5 (CH_3), 28.3 (CH_3), 28.7 (CH), 29.3 (CH_2-oxazoline), 49.5 (CH_2-Im), 66.9, 79.2 (OCH_2), 122.3 (Im), 123.9 (Im), 124.7 (CH), 126.9, 130.1, 131.1 (CH), 131.9, 131.9 (CH), 136.8, 137.7 (Im), 137.9, 139.3, 145.3, 163.3.

MS (ESI+): *m*/*z* (%) = 472 $[M]^+$ (100), 1025 $[2\ M + Br]^+$ (2).

Anal. Calcd for $C_{31}H_{42}BrN_3O{\cdot}2\ H_2O$: C, 63.26; H, 7.88; N, 7.14. Found: C, 63.35; H, 7.86; N, 6.74.

1-(3-{[(4*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl]methyl}-2,4,6-trimethylbenzyl)-3-methylimidazolium Bromide [(*S*)-4]

The above procedure was followed using oxazoline (*S*)-**22** (0.52 g, 1.53 mmol), 1-methyl-1*H*-imidazole (**17**, 0.18 mL, 2.31 mmol), and anhyd DMF (4 mL). The product was obtained as a hygroscopic solid; yield: 68%; ^1H NMR purity: 80%.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.84–1.00 (m, 6 H, CH_3), 1.80–1.90 (m, 1 H, *i*-Pr), 2.18–2.33 (m, 9 H, CH_3), 3.61–3.78 (m, 4 H, CH_2-oxazoline), 3.94–4.02 (m, 6 H), 5.32–5.60 (s, 2 H, CH_2-Im), 6.98 (s, 1 H, Im), 7.19 (s, 1 H), 7.42 (s, 1 H, Im), 10.26 (s, 1 H, Im).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 15.8 (CH_3), 19.3 (CH_3), 19.5 (CH_3), 20.5 (CH_3), 25.1 (CH_3), 28.6 (CH), 36.1 (CH_3-Im), 37.5 (CH_2-oxazoline), 47.9 (CH_2-Im), 56.5 (NCH), 61.4 (OCH_2), 121.2 (Im), 123.3 (Im), 126.0, 130.5 (Im), 131.0 (CH), 132.1, 136.4, 137.6, 139.5, 170.0.

MS (ESI+): *m*/*z* (%) = 358 $[M + H_2O]^+$ (100), 762 $[2\ M + Br]^+$ (2).

1-(3-{[(4*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl]methyl}-2,4,6-trimethylbenzyl)-3-(2,4,6-trimethylphenyl)imidazolium Bromide [(*S*)-5]

The above procedure was followed using oxazoline (*S*)-**22** (0.23 g, 0.69 mmol), 1-mesityl-1*H*-imidazole (**18**, 0.14 g, 0.75 mmol), and anhyd DMF (2 mL). The product was obtained as a white solid; yield: 75%; mp 130–132 °C.

$[\alpha]_D^{20}$ +4.7 (*c* 1.0, MeOH).

IR (KBr): 2959, 1731 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.82 (d, *J* = 1.0 Hz, 3 H, *i*-Pr), 0.86 (d, *J* = 1.0 Hz, 3 H, *i*-Pr), 1.74–1.86 (m, 1 H, *i*-Pr), 2.04–2.09 (m, 6 H, CH_3), 2.24–2.42 (m, 12 H, CH_3), 3.47–3.94 (m, 4 H), 4.08–4.28 (m, 1 H, NCH), 5.76–6.09 (m, 2 H, CH_2-Im), 6.95–7.05 (m, 3 H), 7.09–7.20 (m, 1 H, Im), 7.31–7.39 (m, 1 H, Im), 9.91–10.54 (m, 1 H, Im).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.2 (CH_3), 17.5 (CH_3), 17.5 (CH_3), 19.3 (CH_3), 19.4 (CH_3), 19.9 (CH_3), 20.6 (CH_3), 21.0 (CH_3), 28.8 (CH), 37.7 (CH_2-oxazoline), 48.8 (CH_2-Im), 69.8 (OCH_2), 71.6 (NCH), 122.3 (Im), 124.3 (Im), 126.9, 129.7 (CH), 129.8 (CH), 130.7, 131.2 (CH), 132.0, 133.9, 134.0, 136.8 (Im), 136.9, 137.8, 139.3, 141.0, 170.2.

MS (ESI+): *m*/*z* (%) = 444 $[M]^+$ (53), 462 $[M + H_2O]^+$ (100).

