Enantioselective Aziridination Using Copper Complexes of Biaryl Schiff Bases

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Received January 10, 2002

Racemic 2,2′-diamino-6,6′-dimethylbiphenyl is resolved using simulated moving bed chromatography, and the absolute configuration of the enantiomers is confirmed via the X-ray crystal structure of a derivative. The diamine is condensed with a range of aldehydes to give bidentate aldimine proligands **L**. Molecular structures of the complexes formed between L and Cu(I) fall into two classes; bimetallic double helices ($[Cu_2L_2]^{2+}$) and monometallic ($[CuL]^{+}$). The latter are strikingly more efficient in the aziridination of alkenes than are the former in terms of rate, turnover, and enantioselection. In particular, the imine ligand formed from the diamine and 2,6-dichlorobenzaldehyde gives, in combination with Cu(I) or Cu(II), up to 99% ee in the aziridination of 6-acyl-2,2-dimethylchromene and 88−98% ee for a range of cinnamate esters. Styrenic and other alkenes are converted with lower selectivities (5−54%). The catalytic system shows a linear response in product ee to catalyst ee, and the product ee does not vary significantly during the reaction. UV spectrophotometric investigations indicate that conversion of Cu(I) to Cu(II) is not essential for catalysis but that Cu(II) is probably also a competent system.

Introduction

Aziridines are highly versatile synthetic precursors and have been used as synthons for chiral amines, amino acids, amino alcohols, alkaloids, and β-lactam antibiotics.[1] There are also a number of natural products which contain this functionality: for example, the mitomycins, which display potent antitumor and antibiotic activity.[2] Aziridines have been synthesized from amino alcohols.[3] A number of routes to chiral nonracemic aziridines have been developed using carbohydrates, hydroxy acids, epoxides, and 1,2-diols, as well as some enzymatic methods.[1] Catalytic formation of aziridines has been achieved by the addition of carbenes to imines.[4] The first reported addition of nitrene to olefin was by Kwartz and Khan, whereby they generated nitrene from tosyl azide in the presence of copper powder.[5] The development by Evans et al. of the copper-catalyzed aziridination of a wide range of alkenes using PhINTs (*N*-(*p*-toluenesulfonyl)iminophenyliodinane) as the nitrene source was a breakthrough in this area.[6] Further developments led to catalytic enantioselective reactions with the Evans group using chiral nonracemic bis(oxazoline) ligands[7] and the Jacobsen group using bifunctional Schiff bases derived from *trans*-1,2-diaminocyclohexane.[8]

Biaryl ligands have been used in the formation of catalysts for a number of enantioselective transformations, including hydrogenation,[9] Diels−Alder reactions,[10] cyclopropanation,[11] aldol condensations,[12] formation of chiral nonracemic Mannich bases,[13] and ring-closing and ring-opening olefin metathesis.[14] The success of these ligands is due not least to the fact that the axial chirality

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10.1021/jo025515i CCC: $22.00
Published on Web 04/17/2002

of the ligand is well expressed in the steric environment of the active site and because of the structural rigidity provided by the biaryl backbone.

We have described the synthesis of a number of chiral metal complexes based around the diaminobiphenyl backbone **1**[15] and have found that the salicylaldiminate complexes exhibit nonplanar structures in which coligands (e.g. Cl, alkyls) are forced to occupy mutually cis coordination sites.[15a,b] In contrast, salen-derived Schiff-base ligands such as those used in Jacobsen's catalyst almost exclusively have trans structures.[16] We have recently reported a ruthenium Schiff-base system which, as a result of the nonplanar structure, catalyses alkene cyclopropanation with remarkable enantio- and diastereoselectivity.[17] We have previously communicated principles for the design of biaryldiimine ligands for aziridination[18] and an investigation into their mode of action.[19] In this paper we describe synthetic routes to this precatalyst system and detail the methods for its application to the aziridination of chromenes, cinnamate esters, styrenes, and other alkenes.

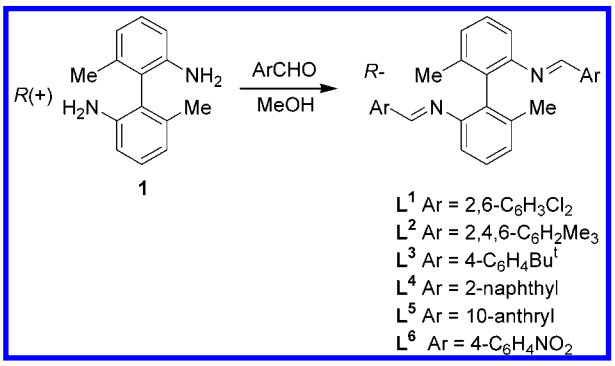
Results and Discussion

Choice, Synthesis, and Resolution of Biaryldiamine. While 1,1′-binaphthyl-2,2′-diamine is commercially available in chiral nonracemic form, it is restrictively expensive for use in exploratory chemistry involving catalyst synthesis and characterization. Also, the potent carcinogen 2-naphthylamine is either used in its synthesis or is a byproduct thereof. In our work on biaryl-bridged chiral diimino ligands we have therefore chosen to use 2,2′-diamino-6,6′-dimethylbiphenyl (**1**).

The diamine was synthesized on a scale of up to 50 g by use of modified literature procedures.[20,21] In particular, the capricious melt-phase Ullmann coupling step was replaced by an adaptation of the Cu/DMF procedure.[22] The subsequent hydrogenation was found to be quantitative in the presence of 5% Pd/C (see the Supporting Information).

The resolution of racemic **1** was attempted using the literature procedure: i.e., repeated crystallization of the tartrate salt.[23] However, while the reported properties of the chiral nonracemic diamines (e.g., melting points and optical rotatory power) were reproduced, we were able to determine by chiral HPLC that chiral nonracemic **1** thus formed had an enantiomeric excess of 82% at best. While exhaustive recrystallization of this material led eventually to an optically pure sample, we found this method inconvenient. The problem of resolution of this compound was finally solved effectively by the use of simulated moving bed (SMB) chromatography.[24]

Scheme 1



A suitable analytical HPLC method was modified to allow maximum throughput without loss of separation. Initial operating conditions for the SMB were obtained after determination of the adsorption isotherm. When the product streams were monitored and the internal concentration profile of the system was determined, good product quality was achieved. It was possible to separate 56 g of racemic **1** in a 24 h period to give the two enantiomers using this method. Enantiomeric excesses of 93.3% for the raffinate and 92.5% for the extract were obtained from an initial pass. Reprocessing of these fractions under the same conditions gave 99.8% ee for the raffinate and 99.1% ee for the extract. Confirmation of the absolute configurations of the diamines produced in this way is described in the following sections.

Schiff Base Ligands. The racemic ligands **L**^{1}−**L**^{6} (Scheme 1) were readily synthesized by condensation of the appropriate aldehyde with the diamine in refluxing methanol or ethanol until precipitation was complete. However, the more soluble chiral nonracemic diimines condensed more slowly and occasionally required some method of dehydration to force the reaction to completion. For example, (*R*)-(+)-**1** and 2,6-dichlorobenzaldehyde were mixed with triethylamine in dichloromethane with dropwise addition of $TiCl_4$ resulting in the formation of (*R*)-**L**^{1}.[25] This latter compound allowed us to confirm the absolute configuration of the diamine by the method described below.

Assignment of Absolute Configuration of (−)-L^1 and Thus (+)-1. Single crystals of **L**^{1} were grown from ether/hexane solution, and the molecular structure was determined. The presence of the relatively heavy Cl atoms in the structure allowed refinement of Flack's parameter *x* to −0.01(8) for the absolute structure (*R*)-(−)-**L**^{1} (see the Supporting Information).[26] The raffinate diamine is thus (*R*)-(+)-**1**, in agreement with Mislow's work, in which *S*-(−)-**1** was synthesized from (*S*)-(−)-6,6′-dinitro-2,2′-bis(bromomethyl)biphenyl.[27]

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Synthesis and Characterization of Cu Complexes. The choice of metal source has played an important role in much of the chemistry of copper-catalyzed aziridination and cyclopropanation reactions. In the latter it was found that Cu(I) was the oxidation state of choice.[6a,b] Evans found that both Cu(I) and Cu(II) were efficient precatalysts for the aziridination of alkenes. For example, both $[Cu(CH_3CN)_4][ClO_4]$ and $[Cu(acac)_2]$ gave a high turnover number.[6b] It was later found that copper(I) triflate was also an excellent catalyst, particularly in combination with chiral ligands such as those of Evans.[6a] Norrby has very recently described detailed calculations on the Jacobsen system which indicate a route by which a Cu(II) starting complex may enter the Cu(I) manifold.[28] Since Cu(I) complexes are diamagnetic, we decided to synthesize precatalysts in this oxidation state.

