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Tetrahedron: *Asymmetry*

Synthesis of a library of chiral α-amino acid-based borate counteranions and their application to copper catalyzed olefin cyclopropanation

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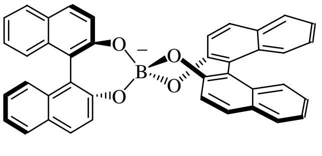
Abstract—Twenty borate counteranions have been prepared from tartaric acid and α-amino acid derivatives. Ion pairing of these anions to a copper cation can be used to induce enantioselectivity into the copper catalyzed cyclopropanation of styrene. Structural modification of the anion provides insight into the importance of each component of the counteranion in asymmetric induction.

1. Introduction

The use of α-amino acids as sources of chirality is important in asymmetric transition metal catalysis.[1,2] A useful feature of this approach is the large pool of natural and non-naturally occurring amino acids that are available. This allows families of amino acid-based ligands to be prepared using the same basic synthetic procedure, and straightforward tuning of substituents to achieve optimal enantiomeric induction.[2] While chiral residues such as α-amino acids are typically associated with transition metal catalysts through tethering to a ligand, we have recently reported that asymmetric induction can be achieved through the ion pairing of a cationic copper center to a chiral counteranion **1** in the catalytic aziridination of styrene, albeit with low enantioselectivities (11% ee).[3] Chiral counteranions have been employed with growing frequency in chemistry,[4] however this represented the first example that ion pairing itself could be used for enantioinduction with a cationic metal catalyst.[5] This suggests that cation/anion interactions can also be employed as an alternative to coordination to associate active metal catalysts to chiral α-amino acid environments.

We report herein the preparation of the first example of a library of α-amino acid-bound borate anions of the form of **2** for use in transition metal catalysis.[6] Studies on their use in the copper catalyzed cyclopropanation of olefins demonstrate that these anions can induce enantioselectivity via ion pairing. The asymmetric induction observed in this system, while low, represents the highest levels reported using a counteranion in catalysis. In addition, variation of the amino acid residues demonstrates how the counteranion structure can be used to affect enantioinduction, as well as the importance of each structural component of the anion on the enantioselectivities observed.



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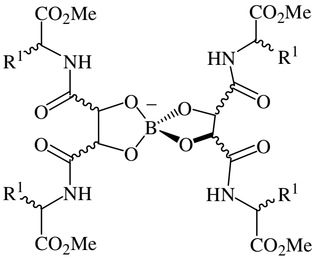

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2. Results

2.1. Synthesis of the α-amino acid based counteranions

The counteranions employed in this study are composed of two C_2-symmetric tartaric acid derived diols connected to a tetrahedral boron center **2**. Complexation of the diols to boron creates a borate counteranion with

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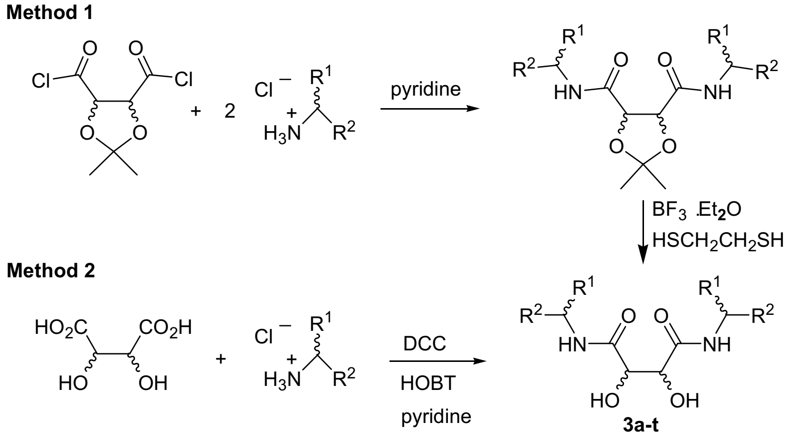
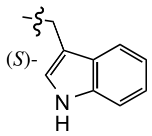
Table 1. Synthesis and structure of Diols **3a**–**t**



