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Influences of phenyl rings on NHC ligands with bicyclic architectures

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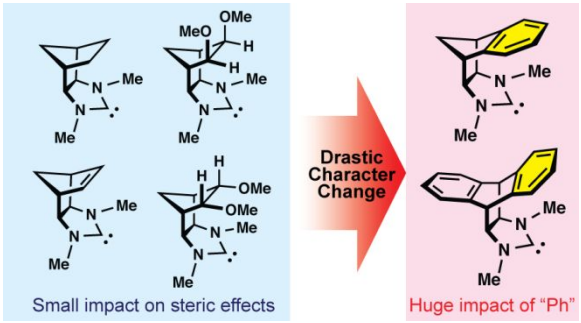


Abstract

In addition to phosphanes, olefins, amines, and amides, over the past two decades N-heterocyclic carbene (NHC) has emerged as a useful alternative ligand. Based on a number of derivatization studies on NHC ligands, imidazol-2-ylidene and imidazolin-2-ylidene became the standard heterocyclic form, and bulky substituents have commonly been introduced on the nitrogen(s) adjacent to carbenic carbons. Our group previously developed NHCs equipped with non-carbenic carbons with a bicyclic architecture that gives them unique steric properties that make them bulky but accessible. In this study,

we synthesized a novel type of NHC ligand that possesses a bicyclo[2.2.1]heptane architecture, and we compared five derivatives using copper-catalyzed allylic arylations with aryl Grignard reagents. The regioselectivity of the substitution obviously indicates that a phenyl ring over an active site has a characteristic effect on the resultant copper catalysts when γ-substitution is the major pathway.

Introduction

The choice of a ligand for use as a transitional metal catalyst is crucial to an effective chemical transformation.[1] In addition to electron-donating ability, Lewis basicity in other words, the steric bulkiness of the ligands is important in the obtainment of effective metal catalysts.[2] Therefore, in the development of an effective catalytic cycle, the steric properties of ligands are routinely tuned. Some parameters such as cone angle[2a] and bite angle[2b] have been used to represent the steric demands of phosphine ligands, and these factors have provided significant insight to an understanding of the mechanism as well as to a prediction of reactivity.

Over the past two decades, N-heterocyclic carbenes (NHC) have become an alternative ligand to phosphines, olefins, amines, or amides because of their unique binding nature that includes strong σ-donation to bound transition metals that results in a remarkably strong and stable complex

under aerial conditions.[3] A number of heterocycles containing carbenic carbons with neighboring nitrogen(s) have been studied, and imidazolin-2-yliden and imidazol-2-yliden have become the general ring system for NHC ligands.[4] These structures possess two nitrogen elements adjacent to carbenic carbons, where many functional groups have been introduced in order to study the steric and electronic effects.[4-5] As a result of these numerous derivations, the steric effects of the substituents on nitrogen elements are recognized as stronger than the electronic effects. Furthermore, the substituents on nitrogen elements structurally influence the environment around the bound metals on a much stronger level than the substituents on non-carbenic carbons. Based on these facts, the steric variety in NHC ligands is due mostly to nitrogen elements (Figure 1a).[3b,6]

Recently, our group developed original NHCs, which we refer to as DHASI, and discovered that DHASI ligands have particular steric properties.[7] The non-carbenic carbons in this series of NHC ligands have a bicyclic architecture, and an aromatic ring is rigidly fixed toward an active site that results in effective steric shielding. Silver and copper complexes of DHASI*i*Pr have isopropyl groups on two nitrogen elements and can be isolated as air-stable crystals, but the copper complex ably catalyzes the borylation of sterically hindered arylbromide, which is a reaction where ubiquitous NHC

ligands are incompatible.[7b] It is worth noting that most imidazolinylidene ligands with *N*-alkyl groups do not have a stabilizing effect sufficient to isolate air-stable copper complexes. The results of the present study indicate that our bicyclic architecture is sufficiently bulky to stabilize the metal complexes yet remains accessible even for sterically demanding substrates (Figure 1b). The DHASI ligands are also useful to nickel catalysts for the Corriu-Kumada-Tamao coupling of tertiary alkyl Grignard reagents[7c] and for Suzuki-Miyaura coupling between aryl/heteroaryl chlorides and aryl/heteroarylboronic acids.[7d]

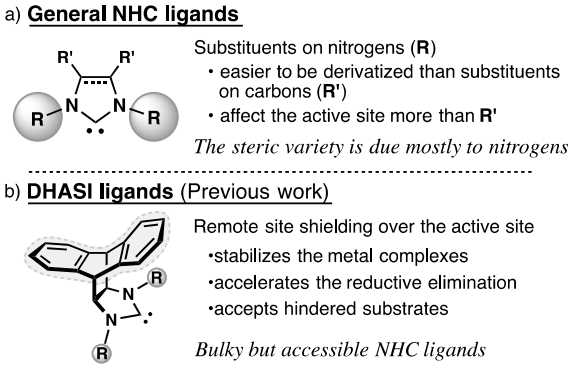


Figure 1. Features of general NHC ligands (a) and of NHC ligands with bicyclic architectures (b).

DHASI ligands, which contain a bicyclo[2.2.2]octadiene system, are synthesized via a Diels-Alder reaction between anthracene and *N,N'*-diacetyl-2-imidazolone with some subsequent chemical transformations (Figure 2).[7b,8] Although DHASI is a version of NHC ligands that shows promise for the realization of unique metal catalysts, the substituents on the bicyclic structure are

difficult to modify. As yet there has been no investigation into how the steric and electronic features of a bicyclic architecture affect the functions of DHASI ligands. Through the development of finely tunable NHC ligands with a bicyclic architecture, we intended to examine the effects that structural change could exert on stabilizing ability as well as on the acceleration of reductive elimination during catalysis. To perform these examinations, we designed a novel type of NHC ligand equipped with another bicyclic ring system, bicyclo[2.2.1]heptane, via the use of cyclopentadiene as a diene in a Diels-Alder reaction.[8] Here, we report the syntheses of NHC ligands with a bicyclo[2.2.1]heptane framework, which include saturated alkyl, unsaturated olefin, *exo,cis*-dimethoxy groups, *endo*,*cis*-dimethoxy groups, and a phenyl ring over active sites. The synthesized NHC ligands were applied to a copper-catalyzed allylic arylation with PhMgBr in order to examine the effect of accelerating the reductive elimination step. The introduced aromatic ring had a unique steric effect and accelerated the reductive elimination step to predominantly produce the γ-product, which also was observed in our previous study using DHASI ligands.

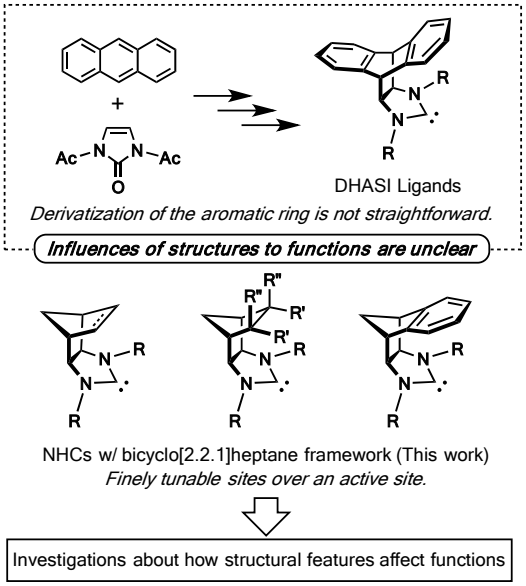


Figure 2. Designs of NHC ligands studied in previous work and in this study.

Results and discussion

Syntheses of novel types of NHC ligands with a bicyclo[2.2.1]heptane framework.

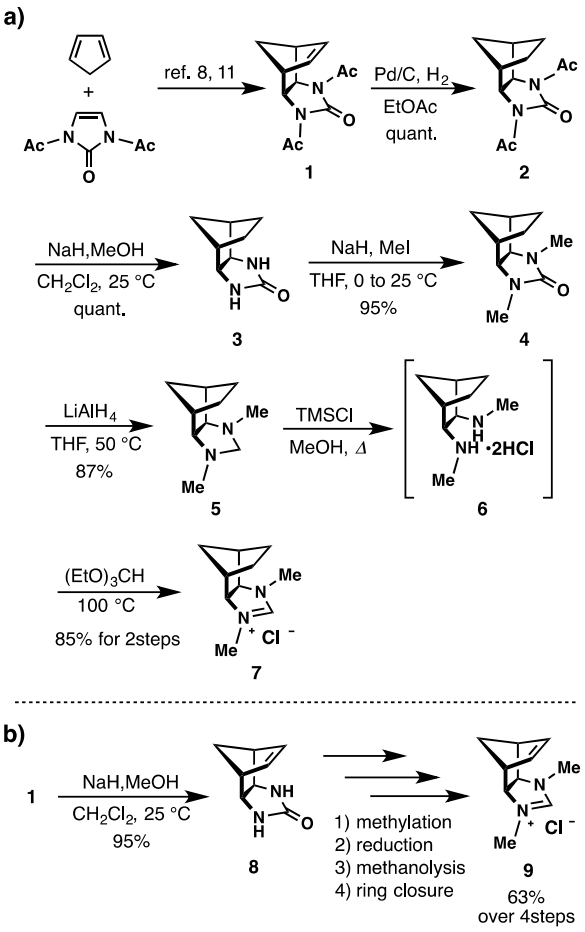
We began our syntheses of novel NHC ligands with a Diels-Alder reaction between freshly cracked cyclopentadiene and *N,N'*-diacetyl-2-imidazolone to afford the known imidazolidinone **1** (Scheme 1a).[8-9] Imidazolidinone **1** has an olefin that allows the subsequent introduction of many types of substituents, which should result in flexible modifications. In this context, we synthesized five derivatives to observe the steric effect of the substituents when introduced on two carbons over an active site.

