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Design and Synthesis of C_2-Symmetric N-Heterocyclic Carbene Precursors and Metal Carbenoids

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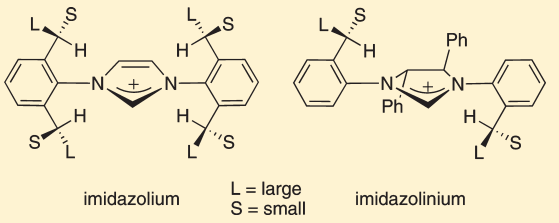
Supporting Information

ABSTRACT: Chiral, C_2-symmetric imidazolium and imidazolinium ions, as well as the corresponding copper- or silver-bound carbenoids, have been prepared. Structural study of these compounds by X-ray crystallography reveals a chiral pocket that surrounds the putative carbene site or the metal−carbene bond, at carbon 2, in three of the four ligands prepared. Preliminary investigation into the application of these complexes has shown one of them to be highly enantioselective in the hydrosilylation of acetophenone.



INTRODUCTION

N-Heterocyclic carbenes (NHCs) and their organometallic complexes have risen to prominence in recent years, in part due to their broad utility in the catalysis of numerous bond-forming reactions.[1] The field of NHC catalysis has evolved rapidly, and a variety of practical uses in synthetic chemistry have been developed.[2]

The immediate precursors to many of the useful NHC catalysts contain *N*,*N*′-diarylimidazolium and -imidazolinium rings. Removal of the C-2 proton of an imidazolium results in the formation of a carbene and retention of aromaticity, deprotonation of an imidazolinium affords a saturated carbene, and complexation of either with a metal affords a metal carbenoid (Figure 1). Consideration of the electronic attributes of each structure can prove useful in the rational design of an NHC catalyst for a given application.

One of the most versatile achiral imidazolium NHCs is the *N*,*N*′-bis(2,6-diisopropylphenyl)imidazol-2-ylidine (IPr) ligand, in which 2,6-diisopropylphenyl groups comprise the aryl substituent on the heterocycle.[3] The X-ray crystal structure of the IPrCuCl complex is displayed in Figure 2, in both wire and space-filling representations. It can be seen that the four methyls of the isopropyl groups are in close proximity to the copper atom, with an average distance of 3.840 Å. One can reasonably speculate that when the IPr NHC is used as a free carbene (organocatalyst), the catalyst-coordinated reactant would be in approximately the same place as the copper, whereas in metal-mediated catalysis, the position of the reactant would be approximately in the position of the chlorine atom, which is ∼4.8 Å distant from the four methyl groups. Analysis of the crystal structure of CuIPr led us to speculate that in NHC a stereocenter at the location of the isopropyl methine could produce a

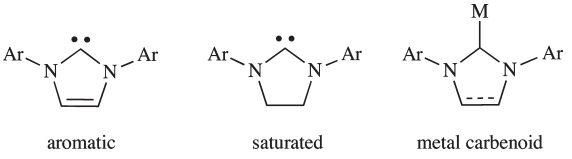


Figure 1. Common NHC structural motifs.

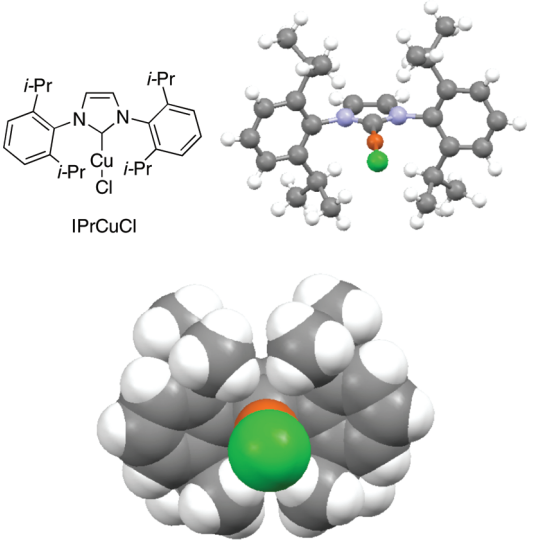


Figure 2. Crystal structure of IPrCuCl.[3]

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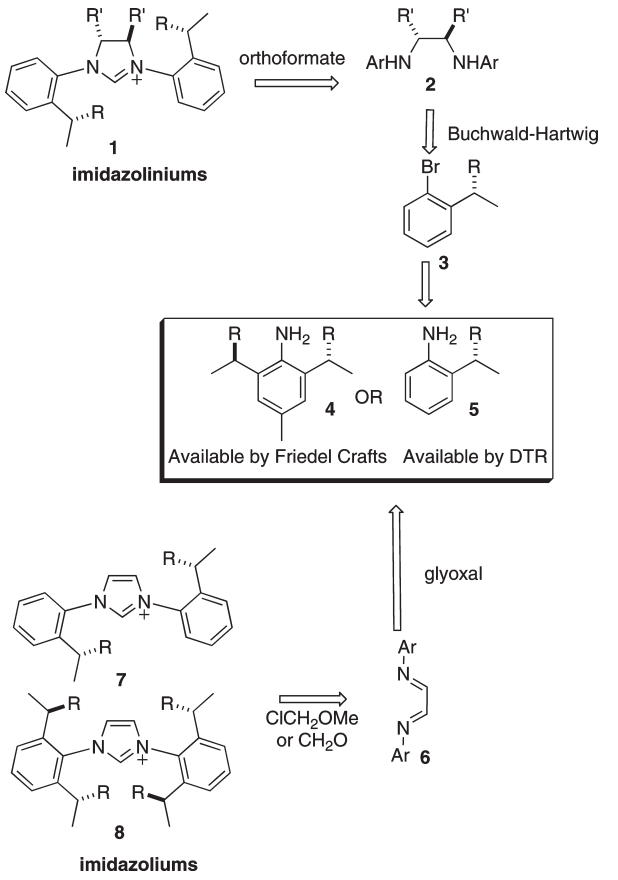
Scheme 1. Retrosynthesis Plan



compound with a well-formed chiral pocket around the catalytic reactive site. A similar chiral pocket could ensue in a C_2-symmetric imidazolinium having *trans*-2,3-diphenyl substituents on the heterocyclic ring and a single *ortho*-substituted *N*-phenyl substituent.[4] If such compounds retain synthetic versatility, they could constitute a useful class of enantioselective NHC catalysts.

A design in which the stereogenic center is γ to the annular nitrogen could produce an NHC that retains the synthetic versatility of the *N*-aryl NHC ligands and simultaneously place the reactive site in a chiral pocket if a C_2-symmetric conformation is retained. To our knowledge, NHC imidazole-derived ligands having stereocenter(s) γ to the nitrogen(s) have not yet been reported. A C_2-symmetric conformation would place two or more stereogenic centers in close proximity to the putative carbene site, whereby large groups would occupy diagonally opposite quadrants around the carbene. We therefore decided to investigate the preparation of such species, characterize them structurally by X-ray crystallography, and test them in the hydrosilylation of acetophenone.

Our decision to pursue asymmetric hydrosilylation as a test of the synthetic design was guided by the high industrial and academic utility of this transformation. The hydrosilylation of ketones provides an attractive alternative to hydrogenation, avoiding the use of expensive precious metal catalysts and harsh reaction conditions that can lead to over-reduction of the product. The resultant silyl ethers are readily cleaved to the corresponding alcohol, or alternatively the silyl group can be retained as a protecting group. Only a small number of NHC hydrosilylation catalysts have been reported to date.[5]

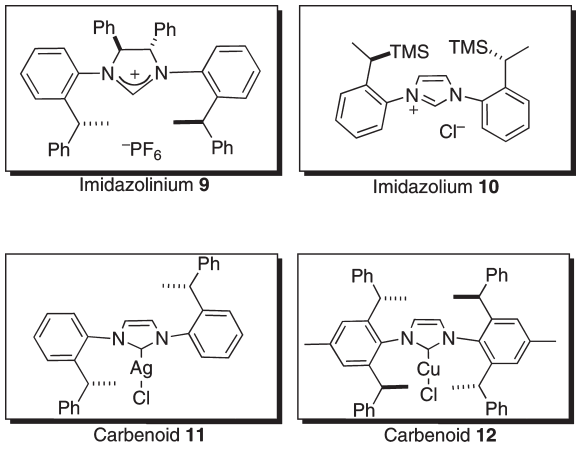


Figure 3. NHC precursors and metal carbenoids.