$[Cu(CH_3CN)_4][BF_4]$ and $[(CuOTf)_2C_6H_6]$ are commercially available but are frequently contaminated with paramagnetic Cu(II). Hence, $[Cu(CH_3CN)_4][BF_4]$ was synthesized by the reaction of copper(I) oxide with tetrafluoroboric acid in refluxing acetonitrile, an adaption of Kubas' procedure.[29] The compound is relatively air and water stable and can be stored in a sealed container for up to 1 month without any appreciable hydrolysis or indefinitely under an inert atmosphere. $[(CuOTf)_2C_6H_6]$ was synthesized by the reaction of copper(I) oxide with trifluoromethanesulfonic anhydride in refluxing benzene, in an adaption of a procedure published by Kochi.[30] The off-white solid can be stored indefinitely under an inert atmosphere.

The copper diimine complexes were synthesized by mixing a slight excess of 1 equiv of the racemic diimine ligand with either of the copper(I) salts $[Cu(CH_3CN)_4][BF_4]$ and $[(CuOTf)_2C_6H_6]$ in dichloromethane, followed by crystallization. The chiral nonracemic complexes crystallized less readily, if at all. The ^1H and $^{13}C\{^1H\}$ NMR spectra in solution of the free ligand $\mathbf{L^1}$ and the diamagnetic complexes $[Cu\mathbf{L^1}(CH_3CN)_2][BF_4]$ or $[Cu\mathbf{L^1}][OTf]$ are all very similar. For example, the singlet resonance for the imine protons appears at ca. 8.5 ppm in all cases. The spectrum obtained by mixing the ligand with substoichiometric amounts of Cu^I has essentially the same appearance; separate ligand/complex peaks are not resolved. This arises from rapid exchange of coordinated and uncoordinated ligands on the ^1H NMR chemical shift time scale, as might be expected for a d^{10} metal center.

Single crystals of the complexes $[Cu\mathbf{L^1}(CH_3CN)_2][BF_4]$ suitable for X-ray structural analysis were grown by concentrating the reaction mixtures in dichloromethane and cooling. Representations of the molecular structure of the cationic unit in $[Cu\mathbf{L^1}(CH_3CN)_2][BF_4]$ are shown in Figure 1. The structure of $[Cu\mathbf{L^2}(CH_3CN)_2][BF_4]$ is similar (see the Supporting Information). The systems are monometallic, with a pseudo-tetrahedral arrangement of the imine nitrogen atoms of the ligand and nitrogen atoms of the two acetonitrile ligands around copper. It is apparent from Figure 1b that the chirality of the diamine is expressed efficiently in the region of the labile acetonitrile ligands. There is a relatively short dative contact between Cl(2) and the metal center (ca. 3.54 Å).

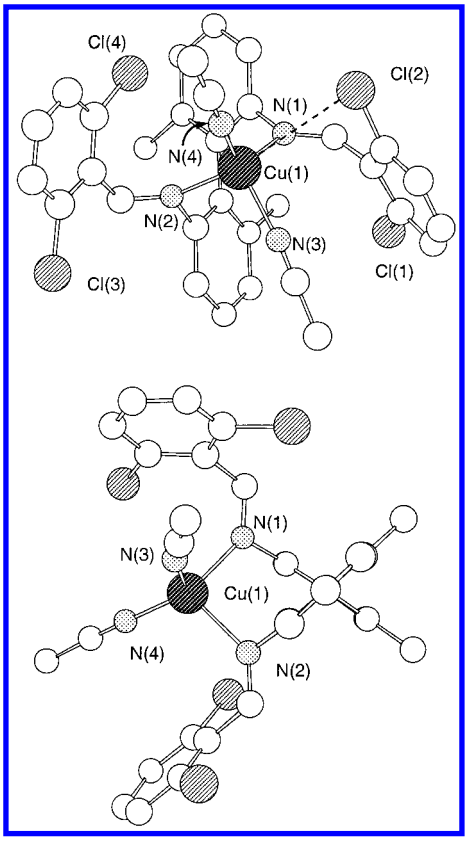

Figure 1. Views (a, top; b, bottom) of the molecular structure of $[Cu\mathbf{L^1}(CH_3CN)_2][BF_4]$.

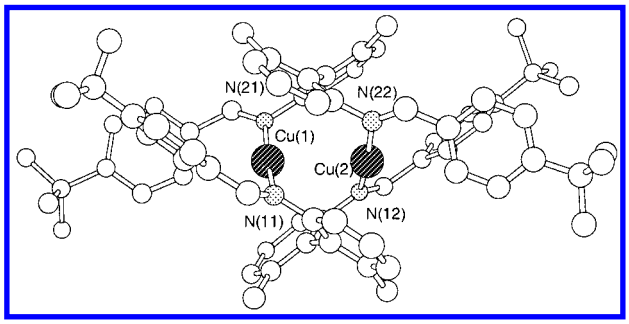

Figure 2. Molecular structure of the dicationic unit in $[Cu_2\mathbf{L^3}_2][OTf]_2$.

The complexes between $\mathbf{L^3}$ and copper sources were synthesized in the same manner and gave NMR spectra similar to those above. However, FAB mass spectra of dichloromethane solutions exhibited ions arising from $[Cu_2\mathbf{L^3}_2][OTf]^+$ (*m*/*z* 1277) and $[Cu_2\mathbf{L^3}_2]^+$ (*m*/*z* 1128) as well as the monometallic $[Cu\mathbf{L^3}]^+$ (*m*/*z* 563). A molecular ion for the monomer unit $[Cu\mathbf{L^3}][OTf]^+$ was not detected as it was for the complexes $[Cu\mathbf{L^1}(OTf)]$ and $[Cu\mathbf{L^1}(OTf)]$.

Subsequently, single crystals of the complexes $[Cu_2\mathbf{L^3}_2][OTf]_2$ were grown from a concentrated solution in dichloromethane. A structural representation is shown in Figure 2, The ligands $\mathbf{L^3}$ bridge between two two-coordinate copper(I) centers. Many linearly coordinated Cu d^{10} compounds have been structurally characterized, including Evans' polymeric bis(oxazoline)copper(I) triflate complex.[6c] In $[Cu_2\mathbf{L^3}_2][OTf]_2$ the biaryl backbone in the ligand dictates that the complex comprises a double helix, both ligands having the same absolute configuration. It

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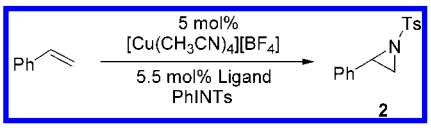
Scheme 2



may be seen from Figure 2 that edge−face contacts between *tert*-butylphenyl rings are present.[31,32]

Hence, there are two distinct structural types present in our precatalysts. The monometallics $[Cu\mathbf{L}(CH_3CN)_2]^+$ arise where ortho substituents are present on the ligand: i.e., for **L**[1], **L**[2], and (according to mass spectra) **L**[5]. Bimetallics $[Cu_2\mathbf{L}_2]^{2+}$ arise where ortho substituents are absent: i.e., **L**[3], **L**[4], and **L**[6].

To investigate the origins of this behavior, we have briefly studied models based on the crystallographically determined structure of the ion $[Cu_2\mathbf{L}^3_2]^{2+}$. Adding 2,6-Cl atoms prevents edge−face orientation of the arenes as in Figure 2, and the face−face conformation is also destabilized by interligand steric compression (between a Cl atom and the biaryl unit of the second ligand). We thus consider that the $[Cu_2\mathbf{L}_2]$ structure is the default type and its formation is prevented by the use of ortho-substituted aromatic rings. This has important implications for turnover, rate, and enantioselectivity in the subsequent catalytic reaction.

Optimization of the Aziridination Reaction. With reference to Evans' procedure, the reaction was optimized for the aziridination of styrene (Scheme 2).[6] A slight excess of the ligand was used to ensure complete complexation of copper ions. The side product *p*-toluenesulfonamide (H_2NTs) was minimized by use of a 5-fold excess of alkene, although high yields of aziridine **2** were obtained when only 1 equiv of the alkene was used. The reaction proceeds very rapidly, and for several reactions all the PhINTs dissolved in less than 1 min.

A wide range of solvents was examined, but only CH_2Cl_2 and MeCN gave reasonable yields. In preliminary enantioselective reactions it was found that CH_2Cl_2 was far superior; it is probable that acetonitrile competes successfully with the diimine ligand, leading to catalysis by achiral derivatives of $[Cu(CH_3CN)_4]^+$.