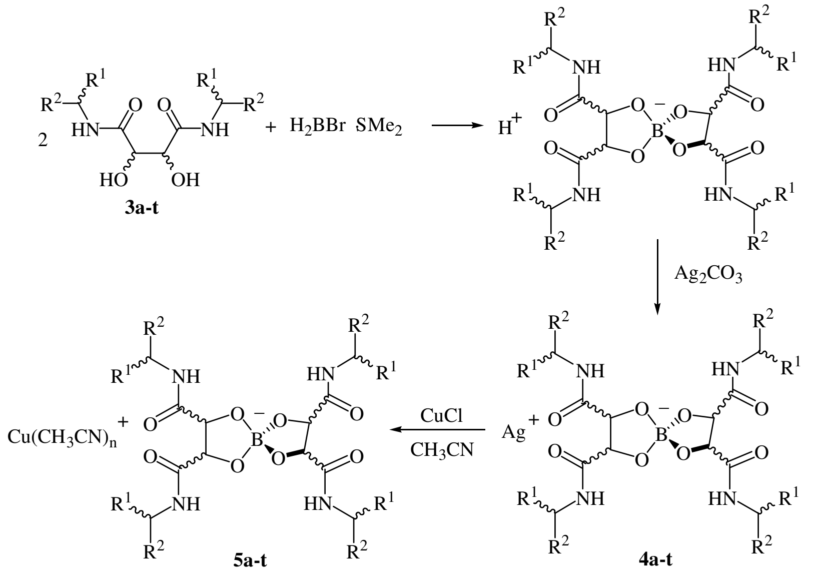
Compound **3**	Tartrate isomer	R^{1a}	R^2
a	(*R*,*R*)	(*R*)-Ph	CO_2CH_3
b	(*R*,*R*)	(*R*)-Ph	CO_2CH_2 Ph
c	(*S*,*S*)	(*S*)-Ph	$CO_2C_6H_{11}$
d	(*R*,*R*)	(*R*)-Ph	CH_2OCH_3
e	(*S*,*S*)	(*S*)-Ph	$C(O)NH_2(CH_2)_3CH_3$
f	(*S*,*S*)	(*S*)- 	CO_2CH_3
g	(*S*,*S*)	(*S*)-$CH_2CH_2CO_2CH_3$	CO_2CH_3
h	(*S*,*S*)	(*S*)-$C(CH_3)_3$	CO_2CH_3
i	(*R*,*R*)	(*S*)-$C(CH_3)_3$	CO_2CH_3
j	(*R*,*R*)	H	CO_2CH_3
k	(*S*,*S*)	(*R*)-Ph	CO_2CH_3
l	(*R*,*R*)	(*S*)-$CH(CH_3)_2$	CO_2CH_3
m	(*S*,*S*)	(*S*)-$CH(CH_3)_2$	CO_2CH_3
n	(*S*,*S*)	(*S*)-CH_2 Ph	CO_2CH_3
o	(*S*,*S*)	(*S*)-Ph	(*S*)-Alanine methyl ester
p	(*S*,*S*)	(*S*)-Ph	(*S*)-Valine methyl ester
q	(*S*,*S*)	(*S*)-Ph	(*S*)-Phenyl alanine methyl ester
r	(*R*,*R*)	(*R*)-Ph	(*R*)-Phenylglycine methyl ester
s	(*R*,*R*)	(*R*)-Ph	(*S*)-Phenylglycine methyl ester
t	(*R*,*R*)	(*S*)-$C(CH_3)_3$	(*S*)-*tert*-Butyl leucine methyl ester

[a] Substituent and stereochemistry at the α-amino acid carbon.

four flexible α-amino ester arms, that can encapsulate a metal cation in a chiral amino acid environment. Diols **3a**–**t** can be readily prepared via either the nucleophilic addition of the α-amino acid derivative (2 equiv) to tartaryl chloride,[7] (Table 1, Method 1), or the *N*,*N*′-dicyclohexylcarbodiimide (DCC) coupling of an α-amino acid derivative (2 equiv) with tartaric acid (Method 2).[8] Representative examples of compounds **3a**–**t**, and their subsequent borate derivatives (vide infra), have been fully characterized by NMR, IR, mass spectrometry, and elemental analysis. All data are consistent with the structures shown.

The addition of 2 equiv **3a**–**t** to 1 equiv $H_2BBr–SMe_2$ results in the liberation of H_2 and HBr to form the corresponding borate acid. The acids can be readily converted into their silver salts **4a**–**t** through their addition to Ag_2CO_3 in acetonitrile (ca. 90% yield). Silver salts **4a**–**t** serve as useful precursors for the incorporation of α-amino acid bound counteranions into transition metal halides via ion exchange. Thus, the mixing of the appropriate silver borate salt with CuCl in acetonitrile results in the immediate precipitation of AgCl, and the formation of copper salts **5a**–**t** as white solids in ca. 90% yield (Scheme 1).