RESULTS AND DISCUSSION

The design we envision for chiral, C_2-symmetric imidazoliums and imidazoliniums is shown in Scheme 1, along with the retrosynthetic plans for their preparation. Cyclization of diamine **2** with an orthoformate affords imidazolinium **1**, whereas cyclization of a diimine, **6**, with a formaldehyde equivalent affords the imidazoliums **7** and **8**. The plan for the preparation of geared imidazoliniums involved Buchwald−Hartwig coupling of an *ortho*-substituted bromobenzene such as **3** with 1,2-diphenylethylenediamine. We planned to make the bromobenzene by Sandmeyer substitution of a 2-substituted aniline, **5**, which is available by dynamic thermodynamic resolution (DTR). The diimine precursor, **6**, of the imidazoliums **7** and **8** could be prepared by condensation of anilines **4** or **5** with glyoxal. The 2,6-disubstituted aniline **4** could be prepared with Friedel−Crafts-type chemistry.

According to this synthetic plan, we have succeeded in the preparation of four novel NHCs and NHC-precursors, depicted in Figure 3 as compounds **9**−**12**. Each of these compounds were characterized by X-ray diffraction and, with the exception of **10**, were found to beautifully illustrate the goal of our synthetic design. The bulk of the *o*-aryl substituents or, in the case of imidazolinium **9**, the gearing of the backbone phenyl moieties, induced the formation of a chiral pocket around C-2, with two stereocenters residing less than 5 Å from the reactive site of the catalyst.

Individual Syntheses: Imidazolinium 9. Imidazolinium **9** was derived from the enantioenriched aniline **16** (Scheme 2). This compound is in turn obtained by the acylation of commercially available 2-benzylaniline with pivaloyl chloride, followed by enantioselective methylation via dynamic thermodynamic resolution and lastly hydrolysis. Compounds **15** and **16** have previously been synthesized by Wilkinson et al.,[6] however, in much lower yield and selectivity. By conducting the DTR in methyl *tert*-butyl ether (MTBE) rather than diethyl ether and employing methyl iodide rather than methyl tosylate as the electrophile, we were able to obtain **15** in 89% yield and 95:5 er, improved from 41% yield and 78:22 er.[6] The improved enantioenrichment obtained by solvation with MTBE was first noted by Beak with the same substrate, **14**, although a methylating electrophile was not included in the scope.[7] Furthermore, the hydrolysis conditions employed below differ from those published by the Hussain group, which removed the pivaloyl group in

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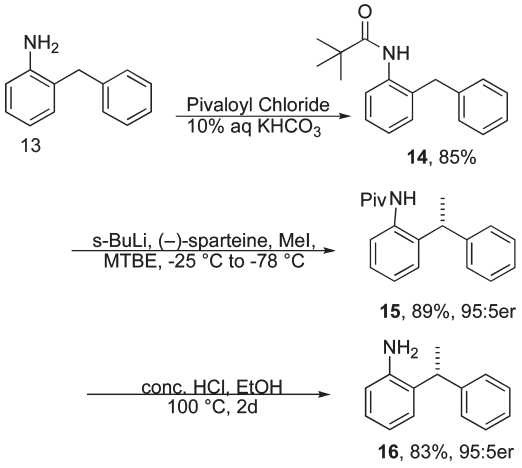
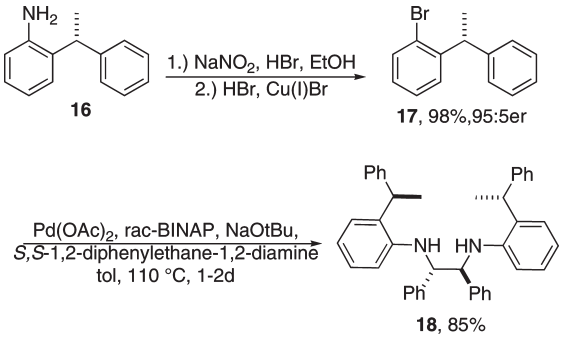
Scheme 2. Synthesis of Enantioenriched Aniline 16



Scheme 3. Synthesis of Chiral Diamine 18



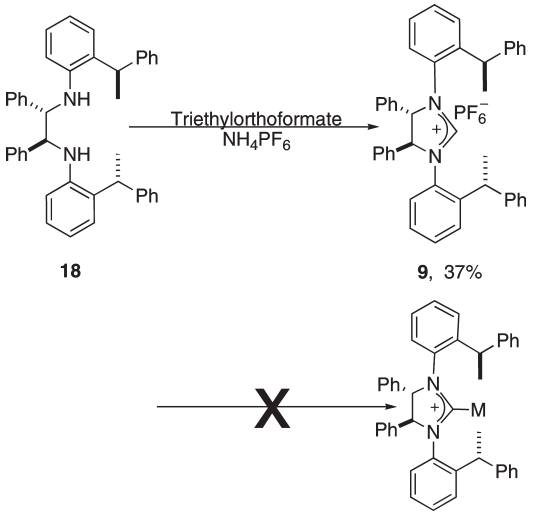
THF using $LiAlH_4$.[6] Refluxing in absolute ethanol and concentrated hydrochloric acid afforded aniline **16** in 83% yield (63% from **13**).[8] Lastly, it should be noted that our assignment of the absolute configuration as *R* was confirmed by the subsequent XRD analysis of both imidazolinium **9** and silver carbenoid **11**, although this assignment differs from that reported by the Hussain group (see Experimental Section for further details). Our assignment is consistent with the report by Beak on the (−)-sparteine-mediated DTR of compound **14**, in which electrophilic addition to the *Re* face of the benzylic carbanion was observed.[7]

Compound **16** was then converted to the corresponding aryl bromide via traditional Sandmeyer reaction conditions[9] in nearly quantitative yield and subjected to a palladium catalyzed coupling[4a] with (*S*,*S*)-1,2-diphenylethane-1,2-diamine to yield the chiral diamine **18** in 85% yield as a single diastereomer (Scheme 3).

Diamine **18** was subjected to Grubbs' cyclization protocol[4b] and gave a 37% yield of the hexafluorophosphate salt **9**, which was purified by recrystallization from ethanol. None of the numerous metalation protocols investigated allowed for the generation of an isolatable metal carbenoid from **9** (Scheme 4).

Crystals of **9** suitable for XRD were grown by slow diffusion of pentane into dichloromethane. The monoclinic crystal (β = 94.5024°) was determined to have the *P*21 space group, and a final *R* factor of 0.0433 was obtained. The crystal structure is shown in Figure 4. The Flack parameter was refined to a value of zero, providing confirmation of the absolute configuration as the (*S*,*S*,*R*,*R*) enantiomer. The phenyl groups of the *o*-aryl substituent

Scheme 4. Synthesis of Imidazolinium 9



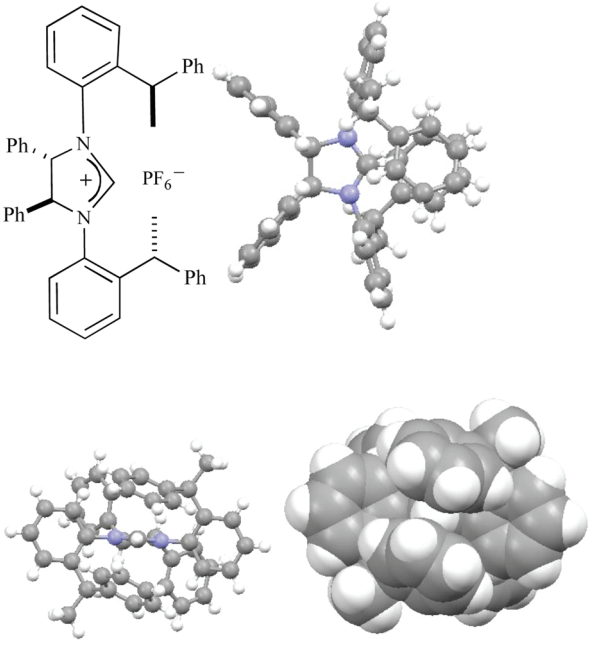


Figure 4. Crystal structure of **9**.

are geared to the front of the imidazolinium ring to avoid steric interaction with the phenyl groups of the imidazolinium backbone, thereby blocking two faces of the carbene center. Encouraged by these results, we sought to achieve the synthesis of an unsaturated NHC containing a similar chiral pocket, formed via the steric interaction of bulky *o*-aryl substituents across the face of the heterocycle rather than by the gearing effect.