First, we developed a saturated *N*,*N*'-dimethyl-4,5-(cyclopentane-1,3-diyl)-imidazolinium chloride **7** for use as an NHC precursor (Scheme 1a). We refer to this NHC motif as CPSI ((cyclopentane-1,3-diyl)-imidazolinylidene). The synthesis of imidazolinium chloride **7** started from the hydrogenation of an olefin using a Pd/C catalyst under a H_2 balloon to obtain the saturated compound **2** in a quantitative yield. The acetyl groups of compound **2** were then cleaved by methanolysis in a quantitative yield.[10] Following methylation of the nitrogen elements in a 95% yield, cyclic urea **4** was reduced by $LiAlH_4$ to afford imidazolidine **5** in an 87% yield. Imidazolidine **5** was treated with HCl in methanol to afford *N*,*N'*-dimethylethylenediamine **6** as a hydrochloride salt, and finally the crude diamine **6** was heated with $(EtO)_3CH$ to afford *N*,*N*'-dimethyl-4,5-(cyclopentane-1,3-diyl)-imidazolinium chloride **7** (CPSIMe•HCl).

Second, we synthesized *N*,*N*'-dimethyl-4,5-(cyclopent-1-ene-3,5-diyl)-imidazolinium chloride **9** (CPESIMe•HCl) under the same synthetic route as CPSIMe•HCl **7** with the exception of omitting hydrogenation of the olefin (Scheme 1b, in a 60% overall yield; see the experimental section for details).

Scheme 1. Syntheses of the NHC precursors with cyclopentane-1,3-diyl and

cyclopent-1-ene-3,5-diyl groups

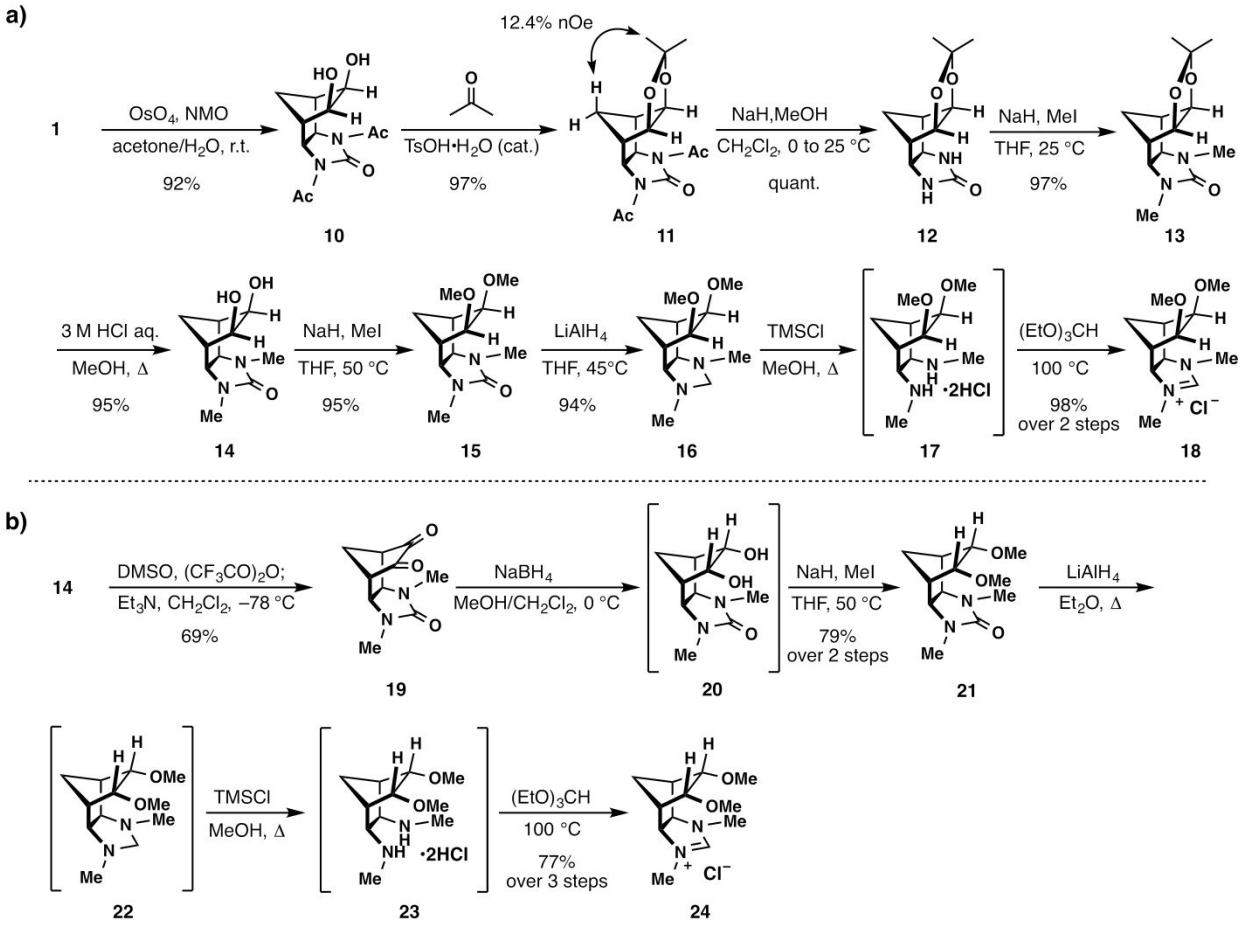


Third and fourth, we introduced two methoxy groups on the *cis* configurations *exo,cis*-dimethoxy derivative **18** and *endo,cis*-dimethoxy derivative **24** (Scheme 2). We expected these two isomers to provide information about the steric effects of the substituents that reside at different distances from a bound metal. The synthesis of *N*,*N*'-dimethyl-4,5-(*exo,cis*-1,2-dimethoxy-cyclopentane-3,5-diyl)-imidazolinium chloride **18**

(*exo*,*cis*-diMeO-CPSIMe•HCl) was started from the dihydroxylation of the olefin of compound **1** catalyzed by OsO_4 (0.5 mol%) with NMO as the terminal oxidant in a 92% yield.[9,11] After a 97% yield of acetonide formation from the *cis*-dihydroxy groups,[9] the NOE spectra of the acetonide **11** was analyzed and 12.4% of it fell between a methyl group of the acetonide and one of the methylene protons, which assured a *exo*,*cis*-configuration for the dihydroxy groups. The acetyl groups were cleaved by methanolysis to yield compound **12**[9] in a quantitative yield, and the resultant free N-H functionality was methylated to afford compound **13** in a 97% yield. At this point, acetonide was deprotected in a 95% yield, and the methylation of the dihydroxy groups gave *exo*,*cis*-dimethoxy compound **15** in a 95% yield. From compound **15**, *exo*,*cis*-diMeO-CPSIMe•HCl **18** was synthesized via a transformation similar to that described above, which amounted to a reduction of the urea moiety (94%), methanolysis of aminal, and ring closure using $(EtO)_3CH$ (98% over 2 steps, Scheme 2a). The *endo*,*cis*-dimethoxy functionality was achieved from the *exo*,*cis*-diol **14** via a three-step conversion that involved Swern oxidation to diketone **19** in a 69% yield,[11] reduction with $NaBH_4$ to *endo*,*cis*-dihydroxy compound **20** in a quantitative yield, and then methylation to afford *endo*,*cis*-dimethoxy compound **21** in a 79% yield. Compound **21** was also transformed to *endo*,*cis*-diMeO-CPSIMe•HCl **24** using the

same synthetic route as other ligands for a 77% overall yield (Scheme 2b).

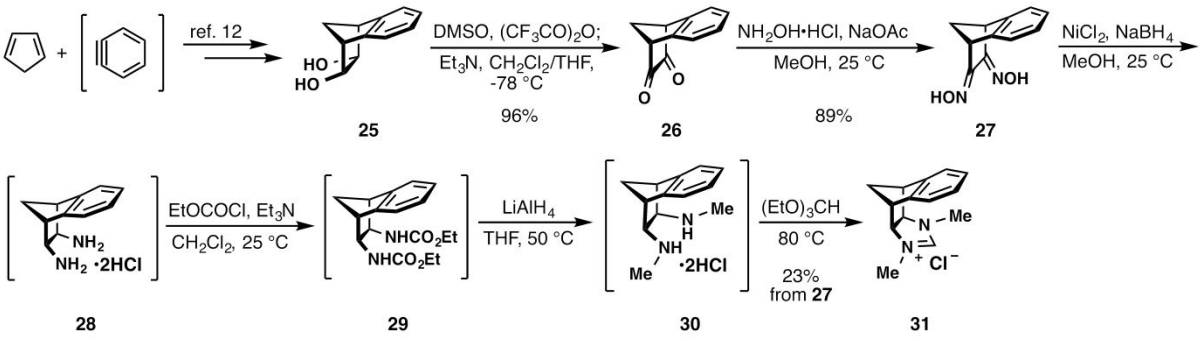
Scheme 2. Syntheses of the NHC precursors with *cis*-1,2-dimethoxy-cyclopentane-3,5-diyl groups



Finally, we introduced an aromatic ring to the same framework based on another synthetic strategy that involved the introduction of amino groups to the known compound **25**,[12] which was synthesized in two steps from cyclopentadiene and benzyne formed *in situ*. This *exo*,*cis*-diol **25** was oxidized to diketone **26**[13] under Swern oxidation conditions in a 96% yield,[11] and then treated with

NH_2OH•HCl to afford dioxime **27** in an 89% yield. The direct reduction of dioxime to diamine using nickel boride[14] gave diamine hydrochloride **28** as a crude product, which was subsequently converted to bis(ethylcarbamate) **29**. Carbamate **29** was reduced with $LiAlH_4$ to afford *N,N'*-dimethylethylenediamine **30** as a crude hydrochloride salt, which was then heated in $(EtO)_3CH$ to afford *N,N'*-dimethyl-4,5-(benzocyclopentane-3,4-diyl)-imidazolinium chloride **31** (BCPSIMe•HCl) in a 23% overall yield from dioxime **27** (Scheme 3).