Spectroscopic data on complexes **5a**–**t** are consistent with their existence as ionized salts in solution. For example, the ^{1}H NMR of **5a** only shows a single set of tartrate and α-amino acid resonances in both polar (CD_3CN) and nonpolar (C_6D_6) solvents. Furthermore, the IR of **5a** reveals only a single ester ($\nu_{CO} = 1740\ cm^{-1}$) and amide ($\nu_{CO} = 1646\ cm^{-1}$) signal in solution (CH_2Cl_2) and in the solid phase (KBr). The fact that the four α-amino acid residues in the counteranion are equivalent in solution, even on the IR timescale, as well as their lack of perturbation in both polar and nonpolar media, argues against any type of static coordination of the borate anion to the copper center. The latter would be expected to create at least some degree of asymmetry in the anion.

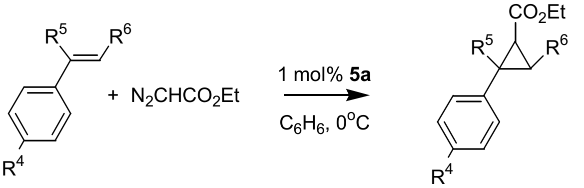


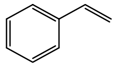
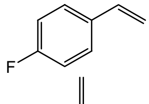
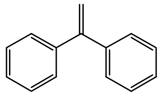
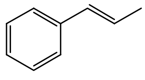
Scheme 1. Synthesis of the copper salts **5a**–**t** from **3a**–**t**.

2.2. Asymmetric catalysis

Cu(I) salts are well known to catalyze the cyclopropanation of styrene derivatives with ethyl diazoacetate.[9] As demonstrated in Table 2, the cationic copper complex **5a** can also mediate this reaction.[10] More importantly, analysis of the reaction products reveals the formation of cyclopropanes in 17% (trans) and 26% (cis) enantiomeric excesses. To study the generality of this ion-pairing influence on enantioselectivity, several other aromatic olefins were examined as substrates. The electron poor 4-fluorostyrene and the 1,2-disubstituted olefin *trans*-β-methylstyrene react smoothly to give *trans*-cyclopropanes with enantioselectivities of 26% and 18%, respectively. While 1,1-diphenylethylene does not produce any cyclopropanes at 0 °C, it did react at room temperature to give 2,2-diphenyl-cyclopropanecarboxylic acid ethyl ester with 23% ee (entry 3).

Table 2. Enantioselective cyclopropanation of olefins with catalyst **5a**



Entry	Olefin	Trans % ee[a]	Cis % ee[a]	Yield[b]
1		17%	26%	21% (1.3)[9]
2		26%	18%	10% (1.2)
3[c]		23%[d]		67%
4		18%	2%	47%[c] (1.1)

[a] Enantiomeric excess and trans/cis ratio determined by chiral GC. All cyclopropanes prepared are known compounds.[9]

[b] Trans:cis ratio in brackets.

[c] Reaction performed at room temperature.

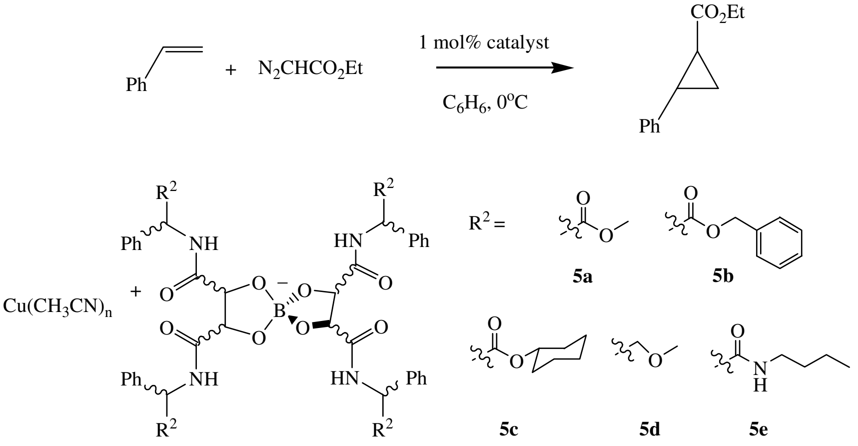
[d] Enantiomeric excess determined by chiral HPLC.