Anal. Calcd for $C_{29}H_{38}BrN_3O{\cdot}1.5\ H_2O$: C, 63.15; H, 7.49; N, 7.62. Found: C, 63.08; H, 7.45; N, 7.22.

Bis(oxazolines) 6 and (*S*,*S*)-7; General Procedure

A soln of $Cd(OAc)_2{\cdot}2\ H_2O$ (0.05 or 0.5 equiv), dinitrile **20** (1 equiv), and amino alcohol **12** or (*S*)-**20** (3.75 equiv) in chlorobenzene was stirred at reflux temperature under an argon atmosphere for 7 d and then the solvent was removed under vacuum. The oily residue was purified by column chromatography (silica gel, hexanes–EtOAc–MeOH mixtures of increasing polarity).

1,3-Bis[(4,4-dimethyl-4,5-dihydrooxazol-2-yl)methyl]-2,4,6-trimethylbenzene (6)

The above procedure was followed using $Cd(OAc)_2{\cdot}2\ H_2O$ (0.07 g, 0.25 mmol), dinitrile **9** (1 g, 5.05 mmol), 2-amino-2-methylpropan-1-ol (**12**, 1.80 mL, 18.90 mmol), and chlorobenzene (25 mL). The product was obtained as a yellow solid; yield: 79%; mp 100–102 °C.

IR (KBr): 1658 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (s, 12 H), 2.31 (s, 6 H), 2.34 (s, 3 H), 3.64 (s, 4 H, CH_2-oxazoline), 3.85 (s, 4 H, OCH_2), 6.87 (s, 1 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.3 (CH_3), 20.4 (CH_3), 24.1 (CH_3), 28.3 (CH_3), 29.6 (CH_2-oxazoline), 66.8, 79.1 (OCH_2), 130.1 (CH), 130.3, 135.9, 136.8, 164.0.

MS (EI): *m*/*z* (%) = 342 $[M^+]$ (100).

Anal. Calcd for $C_{21}H_{30}N_2O_2$: C, 73.65; H, 8.83; N, 8.18. Found: C, 73.68; H, 8.77; N, 8.18.

1,3-Bis{[(4*S*)-4-isopropyl-4,5-dihydrooxazol-2-yl]methyl}-2,4,6-trimethylbenzene [(*S*,*S*)-7]

The above procedure was followed using $Cd(OAc)_2{\cdot}2\ H_2O$ (0.67 g, 2.52 mmol), dinitrile **9** (1 g, 5.05 mmol), (+)-(*S*)-2-amino-3-methylbutan-1-ol [(*S*)-**20**, 1.95 g, 18.90 mmol), and chlorobenzene (25 mL). The product was obtained as a yellow solid; yield: 59%; mp 80–82 °C.

$[\alpha]_D^{20}$ –0.87 (*c* 1.0, MeOH).

IR (KBr): 1661 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.83 (d, *J* = 6.8 Hz, 6 H, *i*-Pr), 0.91 (d, *J* = 6.8 Hz, 6 H, *i*-Pr), 1.68–1.80 (m, 2 H, *i*-Pr), 2.32 (s, 6

H), 2.37 (s, 3 H), 3.66 (s, 4 H, CH_2-oxazoline), 3.84–3.91 (m, 4 H, OCH_2), 4.11–4.21 (m, 2 H, NCH), 6.88 (s, 1 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.4 (CH_3), 17.8 (CH_3), 18.8 (CH_3), 20.4 (CH_3), 29.4 (CH_2-oxazoline), 32.3 (CH), 69.7 (OCH_2), 71.8 (NCH), 130.1, 130.4 (CH), 135.9, 136.6, 165.4.

MS (EI): *m*/*z* (%) = 370 [M^+] (100).

Anal. Calcd for $C_{23}H_{34}N_2O_2 \cdot 0.65\ H_2O$: C, 72.27; H, 9.31; N, 7.33. Found: C, 72.19; H, 9.16; N, 7.57.

Suzuki–Miyaura Reaction with Palladium(II); General Procedure

Under an argon atmosphere, a Schlenk tube was charged with 1,4-dioxane (3 mL), $Pd(OAc)_2$ (see Table 1), ligand (see Table 1), and Cs_2CO_3 (2 mmol). The mixture was heated to 80 °C for 2 h and then the mixture was cooled to r.t. and the aryl halide (1 mmol) and arylboronic acid (1.5 mmol) were added in turn. The Schlenk tube was heated to 80 °C and stirred for 2 h. The mixture was then allowed to cool to r.t., and was purified by filtration through a pad of Celite. It was subsequently concentrated and finally purified by flash chromatography.

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