A number of nitrene sources were examined briefly, and iodinane-type materials such as PhINNs (*N*-(*p*-nitrophenylsulfonyl)iminophenyliodinane),[33] PhINSs (*N*-(2-trimethylsilyl)ethanesulfonylphenyliodinane),[34] and 2-(*tert*-butylsulfonyl)(*p*-toluenesulfonyliminoiodo)-benzene[35] were effective. The more commonly used PhINTs (*N*-(*p*-toluenesulfonyl)iminophenyliodinane) was chosen for detailed study because of its ease of synthesis and so that results could be compared directly with those of others. Chloramine-T did not operate as a nitrene source, although this has been achieved by Taylor in another system.[36]

Scheme 3

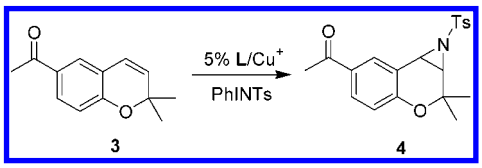


Table 1. Enantioselective Aziridination of Chromene 3[a]

entry	ligand	temp/°C	yield/%	*t*/min[b]	ee/%
1	**L**[3]	room temp	53	900	13
2	**L**[4]	room temp	75	900	16[c]
3	**L**[1]	room temp	83	<10	86
4	**L**[2]	room temp	79	<10	55
5	**L**[5]	room temp	56	<10	65
6	**L**[6]	room temp	0	900	
7[e]	**L**[1]	room temp	85	<10	85
8	**L**[1]	−40	80	300[d]	94
9[e]	**L**[1]	−40	87	300[d]	99

[a] $[Cu^I(CH_3CN)_4]BF_4$ was used as the Cu^I source, unless otherwise stated. Substitution of $[Cu^I_2(OTf)_2]\cdot C_6H_6$ did not affect the results significantly. [b] Time until all PhINTs had dissolved. [c] Opposite enantiomer to other ligand systems. [d] The rate of the low-temperature reactions is probably limited by the rate of dissolution of PhINTs at −40 °C. [e] $[Cu^{II}(CH_3CN)_4][BF_4]_2$ was used as the source of copper.[38]

The performances of the different ligands were assessed in a test reaction involving chromene **3** (Scheme 3). In the case of the systems which form bimetallic $[Cu_2L_2]$ precatalysts**,** dissolution of the sparingly soluble trivalent iodinane nitrene source PhINTs was not complete after 900 min and the enantiomeric excess of the product was very poor (Table 1, entries 1, 2, and 6). The systems having monometallic precatalysts were strikingly more efficient. Dissolution of PhINTs was complete in minutes, isolated yields were good, and the product ee was dramatically improved (entries 3−5).[37]

It is apparent also from Table 1 that the nature of the ortho substituents on the ligand has a pronounced effect on the ee, with dichloro giving the best results. We propose that this arises from the function of Cl as a dative ligand for the copper center, as noted in the structure of $[Cu\mathbf{L}^1(CH_3CN)_2][BF_4]$ and also in our DFT calculations.[19] Such interactions at the metal will help to shape the chiral pocket at the active site, without taking up one of the key tetrahedral positions.

The mass spectrometric data presented above indicate that the structures obtained from X-ray crystallography appear also to be present in solution. Nevertheless, given the rapid ligand exchange possible in Cu systems, it remained that a nonlinear effect[19] might be responsible for the variation in catalyst performance. This possibility is almost certainly excluded by the fact that essentially linear plots were obtained for ee_{ligand} vs $ee_{product}$ for **L**[1], **L**[3], and **L**[4] (Figure 3).

Further in support of a simple, "single-site" catalyst, we have found that the enantiomeric excess of the product obtained does not vary significantly with the percent conversion (Figure 4); it is very unlikely that the nature of the active catalyst changes during the course of the reaction.

The degree of enantiomeric excess obtained, the rate of reaction, and the yield thus relate very strongly to the

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(32) The phenomenon of noncovalent interactions between arene rings is well-documented, and for edge−face interactions the distances between the two ring centroids are found in the range 4.5−7.0 Å, with a theoretical optimum distance of 5.2 Å. In $[Cu_2\mathbf{L}^3_2\}_2][OTf]_2$ the centroid−centroid distances are ca. 4.99 Å. (a) Burley, S. K.; Petsko, G. A. *Science* **1985**, *229*, 23. (b) Jorgensen, W. L.; Severance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768.

(33) (a) Fukuyama, T.; Jow, C.-K.; Cheung, M. *Tetrahedron Lett.* **1995**, *36*, 6373. (b) Fukuyama, T.; Cheung, M.; Jow, C.-K.; Hidai, Y.; Kan, T. *Tetrahedron Lett.* **1997**, *38*, 5831.

(34) Dauban, P.; Dodd, R. H. *J. Org. Chem.* **1999**, *64*, 5304.

(35) Macikenas, D.; Skrzypczak-Jankun, E.; Protasiewicz, J. D. *J. Am. Chem. Soc.* **1999**, *121*, 7164.

(36) Albone, D. P.; Aujla, P. S.; Taylor, P. C.; Challenger, S.; Derrick, A. M. *J. Org. Chem.* **1998**, *63*, 9569.

(37) Strenuous attempts to determine the absolute configuration of the chromene aziridine by crystallographic and synthetic methods were unsuccessful.

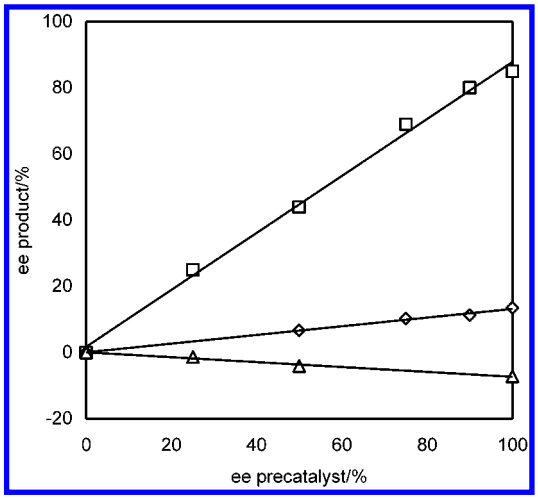


Figure 3. Variation of the enantiomeric excess of the product with that of the precatalyst for the aziridination of chromene **3** with $[Cu(CH_3CN)_4]BF_4$ in the presence of chiral nonracemic **L**: (□) $\mathbf{L^1}$; (◊) $\mathbf{L^3}$; (△) $\mathbf{L^4}$.

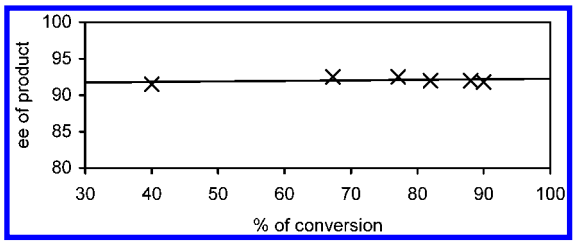


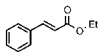
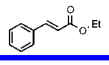
Figure 4. Variation of product ee with conversion for the aziridination of **3** with PhINTs using 5% $[Cu(CH_3CN)_4][BF_4]$ and 5.5% (*R*)-$\mathbf{L^1}$ in CH_2Cl_2.

structure of the precatalyst determined by X-ray crystallography. This could arise for a number of reasons. Since the bimetallic Cu_2L_2 complexes do not have sterically available coordination sites, the aziridination reaction in these cases may be being mediated by an equilibrium amount of an achiral copper complex, e.g. $[Cu(CH_3CN)_n]^+$. The low rates of reaction obtained would thus be due to very low concentrations of this catalyst at equilibrium. The low ee's obtained could arise from catalysis by a small equilibrium amount of the monomeric $[CuL]^+$. It seems less likely that the Cu_2L_2 catalyzes the reaction with low enantioselection.

To ascertain whether this effect holds for other alkene substrate types, catalyst systems of both mono- and bimetallic types were used in the aziridination of styrene and ethyl cinnamate. The results in Table 2 show that, as with chromene, the time for completion of the reaction, yield, and ee are significantly better for the monometallic [CuL] systems than for $[Cu_2L_2]$.

UV Studies. Evans proposes oxidation of Cu(I) to a Cu(II) active catalyst in the bis(oxazoline) ligated system.[7] The identical performance of the two catalysts in terms of yield and ee and indistinguishable UV spectra for the complexes treated with PhINTs strongly support this. In our system it can be seen from Figure 5 that the spectrum (a) of precatalyst $[Cu\mathbf{L^1}(CH_3CN)_2][BF_4]$ is little affected by treatment with PhINTs (b). The analogous Cu(II) spectra behave similarly ((c) and (d)).[38] Comparison of (b) with (d) shows that the addition of PhINTs has apparently not caused oxidation of the Cu(I) complex.