Scheme 3. Synthesis of the NHC precursor with a benzocyclopentane-3,5-diyl group



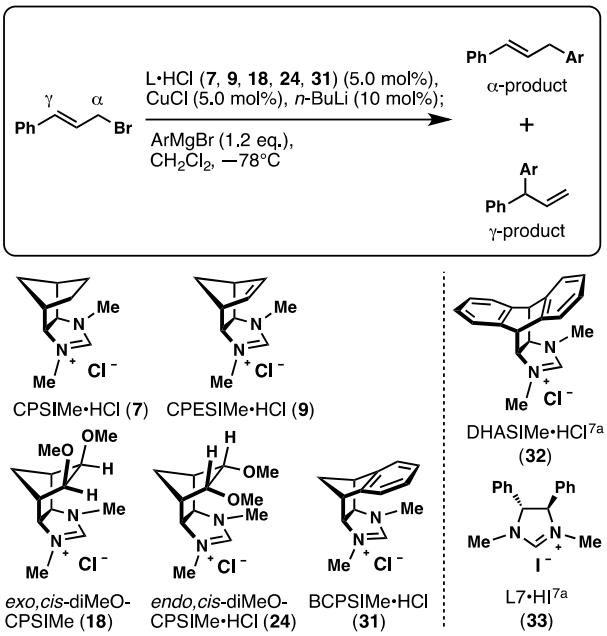
Structural alteration of NHC ligands and its influence on regioselectivity during copper-catalyzed allylic arylations with aryl Grignard reagents

With the five novel NHC ligands in hand, we performed copper-catalyzed allylic arylations of cinnamyl bromide with PhMgBr to investigate the steric effects of the structural differences in a bicyclic[2.2.1]heptane architecture (Table 1).[15] The regioselectivity of this reaction is strongly affected

by the properties of ligands, and greater degrees of sterically hindered and electron-deficient ligands will give the γ-product preferentially. On the other hand, the conjugation of an α-product is longer than that of a γ-substituted product, which results in the preferred α-product, either without ligands or with sterically less-hindered ligands.[7a,16] To evaluate the steric effect that the substituents exert on non-carbenic carbons, we used NHC ligands that were equipped with methyl groups on the nitrogen elements, as shown in Table 1. As shown by entry 1, CPSIMe **7**, which has a bicyclo[2.2.1]heptane ring system, preferentially gave us the α-product relative to the γ-product (α/γ = 2.38/1). Although the α-product was still the major yield, CPESIMe **9** gave a higher ratio of the γ-product (entry 2, α/γ = 1.92/1). The introduction of *exo*,*cis*-dimethoxy groups on the ligand (*exo*,*cis*-diMeO-CPSIMe **18**) resulted in a significant increase in the α-product (α/γ = 3.33/1). To our surprise, the *endo*,*cis*-dimethoxy ligand (*endo*,*cis*-diMeO-CPSIMe **24**), which has the closest site for substituents from bound copper, did not heighten the γ-selectivity, which remained at the same level (α/γ = 2.12/1) as the reaction with CPESIMe **9**. A comparison of those results shows that the NHC ligand with a 1,2,3,4-tetrahydro-1,4-methano-naphthyl group (BCPSIMe **31**) significantly affected the properties of the copper catalyst and gave us the γ-product as the major yield (entry 5, α/γ = 1/7.69), which also

means the steric effect of BCPSIMe **31** was stronger than that of the DHASIMe ligand (**32**, entry 6, α/γ = 1/3.76).[7a] It is noteworthy that the two phenyl rings on the 1,2-diphenylethylenediamine-based NHC (**33**) showed no such steric effect (entry 7, α/γ = 4.00/1).[7a] A comparison of the NHC ligands synthesized in this study indicates that the phenyl ring fixed toward the active site would be the critical element for the acceleration of the reductive elimination step in this reaction by DHASI ligands and by BCPSIMe **31**.[16] We additionally attempted the allylic arylations using two other Grignard reagents (entries 8 to 11). Previous studies clearly established that the copper catalyzed allylic substitutions were significantly affected by the electronic properties of substrates (see reference 16 and references cited therein). The results suggested that the structural changes from DHASI to BCPSI influenced the regio-selectivity regardless of the electronic properties of the nucleophile.

Table 1. Influences of the structures of NHC ligands with bicyclic architectures on regio-selectivity during the copper-catalyzed allylic arylations of cinnamyl bromide with aryl Grignard reagents [a]



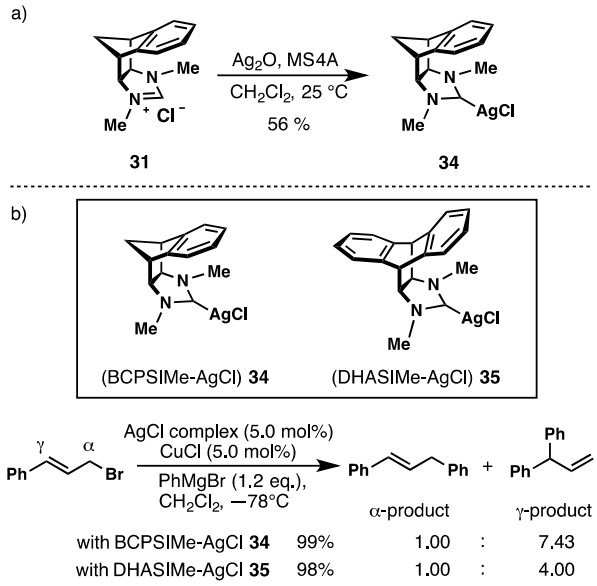
Entry	Ligand	Ar	Combined Yield (%)	Ratio (α:γ)[b]
1	**7**	Ph	84	2.38 : 1
2	**9**	Ph	95	1.92 : 1
3	**18**	Ph	92	3.33 : 1
4	**24**	Ph	86	2.12 : 1
5	**31**	Ph	92	1 : 7.69[c]
6[d]	**32**[7a]	Ph	98	1 : 3.76[c]
7[d]	**33**[7a]	Ph	99	4.00 : 1
8	**32**	4-Me-C_6H_4–	98	1 : 2.81

9	**31**	4-Me-C_6H_4–	99	1 : 5.23
10	**32**	4-Cl-C_6H_4–	98	1 : 4.14
11	**31**	4-Cl-C_6H_4–	99	1 : 8.55

[a] The NHC precursors were converted to the corresponding NHC ligands *in situ*. [b] Calculated using ^{1}H NMR. [c]The averages of two runs are shown. [d]From reference 7a.

We also tried syntheses of silver complexes supported by these novel NHC ligands, and isolation of a bench-top stable silver complex was successful only when we used BCPSIMe as a ligand. The other four NHC ligands gave us highly hygroscopic unstable silver complexes; therefore, we could not characterize these complexes for use as NHC transfer agents.[17] In contrast, BCPSIMe-AgCl **34** was successfully isolated in a 56% yield by a typical synthetic method with use of Ag_2O, as reported by Lin and co-workers.[17] As we had previously reported, DHASIMe-AgCl complex **35**[7a] was also sufficiently stable to allow isolation and characterization, which included crystallographic analysis, as well as for storage under air on a bench. These observations suggested that phenyl rings installed in BCPSIMe and DHASIMe were effective functional groups to stabilize the silver complexes, which allowed isolation and storage under air on a bench. The silver complex **34** was also applied to the allylic arylations

shown in Table 1, and the results were comparable to the *in situ* procedure (Scheme 4), which confirmed that the *in situ* formation of NHC-CuCl aptly worked during the reactions listed in Table 1.[18]



Scheme 4. a) Synthesis of BCPSIMe-AgCl complex **34** b) Allylic arylations using a transmetallation procedure from NHC-AgCl complexes

Structural analyses of some NHC precursors with bicyclic architectures

The structural similarities between BCPSIMe **L5** and DHASIMe **L6** notwithstanding, bicyclo[2.2.1]heptene and bicyclo[2.2.2]octadiene are different bicyclic systems, which generate different environments around a bound metal. To analyze these two structures in detail, we performed X-ray crystallography of DHASIMe•HCl **32**,[7a] which is the precursor of DHASIMe **L6**, and

BCPSIMe•HCl **31**. The ORTEP diagrams, the dihedral angles, and the distances between the pre-carbenic carbon of the imidazolinium ring, C(1), and the centroid of the phenyl ring over the imidazolinium ring are shown in Figure 3. Crystal analysis of **32** revealed two structures in the cell and the means of the dihedral angles and distances are shown. The dihedral angle between the phenyl ring and the imidazolinium ring (angle *a*) on compound **31** (Figure 3b) is ca. 6° smaller than that on DHASIMe•HCl **32** (Figure 3a), and the distances between the carbon C(1) and the centroid of the phenyl ring of compound **31** is ca. 0.15 Å shorter than that of compound **32**. In addition to NHC precursors **31** and **32**, we used X-ray crystallography to analyze silver chloride complexes **34** and **35**[7a]. The distances between silver and centroids of phenyl rings of each complex showed the same trends as the precursors: 4.531 Å for complex **34** and 4.974 Å for complex **35**. The dihedral angle between the phenyl rings and the imidazolinylidene ring were 46.76° for complex **34** and 56.32° for complex **35**, which were smaller than for precursors **31** and **32**. We also analyzed the steric map of these two structures using SambVca 2.0 software developed by Cavallo and co-workers.[19] The buried volume of BCPSIMeAgCl was 28.4%, which was slightly higher than of DHASIMeAgCl (26.1%). The steric maps also indicated a bit higher steric pressure from the phenyl ring for BCPSIMe than that for

DHASIMe (Figure 4). These steric differences could be the reason for the better γ-selectivity of the allylic arylation with BCPSIMe compared with that with DHASIMe. The different environments on these frameworks would be a useful steric variety of NHC ligands, and the N-substituents on these NHCs leave room for the tuning of sterics. Moreover, the phenyl ring of the BCPSI core structure could be derivatized with the use of substituted benzynes or other appropriate dienophiles for Diels-Alder reactions with cyclopentadiene, and this structural flexibility is amenable to the fine-tunings of the properties of NHCs with a bicyclic architecture.