Individual Syntheses: Imidazolium 10 and Silver Carbenoid 11. Imidazolium **10** was derived from the enantioenriched aniline **22** (Scheme 5). This compound was in turn synthesized by the acylation of commercially available 2-ethylaniline with pivaloyl chloride followed by dynamic thermodynamic resolution according to the method of Beak[10] and lastly hydrolysis. While this nearly quantitative hydrolysis of the enriched

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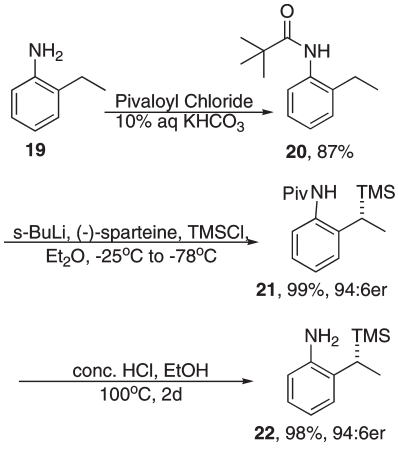
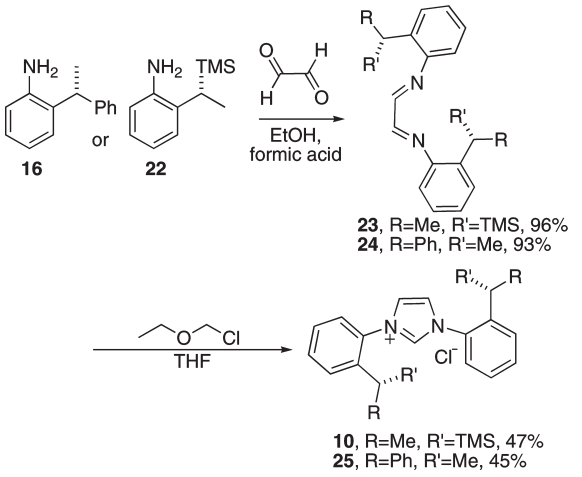
Scheme 5. Synthesis of Enantioenriched Aniline 22



Scheme 6. Synthesis of Imidazoliums 10 and 25



pivanilide is a new protocol, the DTR yielding **21** was performed with comparable yield and selectivity by Beak et al.

The acid-catalyzed condensation of chiral anilines **16** and **22** with glyoxal was achieved in excellent yield (Scheme 6). Subsequent cyclization of diimines **23** and **24** with chloromethylethylether was achieved in 47% and 45% yield, respectively. Imidazolium chlorides **10** and **25** were purified by column chromatography and obtained as single diastereomers.

Characterization of 10. Crystals suitable for X-ray crystallography were obtained for **10** through slow evaporation of a THF solution. The crystal was found to be orthorhombic and determined to have the *P*212121 space group. A final *R* factor of 0.0354 was obtained. The crystal structure is illustrated in Figure 5. The Flack parameter was refined to a value of zero, providing confirmation of the absolute configuration as the (*R*,*R*) enantiomer. We were chagrined to observe that the aryls groups reside in a conformation lacking C_2-symmetry. Both trimethylsily moieties reside on the same face of the heterocycle, indicating that the steric bulk of the *o*-aryl trimethylsilyl substituents is insufficient to enforce C_2-symmetry and create the desired chiral pocket. Our work was consequently focused on the metalation and characterization of **25**.

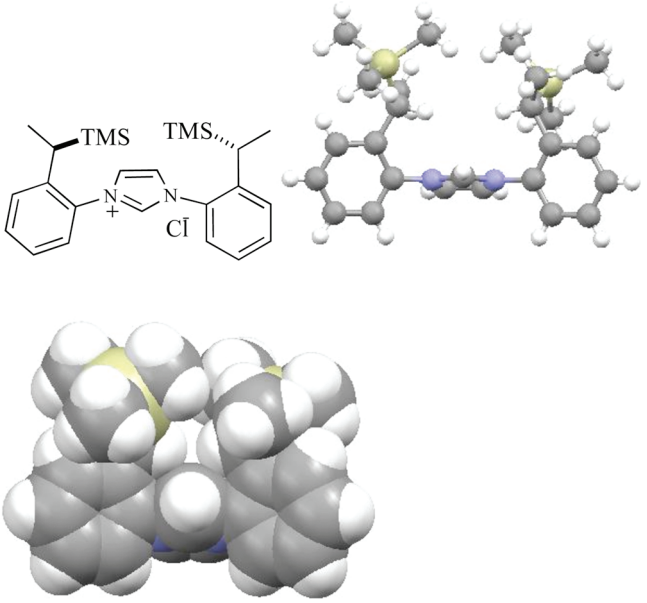
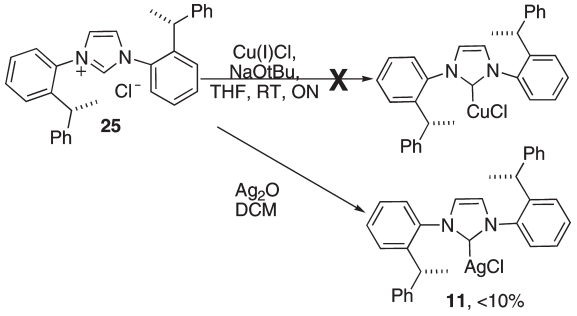


Figure 5. Crystal structure of **10**.

Scheme 7. Synthesis of Silver Carbenoid 11



The metalation of imidazolium chloride **25** was complicated by its decomposition to a formamidine in the presence of base. Even mild organic bases induced decomposition, but a protocol by Wang and Lin[11] utilizing silver(II) oxide as both base and metal source provided for the isolation of **11** in low yield (Scheme 7).

Characterization of 11. Crystals of **11** suitable for X-ray diffraction were grown by slow evaporation of a dichloromethane solution. The monoclinic crystal ($\beta = 116.653°$) was determined to have the *C*2 space group, and a final *R* factor of 0.0409 was obtained. The crystal structure is presented in Figure 6. The Flack parameter was refined to a value of zero, providing confirmation of the absolute configuration as the (*R*,*R*) enantiomer. The crystal structure of the silver carbenoid reveals a nicely formed chiral pocket and served to confirm the rationale of our synthetic design. To our knowledge, compound **11** represents the first example of a structural gearing effect induced not by placement of bulky substituents on the backbone of a saturated imidazolinium but via transannular steric interaction of bulky substituents γ to nitrogen in an unsaturated imidazolium. Nevertheless, the low-yielding metalation step provides a major limitation in the future utility of compound **11** in asymmetric catalysis. Our efforts were thus concentrated on the synthesis of an enantioenriched 2,6-disubstituted aniline.

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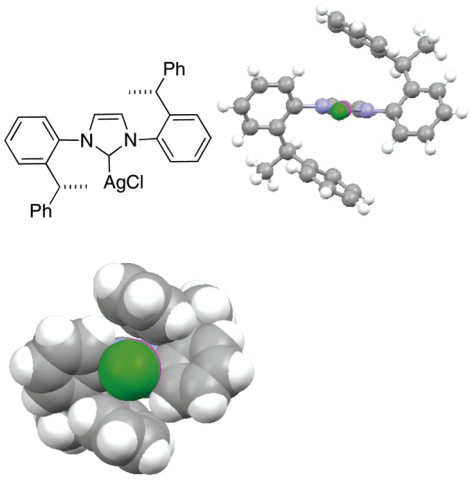
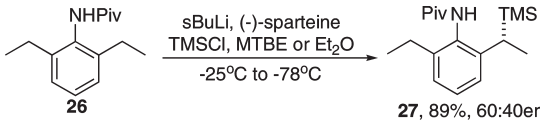


Figure 6. Crystal structure of **11**.