2.3. Structural influences on chiral induction

With this family of counteranions in hand, we turned our attention to whether the structural modification of a counteranion can be used to modulate enantioselectivity in catalysis. As shown in Table 3, modifying the terminal methyl ester in **5a** to a benzyl **5b** or cyclohexyl ester **5c** had only a minor effect on the catalysis (entries 1–3). However, if the methyl ester functionality is replaced with a less basic methyl ether **5d**, the selectivity of the reaction is significantly reduced (trans: 0% ee, cis: 9% ee). While this implies that weak copper interactions with the ester may be important for asymmetric induction, the use of the more basic *N*-butyl amide terminated anion **5e** also led to lower levels of chiral induction (entry 5).

The influence of the homochiral tartrate and amino ester residues of the anions on the enantioselectivity has also been probed. As shown in Table 4, the amino acid residues have the most significant influence on chiral induction. From a structural perspective, increasing the steric bulk of the amino acid substituent leads to a general increase in enantioselectivity, when proceeding from glycine (entry 6, trans ee = 0%, cis ee = 2%) valine (entry 8, trans ee = 21%, cis ee = 7%) to *tert*-leucine (entry 5, trans ee = 34%, cis ee = 19%). In addition, it is the α-amino acid unit residue that determines the overall stereochemical outcome of the reaction, with the (*R*)-amino acid derivatives favoring the *trans*-(1*R*,2*R*) and *cis*-(1*R*,2*S*) products, with the opposite enantiomers observed for the (*S*)-amino acid derivatives. Conversely, while the chirality of the tartaric acid unit can modulate

Table 3. Influence of α-amino acid substitutent R^2 on enantioselectivity

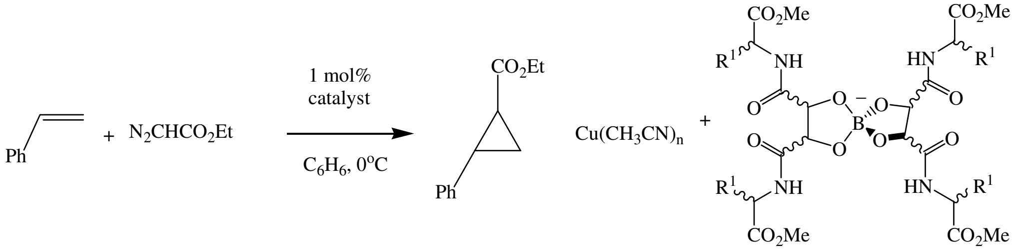


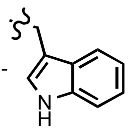
Entry	Catalyst	Trans % ee[a]	Cis % ee[a]	Yield[b]
1	**5a**	17% (1*R*,2*R*)	26% (1*R*,2*S*)	21% (1.3)
2	**5b**	20% (1*R*,2*R*)	20% (1*R*,2*S*)	15% (1.3)
3	**5c**	23% (1*S*,2*S*)	19% (1*S*,2*R*)	36% (1.2)
4	**5d**	0%	9% (1*R*,2*S*)	27% (1.2)
5	**5e**	4% (1*S*,2*S*)	9% (1*S*,2*R*)	26% (1.0)

[a] Enantiomeric excess of trans and cis products, respectively, as determined using the literature procedures.[9c] Absolute stereochemistry of major enantiomer in brackets.

[b] Trans:cis ratio in brackets.

Table 4. Influence of the α-amino acid (*R*[1]) and tartaric acid on enantioselectivity



Entry	Cat.	Tartrate isomer	R[1]	Trans % ee[a]	Cis % ee[a]	Yield[b]
1	**5a**	(*R*,*R*)	(*R*)-Ph	17% (1*R*,2*R*)	26% (1*R*,2*S*)	21% (1.3)
2	**5f**	(*S*,*S*)	(*S*)- 	4% (1*S*,2*S*)	8% (1*S*,2*R*)	3% (1.0)
3[c]	**5g**	(*S*,*S*)	(*S*)-$(CH_2)_2CO_2CH_3$	7% (1*S*,2*S*)	19% (1*S*,2*R*)	35% (1.6)
4	**5h**	(*S*,*S*)	(*S*)-$C(CH_3)_3$	19% (1*S*,2*S*)	11% (1*S*,2*R*)	41% (0.9)
5	**5i**	(*R*,*R*)	(*S*)-$C(CH_3)_3$	34% (1*S*,2*S*)	19% (1*S*,2*R*)	3% (1.0)
6[c]	**5j**	(*R*,*R*)	H	0%	2% (1*R*,2*S*)	12% (1.8)
7	**5k**	(*S*,*S*)	(*R*)-Ph	17% (1*R*,2*R*)	11% (1*R*,2*S*)	14% (1.2)
8	**5l**	(*R*,*R*)	(*S*)-$CH(CH_3)_2$	21% (1*S*,2*S*)	7% (1*S*,2*R*)	17% (1.4)
9	**5m**	(*S*,*S*)	(*S*)-$CH(CH_3)_2$	10% (1*S*,2*S*)	8% (1*S*,2*R*)	31% (1.4)
10	**5n**	(*S*,*S*)	(*S*)-CH_2Ph	17% (1*S*,2*S*)	8% (1*S*,2*R*)	28% (1.4)