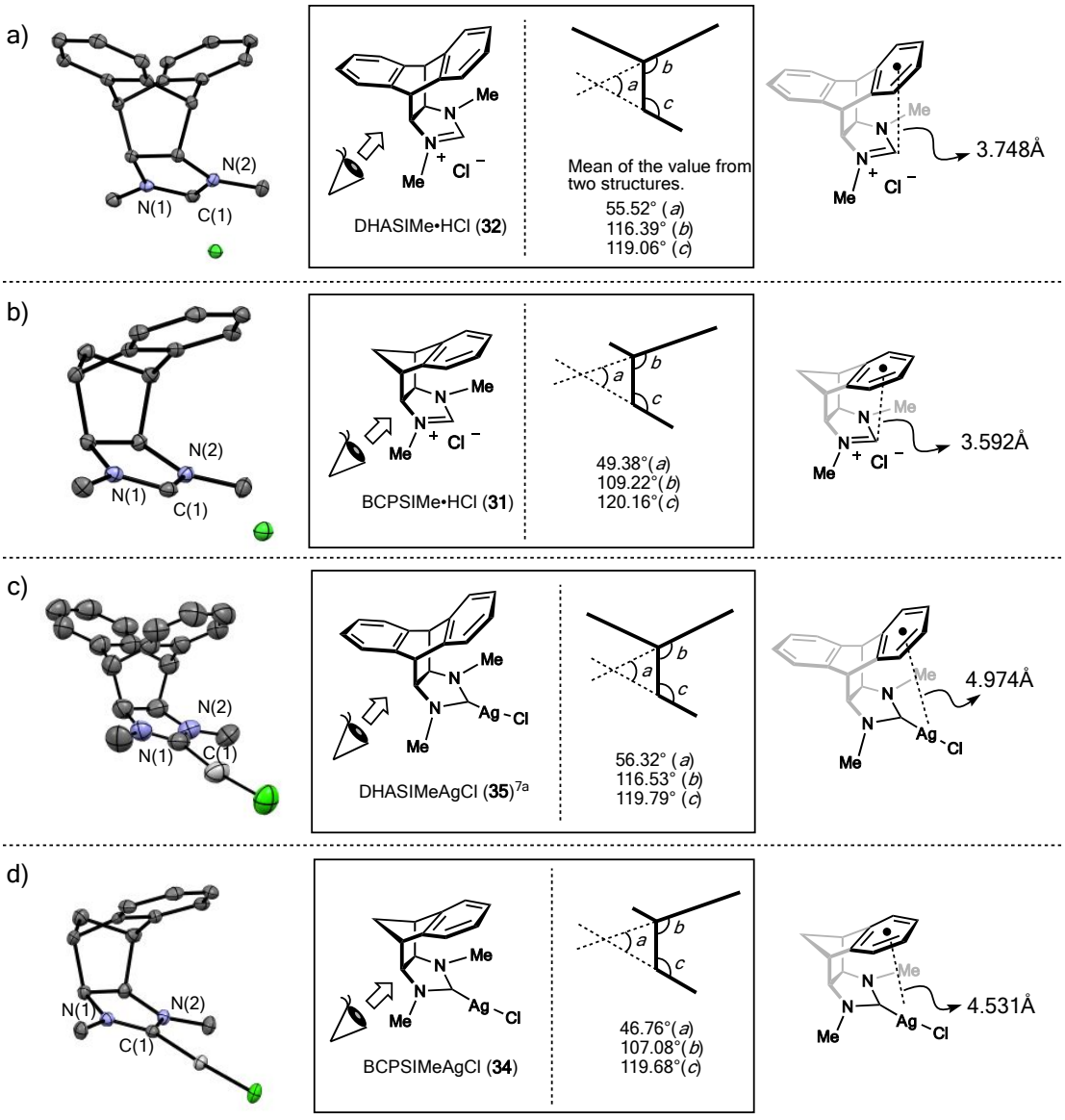


Figure 3. ORTEP diagrams, dihedral angles, and distances between C(1) and the centroids of the phenyl rings of DHASIMe•HCl **32** (a), BCPSIMe•HCl **31** (b), DHASIMeAgCl **35** (c), and BCPSIMeAgCl **34** (d). Selected bond length (Å) and angles (deg): Figure 3a (mean of 2 structures): C(1)–N(1), 1.311; C(1)–N(2), 1.310; N(1)–C(1)–N(2), 113.63, Figure 3b: C(1)–N(1), 1.313; C(1)–N(2),

1.313; N(1)–C(1)–N(2), 113.82, Figure 3c: C(1)–N(1), 1.326; C(1)–N(2), 1.326; N(1)–C(1)–N(2), 109.65, Figure 3d: C(1)–N(1), 1.331; C(1)–N(2), 1.326; N(1)–C(1)–N(2), 109.49.

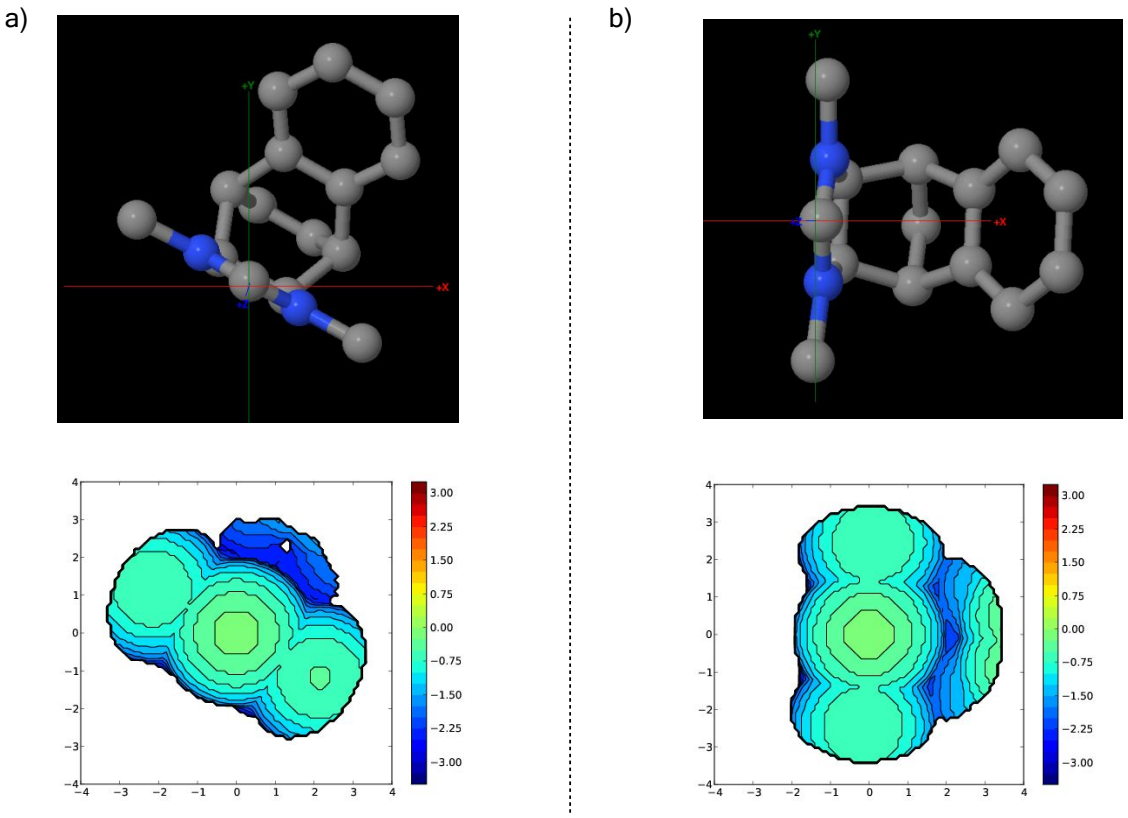


Figure 4. Steric maps of a) DHASIMeAgCl (**35**)[7a] and BCPSIMeAgCl (**34**).

Conclusions

In this study, we synthesized five novel NHC ligand precursors, **7**, **9**, **18**, **24**, and **31**, equipped with bicyclo[2,2,1]heptane architectures on non-carbenic carbons. We applied these NHC ligands to the copper-catalyzed allylic arylations of cinnamyl bromide with PhMgBr. Among the

synthesized NHC ligands, only (benzocyclopentane-3,5-diyl)-NHC **31**, which possesses a phenyl ring fixed to the bound copper, produced the γ-product in a major yield. It must be emphasized here that regioselectivity was not affected by the dimethoxy groups, even those in the *endo*,*cis*-configuration (**24**), which were arguably near enough to the bound copper to be expected to exert some steric effect. DHASIMe **32**, which also has a phenyl ring on a bicyclo[2.2.2]octadiene framework, had previously shown a preference similar to that of the γ-product in this reaction.[7a] These results obviously indicated that the phenyl rings set over the bound copper caused a characteristic effect, that included an acceleration of the reductive elimination step. X-ray diffraction studies of BCPSIMe•HCl **31** and DHASIMe•HCl **32** verified the position of the phenyl ring of BCPSIMe as existing somewhat closer to a bound metal than that of DHASIMe, which would be one reason that the γ-selectivity of BCPSIMe is higher than that of DHASIMe. The established synthetic route enables the flexible derivatization of the aromatic ring, which should be useful for tuning of the properties of NHC ligands. As we further investigate the effects of the steric and electronic properties of the phenyl rings of NHCs with bicyclic architectures in our laboratory, we will apply the novel NHCs synthesized in this study to the development of useful metal catalysts.

Experimental Section

General Procedure and Chemicals

All reactions were carried out under an argon atmosphere with freshly distilled solvents under anhydrous conditions, unless otherwise noted. Anhydrous CH_2Cl_2, DMSO, and THF were purchased and used without further distillation. Et_3N was distilled from CaH_2. Other reagents were used without further purification. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials unless otherwise noted. ^{1}H and ^{13}C NMR spectra were recorded at 600 and 151 MHz, respectively. Chemical shifts are reported in δ ppm and reference either an internal tetramethylsilane or solvent peaks. The following abbreviations are used to indicate the multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; qt = quintet; sex = sextet; sept = septet dd = doublet of doublets; ddd = doublet of doublet of doublets; dddd = doublet of doublet of doublet of doublets; dt = doublet of triplets; app = apparent; m = multiplet; br = broad. Melting points were uncorrected. High-resolution mass spectra were recorded on a double-focusing magnetic-sector mass analyzer operating in a fast atomic bombardment (FAB) mode.