Scheme 8. DTR of 2,6-Diethylpivanilide



Individual Syntheses: Copper Carbenoid 12. We surmised that increasing structural rigidity via the use of a di-*ortho*-substituted aniline precursor could yield a more promising final structure. Initial investigation led us to attempt a lithiation/DTR of 2,6-diethylpivanilide (Scheme 8). While this transformation proceeds in a yield comparable to that of the singly substituted pivanilides, the enantioselectivity is poor (60:40 er).

Numerous methodologies were investigated in attempts to synthesize an enantioenriched 2,6-disubstituted aniline. Ultimately, Friedel−Crafts-type chemistry was employed for the di-*ortho*-substitution of toluidine with either phenylacetylene followed by reduction or styrene, protocols published by Tarantola[12] and Coates,[13] respectively (Scheme 9). Although lengthier by one step, the Tarantola route was found to be a higher-yielding and cleaner way to access compound **28** as a mixture of a racemate and a *meso* diastereomer. This mixture was separated via stacked injection into a semipreparative chiral stationary phase SFC (Figure 7).

Each of the stereoisomers were independently analyzed. It was found that the first to elute is (+)-**28**, the second is (−)-**28**, and the third is the optically inactive *meso* **28**. Subsequent XRD analysis of the copper carbenoid **12**, prepared from (+)-**28**, revealed it to be the (*S*,*S*) enantiomer (see below).

The following synthesis was optimized with *meso*-**28**, as it has no potential in asymmetric catalysis. For clarity's sake, we will illustrate the synthesis with (+)-(*S*,*S*)-**28**. Enantioenriched aniline (+)-(*S*,*S*)-**28** was condensed with glyoxal in quantitative yield to give diimine (*S*,*S*)-**29** (Scheme 10). The cyclization and purification of this product, however, required extensive optimization. Fortunately, minimal revisions to a cyclization protocol by Markó,[14] which utilizes zinc chloride to coordinate the diimine in the reactive *s-cis* conformation, provided for isolation of pure (*S*,*S*,*S*,*S*)-**30** in 87% yield after recrystallization.

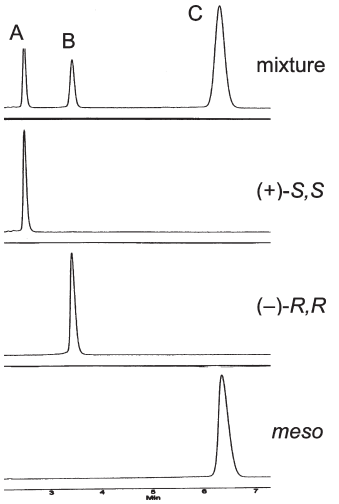


Figure 7. Analytical results of the preparative separation of the stereoisomers of **28**.

When *meso*-**28** was condensed and cyclized, some interesting stereochemical features were discovered in the characterization of *meso*-**30**. The NMR spectra exhibited quadrupling of the aliphatic signals. Further consideration of this phenomenon led us to conclude that *meso*-**30** exists as a mixture of three rotamers (Figure 8). We hypothesize that conformer A is the most highly populated species: one can imagine that the cyclization of the diimine to the imidazolium is facilitated by a conformation that places the forming imidazole carbon in the least sterically hindered environment. Rotation around both *N*-aryl bonds would give conformer B,[15] likely the least populated species because carbon 2 is in a highly crowded environment in the midst of four bulky phenyl groups. Rotation around only one of the rightmost *N*-aryl bonds of A or B gives compound C. The two depictions of compound C are identical; however, the methyl groups γ to the heterocyclic nitrogen are diastereotopic, resulting in their nonequivalence in the proton NMR spectrum.

Imidazolium chlorides (*R*,*R*,*R*,*R*)-**30** and (*S*,*S*,*S*,*S*)-**30** were both subjected to metalation in the presence of copper(I) chloride and NaO*t*-Bu (Scheme 11). Copper carbenoids (*R*,*R*,*R*,*R*)-**12** and (*S*,*S*,*S*,*S*)-**12** were obtained in good yield via this protocol.

Crystals of (*S*,*S*,*S*,*S*)-**12** suitable for X-ray diffraction were grown by slow diffusion of hexanes into ether. The monoclinic crystal (β = 115.097°) was determined to have the *C*2 space group; a final *R* factor of 0.0438 was obtained. The crystal structure is presented in Figure 9. The Flack parameter was refined to a value of zero, establishing the absolute configuration as the (*S*,*S*,*S*,*S*). We were pleased to observe the formation of a chiral pocket at the site of the putative carbene. Compound **12** successfully places four stereocenters in close proximity to the C-2 reactive site.

Application. Of the four novel NHC precursors and metal carbenoids we were able to access synthetically, three served to confirm the feasibility of the design motif. With these compounds in hand, we set out to test this new class of NHCs in an enantioselective reaction. The hydrosilylation of prochiral ketones provides access to enantioenriched alcohols without the use of high pressure reactors and expensive metal catalysts. Simmons and Hartwig recently showed that racemic (hydrido)-silyl ethers of 1-phenyl alcohols can be used to activate the

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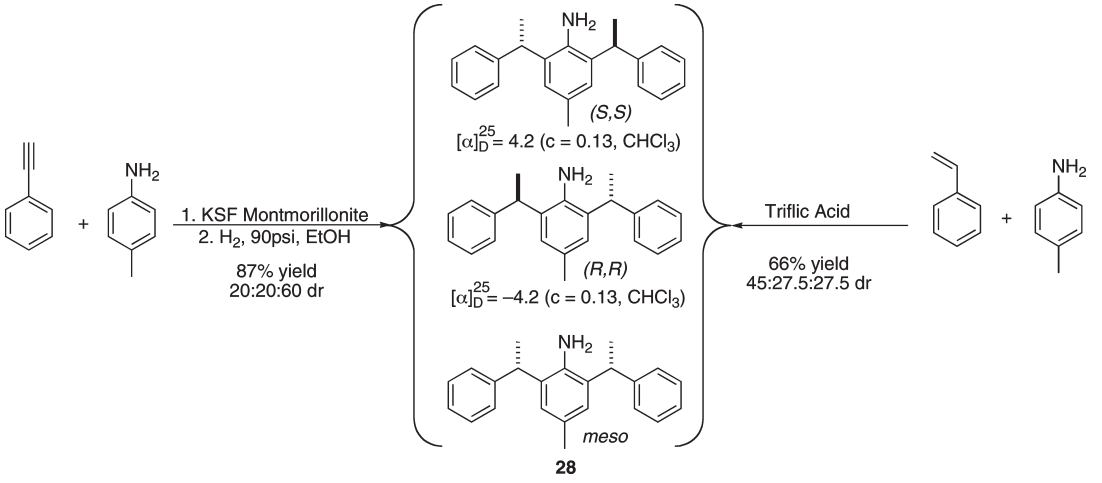
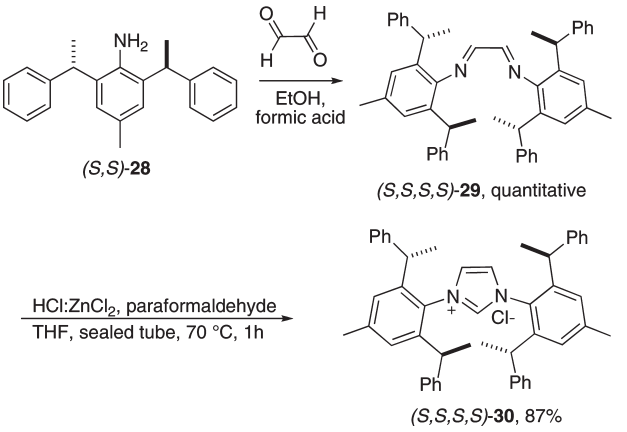
Scheme 9. Syntheses of 28 as a Mixture of Stereoisomers



Scheme 10



ortho C−H bond to make benzoxasiloles, which can then be further functionalized in a number of useful ways.[16] Furthermore, the catalytic cycle using the CuIPr NHC has been studied in detail.[17] As our novel class of metal bound NHCs and NHC precursors can be considered chiral analogues of the CuIPr NHC, with chiral centers incorporated at the location of the isopropyl methine, we chose this transformation for the investigation of compounds **9**, **11**, and **12** as asymmetric catalysts (Scheme 12 and Table 1).