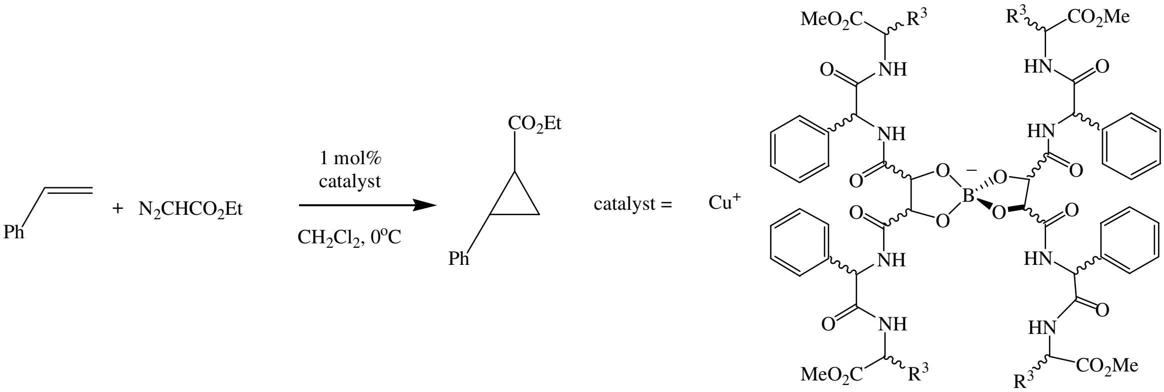
[a] Enantiomeric excess of trans and cis products, respectively, as determined using the literature procedures.[9c] Absolute stereochemistry of major enantiomer in brackets.

[b] Trans:cis ratio in brackets.

[c] Reaction performed in CH_2Cl_2.

enantioselectivity (entries 1–9), it does not directly influence the stereochemical preference of the reaction. Consistent with this, the use of the achiral glycine α-amino methyl ester with a chiral tartrate backbone **5j** results in a racemic product (entry 6). Overall, the enantioselectivities obtained with the *tert*-butyl substituted catalyst

Table 5. Dipeptide-containing counteranions in catalysis[12]



Entry	Catalyst	R^3	Trans % ee[a]	Cis % ee[a]	Yield[b]
1	**5o**	(*S*)-CH_3	5% (1*S*,2*S*)	7% (1*S*,2*R*)	46% (1.2)
2	**5p**	(*S*)-$CH(CH_3)_2$	11% (1*S*,2*S*)	18% (1*S*,2*R*)	29% (1.4)
3[c]	**5q**	(*S*)-CH_2 Ph	13% (1*S*,2*S*)	15% (1*S*,2*R*)	90% (1.2)
4	**5r**	(*R*)-Ph	14% (1*R*,2*R*)	24% (1*R*,2*S*)	32% (1.3)
5	**5s**	(*S*)-Ph	7% (1*S*,2*S*)	1% (1*R*,2*S*)	47% (0.9)
6	**5t**	(*S*)-$C(CH_3)_3$	20% (1*S*,2*S*)	7% (1*R*,2*S*)	6% (1.6)
7	**5a**	—	17% (1*R*,2*R*)	18% (1*R*,2*S*)	35% (1.3)

[a] Enantiomeric excess of trans and cis products, respectively, as determined using literature procedures.[9c] Absolute stereochemistry of major enantiomer in brackets.

[b] Trans:cis ratio in brackets.

[c] Reaction performed at room temperature.

5i (trans ee = 34%, cis ee = 19%)[11] represent the highest yet observed for a chiral counteranion induced asymmetric metal catalyzed reaction.