(3a*R*,4*S*,7*R*,7a*S*)-1,3-Diacetyl-3a,4,7,7a-tetrahydro-4,7-methanobenzo[4,5-*d*]imidazol-2-one **(1)**[8–10]

A mixture of 1,3-diacetylimidazolin-2-one (17.7 g, 105 mmol) and an excess of freshly cracked cyclopentadiene (88.8 ml, 1.05 mol) in *m*-xylene (105 mL) was stirred in a sealed tube at 150°C for 72 h. The resultant mixture was then cooled to room temperature and concentrated under reduced pressure. *n*-Hexane was added to the residue, and the crude precipitate was filtered and washed with *n*-hexane. The crude solid containing the title product and a small amount of unreacted imidazolone was dissolved in MeOH (250 mL), and 2M HCl aq. (250 mL) was added to the solution to decompose the imidazolone. The resultant mixture was stirred at 25 °C for 30 min, and then MeOH was removed under reduced pressure. The residual aqueous layer was extracted with CH_2Cl_2 (200 mL × 3), and the combined organic extracts were washed with brine (200 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford the title compound **1** (13.3 g, 54%) as a white solid. mp 116–117 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 6.04 (dd, *J* = 1.8, 1.8 Hz, 2H), 4.42 (dd, *J* = 1.8, 1.8 Hz, 2H), 3.53 (sep, *J* = 1.8 Hz, 2H), 2.47 (s, 6H), 1.70 (ddd, *J* = 10.2, 1.8, 1.8 Hz, 1H), 1.39 (d, *J* = 10.2 Hz, 1H) ppm. Other spectral data matched the reported data.[8–10]

(3a*R*,4*R*,7*S*,7a*S*)-1,3-Diacetylperhydro-4,7-methanobenzo[4,5-*d*]imidazol-2-one (2)

EtOAc (80 mL) was added to a flask charged with 10% Pd/C (70 mg) and a magnetic stirrer bar under

Ar. A solution of diacetylimidazolidinone **1** (7.01 g, 30.0 mmol) and in EtOAc (20 mL) was added to the resultant flask, and then the argon balloon was replaced with a hydrogen balloon. The reaction flask was evacuated and backfilled with hydrogen, and this sequence was repeated three times. The resultant reaction mixture was stirred at 25 °C under hydrogen atmosphere for 1 h, and the reaction mixture was filtered through a Celite pad, washed with EtOAc (100 mL). The filtrate and washings were combined and concentrated under reduced pressure to afford the title compound **2** (7.06 g, quantitative) as a white solid. The purity of the product was sufficient without further purification. mp 111−112 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 296 K): δ = 4.21 (dd, *J* = 1.8, 1.8 Hz, 2H), 2.82 (sep, *J* = 1.8 Hz, 2H), 2.55 (s, 6H), 1.56–1.54 (m, 2H), 1.43–1.40 (m, 1H), 1.18 (dd, *J* = 7.8, 7.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 170.9, 152.8, 55.6, 39.7, 36.1, 24.4, 21.4 ppm; IR (KBr pellet): ν_{max} = 1739 (C=O), 1698 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{12}H_{17}N_2O_3$ $[M + H]^+$: 237.1239; found: 237.1220.

(3a*R*,4*R*,7*S*,7a*S*)-Perhydro-4,7-methanobenzo[4,5-*d*]imidazol-2-one (3)[10]

MeOH (7 mL) and CH_2Cl_2 (35 mL) were added to a flask charged with diacetylimidazolidinone **2** (1.92 g, 8.15 mmol) and a magnetic stir bar at 25 °C. After cooling to 0 °C in an ice bath, NaH (60% in mineral oil, 163 mg, 4.07 mmol) was added to the resultant solution in small portions, and the reaction

mixture was stirred at 25 °C for 4 h. The reaction was then quenched with sat. NH_4Cl aq. (30 mL) at 0 °C and extracted with CH_2Cl_2 (100 mL × 8). The combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was triturated with *n*-hexane, and the solid precipitated was filtered, washed with *n*-hexane, and dried under reduced pressure to afford the title compound **3** (1.25 g, quantitative) as a white powder. The purity of the product was sufficient without further purification. ^{1}H NMR (600 MHz, DMSO-d_6, 296 K): δ = 6.23 (s, 2H), 3.71 (s, 2H), 2.14 (s, 2H), 1.52 (ddd, J = 6.0, 6.0, 1.8 Hz, 2H), 1.34–1.30 (m, 1H), 1.22–1.21 (m, 2H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 163.5, 57.0, 40.8, 36.2, 21.5 ppm. Other spectral data matched the reported data.[10]

(3a*R*,4*R*,7*S*,7a*S*)-1,3-Dimethylperhydro-4,7-methanobenzo[4,5-*d*]imidazol-2-one (4)

A solution of imidazolidinone **3** (304 mg, 2.00 mmol) and MeI (0.50 mL, 8.00 mmol) in THF (10 mL) was cooled to 0 °C in an ice bath. NaH (60% in mineral oil, 288 mg, 4.80 mmol) was added to the solution in small portions at 0 °C, and the reaction mixture was stirred at 25 °C for 4 h. The reaction was quenched with MeOH (0.4 mL) at 0 °C, and the resultant solution was stirred for 30 min at 25 °C. Sat. NH_4Cl aq. (1.0 mL) and H_2O (8.0 mL) were added to this solution at 0 °C, and extracted with

CH_2Cl_2 (50 mL × 3). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (80% EtOAc/*n*-hexane) on silica gel (60 mL) to afford the title compound **4** (343 mg, 95%) as a yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 3.59 (dd, *J* = 1.8, 1.8 Hz, 2H), 2.74 (s, 6H), 2.41 (sep, *J* = 1.8 Hz, 2H), 1.49 (ddd, *J* = 10.8, 1.8, 1.8 Hz, 1H), 1.41 (ddd, *J* = 10.8, 1.8, 1.8 Hz, 1H), 1.35–1.31 (m, 4H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 301 K): δ = 160.3, 60.1, 39.4, 35.9, 29.4, 21.4 ppm; IR (film): ν_{max} = 1679 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{10}H_{17}N_2O$ [M + H]$^+$: 181.1341; found: 181.1334.

(3a*R*,4*R*,7*S*,7a*S*)-1,3-Dimethylperhydro-4,7-methanobenzo[4,5-*d*]imidazole (5)

THF (17.3 mL) was added to a flask charged with dimethylimidazolidinone **4** (623 mg, 3.46 mmol) and a magnetic stir bar at 25 °C. After cooling to 0 °C in an ice bath, $LiAlH_4$ (262 mg, 6.92 mmol) was added to the resultant solution in small portions, and the reaction mixture was stirred at 50 °C for 2 h. The reaction mixture was then cooled to 0 °C in an ice bath and diluted with 34 mL of THF. H_2O (0.26 mL), 15% NaOH aq. (0.26 mL), and H_2O (0.79 mL) were added to the mixture sequentially at the same temperature. The resultant mixture was stirred at 25 °C for 30 min, and the solution was filtered

through a Celite pad, washed with THF (20 mL × 3), and the combined filtrate and washings were concentrated under reduced pressure. The crude residue was passed through a short pad of silica gel, eluted with EtOAc, and the eluent was concentrated under reduced pressure to afford the title compound **5** (498 mg, 87%) as a yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 3.98 (d, *J* = 3.6 Hz, 1H), 3.01 (d, *J* = 3.6 Hz, 1H), 2.67 (s, 2H), 2.23 (s, 6H), 2.09 (sep, *J* = 1.8 Hz, 2H), 1.93 (d, *J* = 7.2 Hz, 2H), 1.50 (s, 2H), 1.28–1.24 (m, 2H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 85.3, 71.9, 40.1, 39.5, 39.4, 22.2 ppm; HRMS (FAB+) *m/z* calcd. for $C_{10}H_{19}N_2^+$ $[M + H]^+$: 167.1548; found: 167.1553.

(4*R*,5*S*)-1,3-Dimethyl-4,5-(1*R*,3*S*-cyclopentane-1,3-diyl)-imidazolinium chloride (7)

Chlorotrimethylsilane (1.9 mL) was added to MeOH (5.0 mL) with stirring at 0 °C, and the resultant solution was added to a flask charged with dimethylimidazolidine **5** and a magnetic stir bar. The reaction solution was heated at 65 °C with a distillation apparatus until TMS−OMe was distilled off. The distillation apparatus was removed, and equipped with a reflux condenser. The resultant mixture was then heated at reflux for 19 h. The resultant solution was concentrated under reduced pressure to afford the crude *N*,*N'*-dimethylethylenediamine hydrochloride **6**. $(EtO)_3CH$ (20.5 mL) was added to a

flask charged with the crude **6**, and the resultant suspension was heated at 100 °C in an oil bath for 20 h. The reaction mixture was concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2, and Et_2O was added to precipitate the crude title compound **7**. The precipitate was filtered, washed with a 1 : 1 mixture of CH_2Cl_2 and Et_2O, and dried under reduced pressure to afford the title compound **7** (350 mg, 85% over two steps) as an off-white powder. mp 247–249 °C (decomp.); ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 10.3 (s, 1H), 4.24 (s, 2H), 3.27 (s, 6H), 2.69 (s, 2H), 1.64 (d, J = 11.4 Hz, 1H), 1.61 (d, J = 8.4 Hz, 2H), 1.54 (d, J = 11.4 Hz, 1H), 1.33 (dd, J = 8.4, 2.4 Hz, 2H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 158.5, 68.6, 39.6, 37.2, 34.4, 21.7 ppm; IR (KBr pellet): ν_{max} = 1653 (C=N) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{10}H_{17}N_2^+$ [M - Cl]$^+$: 165.1392; found: 165.1397.

(3a*R*,4*S*,7*R*,7a*S*)-3a,4,7,7a-tetrahydro-4,7-methanobenzo[4,5-*d*]imidazol-2-one **(8)**[10]

MeOH (13.5 mL) and CH_2Cl_2 (68.5 mL) were added to a flask charged with diacetylimidazolidinone **1** (3.80 g, 16.2 mmol) and a magnetic stir bar at 25 °C. After cooling to 0 °C in an ice bath, NaH (60% in mineral oil, 325 mg, 8.10 mmol) was added to the resultant solution in small portions, and the reaction mixture was stirred at 25 °C for 4 h. The reaction was quenched with sat. NH_4Cl aq. (50 mL) and

extracted with CH_2Cl_2 (100 mL × 8). The combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was triturated with *n*-hexane, and the solid precipitated was filtered, washed with *n*-hexane, and dried under reduced pressure to afford the title compound **8** (2.31 g, 95%) as a white powder. mp 230–231 °C (decomp); ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 6.17 (dd, *J* = 1.8, 1.8 Hz, 2H), 4.67 (br s, 2H), 4.13 (s, 2H), 3.03 (sep, *J* = 1.8 Hz, 2H), 1.56 (ddd, *J* = 9.6, 1.8, 1.8 Hz, 1H), 1.19 (d, *J* = 9.6 Hz, 1H) ppm. Other spectral data matched the reported data.[10]

(4*R*,5*S*)-1,3-Dimethyl-4,5-(3*S*,5*R*-cyclopent-1-ene-3,5-diyl)-imidazolinium chloride (9)

Imidazolidinone **8** was methylated in a 76% yield under the same reaction conditions as the synthesis of dimethylimidazolidine **4**. Data for the dimethylimidazolidinone **S1**: state: yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$, 299 K): δ = 6.01 (dd, *J* = 1.8, 1.8 Hz, 2H), 3.88 (dd, *J* = 1.8, 1.8 Hz, 2H), 3.14 (sep, *J* = 1.8 Hz, 2H), 2.71 (s, 6H), 1.62 (ddd, *J* = 9.6, 1.8, 1.8 Hz, 1H), 1.22 (d, *J* = 9.6 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 160.3, 133.9, 59.8, 45.6, 44.3, 28.9 ppm; IR (film): ν_{max} = 1693 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{10}H_{15}N_2O$ $[M + H]^+$: 179.1184; found: 179.1189.