Table 2

Entry	Ligand	Substrate	Time	Yield / %	ee / %
1	$\mathbf{L^1}$		30 min	91	27
2	$\mathbf{L^4}$		15 h	69	5
3	$\mathbf{L^1}$		10 min	63	75
4	$\mathbf{L^4}$		O/N	45	40

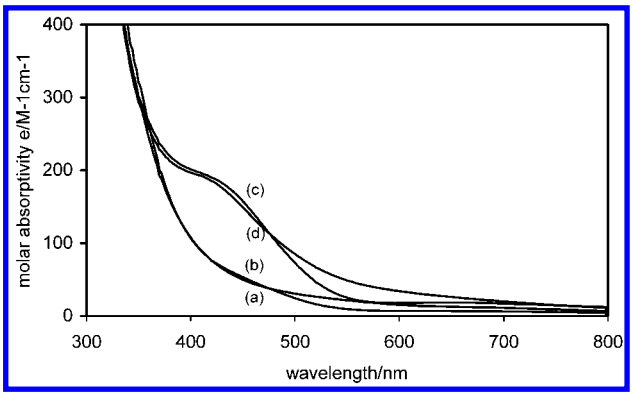
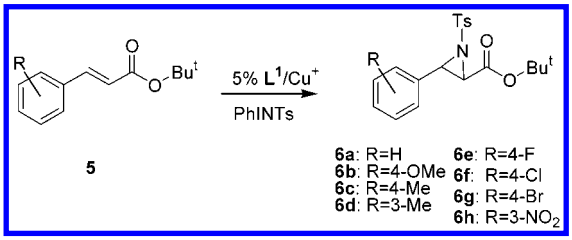


Figure 5. UV spectra of Cu(I) and Cu(II) complexes reacted with PhINTs in CH_2Cl_2: (a) $[Cu^I(CH_3CN)_4][BF_4] + \mathbf{L^1}$, 10 mM in CH_2Cl_2; (b) $[Cu^I(CH_3CN)_4][BF_4] + \mathbf{L^1}$ + PhINTs, 10 mM in CH_2Cl_2; (c) $[Cu^{II}(CH_3CN)_4][BF_4]_2 + \mathbf{L^1}$, 10 mM in CH_2Cl_2; (d) $[Cu^{II}(CH_3CN)_4][BF_4]_2 + \mathbf{L^1}$ + PhINTs, 10 mM in CH_2Cl_2.

Scheme 4



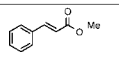
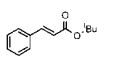
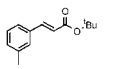
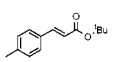
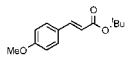
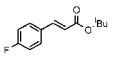
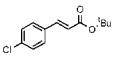
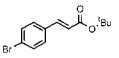
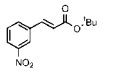
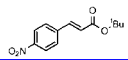
These observations indicate that in the present system the conversion of Cu(I) to Cu(II) is not essential for catalysis. Nevertheless, it seems either that Cu(II) is also a competent catalyst or that a small amount of Cu(II) is reduced to a Cu(I) catalyst in situ, perhaps by the Norrby mechanism.[28]

Enantioselective Aziridination of Cinnamate Esters. We set out to optimize the aziridination of cinnamate esters, the products of which may allow access to phenylalanine analogues.[39] The ligand $\mathbf{L^1}$ (Scheme 4) was used throughout the experiments, whose results are shown in Table 3. In most cases a significant improvement in yield and ee was observed for reactions performed at −40 °C compared to those at room temperature. At still lower temperatures the rate was made

(38) (a) Hathaway, B. J.; Underhill, A. E. *J. Chem. Soc.* **1960**, 3705. (b) Hathaway, B. J.; Holah, D. G.; Underhill, A. E. *J. Chem. Soc.* **1962**, 2444.

(39) (a) Dauban, P.; Dodd, R. H. *Tetrahedron Lett.* **1998**, *39*, 5739. (b) Rousseau, J.-F.; Dodd, R. H. *J. Org. Chem.* **1998**, *63*, 2731.

Table 3. Aziridination of Cinnamate Esters

Entry	Cinnamate	Yield %[a]		EE %[b]		Config.
		R.T	-40°C	R.T	-40°C	
1		70	-	69[c]	-[c]	2S, 3R (-)
2		59	77	77	89	2*S*, 3*R* (-)
3		58	56	81[c]	96[c]	(-)
4		59	82	60[c]	88[c]	(-)
5		51	67	87	93	(+)
6		66	45	92	98	(-)
7		69	89	85	92	(-)
8		45	59	96	98	(-)
9		28	32	61	96	(-)
10		0	0	-	-	(-)

[a] Recovered yield. [b] Enantiomeric excess determined by HPLC using Chiralpak Chiralcel OD column 15 cm × 0.46 cm i.d. with mobile phase hexane/propan-2-ol (various ratios) unless otherwise stated. [c] Enantiomeric excess determined by ^{1}H NMR in the presence of the chiral shift reagent Eu(hfc)$_3$.

inconveniently slow, probably limited by the rate of dissolution of PhINTs. It was first noted that the size of the ester alkyl substituent has a small but significant influence on enantioselection; the *tert*-butyl compound (entry 2) gave a higher ee than the methyl (entry 1) and ethyl compounds (entry 4, Table 2). For this reason, the *tert*-butyl esters **5**, synthesized readily from the commercially available acids (see the Supporting Information) were used in subsequent studies. Arene substitution with various groups appears to have little effect on enantioselection, although the 3-NO_2 compound gave low yields (entries 2−8). Significantly, no cis/trans isomerism was observed; only anti isomers of the aziridines were detected. The absolute configuration of the unsubstituted aziridine (entry 2) was determined by comparison of the observed optical rotation with the literature value[7] and confirmed by X-ray crystallography (see the Supporting Information). The 2*S*,3*R* configuration is as predicted by our previously communicated model.[19]

Aziridination of Styrenic Alkenes. The results for aziridination of a number of styrenic and other alkenes are given in Table 4. Although yields are reasonable, enantiomeric excesses for these substrates are low in comparison to those with the functionalized systems above. The contrast with cinnamates is significant and can be attributed to a lack of secondary binding of the substrate.[19] Evans observed similar selectivities for the cinnamate and styrenic substrates.[7] Unlike the cinnamate esters, significant levels of trans/cis isomerization are apparent in some cases. Similarly to Evans,[7] we found that the absolute configuration of styrene-derived aziridine was opposite to that for the trans substrates *β*-methylstyrene and methyl cinnamate.[40]

Table 4. Aziridination of Olefins Using Cu^{I}/L^{1} as Catalyst

Entry	*Olefin*	Temp.	Yield %	*Trans*:*Cis*	ee %
1		R.T.	40	90:10	26[a,b]/18[c]
2		-40°C	88	97:3	28[b]
3		R.T.	64	100:0	6.5
4		-40°C	66	100:0	5.1
5		R.T.	60	8:92	meso
6		-40°C	63	5:95	meso
7		R.T.	60	-	54[d]
8		-40°C	60	-	36[d]
9		R.T.	17	-	meso

[a] Absolute configuration 2*R*,3*R*-(−) determined by comparison with data from ref 7. [b] ee for trans product. [c] ee for cis product. [d] Absolute configuration 2*S*,3*R*-(−) determined by comparison with data from ref 8b.

Conclusions

Efficient, and in some cases highly enantioselective, catalysts for the aziridination of alkenes have been produced using a biaryldiimine ligand set **L^n** at copper. The performance of the catalysts is highly dependent on the substitution pattern of the ligand arylimine unit, which determines catalyst speciation; ortho disubstitution is required to furnish monometallic, active systems. By some way the highest enantioselectivities are obtained for **L^1**, which contains *o*-dichlorophenyl groups. Interestingly, the most successful ligands in Jacobsen's diiminocyclohexane[8] system and Suga and co-workers' binaphthyldiimine catalysts[11c] for aziridination and cyclopropanation repectively, also incorporate this unit. In the former case this may be due to the presence of Cl···Cu dative interactions.[19] In the latter, catalyst speciation as described above is likely to be the determining factor.

Experimental Section

General Experimental Procedures. Catalytic procedures were carried out under an inert atmosphere of argon by using a dual-manifold vacuum/argon line and standard Schlenk techniques. Solvents were dried by refluxing over the appropriate drying agent (calcium hydride for dichloromethane, potassium for THF) for 3 days under dinitrogen. All glassware, cannulas, and Celite were stored in an oven (>100 °C) and

(40) This refers to the configuration of the benzylic carbon.

flame-dried immediately prior to use. Deuterated chloroform was dried in the bottle in air over molecular sieves (4 Å).

Infrared spectra were obtained either as Nujol mulls or by evaporation of dichloromethane solutions onto IR plates. SMB separation was performed on a Novasep Licoseplab with 8 × Chiralpak AD columns, 10 cm bed length × 26 mm id. The eluent was hexane/IPA in the ratio 60:40 maintained at 28 °C. HPLC experiments were performed on a Kontron instrument: Model 332 detector, Model 320 system. The columns used were Chiracel OD and AD, 15.0 cm × 0.46 cm i.d. Column chromatography was performed using a selection of column widths and Merck silica gel 60. Thin-layer chromatography was performed using Merck 0.25 mm silica layer foil-backed plates.