2.4. Dipeptide based counteranions

A useful feature of these counteranions is that the α-amino acid unit can be extended to create peptide-tethered anions. In principle, these would possess a deeper chiral pocket for the metal cation to reside, which may lead to more selective catalysis. As a preliminary test of this phenomenon, a series of dipeptide-based counteranions were examined (Table 5). Building of an initial phenylglycine unit, modification of the second amino acid residue from alanine (entry 1), to phenyl alanine (entry 3), to valine (entry 2), to phenylglycine (entry 4) led to an increase in the enantioselectivity of the *cis*-cyclopropane product (7%, 15%, 18%, and 24% ee, respectively). In addition, a change in the chirality of the second amino acid can also modulate enantioselectivity **5s**. The highest level of asymmetric induction using the dipeptide based anions was observed using catalyst **5r** (cis = 24% ee, trans = 14% ee). Notably, this selectivity is slightly higher than its mono amino acid counterpart under the same reaction conditions, CH_2Cl_2, 0 °C (entry 7).[12]

3. Discussion

The principle of using chiral counteranions to create energetically non-equivalent ion-pairs in transition metal complexes is well established. This has been perhaps most significantly exploited in the solid phase, with the selective crystallization of diastereomeric salts.[4] In addition, chiral phase transfer catalysts have been shown to induce high levels of enantioselectivity into their reaction products,[5] and chiral counteranions have been shown to allow the resolution of cationic transition metal enantiomers for solution ^1H NMR analysis,[13] as well as influence the stereochemistry of metal centers that are rapidly inter-converting between enantiomers.[14] As this study demonstrates, these principles appear to be equally applicable to asymmetric metal catalysis. Enantiomeric product formation with anion **2** likely results from a similar phenomenon to that with chiral ligands, where in this case selectivity results from the generation of non-equivalent diastereotopic ion pairs (rather than static coordination complexes) as intermediates and/or transition states during the reaction. While the difference in energy between these ion pairs is not anticipated to be as significant as those within a coordination complex, the results in this study show it is important.

As shown in Tables 3–5, every structural feature of these counteranions plays a role in the enantioselectivities observed, demonstrating that even subtle influences on ion pairing can translate themselves into an effect in catalytic selectivity. The diverse set of counteranions employed allows for the development of a preliminary model to explain the observed asymmetric induction. While modification of the tartrate chirality affects the level of enantioselectivity observed, it does not change the stereochemical outcome of the reaction (Table 4). Furthermore, in the absence of chiral α-amino acid residues, the tartrate units do not induce enantioselectivity (Table 4, entry 6). This is in contrast to the chirality of the

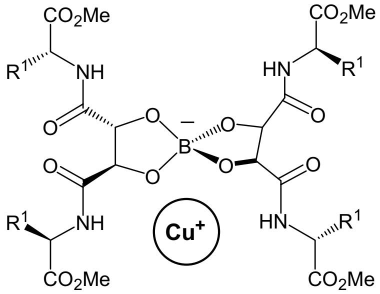


Figure 1. Plausible ion-pairing contact between the copper cation and the counteranion during catalysis.

α-amino acid units themselves, which are mostly responsible for the overall enantioinduction. This suggests that at least one of the amino acid residues on the anion remains near the copper cation during catalysis. Based on this, a reasonable hypothesis is that the copper catalyst resides in a pocket created by the α-amino acid residues of two separate diols (Fig. 1). This would provide the site of closest ion-pairing contact between the cationic copper and the negative charge on the boron, and places the copper in a pseudo-C_2-symmetric chiral pocket created by two separate amino acid residues. In this general environment, the tartrate units are removed from the copper center, and their influence on enantioselectivity likely occurs through changing the relative orientation of the α-amino acid residues.

It should be noted that this interpretation of the chiral counteranion influence on stereoselectivity employs a static ion-pairing complex; which is unlikely for an ion pair in solution. Nevertheless, transition metal ion pairs have been shown to have preferred orientations in solution.[15] In our case, this configuration leads to the partial encapsulation of the copper center within the chiral α-amino acid residues of the anion. The results with the dipeptide residues are consistent with this idea, which would place the metal cation into an even deeper chiral cavity for higher enantioselectivity.