Imidazolinium chloride **9** was synthesized via reduction of the cyclic urea moiety, methanolysis of the

aminal, and cyclization with use of $(EtO)_3CH$ under the same reaction conditions as the synthesis of compound **7**. The title compound **9** was obtained in 63% over four steps (81 mg) as a black powder. mp 192−195 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 299 K): δ = 9.85 (s, 1H), 6.19 (s, 2H), 4.55 (s, 2H), 3.42 (s, 2H), 3.21 (s, 6H), 1.79 (d, *J* = 9.6 Hz, 1H), 1.35 (d, *J* = 9.6 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 158.6, 134.6, 68.5, 46.0, 45.7, 33.8 ppm; IR (KBr pellet): ν_{max} = 1652 (C=N) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{10}H_{15}N_2^+$ [M - Cl]$^+$: 163.1235; found: 163.1244.

(3a*R*,4*R*,5*R*,6*S*,7*S*,7a*S*)-1,3-Diacetyl-5,6-dihydroxyperhydro-4,7-methanobenzo[4,5-*d*]imidazol-2-one **(10)**[9]

Diacetylimidazolidinone **1** (360 mg, 1.54 mmol) was dissolved in a mixture of acetone/water (15 mL, 4 : 1) at 25 °C. *N*-Methylmorpholine *N*-oxide (4.8 M in H_2O, 0.35 mL, 1.69 mmol) was added to this solution, followed by (after 5 min) an addition of a commercial solution of OsO_4 (0.02 mL, 2 wt % in water). After stirring at 25 °C for 20 h., the reaction mixture was concentrated under reduced pressure, and the remaining aqueous solution extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford the title compound **10** (379 mg, 92%) as a white solid. The purity of this product was sufficient

without further purification. mp 178–179 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 4.42 (app.d, *J* = 0.6 Hz, 2H), 4.22 (s, 2H), 3.15 (s, 2H), 2.90 (s, 2H), 2.49 (s, 6H), 1.40 (ddd, *J* = 12.0, 1.8, 1.8 Hz, 1H), 1.31 (d, *J* = 12.0 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 303 K): δ = 171.1, 152.1, 68.6, 53.8, 46.4, 30.8, 24.4 ppm. Other spectral data matched the reported data.[9]

(3a*R*,4*R*,4a*R*,7a*S*,8*S*,8a*S*)-5,7-Diacetyl-2,2-dimethylperhydro-4,8-methano[1,3]dioxolo[4,5-*f*]benzoimidazol-6-one **(11)**[9]

Acetone (33 mL) was added to a flask charged with *exo*-diol **10** (435 mg, 1.62 mmol) and a magnetic stir bar at 25 °C. *p*-Toluenesulphonic acid monohydrate (30.9 mg, 0.16 mmol) was added to the resultant solution, and the reaction mixture was heated at reflux for 1 h. The solution was concentrated under reduced pressure, and the crude residue was passed through a short pad of silica gel, eluted EtOAc, and concentrated under reduced pressure to afford the title compound **11** (486 mg, 97%) as a white solid. mp 176–177 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 4.32 (dd, *J* = 1.8, 1.8 Hz, 2H), 4.00 (d, *J* = 1.8 Hz, 2H), 2.96 (ddd, *J* = 1.8, 1.8, 1.8 Hz, 2H), 2.55 (s, 6H), 1.90 (ddd, *J* = 11.4, 1.8, 1.8 Hz, 1H), 1.44 (s, 3H), 1.29 (ddd, *J* = 11.4, 1.8, 1.8 Hz, 1H), 1.26 (s, 3H) ppm. Other spectral data matched the reported data.[9]

(3a*R*,4*R*,4a*R*,7a*S*,8*S*,8a*S*)-2,2-dimethylperhydro-4,8-methano[1,3]dioxolo[4,5-*f*]benzoimidazol-6-one **(12)**[9]

The title compound **12** was synthesized under the same reaction conditions as the synthesis of compound **3**. The title compound was quantitatively obtained (351 mg) as a white powder. mp 310–312 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 4.53 (d, *J* = 1.2 Hz, 2H), 4.48 (s, 2H), 4.09 (app.d, *J* = 1.2 Hz, 2H), 2.47 (s, 2H), 1.84 (d, *J* = 10.8 Hz, 1H), 1.46 (s, 3H), 1.31 (s, 3H), 1.16 (ddd, *J* = 11.4, 1.2, 1.2 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 162.5, 108.6, 54.6, 44.1, 30.7, 25.5, 24.0 ppm. Other spectral data matched the reported data.[9]

(3a*R*,4*R*,4a*R*,7a*S*,8*S*,8a*S*)-2,2,5,7-tetramethylperhydro-4,8-methano[1,3]dioxolo[4,5-*f*]benzo-imidazol-6-one (13)

The title compound **13** was synthesized under the same reaction conditions as the synthesis of compound **4**. The title compound was obtained in a 97% yield (970 mg) as a white powder. mp 158–161 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 4.16 (s, 2H), 3.72 (dd, *J* = 2.4, 2.4 Hz, 2H), 2.81 (s, 6H), 2.57 (s, 2H), 1.87 (d, *J* = 10.8 Hz, 1H), 1.45 (s, 3H), 1.27 (s, 3H), 1.18 (d, *J* = 10.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 159.7, 108.6, 57.8, 42.8, 30.4, 29.7, 25.5, 24.0

ppm; IR (KBr pellet): ν_{max} = 1689 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{13}H_{21}N_2O_3$ $[M + H]^+$: 253.1552; found: 253.1567.

(3a*R*,4*R*,5*R*,6*S*,7*S*,7a*S*)-5,6-dihydroxy-1,3-dimethylperhydro-4,7-methanobenzo[4,5-*d*]imidazol-2-one (14)

Acetonide **13** (536 mg, 2.53 mmol) was dissolved in MeOH (25 mL), and 3M HCl (25 mL) was added to the solution. The reaction mixture was then heated at reflux for 2 h. The solution was concentrated under reduced pressure to afford the title compound **14** (508 mg, 95%) as a yellow solid. mp 159–162 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 3.69 (s, 4H), 3.49 (br s, 2H), 2.80 (s, 6H), 2.46 (s, 2H), 1.99 (d, *J* = 11.4 Hz, 1H), 1.23 (d, *J* = 11.4 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 160.3, 68.7, 58.8, 45.9, 30.7, 29.7 ppm; IR (KBr pellet): ν_{max} = 3436 (-OH), 1667 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{10}H_{17}N_2O_3$ $[M + H]^+$: 213.1239; found: 213.1248.

(3a*R*,4*R*,5*R*,6*S*,7*S*,7a*S*)-5,6-dimethoxy-1,3-dimethylperhydro-4,7-methanobenzo[4,5-*d*]imidazol-2-one (15)

The title compound **15** was synthesized under the same reaction conditions as the synthesis of compound **4** except for stirring at 50 °C rather than 25 °C. The title compound was obtained in a 95%

yield (173 mg) as a yellow amorphous. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 3.67 (dd, *J* = 1.8, 1.8 Hz, 2H), 3.43 (d, *J* = 1.8 Hz, 2H), 3.38 (s, 6H), 2.80 (s, 6H), 2.54 (ddd, *J* = 1.8, 1.8, 1.8 Hz, 2H), 2.01 (ddd, *J* = 11.4, 1.8, 1.8 Hz, 1H), 1.23 (ddd, *J* = 10.8, 1.8, 1.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 159.9, 79.6, 58.9, 58.4, 43.1, 31.8, 29.6 ppm; IR (KBr pellet): ν_{max} = 1697 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{12}H_{21}N_2O_3$ $[M + H]^+$: 241.1552; found: 241.1566.

(3a*R*,4*R*,5*R*,6*S*,7*S*,7a*S*)-5,6-Dimethoxy-1,3-dimethylperhydro-4,7-methanobenzo[4,5-*d*]imidazole (16)

THF (6.0 mL) was added to a flask charged with compound **15** (146 mg, 0.61 mmol) and a magnetic stir bar at 25 °C. After cooling to 0 °C in an ice bath, $LiAlH_4$ (46 mg, 1.22 mmol) was added to the resultant solution, and the reaction mixture was stirred at 45 °C for 2 h. An aqueous solution of Rochelle salt (30 wt %, 1.0 mL) was then added to the resultant mixture at 0 °C, and stirred at 25 °C for 30 min. The resultant solution was extracted with CH_2Cl_2 (15 mL × 3), and the combined organic extracts were washed with brine (15 mL × 1), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, and the resultant solution was passed through a short pad of silica gel, eluted with 5% MeOH/CH_2Cl_2. The eluent was concentrated under reduced pressure

to afford the title compound **16** (111 mg, 81%) as a yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 4.04 (d, *J* = 1.2 Hz, 2H), 3.86 (d, *J* = 4.2 Hz, 1H), 3.41 (s, 6H), 2.94 (d, *J* = 4.2 Hz, 1H), 2.75 (dd, *J* = 1.8 Hz, 2H), 2.24 (s, 6H), 1.99 (d, *J* = 10.2 Hz, 1H), 1.28 (ddd, *J* = 10.2, 1.2, 1.2 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 300 K): δ = 84.6, 80.3, 69.8, 58.5, 43.1, 39.2, 35.6 ppm; HRMS (FAB+) *m/z* calcd. for $C_{12}H_{22}N_2O_2Na$ $[M + Na]^+$: 249.1579; found: 249.1581.