Imidazolinium **9** was found to be the least effective in the hydrosilylation of acetophenone, achieving only minimal conversion to the silylether after 24 h. The enantioselectvity of the transformation was very poor. Unsaturated imidazoliums **25** and **12** were found to give nearly quantitative conversion to the silylether at room temperature in 4 and <1 h, respectively. Whereas **25** yields the product with only very moderate enantioenrichment, **12** provides for isolation of nearly enantiopure silylether. The absolute configuration of the silylether was determined by co-injection of an enantiopure authentic sample and found to be *S* when using the (*R*,*R*,*R*,*R*) stereoisomer of **12**.

The usually accepted[18] catalytic cycle (Scheme 13) proceeds via the formation of a copper hydride followed by coordination of the ketone and σ bond metathesis. There is precedent for the in situ formation of the copper carbenoid,[19] so imidazolinium **9** and imidazolium **25**, for which we lack efficient metalation procedures, were investigated in this manner.

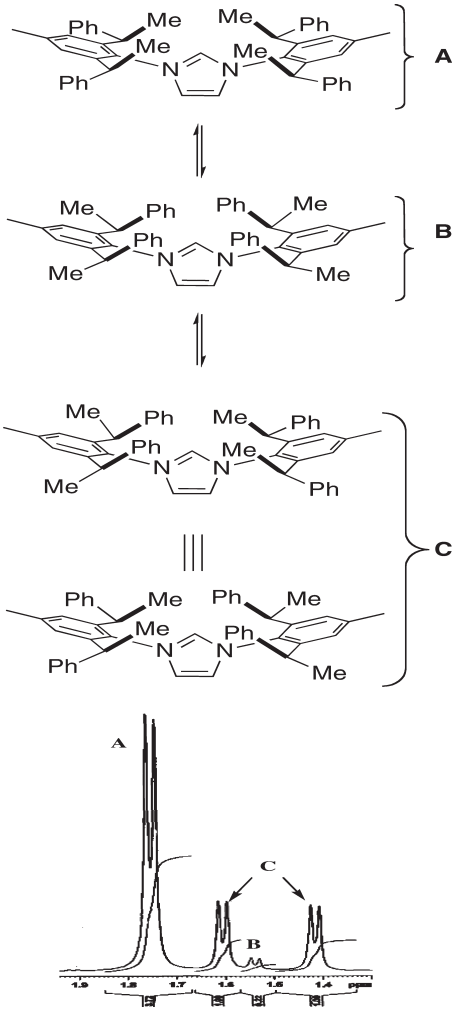


Figure 8. Rotamers of *meso*-**30**.

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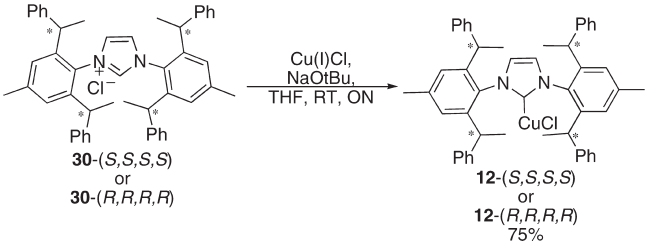
Scheme 11. Synthesis of Copper Carbenoid 12



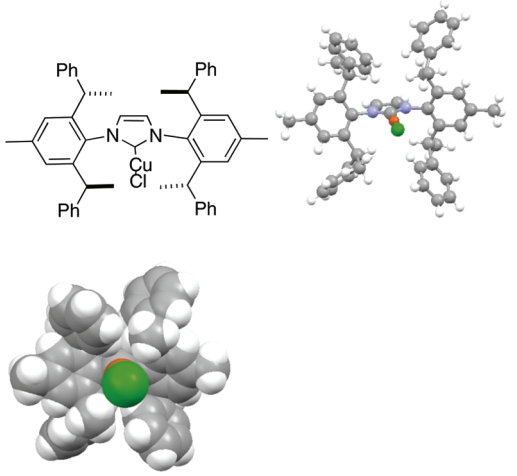
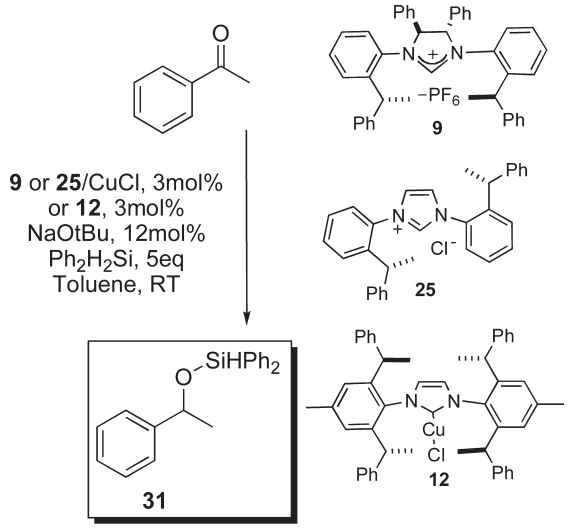


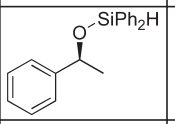
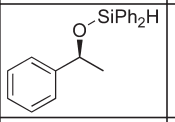
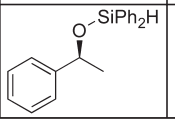
Figure 9. Crystal structure of (*S*,*S*,*S*,*S*)-**12**.

Scheme 12. Hydrosilylation of Acetophenone



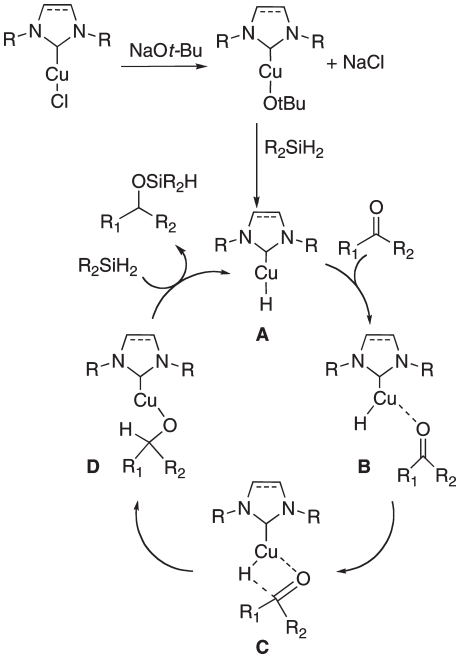
In order to obtain better insight into the steric course for the hydrosilylation of acetophenone catalyzed by **12**, a DFT minimization (B3LYP 3-21 g-d) was carried out on two conformations of intermediate **B** in the catalytic cycle using the PQS ab initio molecular modeling software.[20] The minimized structures are shown in Figure 10, with two of the *ortho N*-aryl substituents drawn as R groups for clarity. In the lowest energy conformation of **B**, the copper, the hydride, and the carbonyl of acetophenone

Table 1. Hydrosilylation of Acetophenone

Catalyst	Time (h)	Product	%conversion* (er, *S*:*R*)
9	24		29 (60:40)
25	4		95 (73:27)
12	0.75		100 (98:2)

*Determined by GC.

Scheme 13. Hydrosilylation Catalytic Cycle[18]



lie in a common plane, and more critically, this plane is roughly orthogonal to the plane of the heterocycle. Recalling that **12** has C_2-symmetry, examination of the minimized structures reveals that the phenyl group of acetophenone preferentially resides in the less crowded upper right quadrant and thereby exposes the *Re* face of the carbonyl to the hydride residing on copper. Delivery of the hydride in this manner would lead to formation of the (*S*)-enantiomer of the silyl ether, as is observed experimentally. The relative energy between these two intermediates was found to be 3.6 kcal/mol.