4. Conclusions

In summary, we have developed a convenient route to prepare a diverse set of chiral counteranions that incorporate four pendant α-amino ester arms. The ion pairing with these anions provides a straightforward, outer-sphere method to associate metal catalysts with amino acid or peptide residues. While the metal catalyst is only associated to the chiral anion by weak ion-pairing influences, even in this model study it can lead to enantioselectivities of up to 34% in the catalytic cyclopropanation of styrene. Considering the structural versatility of these α-amino acid containing counteranions, and their potential use in concert with chiral ligands, this approach may allow the scanning of catalytic systems for higher levels of enantioselectivity. Studies directed towards this, as well as the use of these anions to associate other cationic fragments to peptide-like environments, are currently underway.

5. Experimental section

5.1. General

All manipulations of air or moisture sensitive compounds were performed under an inert atmosphere in a Vacuum Atmosphere 553-2 dry box or by using standard Schlenk techniques. All reagents, unless otherwise noted, were purchased from commercial suppliers and used without further purification. (*R*)-2-Phenylglycine methyl ether hydrochloride,[16] 2,3-*O*-isopropylidene tartaric acid dichloride,[7] (*S*)-*tert*-leucine methyl ester hydrochloride[17] and α-amino acid derivatives[18] were synthesized in analogy to literature procedures. Benzene and diethyl ether were distilled from sodium/benzophenone under nitrogen. Acetonitrile and methylene chloride were distilled from CaH_2 under nitrogen. Deuterated solvents were dried as their protonated analogues, and transferred under vacuum from the drying agent and stored over 4 Å molecular sieves. d_6-DMSO was degassed dry using 4 Å molecular sieves. All manipulations involving silver salts were performed with a minimum amount of light present. NMR spectra were recorded on JEOL-270, Varian 400, or Varian 300 spectrometers. Infrared spectra were recorded on a Bruker IFS-48 or Nicolet Avatar 360 FT-IR spectrometer. GC analysis was performed using a Hewlett Packard 6890 Series GC with a Chirasil-DEX CB column with a hexadecane internal standard. HPLC analysis was performed on a Waters 600 HPLC using a Waters 486 UV detector and a CHIRACEL OD column. Compounds **3a**–**5a**, **3i**–**5i**, **3j**–**5j**, and **5q** were selected as representative compounds and fully characterized by NMR spectroscopy, IR spectroscopy, elemental analysis. The remaining compounds were characterized using ^{1}H, ^{13}C, and ^{11}B NMR spectroscopy.

5.2. Preparation of (*R*)-2-phenylglycine benzyl ester *p*-toluene sulfonic acid[18]

A mixture of (*R*)-2-phenylglycine (3.0 g, 0.0198 mol), *p*-toluene sulfonic acid monohydrate (4.14 g, 0.0218 mmol) and benzyl alcohol (8.0 ml, 0.0773 mol) was refluxed in 30 ml toluene overnight. The solution was then cooled to room temperature and the resulting crystals filtered to yield a white solid (7.3 g, 89%). ^{1}H NMR: (300 MHz, d_6-DMSO): δ 8.90 (br s, 3H), 7.19–7.48 (m, 12H), 7.09 (d, 2H), 5.38 (s, 1H), 5.23 (d, 1H), 5.17 (d, 1H). ^{13}C NMR: (75 MHz, d_6-DMSO): δ 169.0, 146.2, 138.4, 135.7, 133.1, 130.3, 129.7, 129.1, 129.0, 128.9, 128.8, 128.5, 126.2, 67.9, 56.1.

5.3. Preparation of (*S*)-2-phenylglycine cyclohexyl ester *p*-toluene sulfonic acid[18]

A mixture of (*S*)-2-phenylglycine (5.0 g, 0.033 mol), *p*-toluene sulfonic acid monohydrate (7.5 g, 0.040 mol) and cyclohexanol (17.5 ml, 0.165 mol) in 100 ml toluene was refluxed overnight using a Dean Stark trap. The resulting solution was cooled to room temperature at which point a white solid crystallized. The product was then filtered and washed with toluene (9.33 g, 70%). ^{1}H NMR: (300 MHz, d_6-DMSO): δ 8.83 (br s, 3H), 7.46 (m, 7H), 7.10 (d, 2H), 5.26 (s, 1H), 4.79 (m, 1H), 2.27 (s, 6H), 1.18–1.73 (m, 10H). ^{13}C NMR: (75 MHz, *d*$_6$-DMSO): δ 168.5, 146.2, 138.4, 133.4, 130.2, 129.7, 128.8, 128.7, 126.2, 74.9, 56.1, 31.3, 30.9, 25.3, 23.3, 23.0, 21.5.