(4*R*,5*S*)-1,3-Dimethyl-4,5-(1*S*,2*R*,3*R*,5*S*-1,2-dimethoxy-cyclopentane-3,5-diyl)-imidazolinium chloride (18)

The title compound **18** was synthesized via methanolysis of the aminal moiety and cyclization using $(EtO)_3CH$ under the same reaction conditions as the synthesis of compound **7**. The title compound **18** was obtained in a 98% yield (250 mg) over two steps as a pale yellow powder. mp 215–217 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 10.1 (s, 1H), 4.35 (s, 2H), 3.47 (s, 2H), 3.44 (s, 6H), 3.34 (s, 6H), 2.73 (s, 2H), 2.17 (d, *J* = 11.4 Hz, 1H), 1.38 (d, *J* = 11.4 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 159.3, 78.9, 66.7, 59.3, 43.1, 34.4, 33.2 ppm; IR (KBr pellet): ν_{max} = 1646 (C=N) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{12}H_{21}N_2O_2^+$ $[M - Cl]^+$: 225.1603; found: 225.1606.

(3a*R*,4*R*,7*S*,7a*S*)-1,3-Dimethyl-5,6-dioxoperhydro-4,7-methanobenzo[4,5-*d*]imidazol-2-one (19)

Trifluoroacetic anhydride (0.10 mL, 0.72 mmol) was added very slowly to a solution of dry DMSO (0.05 mL) in dry CH_2Cl_2 (2 mL) at -78 °C, and the mixture was stirred for 10 min. Compound **14** (50 mg, 0.24 mmol) in CH_2Cl_2 (4 mL) was added and the reaction mixture was stirred at -78 °C for 2.5 h. Dry Et_3N (0.18 mL) was then added to the solution, and the reaction mixture was stirred at -78 °C for a further 3 h, allowed to reach 0 °C, transferred to an ice bath, acidified with 3 M HCl, and extracted with CH_2Cl_2 (10 mL × 3). The combined organic extracts were washed with brine (10 mL × 1), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (0−10% EtOAc in CH_2Cl_2) on silica gel (20 mL) to afford the title compound **19** (34 mg, 69%) as a yellow solid. mp 163–164 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 4.24 (dd, J = 2.4, 2.4 Hz, 2H), 3.48 (d, J = 0.6 Hz, 2H), 2.80 (s, 6H), 2.16 (s, 2H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 300 K): δ = 197.7, 158.5, 59.8, 52.6, 29.1, 28.7 ppm; IR (KBr pellet): ν_{max} = 1755 (C=O), 1696 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{10}H_{13}N_2O_3$ $[M + H]^+$: 209.0926; found: 209.0914.

(3a*R*,4*R*,5*S*,6*R*,7*S*,7a*S*)-5,6-Dimethoxy-1,3-dimethylperhydro-4,7methanobenzo[4,5-*d*]imidazol-2-one (21)

MeOH (0.9 mL) and CH_2Cl_2 (3.6 mL) were added to a flask charged with compound **19** (90 mg, 0.43

mmol) and a magnetic stir bar at 25 °C. After cooling to 0 °C in an ice bath, $NaBH_4$ (33 mg, 0.86 mmol) was added to the resultant solution in small portions, and the reaction mixture was stirred at 0 °C for 1 h. The reaction was then quenched with acetone and acidified with HOAc (0.05 mL) at 0 °C, and the resultant solution was concentrated under reduced pressure. The crude residue was passed through a short pad of silica gel, eluted with 10% MeOH/CH_2Cl_2, and concentrated under reduced pressure to afford the *endo*,*cis*-diol **20** (91 mg) as a crude product. (^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 4.15 (s, 2H), 3.83 (app.d, *J* = 0.6 Hz, 2H), 2.86 (s, 6H), 2.76 (sep, *J* = 1.8 Hz, 2H), 1.34 (ddd, *J* = 11.4, 1.8, 1.8 Hz, 1H), 1.30 (ddd, *J* = 10.2, 1.8, 1.8 Hz, 1H) ppm). This product was somewhat unstable; therefore, we used this crude imidazolidinone **20** without further purification. The title compound **21** was methylated under the same reaction conditions as the synthesis of compound **4** except for the following differences. One was the stirring at 50 °C instead of at 25 °C, and the other was the usage of double amounts of NaH and MeI. The title compound **21** was obtained in a 79% yield over 2 steps (61 mg) as a yellow powder. mp 111–114 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 3.81 (dd, *J* = 1.2, 1.2 Hz, 2H), 3.71 (dd, *J* = 1.2, 1.2 Hz, 2H), 3.38 (s, 6H), 2.78 (s, 6H), 2.72 (sep, *J* = 1.8 Hz, 2H), 1.28 (ddd, *J* = 11.4, 1.8, 1.8 Hz, 1H), 1.22 (ddd, *J* = 11.4, 1.8, 1.8 Hz, 1H) ppm; ^{13}C{^{1}H}

NMR (151 MHz, $CDCl_3$, 302 K): δ = 159.9, 80.0, 59.7, 59.4, 42.4, 29.9, 29.7 ppm; IR (KBr pellet): ν_{max} = 1685 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{12}H_{21}N_2O_3$ $[M + H]^+$: 241.1552; found: 241.1555.

(4*R*,5*S*)-1,3-Dimethyl-4,5-(1*R*,2*S*,3*R*,5*S*-1,2-dimethoxy-cyclopentane-3,5-diyl)-imidazolinium chloride (24)

The urea moiety of compound **21** was reduced under the same reaction conditions as the synthesis of compound **16** except for the usage of Et_2O instead of THF. The title compound **24** was synthesized via methanolysis of the aminal moiety and cyclization using $(EtO)_3CH$ under the same reaction conditions as the synthesis of compound **7**. The title compound **24** was obtained in a 77% yield (57.4 mg) over three steps as a pale yellow powder. mp 205–207 °C; ^1H NMR (600 MHz, $CDCl_3$, 298 K): δ = 8.93 (s, 1H), 4.48 (s, 2H), 3.81 (dd, *J* = 2.4, 2.4 Hz, 2H), 3.40 (s, 6H), 3.28 (s, 6H), 2.97 (s, 2H), 1.45 (ddd, *J* = 12, 1.8, 1.8 Hz, 1H), 1.36 (app. d, *J* = 12 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$, 303 K): δ = 159.3, 79.5, 67.6, 60.4, 43.6, 35.2, 31.8 ppm; IR (KBr pellet): ν_{max} = 1660 (C=N) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{12}H_{21}N_2O_2^+$ $[M - Cl]^+$: 225.1603; found: 225.1602.

(1*R*,2*R*,3*S*,4*S*)-1,2,3,4-Tetrahydro-1,4-methanonaphthalene-2,3-diol (25)[12]

t-BuOH (7.8 mL) and H_2O (2.3 mL) were added to a flask charged with 1,4-dihydro-1,4-methanonapthalene[20] (1.00g, 7.03 mmol) and a magnetic stir bar at 25 °C. A solution of *N*-methylmorpholine *N*-oxide (4.8 M in H_2O, 6.4 mL, 30.7 mmol) was added to the flask, followed by (after 5 min) a commercial solution of OsO_4 (0.02 mL, 2 wt % in water), and the resultant solution was stirred at 60 °C for 20 h. The reaction mixture was then concentrated under reduced pressure, and the remaining aqueous solution was extracted with EtOAc (100 mL × 3). The combined organic extracts were washed with brine (100 mL × 1), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was triturated with acetone, filtered, washed with cold acetone, and dried under reduced pressure to afford the title compound **25** (928 mg, 75%) as a white powder. mp 179–180 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 7.19 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.09 (dd, *J* = 5.4, 3.0 Hz, 2H), 3.83 (ddd, *J* = 3.6, 1.8, 1.8 Hz, 2H), 3.22 (dd, *J* = 1.8, 1.8 Hz, 1H), 2.82–2.81 (m, 2H), 2.23 (ddd, *J* = 10.8, 1.8, 1.8 Hz, 1H), 1.93 (dddd, *J* = 10.8, 1.8, 1.8, 1.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 145.1, 126.5, 122.0, 71.3, 50.6, 42.8 ppm; IR (KBr pellet): ν_{max} = 3391 (-OH), 3242 (-OH) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{11}H_{12}O_2Na$ $[M + Na]^+$:199.0735; found: 199.0764.

(1*R*,4*S*)-1,2,3,4-Tetrahydro-1,4-methanonaphthalene-2,3-dione (26)[21]

Trifluoroacetic anhydride (0.62 mL, 4.50 mmol) was added very slowly to a solution of dry DMSO (0.34 mL) in dry CH_2Cl_2 (10 mL) at -78 °C, and the mixture was stirred for 10 min. Diol **25** (264 mg, 1.50 mmol) in dry THF (5 mL) was added and the reaction mixture was stirred at -78 °C for 2.5 h. Et_3N (1.11 mL) was added to the solution, and the reaction mixture was stirred at -78 °C for a further 3 h, allowed to reach 0 °C, transferred to an ice bath, quenched with sat. NH_4Cl aq. (10 mL), and extracted with Et_2O (30 mL × 3). The combined organic extracts were washed with brine (30 mL × 1), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (20 to 30% EtOAc in hexane) on silica gel (30 mL) to afford the title compound **26** (249 mg, 96%) as a yellow solid. mp 77–79 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 7.36 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.29 (dd, *J* = 5.4, 3.0 Hz, 2H), 3.89 (dd, *J* = 1.8, 1.8 Hz, 2H), 3.12 (ddd, *J* = 10.8, 1.8, 1.8 Hz, 1H), 2.66 (ddd, *J* = 10.8, 1.8, 1.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 301 K): δ = 196.2, 140.5, 129.6, 124.3, 54.3, 44.0 ppm; IR (KBr pellet): ν_{max} = 1758 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{11}H_8O_2Na$ $[M + Na]^+$: 195.0422; found: 195.0425.