SUMMARY AND CONCLUSION

New, chiral C_2-symmetric NHC ligands have been prepared. These NHCs and metal carbenoids exhibit the structural motif of having two or four stereocenters γ to the heterocyclic nitrogen. The imidazolinium **9** induces these chiral "arms" to reside in

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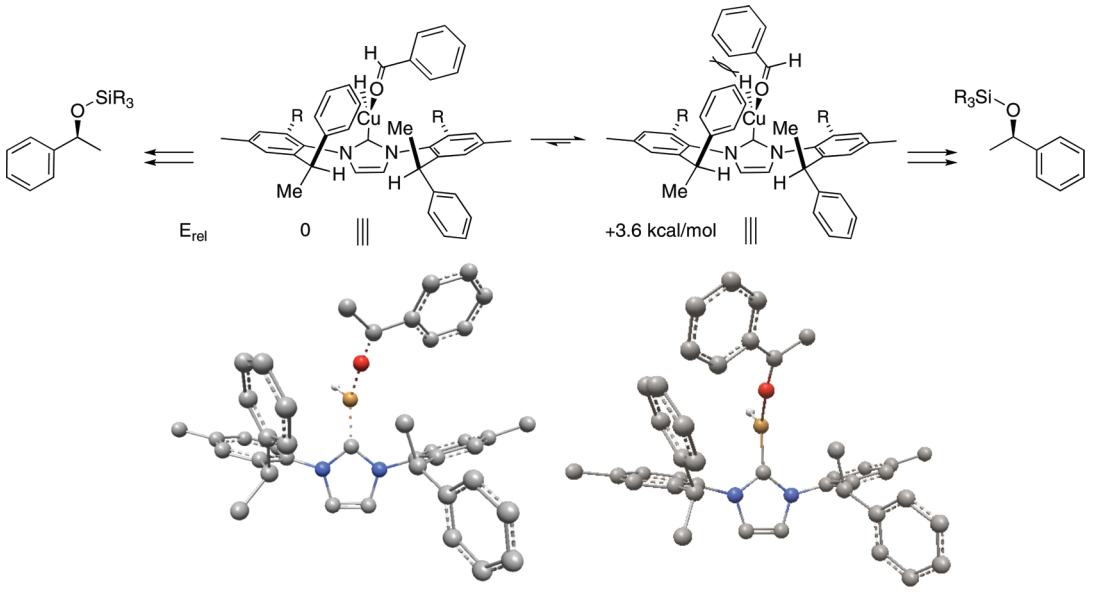

Figure 10. DFT Minimization of Intermediate **B**.

close proximity to the putative carbene via the gearing effect, while the conformation of metal carbenoid **11** is geared by transannular steric interaction of the bulky *o*-aryl substituents. Copper carbenoid **12**, CuPhEt, has little conformational mobility, and so the chiral pocket created by the α-phenethyl arms is essentially fixed. Initial investigation into the application of this novel class of NHCs has revealed **12** to be a powerful catalyst for the hydrosilylation of acetophenone, achieving this transformation at room temperature in 45 min in quantitative conversion and high enantiopurity. Further investigation into the mechanism, stereoselectivity, and application of these catalysts is ongoing and will be reported in due course.

EXPERIMENTAL SECTION

General. All reagents and solvents were used as received, unless indicated below. Diethyl ether (Et_2O), *tert*-butyl methyl ether (MTBE), and tetrahydrofuran (THF) were distilled over Na/benzophenone ketyl under N_2 immediately prior to use. Toluene was dried over CaH_2 followed by distillation and storage over 3 Å molecular sieves. Methylene chloride was distilled over CaH_2 under N_2 immediately prior to use. *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) was vacuum distilled over CaH_2 and stored over 4 Å molecular sieves. (−)-Sparteine was vacuum distilled over CaH_2 and stored over 4 Å molecular sieves. Solutions of *s*-BuLi in cyclohexane were titrated against *N*-pivaloyl-*o*-benzaniline. ^{1}H NMR spectra were collected at 300 or 400 MHz in $CDCl_3$ unless otherwise noted. Coupling constants (*J*) are reported in Hz. Supercritical fluid chromatography was used to determine enantiomer ratios on a Daicel Chiracel OD-H column or a Whelk-O column using absolute ethanol as modifier. Details of these separations can be found in the Supporting Information.

Compounds **13** and **19** are commercially available and were used as received without further purification. The following compounds have been previously reported, and their spectra were consistent with that of the published data: pivanilides **14**, **15**, **20**, **21**;[6,10] anilines **16**,[6] **28**;[13] aryl bromide **17**;[21] and diphenylsilylether **31**.[22]

The characterization of the following compounds is detailed below: imidazolinium **9**; imidazoliums **10**, **25**, **30**; silver carbenoid **11**; copper carbenoid **12**; diamine **18**; aniline **22**; diimines **23**, **24**, **29**; and pivanilides **27**, **29**, **30**. If synthesized according to a known procedure, the reference is given. Any alterations to the published procedure are noted. Otherwise details of the synthetic protocol can be found below.

General Procedure for Dynamic Thermodynamic Resolution. To an oven-dried, argon-purged, 250 mL round-bottom flask was added the pivanilide **14**, **20**, or **26** (14.6 mmol) in 120 mL of freshly distilled MTBE or Et_2O, and the mixture was cooled to −25 °C. Some crystallization occurs. To this was added dropwise 35 mL of 1.4 M *s*-BuLi in cyclohexane (49.0 mmol). After 2 h, (−)-sparteine (50.0 mmol) was added, and the mixture was stirred for 45 min and then rapidly cooled to −78 °C. After 30 min, the electrophile (TMSCl or MeI, 29.5 mmol) was added, and the mixture was stirred for 16 h. The reaction was quenched with 15 mL of MeOH followed by 15 mL of water and warmed to room temperature. The contents were transferred to a separatory funnel, diluted with 50 mL of water, and washed with 3 × 25 mL of EtOAc. The combined organic layers were washed with 3 × 20 mL of 5% H_3PO_4, and 3 × 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a pale tan oil that was used without further purification for subsequent reactions (89−99% yield). An analytical sample was prepared by radial chromatography on silica, eluting with 95% hexanes/4.5% EtOAc/0.5% NH_4OH followed by recrystallization via slow evaporation of hexanes. NMR data of **15** and **21** match the literature data.[6,10]

***N*-(2-Ethyl-6-(1-(trimethylsilyl)ethyl)phenyl)pivalamide (*R*)-27.** ^{1}H NMR ($CDCl_3$): −0.0 (9H,s), 1.2 (3H, t, *J* = 7.5), 1.3 (3H, d, *J* = 7.5), 1.4 (9H, s), 2.3 (1H, q, *J* = 7.5), 2.5 (2H, q, *J* = 7.5), 6.7 (1H, bs), 7.0 (2H, m), 7.2 (1H, t, *J* = 7.6). ^{13}C NMR ($CDCl_3$): −2.8 (CH_3), 14.7 (CH_3), 15.7 (CH_3), 23.6 (CH), 25.5 (CH_2), 28.0 (CH_3), 39.4 (C), 124.9 (2-CH), 127.7 (CH), 131.9 (C), 141.5 (C), 144.0 (C), 176.6 (C). MS (CI/MH+): 306. Anal. Calcd for $C_{18}H_{31}NOSi$: C, 70.76; H, 10.23. Found: C, 70.62; H, 10.26. er = 60:40.

General Procedure for Pivanilide Hydrolysis. To a 100 mL round-bottom flask equipped with a stir bar were added the pivanilide (2.88 mmol), absolute ethanol (30 mL), and concentrated hydrochloric acid (30 mL). The reaction solution was fitted with a condenser and refluxed at 100 °C for 2d after which time the reflux condensor was replaced with a distillation short path, and the reaction volume was reduced to approximately 5 mL. The crude reaction solution was then cooled to room temperature, diluted with diethyl ether, and neutralized with potassium hydroxide. The organic layer was extracted thrice with

diethyl ether (10 mL) and washed with distilled water before drying over $MgSO_4$. The reaction solution was filtered and concentrated in vacuo to give the corresponding anilide.

2-(1-Phenylethyl)benzenamine (*R*)-16. ^{1}H NMR ($CDCl_3$): 1.7 (3H, d, J = 7.2), 3.5 (2H, s), 4.1 (1H, q, J = 7.2), 6.7 (1H, dd, J = 1.2, 7.8), 6.9 (1H, dt, J = 1.2, 7.5), 7.1 (1H, dt, J = 1.5, 7.5), 7.2−7.3 (3H, m), 7.3−7.4 (3H, m). ^{13}C ($CDCl_3$): 22.0 (CH_3), 40.4 (CH), 116.4 (CH), 118.9 (CH), 126.6 (CH), 127.4 (CH), 127.6 (CH), 128.9 (CH), 129.9 (C), 144.5 (C), 145.8 (C). MS (CI/MH+): 198. Anal. Calcd for $C_{14}H_{15}N$: C, 85.24; H, 7.66. Found: C, 85.27; H, 7.75.[6] er = 95:5.