Synthesis of Ligands L¹−L⁶. (±)-*N*,*N*′-Bis(2,6-dichlorobenzylidene)-6,6′-dimethylbiphenyl-2,2′-diamine (L¹). The following represents the general procedure for ligand synthesis. (±)-2,2′-Diamino-6,6′-dimethylbiphenyl (**1**; 1.06 g, 5.0 mmol) and 2,6-dichlorobenzaldehyde (0.88 g, 5.0 mmol) were dissolved in methanol (10 mL) and stirred at room temperature for 3 h to produce a yellow crystalline solid. The reaction mixture was cooled to −30 °C, and the resultant crystals of the Schiff base were isolated by vacuum filtration, washed with cold methanol, and dried in vacuo. Yield: 2.2 g, 89%. Mp: 166 °C. ^{1}H NMR ($CDCl_3$; δ):, 2.05 (s, 6H), 6.86 (d, 2H, J = 7.3 Hz), 7.07−7.29 (m, 10H), 8.51 (s, 2H). ^{13}C NMR ($CDCl_3$; δ): 19.8, 115.7, 127.3, 128.5, 130.1, 131.8, 132.4, 135.0, 137.1, 151.0, 155.7. MS (EI$^+$): m/z 527 (M^+), 511 ($M^+ - CH_3$), 353 ($M^+ - NC_7H_4Cl_2$). IR (CD_2Cl_2; ν, cm^{-1}): 3056, 2915, 2358, 1635, 1575, 1557, 1455, 1430, 775, 749. Anal. Calcd for $C_{28}H_{20}N_2Cl_4$: C, 63.90; H, 3.83; N, 5.32. Found: C, 63.89; H, 3.80; N, 5.36.

(*R*)-(−)-L¹. (*R*)-**1** (1.06 g, 5.0 mmol) and 2,6-dichlorobenzaldehyde (0.88 g, 5 mmol) were placed in a 100 mL round-bottom flask, and dichloromethane (20 mL) and Et_3N (2.5 mL) were added. The solution was cooled to 0 °C in an ice/salt bath. A solution of $TiCl_4$ in dichloromethane (2.5 mmol) was added over 5 min. The solution was stirred overnight and then filtered through Celite before evaporation in vacuo. The residue was redissolved in toluene, and the solution was stirred for 30 min. After filtration the toluene was removed in vacuo and the crude residue was recrystallized from ether/hexane. Yield: 1.4 g, 56%. $[\alpha]_D^{25} = -28.1°$ (c 0.360, CH_2Cl_2). A crystal suitable for X-ray structural determination was chosen and the molecular structure solved. Refinement of the Flack parameter showed that the correct absolute structure was the *R* isomer.

(±)-*N*,*N*′-Bis(2,4,6-trimethylbenzylidene)-6,6′-dimethylbiphenyl-2,2′-diamine (L²). Yellow crystalline solid. Yield: 4.9 g, 87%. Mp: 138 °C. ^{1}H NMR ($CDCl_3$; δ): 2.03 (s, 6H). 2.09 (s, 12H), 2.22 (s, 6H), 6.75 (s, 4H), 6.75 (d, 2H, J = 7.6 Hz), 7.06 (d, 2H, J = 7.6 Hz), 7.22 (t, 2H, J = 7.6 Hz), 8.55 (s, 2H). ^{13}C NMR ($CDCl_3$; δ): 19.9, 20.5, 21.0,. 115.4, 126.4, 127.7, 129.5, 130.1, 132.4, 136.7, 138.7, 139.2, 152.3, 159.3. MS (EI$^+$; m/z): 472 (M^+), 457 ($M^+ - CH_3$). IR (CD_2Cl_2; ν, cm^{-1}): 3057, 2917, 2860, 2358, 1925, 1631, 1607, 1573, 1453, 1377, 845, 778, 743. Anal. Calcd for $C_{34}H_{36}N_2$: C, 86.40; H, 7.68; N, 5.93. Found: C, 86.47; H, 7.70; N, 5.91.

(*R*)-(−)-L². Yield: 52%. $[\alpha]_D^{25} = -578.2°$ (c 0.188, CH_2Cl_2).

(±)-*N*,*N*′-Bis(4-*tert*-butylbenzylidene)-6,6′-dimethylbiphenyl-2,2′-diamine (L³). White crystalline solid. Yield: 0.76 g, 65%. Mp: 165 °C. ^{1}H NMR ($CDCl_3$; δ): 1.31 (s, 18H), 2.05 (s, 6H,), 6.79 (d, 2H, J = 8.7 Hz), 7.07 (d, 2H, J = 8.7 Hz), 7.21 (t, 2H, J = 9.3 Hz), 7.35 (d, 4H, J = 9.9 Hz), 7.48 (d, 4H, J = 9.9 Hz), 8.18 (s, 2H). ^{13}C NMR ($CDCl_3$; δ): 20.4, 31.6, 116.0, 125.8, 126.9, 128.0, 128.7, 132.4, 134.4, 137.3, 159.6 151.7, 154.6. MS (EI$^+$; m/z) 500 (M^+), 485 (M^+ − Me). MS (CI$^+$; m/z) 501 (MH^+). IR (CH_2Cl_2; ν, cm^{-1}): 3056, 2961, 2865, 1630, 1566, 1456, 830, 746. Anal. Calcd for $C_{36}H_{40}N_2$: C, 86.35; H, 8.05; N, 5.60. Found: C, 86.44; H, 8.05; N, 5.57.

(*R*)-(−)-L³. Yield: 1.1 g, 90%. $[\alpha]_D^{25} = -765.4°$ (c 0.156, CH_2Cl_2).

(±)-[*N*,*N*′-Bis(2-naphthylidene)-6,6′-dimethylbiphenyl-2,2′-diamine (L⁴). Yield: 2.1 g, 85%. Mp: 168 °C. ^{1}H NMR ($CDCl_3$; δ): 2.12 (s, 6H). 6.84 (d, 2H, J = 7.5 Hz), 7.12 (d, 2H, J = 7.5 Hz), 7.23−7.28 (m, 3H), 7.45−7.65 (m, 4H), 7.80−7.83 (m, 10H), 8.25 (s, 2H). ^{13}C NMR ($CDCl_3$; δ): 20.0 (Me). 115.5 (Ar), 123.8, 126.4, 126.8, 127.2, 127.8, 128.3, 128.6, 130.8, 132.1, 132.9, 134.2, 134.8, 136.9, 151.4, 159.6. MS (EI$^+$; m/z): 488 (M^+), 473 (M^+- CH_3). IR (CD_2Cl_2; ν, cm^{-1}): 3054, 2917, 2859, 1925, 1620, 1571, 1453, 819, 764, 745. Anal. Calcd for $C_{36}H_{28}N_2$: C, 88.49; H, 5.77; N, 5.73. Found: C, 87.85; H, 5.72; N, 5.72.

(*R*)-(−)-L⁴. Yield: 1.8 g, 80%. $[\alpha]_D^{25} = -832.4°$ (c 0.250, CH_2Cl_2). HPLC (Chiracel OD, hexane/IPA 90:10, 0.5 mL/min): t_R = 9.8 (0.4%), 11.5 (99.6%) min; ee = 99.2%.

(*R*)-(−)-*N*,*N*′-Bis(anthracen-9-ylidene)-6,6′-dimethylbiphenyl-2,2′-diamine ((*R*)-(−)-L⁵). Yellow powder. Yield: 2.56 g, 93%. ^{1}H NMR ($CDCl_3$; δ): 2.24 (s, 6H), 7.18−7.25 (m, 6H), 7.33−7.39 (m, 6H), 7.54 (t, 2H, J = 7.7 Hz), 7.89 (d, 4H, J = 8.5 Hz), 8.18 (d, 4H, J = 9.0 Hz), 8.38 (s, 2H), 9.48 (s, 2H). ^{13}C NMR (CD_2Cl_2; δ): 20.7, 117.1, 125.5, 126.0, 127.7, 128.0, 128.3, 129.4, 129.5, 131.0, 131.1, 131.9, 133.7, 138.1, 153.4, 160.3. MS (EI$^+$; m/z): 588 (M^+). MS (CI$^+$; m/z): 607 (MNH_4^+), 589 (MH^+). IR (CH_2Cl_2; ν, cm^{-1}): 3051, 2918, 2862, 1671, 1626, 1572, 1520, 1451, 1263, 1239, 890, 784, 732. Anal. Calcd for $C_{44}H_{32}N_2$: C, 89.76; H, 5.48; N, 4.76. Found: C, 89.33; H, 5.34; N, 4.84. $[\alpha]_D^{25} = -6.1°$ (c 0.114, CH_2Cl_2).