(1*R*,4*S*)-1,2,3,4-Tetrahydro-1,4-methanonaphthalene-2,3-dioxime (27)

NaOAc (389 mg, 4.75 mmol) was added to a solution of diketone **26** (400 mg, 1.98 mmol) in MeOH (10 mL), followed by NH_2OH•HCl (550 mg, 7.92 mmol), and the resultant mixture was stirred at 25 °C for 4 h. The reaction mixture was then concentrated under reduced pressure, and H_2O was added to the residue. The resultant mixture was extracted with EtOAc (50 mL × 3), and the combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was dissolved in EtOAc, and hexane was added to precipitate the title compound **27**. The precipitate was filtered, washed with a 1 : 1 mixture of EtOAc and hexane, and dried under reduced pressure to afford the title compound **27** (356 mg, 89%) as a white powder. mp 231–234 °C; ^{1}H NMR (600 MHz, CD_3OD, 299 K): δ = 7.31 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.13 (dd, *J* = 5.4, 3.0 Hz, 2H), 4.64 (dd, *J* = 1.8, 1.8 Hz, 2H), 2.25 (ddd, *J* = 9.6, 1.8, 1.8, 1H), 2.04 (ddd, *J* = 9.6, 1.8, 1.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, MeOD, 302 K): δ = 156.0, 144.4, 126.7, 122.0, 48.7, 44.4 ppm; IR (KBr pellet): ν_{max} = 3352 (-OH) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{11}H_{11}N_2O_2$ $[M + H]^+$: 203.0821; found: 203.0814.

(4*R*,5*S*)-1,3-Dimethyl-4,5-(1*S*,3*R*-benzocyclopentane-1,3-diyl)-imidazolinium chloride (31)

$NiCl_2$ anhydrous (454 mg, 3.50 mmol) was added to a solution of dioxime **27** (354 mg, 1.75 mmol) in

MeOH (17 mL) at 25 °C, and the mixture was stirred for 10 min. After cooling to 0 °C in an ice bath, $NaBH_4$ (662 mg, 17.5 mmol) was added to the resultant solution in small portions, and the reaction mixture was stirred at 25 °C for 4 h. The reaction mixture was then concentrated under reduced pressure, and the crude residue was dissolved in CH_2Cl_2, filtered through a Celite pad, washed with CH_2Cl_2 (30 mL × 3). The combined filtrate and washings were extracted with 2 M HCl aq. (50 mL × 1), and the aqueous layer was washed with CH_2Cl_2 (10 mL × 1) and concentrated under reduced pressure to afford a crude *cis*-diamine hydrochloride **28** (471 mg) (^{1}H NMR (600 MHz, CD_3OD, 299 K): δ = 7.46 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.37 (dd, *J* = 5.4, 3.0 Hz, 2H), 4.35 (dd, *J* = 1.8, 1.8 Hz, 2H), 3.70 (s, 2H), 2.10 (ddd, *J* = 10.8, 1.8, 1.8 Hz, 1H), 2.05 (ddd, *J* = 10.2, 1.8, 1.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, CD_3OD, 303 K): δ = 142.2, 130.0, 125.9, 53.0, 48.5, 47.7 ppm. Product **28** seemed to contain some nickel salts. Et_3N (1.46 mL) was added to a solution of the crude diamine **28** hydrochloride (471 mg) in CH_2Cl_2 (17.5 mL) at 0 °C, followed by ethyl chloroformate (0.67 mL), and the resultant mixture was stirred at 25 °C for 4 h. H_2O was then added to the reaction solution at 0 °C, and extracted with CH_2Cl_2 (30 mL × 3). The combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was

passed through a short pad of silica gel, eluted with 20% EtOAc/CH_2Cl_2, and the eluent was concentrated under reduced pressure to afford the crude bis(ethylcarbamate) **29** (335 mg) as a white solid. THF (10.6 mL) was added to a flask charged with crude bis(ethylcarbamate) **29** (335 mg) and a magnetic stir bar at 25 °C. After cooling to 0 °C in an ice bath, $LiAlH_4$ (160 mg, 4.22 mmol) was added to the resultant solution in small portions, and the reaction mixture was stirred at 50 °C for 2 h. The reaction mixture was then cooled to 0 °C in an ice bath and diluted with 21 mL of THF. H_2O (0.15 mL), 15% NaOH aq. (0.15 mL), and H_2O (0.45 mL) were added sequentially to the mixture at the same temperature. The resultant mixture was stirred at 25 °C for 30 min, and the solution was filtered through a Celite pad, washed with THF (15 mL × 3), and the combined filtrate and washings were concentrated under reduced pressure. In another flask, chlorotrimethylsilane (1.7 mL) was added to MeOH (4.2 mL) with stirring at 0 °C, and the resultant solution was added to the flask charged with the earlier crude residue and a magnetic stir bar. The resultant solution was stirred at 25 °C for a few minutes, and Et_2O was added to precipitate a crude *N*,*N'*-dimethylethylenediamine hydrochloride **30**. The precipitate was filtered, washed with Et_2O, and dried under reduced pressure to afford the crude compound **30** (193 mg) as a yellow powder. $(EtO)_3CH$ (2.9 mL) was added to a flask charged with the

crude compound **30**, and the resultant suspension was heated to 80 °C in an oil bath for 14 h. The reaction mixture was then concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2, and Et_2O was added to precipitate the title imidazolinium chloride **31**. The precipitate was filtered, washed with a 1 : 1 mixture of CH_2Cl_2 and Et_2O, and dried under reduced pressure to afford the title compound **31** (101 mg, 23% over four steps) as a pale yellow powder. A single crystal for X-ray diffraction analysis was grown by the slow vapor diffusion of Et_2O into a CH_2Cl_2 solution. mp 281–283 °C (decomp.); ^{1}H NMR (600 MHz, $CDCl_3$, 299 K): δ = 9.08 (s, 1H), 7.28-7.26 (m, 2H), 7.21 (dd, *J* = 4.8, 3.0 Hz, 2H), 4.85 (s, 2H), 3.85 (s, 2H), 3.12 (s, 6H), 2.07 (d, *J* = 10.2 Hz, 1H), 1.80 (d, *J* = 10.2 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 302 K): δ = 157.9, 140.9, 128.0, 123.1, 68.5, 47.6, 46.5, 33.5 ppm; IR (KBr pellet): ν_{max} = 1653 (C=O) cm^{-1}; HRMS (FAB+) *m/z* calcd. for $C_{14}H_{17}N_2^+$ [M - Cl]$^+$: 213.1392; found: 213.1378.

(4*R*,5*S*)-1,3-Dimethyl-4,5-(1*S*,3*R*-benzocyclopentane-1,3-diyl)-imidazolin-2-ylidene silver chloride (34) Ag_2O (36.4 mg, 157 μmol), imidazolinium chloride **31** (26.1 mg, 105 μmol), and a magnetic stir bar was added to a flask, and the flask was evacuated and backfilled with argon (repeated three times). CH_2Cl_2 (1.05 mL) was added to the resultant flask, and the reaction mixture was stirred for 24 h with a

cover of aluminum foil to darken at room temperature. The resultant mixture was then filtered through a short pad of Celite, and the filter cake was washed with CH_2Cl_2 (2.0 mL× 3), and the combined filtrate and washings were concentrated under reduced pressure to reduce the volume of the solution to ca. 1mL. Et_2O was added to the resultant solution to precipitate the complex, and the precipitate was filtered to afford the silver complex **34** (21 mg, 56%) as a colorless crystalline solid. A single crystal for X-ray diffraction analysis was grown by the slow diffusion of *n*-hexane into a CH_2Cl_2 solution. mp 148-149 °C (decomp); mp 148-149 °C (decomp); ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.22-7.21 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.16-7.14 (dd, *J* = 5.4, 3.0 Hz, 2H), 4.48 (dd, *J* = 1.8, 1.8 Hz, 2H), 3.69 (s, 2H), 2.95 (s, 6H), 2.02-2.00 (d, *J* = 10.2 Hz, 1H), 1.68-1.67 (d, *J* = 10.2 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 302 K): δ = 202.5 (dd, $^1J_{C-Ag}$=259, 219 Hz), 141.7, 127.5, 122.8, 69.7 (d, $^3J_{C-Ag}$= 7.6 Hz), 48.1, 46.8, 36.3 ppm; HRMS (FAB+) *m/z* calcd. for $C_{28}H_{32}N_4Ag^+$ $[L_2Ag]^+$: 531.1678; found: 531.1697; Although the MS spectrum showed that m/z L_2Ag^+ was the parent peak, on the basis of our previous work,[7a] we proposed that the structure shown in Scheme 4 (L-Ag-Cl form rather than L_2Ag-$AgCl_2$ form) seems to be the structure in a solid state. Coupling constant of C-Ag also indicated that complex **34** would be present as a L-Ag-Cl form even in a solution state.[22]

Typical procedure for an allylic arylation

CH_2Cl_2 (0.50 mL) was added to a flask charged with CuCl (2.5 mg, 25 mmol), an imidazolinium salt **7**, **9**, **18**, **24**, or **31** (25 mmol), and magnetic stir bar at 25 °C. The resultant suspension was cooled in a dry-ice/EtOH bath, and *n*-BuLi (1.55 M in hexane, 32 μL) was added to the mixture. After being stirred at the same temperature for 30 min, a solution of cinnamyl bromide (99 mg, 0.50 mmol) in CH_2Cl_2 (0.50 mL) was added to the resultant mixture. A solution of PhMgBr (0.20 mL of 3.0 M solution in Et_2O diluted with 0.25 mL of CH_2Cl_2) was added to the reaction mixture by a syringe pump over 15 min. Once the addition was complete, the resultant mixture was stirred for another 1 h at the same temperature. The reaction mixture was then diluted with Et_2O (2.0 mL) and quenched with 2 M HCl aq. (2.0 mL) at -78 °C. The resultant mixture was allowed to warm to 25 °C and extracted with Et_2O (3 × 4 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was dissolved in CH_2Cl_2, and anthracene (89 mg, 0.5 mmol) was added to the solution as an external standard to calculate the yield based on the crude ^{1}H NMR. After the removal of the solvent, the ratios of the products were calculated based on the crude ^{1}H NMR.

Supporting Information. Copies of the ^{1}H and ^{13}C NMR spectra of all new compounds and compound **1**, **3**, **8**, **10**, **11**, **12**, **25**, and **26**, the NOE spectra of compound **11**, and the crystallographic data of compounds **31** and **32**. This material is available free of charge via the Internet at http://pubs.acs.org.

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