2-(1-(Trimethylsilyl)ethyl)benzenamine (*R*)-22. ^{1}H NMR ($CDCl_3$): 0.0 (9H, s), 1.4 (3H, d, J = 7.5), 2.1 (1H, q, J = 7.5), 3.5 (2H, bs), 6.7 (1H, dd, J = 1.2, 7.8), 6.8 (1H, dt, J = 1.2, 7.5), 6.9−7.0 (2H, m). ^{13}C NMR ($CDCl_3$): −2.7 (CH_3), 15.4 (CH_3), 22.3 (CH), 116.0 (CH), 119.3 (CH), 125.1 (CH), 127.0 (CH), 131.2 (C), 143.1 (C). MS (CI/MH+): 194. Anal. Calcd for $C_{11}H_{19}NSi$: C, 68.33; H, 9.90. Found: C, 68.23; H, 9.93. er = 94:6.

General Procedure for Sandmeyer Reaction. The following is revised from the published protocol for a different aniline substrate.[9] To a 50 mL round-bottom flask was added $NaNO_2$ (14.5 mmol) in 10 mL of DMSO. To this solution were added CuBr (7.0 mmol) and the aniline substrate **16**, (3.9 mmol). The resulting suspension was cooled to 0 °C and treated dropwise with a solution of HBr (5 mL, 48%) in DMSO (10 mL). The reaction solution was stirred for an additional 30 min before warming to room temperature and stirring for 1 h. The reaction solution was then transferred to a separatory funnel, diluted with water (50 mL), and washed with diethyl ether (3 × 20 mL). The combined organic layers were washed with water (3 × 15 mL), then dried over $MgSO_4$, filtered, and concentrated in vacuo.

1-(1-(2-Bromophenyl)ethyl)benzene (*R*)-17. ^{1}H NMR ($CDCl_3$): 1.7 (3H, d, J = 7.2), 4.7 (1H, q, J = 7.2), 7.1 (1H, m), 7.2−7.4 (7H, m), 7.6 (1H, dd, J = 1.2, 7.8). ^{13}C NMR ($CDCl_3$): 21.5 (CH_3), 43.7 (CH), 125.0 (C), 126.4 (CH), 127.8 (CH), 127.9 (CH), 128.0 (CH), 128.5 (CH), 129.0 (CH), 133.1 (CH), 145.1 (C), 145.6 (C). MS (EI): 260.262. er = 95:5. As compound **17** was reported in 1973,[21] we have included our spectra in the Supporting Information to provide more detailed characterization.

1,2-Diphenyl-*N*,*N*′-bis[(*R*)-2-(1-phenyl-ethyl)-phenyl]-ethane-(*S*,*S*)-1,2-diamine 18. (New compound synthesized with a previously published procedure.[4a]) ^{1}H NMR ($CDCl_3$): 1.6 (6H, d, J = 7.2), 3.9 (2H, q, J = 7.2), 4.2 (2H, d, J = 6.3), 4.5 (2H, d, J = 6.9), 6.4 (6H, d, J = 7.5), 6.7 (2H, dt, J = 0.6, 7.5), 6.9 (4H, m), 7.0 (4H, m), 7.1−7.2 (8H, m), 7.3 (4H, m). ^{13}C NMR ($CDCl_3$): 22.3 (CH_3), 40.1 (CH), 61.9 (CH), 112.1 (CH), 117.4 (CH), 126.3 (CH), 126.8 (CH), 127.4 (CH), 127.5 (CH), 127.8 (CH), 128.0 (CH), 128.2 (CH), 128.8 (CH), 130.0 (C), 139.2 (C), 144.0 (C), 145.7 (C). MS (ESI/MH+): 573. Anal. Calcd for $C_{42}H_{40}N_2$: C, 88.07; H, 7.04. Found: C, 88.25; H, 7.20. Single diastereomer.

(*S*,*S*)-4,5-Diphenyl-1,3-bis[(*R*)-2-(1-phenyl-ethyl)-phenyl]-4,5-dihydro-3*H*-imidazol-1-inium; hexafluorophosphate 9. (New compound synthesized with a previously published procedure.[4b]) ^{1}H NMR ($CDCl_3$)1.2 (6H, d, J = 6.9), 3.9 (2H, q, J = 6.9), 5.8 (2H, s), 6.9 (4H, d, J = 7.5), 7.1−7.4 (22H, m), 7.5 (1H, s). ^{13}C NMR ($CDCl_3$): 22.8 (CH_3), 39.5 (CH), 76.5 (CH), 127.2 (CH), 127.5 (CH), 128.6 (CH), 128.7 (CH), 128.8 (CH), 129.2 (CH), 129.3 (CH), 130.0 (CH), 130.8 (CH), 130.8 (CH), 132.1 (C), 132.4 (C), 140.4 (C), 144.8 (C), 157.3 (CH). MS (ESI/-PF_6): 583. Anal. Calcd for $C_{42}H_{40}N_2 \cdot 1/2\ H_2O$: C, 70.00; H, 5.46. Found: C, 69.83; H, 5.33. XRD analysis of **9** resulted in refinement of the Flack parameter to a value of zero, providing confirmation of the absolute configuration as (*S*,*S*,*R*,*R*).

General Procedure for Glyoxal Condenstion and Cyclization of 16 and 22. To a 25 mL round-bottom flask was added chiral aniline **16** or **22** (5.80 mmol) in 3 mL of EtOH. To this was added 40% glyoxal (2.9 mmol). The reaction mixture was refluxed and monitored by TLC until all starting material had been consumed, taking approximately 2 h. The contents were then concentrated in vacuo to a dark purple foam. After drying, the product (**23** or **24**) was recovered (93−96% yield), and 2.7 mmol was added to a 50 mL round-bottom flask under inert atmosphere. To this were added chloromethylethylether (3.5 mmol) in 5 mL of THF and a couple of drops of water. This was stirred at 50 °C for 16 h. The contents were concentrated in vacuo and purified by silica column chromatography 2% MeOH/DCM. The resulting residue was sonicated in ether and filtered (45−47% yield). These diimines were used without further purification.

***N*,*N*′-Bis{2-[1-(trimethyl-silanyl)-ethyl]-phenyl}-ethane-1,2-diylidenediimine (*R*,*R*)-23.** ^{1}H NMR ($CDCl_3$): −0.098 (18H, s), 1.4 (6H, d, J = 7.8), 3.1 (2H, q, J = 7.8), 6.9−7.1 (2H, m), 7.1−7.3 (6H, m), 8.3 (2H, s).

***N*,*N*′-Bis[2-(1-phenyl-ethyl)-phenyl]-ethane-1,2-diylidene-diimine (*R*,*R*)-24.** ^{1}H NMR ($CDCl_3$): 1.7 (6H, d, J = 7.2), 4.8 (2H, J = 7.2), 6.9−7.4 (18H, m), 8.2 (2H, s).

1,3-Bis{2-[1-(trimethyl-silanyl)-ethyl]-phenyl}-1*H*-imidazolium Chloride (*R*,*R*)-10. ^{1}H NMR ($CDCl_3$): −0.066 (18H, s), 1.4 (6H, d, J = 7.2), 1.9 (2H, q, J = 7.2), 7.2−7.3 (4H, m), 7.4−7.5 (2H, m), 7.6−7.7 (2H, m), 8.2 (2H, d, J = 7.8). 9.4 (1H, s). ^{13}C NMR ($CDCl_3$): −2.7 (CH_3), 16.6 (CH_3), 23.8 (CH), 124.8 (CH), 126.7 (CH), 128.2 (CH), 128.8 (CH), 131.4 (CH), 132.4 (CH), 137.9 (C), 141.7 (C). ESI (MS/-Cl): 421. Anal. Calcd for $C_{25}H_{37}\ ClN_2Si_2$: C, 65.68; H, 8.16. Found: C, 65.41; H, 8.23. Single diastereomer. XRD analysis of **10** resulted in refinement of the Flack parameter to a value of zero, providing confirmation of the absolute configuration as (*R*,*R*).