(±)-*N*,*N*′-Bis(4-nitrobenzylidene)-6,6′-dimethylbiphenyl-2,2′-diamine (L⁶). Yellow crystalline solid. Yield: 2.0 g, 88%. Mp: 278 °C. ^{1}H NMR ($CDCl_3$; δ): 2.04 (s, 6H), 6.88 (d, 2H, J = 7.7 Hz), 7.16 (d, 2H, J = 7.5 Hz), 7.28 (t, 2H, J = 7.7 Hz), 7.62 (d, 4H, J = 8.7 Hz), 8.17 (d, 4H, J = 8.9 Hz), 8.28 (s, 2H). ^{13}C NMR ($CDCl_3$; δ): 19.9, 114.4, 123.8, 127.9, 128.1, 128.9, 132.5, 137.3, 141.7, 149.0, 149.6, 156.3. MS (EI$^+$; m/z): 478 (M^+). IR (CD_2Cl_2; ν, cm^{-1}): 3010, 2359, 1638, 1600, 1523, 1343, 855, 841, 744, 689. Anal. Calcd for $C_{28}H_{22}N_4O_4$: C, 70.28; H, 4.63; N, 11.71. Found: C, 70.19; H, 4.66; N, 11.63.

Copper Complexes. [CuL¹(CH₃CN)₂][BF₄]·CH₂Cl₂. A Schlenk vessel was charged with $[Cu(CH_3CN)_4][BF_4]$ (72.4 mg, 230 μmol) and **(±)-L¹** (133 mg, 253 μmol). The two solids were dissolved in dichloromethane with stirring, and an equal volume of pentane was added to the yellow solution. When the mixture was cooled, yellow needlelike crystals formed. The crystals were of sufficient quality for X-ray analysis. Drying in vacuo caused loss of 1 mol of dichloromethane of crystallization. ^{1}H NMR (CD_2Cl_2; δ): 1.95 (s, 6H), 2.05 (s, 6H), 7.00−7.44 (m, 12H), 8.54 (s, 2H). ^{13}C NMR (CD_2Cl_2; δ): 2.5, 20.2, 118.2, 129.5, 129.96, 130.04, 132.1, 133.0, 135.0, 139.7, 162.6. Anal. Calcd for $C_{33}H_{28}BCl_6CuF_4N_4$: C, 46.96; H, 3.35; N, 6.64. Found: C, 47.44; H, 3.37; N, 6.35.

[CuL¹][OTf]. (±)-L¹ (13.4 mg, 25.4 μmol) and $(CuOTf)_2 \cdot C_6H_6$ (6.0 mg, 12.0 μmol) were dissolved in d_2-dichloromethane. ^{1}H NMR (CD_2Cl_2; δ): 1.89 (s, 6H). 7.20−7.30 (m, 15H), 8.46 (s, 2H). ^{13}C NMR (CD_2Cl_2; δ): 20.31, 118.75, 129.07, 129.75, 130.08, 131.25, 132.97, 135.10, 162.56. IR (CD_2Cl_2; ν, cm^{-1}): 3339, 3121, 2302, 2196, 1750, 1628, 1579, 1560, 1433, 1385, 1313, 1270, 1234, 1211, 1170. MS (EI; m/z): 738 [Cu**L¹**][OTf]$^+$, 589 [Cu**L¹**]$^+$, 527 [**L¹**] $^+$. MS (CI; m/z): 589 [Cu**L¹**]$^+$, 527 [L¹] $^+$.

[CuL²(CH₃CN)₂][BF₄]. (±)-L² (12.0 mg, 25.4 μmol) and $[Cu(CH_3CN)_4][BF_4]$ (7.3 mg, 23.0 μmol) were dissolved in d_2-dichloromethane with warming. The sample was placed in the freezer (−30 °C). The yellow crystals obtained were suitable for X-ray structural determination. Drying in vacuo caused complete loss of the solvent of crystallization. ^{1}H NMR ($CDCl_3$; δ): 1.86 (s, 6H). 1.94 (s, 12H), 2.02 (s, 6H), 2.23 (s, 6H), 6.81 (s, 4H), 6.94 (d, 2H, J = 7.6 Hz), 7.25 (d, 2H, J = 7.6 Hz), 7.39 (t, 2H, J = 7.6 Hz), 8.55 (s, 2H). IR (CH_2Cl_2; ν, cm^{-1}): 2360, 2342, 1573, 1385, 1299, 1242, 1210, 1057, 872, 850, 784, 741. Anal. Calcd for $C_{38}H_{42}BCuF_4N_4$: C, 64.73; H, 6.00; N, 7.95. Found: C, 64.44; H, 6.06; N, 8.05.

[CuL²][OTf]. (±)-L² (13.0 mg, 27.5 μmol) and $(CuOTf)_2 \cdot C_6H_6$ (6.3 mg, 12.5 μmol) were dissolved in d_2-dichloromethane. ^{1}H NMR (CD_2Cl_2; δ): 1.91 (s, 6H), 1.94 (s, 12H), 2.14 (s, 6H), 6.73 (s, 4H), 6.93 (d, 2H, J = 7.7 Hz), 7.18 (d, 2H, J = 7.5 Hz), 7.22 (s, 3H, C_6H_6), 7.30 (t, 2H, J = 7.7 Hz), 8.54 (s, 2H). ^{13}C NMR (CD_2Cl_2; δ): 20.2, 20.3, 21.7, 129.8 (C_6H_6), 119.2, 128.9, 1230.0, 130.3, 130.8, 131.0, 137.5, 139.1, 141.5, 149.2, 169.4. MS (FAB$^+$; m/z): 684 ([Cu**L²**][OTf]$^+$), 535 ([Cu**L²**]$^+$), 471 [**L²**]$^+$.

[$Cu_2L^3_2$][OTf]$_2$. (±)-L^3 (12.5 mg, 25.0 μmol) and (CuOTf)$_2$·C_6H_6 (6.0 mg, 12 μmol) were dissolved in d_2-dichloromethane. After NMR analysis, concentration of the solution resulted in formation of crystals suitable for X-ray diffraction. Drying in vacuo caused complete loss of the solvent of crystallization. ^{1}H NMR (CD_2Cl_2; δ): 1.12 (s, 36H), 1.73 (s, 12H), 7.00 (d, 8H, J = 8.3 Hz), 7.15 (d, 8H, J = 7.5 Hz), 7.19 (t, 4H, J = 7.5 Hz), 7.42 (d, 8H, J = 8.3 Hz), 7.26 (s, C_6H_6), 8.62 (s, 4H). ^{13}C NMR (CD_2Cl_2; δ): 20.4, 31.4, 129.1 (C_6H_6), 122.0, 126.8, 129.7, 129.9, 130.8, 132.0, 133.1, 140.3, 160.7, 149.6, 173.0. MS (EI$^+$; *m*/*z*): 712 [{Cu^I**L^3**}][OTf]$^+$, 500 [**L^3**]$^+$, 485 [**L^3** − CH_3^+]. MS (CI$^+$; *m*/*z*): 713 [Cu^I**L^3**][OTf][H]$^+$, 649 [(M$^+$) − Cu], 563 [Cu^I**L^3**]$^+$, 485 [**L^3** − CH_3^+], 340 [**L^3** − N=$CHC_6H_4C(CH_3)_3$+]. MS (FAB$^+$; *m*/*z*): 1277 ([$Cu_2L^3_2$][OTf]$^+$), 1128 [Cu_2**L$^3_2$**$^+$], 1063 [Cu**L$^3_2$**]. High-resolution MS (EI$^+$): calcd mass (M$^+$) 712.200 774, found 712.193 039. Anal. Calcd for $C_{74}H_{80}Cu_2F_6N_4O_6S_2$: C, 62.30; H, 5.65; N, 3.93. Found: C, 62.30; H, 6.00; N, 4.15.

[$Cu_2L^4_2$][OTf]$_2$. (±)-L^4 (12.0 mg, 24.6 μmol) and (CuOTf)$_2$·C_6H_6 (6.0 mg, 12 μmol) were dissolved in d_2-dichloromethane. Concentration of the solution resulted in the formation of crystals suitable for X-ray diffraction. ^{1}H NMR (CD_2Cl_2; δ): 1.96 (s, 12H), 6.64 (d, 4H, J = 8.6 Hz), 6.84 (d, 4H, J = 8.7 Hz), 7.06 (d, 4H, J = 7.9 Hz), 7.26 (s, C_6H_6), 7.74 (s, 4H), 7.38−7.14 (m, 16H), 8.77 (s, 4H). ^{13}C NMR (CD_2Cl_2; δ): 20.7, 121.7, 122.3, 128.0, 128.4, 129.1, 129.2, 129.4, 129.6, 130.5, 132.4, 132.6, 133.1, 136.3, 149.9, 140.5, 164.9, 174.0. MS (FAB$^+$; *m*/*z*): 1253 ([{Cu**L^4**}$_2$][OTf]$^+$), 1104 ([{Cu**L^4**}$_2$]$^+$), 1040 ([(Cu**L^4**)$_2$]$^+$), 552 ([Cu**L^4**]$^+$). Anal. Calcd for $C_{74}H_{56}Cu_2F_6N_4O_6S_2$: C, 63.37; H, 4.02; N, 3.99. Found: C, 63.30; H, 4.10; N, 3.95.

[CuL^5][OTf]. (*R*)-**L^5** (15.0 mg, 25.5 μmol) and (CuOTf)$_2$·C_6H_6 (6.0 mg, 12 μmol) were dissolved in d_2-dichloromethane. ^{1}H NMR (CD_2Cl_2; δ): 2.06 (s, 6H), 7.23 (s, C_6H_6), 6.79−8.11 (m, 26H), 9.38 (s, 2H). ^{13}C NMR (CD_2Cl_2; δ): 20.5, 119.9, 123.0, 124.7, 125.0, 128.4, 129.0, 129.1 (C_6H_6), 129.2, 130.5, 130.8, 131.1, 131.3, 131.4, 132.8, 135.9, 139.9, 149.6, 164.4, 169.2. MS (FAB$^+$; *m*/*z*): 651 ([Cu**L^5**]$^+$). IR (CD_2Cl_2; ν, cm^{-1}): 3485, 3054, 1666, 1623, 1606, 1553, 1446, 1261, 1235, 1173, 1030, 954, 896, 736.

General Procedure for Aziridination. A round-bottom flask with a sidearm incorporating a PTFE stopcock was charged with the metal salt (5 mol %) and the diimine ligand (6 mol %) and was flushed with argon. Solvent (6 mL), usually dichloromethane, was added, and the resulting mixture was stirred for 15 min. Reactions were performed at room temperature or in a bath of 2-propanol cooled to −40 °C using an immersion cooler. The olefin (1−5 equiv) was added to the stirred solution either via syringe or by solid addition against a slow positive flow of argon. The solid nitrene source (1 equiv) was added in a similar manner in a single portion to the stirred solution. The reaction mixture was quenched by dilution with hexane and was filtered through a small plug of silica. The mixture was then concentrated to dryness on silica and separated by flash chromatography. The product was identified by NMR spectroscopy. Cis/trans ratios were calculated from ^{1}H NMR spectroscopy, and enantiomeric excesses (if applicable) were determined using (+)-Eu(hfc)$_3$ as the chiral shift reagent or by chiral HPLC on a Chiracel OD column, as appropriate.

Preparation of Aziridines. *N*-(*p*-Tolylsulfonyl)-2,3-(6-acetyl-2,2-dimethylchroman-3,4-yl)aziridine (4). White solid. Yield: 79%. Mp (DSC): 160 °C. ^{1}H NMR ($CDCl_3$; δ): 1.25 (s, 3H), 1.31 (s, 3H), 2.43 (s, 3H), 2.54 (s, 3H), 3.37 (d, 1H, J = 7.3 Hz), 3.97 (d, 1H, J = 7.3 Hz), 6.81 (d, 1H, J = 8.4 Hz), 7.33 (d, 2H, J = 8.1 Hz), 7.85−7.82 (m, 3H), 7.93 (s, 1H). ^{13}C NMR ($CDCl_3$; δ): 19.6, 21.7, 23.8, 24.3, 37.6, 47.6, 70.9, 115.9, 116.3, 126.0, 127.7, 128.0, 128.8, 128.9, 132.7, 142.9, 154.8, 194.2. IR (Nujol; ν, cm^{-1}): 1669, 1456, 1377, 1365, 1328, 1267, 1160, 904, 868, 830, 825. MS (EI$^+$; *m*/*z*): 372 (M + H$^+$), 216 (M$^+$ − $SO_2C_6H_4CH_3$), 91 ($C_6H_4CH_3^+$), 43 (CH_3CO^+). High-resolution MS (EI$^+$): calcd mass (M$^+$ − Ts) 216.102 454, found 216.101 996. Anal. Calcd for $C_{20}H_{21}NO_4S$: C, 64.67; H, 5.70; N, 3.77. Found: C, 64.48; H, 5.74; N, 3.61. Chiral HPLC analysis (hexane/IPA (90:10), 1 mL/min): t_r = 14.9 min (major), 18.8 min (minor).

***N*-(*p*-Tolylsulfonyl)-2-carbo-*tert*-butoxy-3-phenylaziridine (6a).** Pale, off-white solid. Yield: 144 mg, 77%. Mp: 55−57 °C. IR (NaCl plates; ν_{max}, cm^{-1}): 3026, 2981, 2937, 1739, 1600, 1350, 1160, 1084, 909. ^{1}H NMR ($CDCl_3$; δ): 1.47 (s, 9H), 2.34 (s, 3H), 3.34 (d, 1H, J = 4.0 Hz), 4.31 (d, 1H, J = 4.0 Hz), 7.19 (m, 5H), 7.73 (d, 2H, J = 8.3 Hz). ^{13}C NMR ($CDCl_3$; δ): 20.6, 26.8, 46.6, 47.7, 82.5, 126.2, 126.4, 127.5, 127.7, 128.5, 132.1, 136.6, 143.1, 163.6. MS (CI; *m*/*z*): 391 (M + NH_4^+), 374 (M + H$^+$). Enantiomeric excess determined by ^{1}H NMR using Eu(hfc)$_3$; ee = 89%. $[\alpha]_D^{25}$ = −49.2° (*c* 1.00, CH_2Cl_2).[7] Crystals obtained were suitable for X-ray structural determination (see Supporting Information).

***N*-(*p*-Tolylsulfonyl)-2-carbo-*tert*-butoxy-3-((4-methyloxy)phenyl)aziridine (6b).** Yellow oil. Yield: 136.7 mg, 67%. IR (NaCl plates; ν_{max}, cm^{-1}): 2977, 2927, 1746, 1614, 1516, 1368, 1332, 1253, 1161, 1091, 1032, 816. ^{1}H NMR ($CDCl_3$; δ): 1.15 (s, 9H), 2.42 (s, 3H), 3.56 (d, 1H, J = 7.6 Hz), 3.74 (s, 3H), 4.29 (d, 1H, J = 7.6 Hz), 6.78 (dd, 2H, J = 6.7, 1.8 Hz), 7.22 (dd, 2H, J = 6.7, 1.8 Hz), 7.33 (d, 2H, J = 8.2 Hz), 7.90 (d, 2H, J = 8.2 Hz). ^{13}C NMR ($CDCl_3$; δ): 22.1, 28.1, 44.7, 45.2, 55.7, 83.7, 113.9, 128.4, 129.2, 130.2, 164.0. MS (EI; *m*/*z*): 403 (M$^+$), 347(M − $C_4H_8^+$), 330 (M − OC_4H_9). HRMS (CI; *m*/*z*): 404.1534, calcd [M$^+$ + 1] 404.1550. Anal. Calcd for $C_{21}H_{25}NO_5S$: C, 62.51; H, 6.25; N, 3.47. Found: C, 62.49; H, 6.32; N, 3.37. Enantiomeric excess determined by HPLC: Chiralcel OD, 15 cm × 0.46 cm i.d.; mobile phase hexane/propan-2-ol (95:5), t_r(major) = 16.41 min, t_r(minor) = 20.17 min, ee = 93%. $[\alpha]_D^{26}$ = +30.4° (*c* 1.06, CH_2Cl_2).

***N*-(*p*-Tolylsulfonyl)-2-carbo-*tert*-butoxy-3-(4-methylphenyl)aziridine (6c).** Yellow oil. Yield: 114.3 mg, 59%. IR (NaCl plates; ν_{max}, cm^{-1}): 2978, 2931, 1738, 1597, 1336, 1162, 1088, 921, 813, 677. ^{1}H NMR ($CDCl_3$; δ): 1.46 (s, 9H), 2.24 (s, 3H), 2.33 (s, 3H), 3.35 (d, 1H, J = 4.0 Hz), 4.26 (d, 1H, J = 4.0 Hz), 7.05 (m, 4H),7.19 (d, 2H, J = 8.5 Hz), 7.71 (d, 2H, J = 8.5 Hz). ^{13}C NMR ($CDCl_3$; δ): 21.6, 22.0, 28.2, 48.2, 48.7, 83.8, 127.6, 127.7, 129.6, 129.9, 130.3, 138.1, 139.1, 144.4, 165.1. MS (EI; *m*/*z*): 387 (M$^+$), 332 (M − C_4H_8). HRMS (CI; *m*/*z*): found 388.1589, calcd [M$^+$ + 1] 388.1601. Anal. Calcd for $C_{21}H_{25}NO_4S$: C, 65.09; H, 6.50; N, 3.61. Found: C, 64.98; H, 6.29; N, 3.53. Enantiomeric excess determined by ^{1}H NMR using Eu(hfc)$_3$, ee = 88%. $[\alpha]_D^{30}$ = −18.9° (*c* 0.84, CH_2Cl_2).