1,3-Bis[2-(1-phenyl-ethyl)-phenyl]-1*H*-imidazolium Chloride (*R*,*R*)-25. ^{1}H NMR ($CDCl_3$): 1.6 (6H, d, J = 6.9), 4.3 (2H, q, J = 6.9), 6.9 (4H, m), 7.1−7.3 (8H, m), 7.4−7.5 (4H, m), 7.5−7.7 (4H, m), 8.9 (1H, s). ^{13}C NMR ($CDCl_3$): 22.8 (CH_3), 39.9 (CH), 124.7 (CH), 127.0 (CH), 127.1 (CH), 127.9 (CH), 128.5 (CH), 129.0 (CH), 129.2 (CH), 131.9 (CH), 133.7 (C), 140.6 (C), 145.6 (C). ESI-FTMS calcd $[M^+]$ $C_{31}H_{29}N_2$ $[M]^+$ = 429.2331, found $[M]^+$ = 429.2328. Single diastereomer.

4-Methyl-2,6-bis(1-phenylethyl)benzenamine (mixture of stereoisomers)-28. A 25 mL round-bottom flask equipped with a stir bar was charged with toluidine (10.0 mmol), KSF montmorillonite (1.0 g), and phenyl acetylene (40.0 mmol). The round-bottom was fitted with a reflux condenser, and the heterogeneous slurry was refluxed with vigorous stirring at 140 °C for 8 h. The reaction vessel was allowed to cool to room temperature before dilution with ethyl acetate and filtration. The solvent was removed from the mother liquor under reduced pressure, and the resultant red oil was purified via column chromatography with 50:50 dichloromethane and hexanes. The product (4-methyl-2,6-bis(1-phenylvinyl)benzenamine) was obtained as an off-white solid in 88% yield. ^{1}H NMR ($CDCl_3$): 2.2 (3H, s), 3.3 (2H, s), 5.3 and 5.7 (4H, dd), 6.9 (2H, s), 7.1−7.4 (10H, m). ^{13}C NMR ($CDCl_3$): 20.5, 116.2, 126.5, 127.8, 128.3, 128.7, 131.0, 139.3, 139.9, 147.5. A Parr shaker was charged with 4-methyl-2,6-bis(1-phenylvinyl)benzenamine (8.8 mmol), 10% w/w Pd/C (0.88 mmol), and absolute ethanol (25 mL). The shaker was thrice purged with hydrogen before it was pressurized to 90 psi and shaken overnight. The black hetergeneous solution was filtered, and the solvent was removed from the mother liquor under reduced pressure to give compound **28** in nearly quantitative yield (99%) with a diastereomer ratio of 60:20:20. The details of the preparative separation of **28** can be found in the Supporting Information.

***N*,*N*′-Bis[4-methyl-2,6-bis(1-phenylethyl)phenyl]-ethane-1,2-diylidenediimine 29.** To a 25 mL round-bottom flask was added chiral or meso aniline **28** (5.80 mmol) in 3 mL of EtOH. To this were added 40% glyoxal (2.9 mmol) and one drop of formic acid. The reaction mixture was sonicated overnight at room temperature. The contents were then filtered to give a bright yellow solid. The mother liquor was concentrated and recrystallized from ethanol. These combined batches yielded the product diimine **29** quantitatively (2.88 mmol) as a single diastereomer. ^{1}H NMR ($CDCl_3$): 1.6 (12H, d, J = 6.3), 2.3 (6H, s), 4.0 (4H, q, J = 6.5), 7.0 (s, 4H), 7.2 (m, 20H), 7.4 (s, 2H). ^{13}CNMR

($CDCl_3$): 21.4, 22.1, 39.1, 125.9, 126.2, 127.8, 128.6, 134.5, 146.6, 164.0. $[\alpha]_D$ = 66.3, (c = 1.76, dichloromethane). ESI-FTMS calcd $[M + H]^+$ $C_{48}H_{49}N_2$ = 653.38957, found $[M + H]^+$ = 653.38923.

1,3-Bis[2,6-(*S*,*S*)-(1-phenyl-ethyl)-phenyl]-1*H*-imidazolium Chloride 30. The following procedure is a revision of the protocol published by Markó.[14] A solution of zinc(II) chloride and paraformaldehyde in concentrated hydrochloric acid was prepared (1:1:2, ~4.2 M in paraformaldehyde). A test tube with a screw cap was charged with the diimine (**31**, 0.31 mmol) in freshly distilled THF (8 mL) under inert atmosphere and was treated with the acid solution (0.372 mmol paraformaldehyde, 1.2 equiv). The reaction solution was then heated to 70 °C in the sealed tube for 1 h before cooling to room temperature and removal of the solvent in vacuo. The resultant residue was then dissolved in dichloromethane (2 mL) and washed with water (3 × 1 mL) and saturated $NaHCO_3$ (1 × 1 mL) before drying over $MgSO_4$, filtration, and removal of the solvent in vacuo. The off white solid was then recrystallized from diethyl ether and dichloromethane. ^{1}H NMR ($CDCl_3$): 1.4 (6H, d, *J* = 6.7), 1.6 (6H, d, *J* = 6.7), 2.3 (6H, s), 3.75 (2H, q, *J* = 6.6), 3.85 (2H, q, *J* = 6.6), 6.5 (2H, s), 6.7 (4H, d, *J* = 7.5), 6.9 (2H, s), 7.0−7.5 (18H, m), 11.6 (1H, s). ^{13}CNMR ($CDCl_3$): 21.8, 21.85, 22.7, 38.5, 40.0, 124.3, 126.5, 126.8, 127.1, 127.6, 127.8, 128.3, 128.5, 129.1, 141.3, 141.9, 142.8, 143.5, 145.6. ESI-FTMS calcd $[M^+]$ $C_{49}H_{49}N_2$ = 665.38957, found $[M^+]$ = 665.38957. Single diastereomer.

Copper Carbenoid (*S*,*S*,*S*,*S*)-12. ^{1}H NMR ($CDCl_3$): 1.25 (6H, d, *J* = 8.0), 1.4 (6H, d, *J* = 8.0), 2.15 (6H, s); 3.65 (m, overlapping quartets, *J* = 5.3); 6.3 (2H, s), 6.6−7.3 (m, 24H). ^{13}CNMR ($CDCl_3$): 21.7, 21.9, 22.7, 38.0, 39.6, 123.0, 126.0, 126.5, 127.0, 127.5, 128.0, 129.1, 133.2, 140.5, 142.3, 144.0, 144.3, 145.9, 181.2. ESI-FTMS calcd $[M^+]$ $C_{49}H_{48}CuN_2$ = 727.31135, found $[M^+]$ = 727.31176. XRD analysis of **12** resulted in refinement of the Flack parameter to a value of zero, providing confirmation of the absolute configuration as (*S*,*S*,*S*,*S*).

General Procedure for Hydrosilylation (following the procedure of Nolan[18]). To an oven-dried vial fitted with a septum screw cap was added *either* copper carbenoid **12** (6.0 μmol) and sodium *tert*-butoxide (0.024 mmol) *or* imidazolium **25** or imidazolinium **9** (6.0 μmol), Cu(I)Cl (6.0 μmol), and sodium *tert*-butoxide (0.024 mmol) in freshly distilled toluene (2 mL). The cloudy white reaction solution was stirred for 10 min at room temperature before addition of the silane (1.0 mmol). An immediate color change to bright yellow was observed, and the reaction was stirred for an additional 20 min before addition of acetophenone (0.2 mmol). The reaction progress was monitored by GC. Upon completion (or observation of the cessation of product formation), the reaction solution was treated with charcoal and filtered first through a plug of Celite and then a plug of silica gel. The solvent was removed under reduced pressure and the residue was analyzed by supercritical fluid chromotography. Diphenylsilyl ether **31** was separated on a Daicel Chiralcel OD-H (chiral stationary phase: 4-cellulose tris(3,5-dimethylphenylcarbamate) coated on 5 μm silica gel) at a flow rate of 2.0 mL/min, with polarity modifier = 2.0% EtOH and outlet pressure and oven temperature of 150 psi and 35 °C, respectively. Alternatively, the enantiomers of **31** were resolved via CSP-GC with a β-Dex column (temperature program 100 °C isothermal).

■ ASSOCIATED CONTENT

Supporting Information. Spectroscopic data for all compounds synthesized in the course of this investigation but not included in the text of the paper, as well all XRD data. This material is available free of charge via the Internet at http://pubs.acs.org.

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