***N*-(*p*-Tolylsulfonyl)-2-carbo-*tert*-butoxy-3-(3-methylphenyl)aziridine (6d).** Yellow oil. Yield: 109 mg, 56%. IR (NaCl plates; ν_{ma}, cm^{-1}):$_x$ 2979, 2926, 1736, 1638, 1337, 1163, 1087, 784, 690. ^{1}H NMR ($CDCl_3$; δ): 1.53 (s, 9H), 2.28 (s, 3H), 2.40 (s, 3H), 3.39 (d, 1H, J = 4.0 Hz), 4.31 (d, 1H, J = 4.0 Hz), 6.99−7.28 (m, 6 H), 7.78 (d, 2H, J = 8.6 Hz). ^{13}C NMR ($CDCl_3$; δ): 20.8, 20.6, 26.8, 46.6, 47.5, 82.4, 123.2, 126.4, 127.0, 127.4, 128.5, 128.5, 132.0, 136.5, 137.3, 143.0, 163.6. MS (CI; *m*/*z*): 405 (M + NH_4^+), 388 (M + H$^+$). HRMS (CI; *m*/*z*): found 388.1581, calcd [M$^+$ + 1] 388.1601. Anal. Calcd for $C_{21}H_{25}NO_4S$: C, 65.09; H, 6.50; N, 3.61. Found: C, 65.11; H, 6.59; N, 3.67. Enantiomeric excess determined by ^{1}H NMR using Eu(hfc)$_3$, ee = 96%. $[\alpha]_D^{28}$ = −19.9° (*c* 0.24, CH_2Cl_2).

***N*-(*p*-Tolylsulfonyl)-2-carbo-*tert*-butoxy-3-(4-fluorophenyl)aziridine (6e).** Yellow oil. Yield: 130.0 mg, 66%. IR (NaCl plates; ν_{max}, cm^{-1}): 2982, 1732, 1608, 1515, 1336, 1222, 1088, 925, 814, 738, 690. ^{1}H NMR ($CDCl_3$; δ): 1.52 (s, 9H), 2.40 (s, 3H), 3.39 (d, 1H, J = 4.0 Hz), 4.33 (d, 1H, J = 4.0 Hz), 6.97 (dd, 2H, J = 8.5 Hz), 7.17−7.28 (m, 4H), 7.77 (d, 2H, J = 8.5 Hz). ^{13}C NMR ($CDCl_3$; δ): 20.6, 26.8, 45.9, 47.5, 82.6, 114.4, 114.7, 126.5, 128.0, 128.1, 128.5, 136.4, 143.2, 163.5. MS (CI; *m*/*z*): 409 (MNH_4^+), 392 (MH$^+$). HRMS (CI; *m*/*z*): found 392.1337, calcd [M$^+$ + 1] 392.1351. Anal. Calcd for $C_{20}H_{22}FNO_4S$: C, 61.36; H, 5.66; N, 3.58. Found: C, 61.48; H, 5.29; N, 3.73. Enantiomeric excess determined by HPLC: Chiralcel OD, 15 cm × 0.46 cm i.d.; mobile phase hexane/propan-2-ol (95:5), t_r(major) = 15.56 min, t_r(minor) = 19.37 min, ee = 98%. $[\alpha]_D^{30}$ = −42.2° (*c* 0.25, CH_2Cl_2).

***N*-(*p*-Tolylsulfonyl)-2-carbo-*tert*-butoxy-3-(4-chlorophenyl)aziridine (6f).** Yellow oil. Yield: 174 mg, 89%. IR (NaCl plates; ν_{max}, cm^{-1}): 2980, 2931, 1738, 1598, 1495, 1339, 1164, 1090, 915, 814, 731, 686. ^{1}H NMR ($CDCl_3$; δ): 1.52 (s, 9H), 2.40 (s, 3H), 3.36 (d, 1H, J = 4.0 Hz), 4.32 (d, 1H, J = 4.0 Hz), 7.15 (dd, 2H, J = 8.9 Hz),7.17−7.28 (m, 4H), 7.77 (d, 2H, J =

8.6 Hz). ^{13}C NMR ($CDCl_3$; δ): 20.6, 26.8, 45.8, 47.7, 82.7, 126.3, 127.6, 128.6, 130. 7, 133.7, 136.4, 143.3, 163.3 (*C*═O). MS (CI; *m*/*z*): 428 (MNH_4^+), 408 (MH^+). HRMS (CI; *m*/*z*): found 408.1041, calcd [M^+ + 1] 408.1055. Anal. Calcd for $C_{20}H_{22}ClNO_4S$: C, 58.89; H, 5.44; N, 3.43. Found: C, 58.99; H, 5.35; N, 3.37. Enantiomeric excess determined by HPLC: Chiralcel OD 15 cm × 0.46 cm i.d; mobile phase hexane/propan-2-ol (95:5), t_r(major) 8.99 min, t_r(minor) = 10.43 min, ee = 93%. $[\alpha]_D^{26}$ = −41.0° (*c* 0.66, CH_2Cl_2).

***N*-(*p*-Tolylsulfonyl)-2-carbo-*tert*-butoxy-3-(4-bromophenyl)aziridine (6g).** Colorless oil. Yield: 130 mg, 57%. IR (NaCl plates; ν_{max}, cm^{-1}): 2980, 2928, 1738, 1597, 1338, 1163, 1087, 916, 812. ^{1}H NMR ($CDCl_3$; δ): 1.53 (s, 9H), 2.41 (s, 3H, 3.36 (d, 1H, *J* = 4.0 Hz), 4.31 (d, 1H, *J* = 4.0 Hz), 7.09 (dd, 2H, *J* = 6.7, 1.8 Hz), 7.27 (d, 2H, *J* = 8.2 Hz), 7.41 (dd, 2H, *J* = 6.7, 1.8 Hz), 7.79 (d, 2H, *J* = 8.2 Hz). ^{13}C NMR ($CDCl_3$; δ): 22.0, 28.2, 47.2, 49.1, 84.1, 123.3, 127.7, 129.2, 130.0, 132.1, 132.6, 137.8, 144.7, 164.7. MS (CI; *m*/*z*): 452/454 (MH^+). HRMS (CI; *m*/*z*): found 452.0525, calcd [M^+ + 1] 452.0550. Anal. Calcd for $C_{20}H_{22}BrNO_4S$: C, 53.10; H, 4.90; N, 3.10. Found: C, 53.16; H, 4.79; N, 3.21. Enantiomeric excess determined by HPLC: Chiralcel OD 15 cm × 0.46 cm i.d.; mobile phase hexane/propan-2-ol (95:5), t_r(major) 15.89 min, t_r(minor) = 23.21 min, ee = 98%. $[\alpha]_D^{30}$ = −41.8° (*c* 0.33, CH_2Cl_2).

***N*-(*p*-Tolylsulfonyl)-2-carbo-*tert*-butoxy-3-(3-nitrophenyl)aziridine (6h).** Yellow oil. Yield: 109 mg, 56%. IR (NaCl plates; ν_{max}, cm^{-1}): 2964, 2929, 1730, 1597, 1532, 1439, 1260, 1162, 108, 803, 737, 679. ^{1}H NMR ($CDCl_3$; δ): 1.54 (s, 9H), 2.41 (s, 3H), 3.41 (d, 1H, *J* = 4.0 Hz), 4.42 (d, 1H, *J* = 4.0 Hz), 7.30 (d, 2H, *J* = 8.2 Hz), 7.45 (dd, 1H, *J* = 7.6 Hz), 7.58 (dd, 1H, *J* = 7.6 Hz), 7.78 (d, 2H, *J* = 8.2 Hz), 8.03 (s, 1H), 8.13 (dd, 1H, *J* = 8.3 Hz). ^{13}C NMR ($CDCl_3$; δ): 20.6, 26.8, 44.8, 47.9, 83.1, 121.1, 121.6, 122.7, 122.8, 126.4, 126.6, 128.7, 132.4, 132.6, 134.6, 143.7, 163.4. MS (CI; *m*/*z*): 405 ($M + NH_4^+$), 388 ($M + H^+$). HRMS (CI; *m*/*z*): found 419.1282, calcd [M^+ + 1] 419.2288. Anal. Calcd for $C_{20}H_{22}N2O_6S$: C, 57.40; H, 5.30; N, 6.69. Found: C, 57.51; H, 5.29; N, 6.54. Enantiomeric excess determined by HPLC: Chiralcel OD, 15 cm × 0.46 cm i.d.; mobile phase hexane/propan-2-ol (98:2), t_r(major) 35.65 min, t_r(minor) = 39.79 min, ee = 96%. $[\alpha]_D^{30}$ = −53.8° (*c* 0.41, CH_2Cl_2).

Acknowledgment. We thank EPSRC for a postdoctoral fellowhip to K.M.G.

Supporting Information Available: Details of synthesis of 2,2′-diamino-6,6′-dimethylbiphenyl, copper sources, and butyl cinnamates **5a**−**j** and crystallographic data for (*R*)-(−)-**L**^{1}, four copper complexes, and **6a**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO025515I