5.4. Preparation of (*S*)-2-phenylglycine *n*-butyl amide hydrochloride[18]

To a solution of *N*-*tert*-butoxycarbonyl-(*S*)-phenylglycine (3.0 g, 0.012 mol), *n*-butylamine (2.4 ml, 0.024 mol) and 1-hydroxybenzotriazole hydrate (1.6 g, 0.012 mol) in 30 ml CH_2Cl_2 at 0 °C was added dicyclohexylcarbodiimide (2.5 g, 0.012 mol). The resulting mixture was stirred overnight as it was warmed to room temperature at which point it was filtered. The organic layer was then washed with satd $NaHCO_{3(aq)}$ (2×50 ml), 10% $HCl_{(aq)}$ (2×50 ml) and satd NaCl(aq) (1×50 ml). The organic layer was then dried over $MgSO_4$, filtered, and evaporated to dryness. The solid was dissolved in ethyl acetate and precipitated with hexanes to yield *N*-*tert*-butoxycarbonyl-(*S*)-phenylglycine *n*-butyl amide as a white solid (2.68 g, 0.0088 mol). To a solution of *N*-*tert*-butoxycarbonyl-(*S*)-phenylglycine *n*-butyl amide (2.5 g, 8.16 mmol) in 5 ml, 1,4-dioxane was added in 10 ml of HCl (4.0 M in 1,4-dioxane). The resulting solution was stirred for 30 min. The solvent was removed under reduced pressure to give a clear oil. Diethyl ether was then added, and the white precipitate that formed was filtered and washed with ether to yield the (*S*)-2-phenylglycine *n*-butyl amide (1.92 g, 97%). ^{1}H NMR: (270 MHz, *d*$_6$-DMSO): δ 8.82 (br s, 3H), 7.58 (m, 2H), 7.42 (m, 3H), 4.99 (s, 1H), 3.05 (m, 2H), 1.33 (m, 2H), 1.18 (m, 2H), 0.79 (t, 3H). ^{13}C NMR: (68 MHz, *d*$_6$-DMSO): δ 167.6, 135.0, 129.4, 129.2, 128.2, 66.9, 55.8, 31.3, 19.9, 14.1.

5.5. General procedure for 3a–t

5.5.1. Method 1. (*R*,*R*)- or (*S*,*S*)-2,3-*O*-isoproplylidene tartaric acid dichloride (1.0 g, 3.86 mmol) was added to a mixture of the amino acid derivative hydrochloride salt (8.0 mmol) and pyridine (1.0 ml) in 50 ml CH_2Cl_2. The mixture was stirred for 30 min and then quenched with 10 ml of H_2O. The organic layer was then washed with 10% HCl (3×50 ml), satd $NaHCO_3$ (2×50 ml), and satd NaCl (50 ml). After drying with $MgSO_4$, the solvent was removed under reduced pressure to give the crude acetonide, which was purified by column chromatography. To a solution of acetonide (2.00 mmol) in 15 ml of CH_2Cl_2 was added $BF_3 \cdot Et_2O$ (300 µl, 2.40 mmol) and then ethane dithiol (200 µl, 2.40 mmol). The solution was stirred overnight at room temperature and then quenched with 50 ml H_2O and 75 ml CH_2Cl_2. The two phases were mixed for 10 min and then separated. The organic layer was then washed with 10% HCl (2×50 ml), satd $NaHCO_3$ (2×50 ml) and satd NaCl (1×50 ml). After drying over $MgSO_4$, the solution was filtered and evaporated under reduced pressure to give the crude diol.

5.5.2. Method 2. A mixture of (2*R*,3*R*)- or (2*S*,3*S*)-tartaric acid (500 mg, 3.33 mmol), amino acid derivative (7.32 mmol), 1-hydroxybenzotriazole hydrate (1.08 g, 7.99 mmol), and pyridine (0.8 ml) in 10 ml DMF was cooled to 0 °C. DCC (1.65 g, 7.99 mmol) was added and the mixture was stirred overnight as the solution warmed to room temperature. The resulting mixture was then filtered and the precipitate washed with 50 ml ethyl acetate. The organic layers were combined and washed with saturated $NaHCO_3$ (2×50 ml), 10% HCl (2×50 ml) and brine (50 ml). The organic layer was then dried over $MgSO_4$, filtered, and evaporated to dryness to give the crude diol.

Compound **3a**: (Method 2) The product precipitated when the organic solution was washed with water. This was filtered and recrystallized from CH_3CN. Dried with 4 Å sieves in $CHCl_3$ for two days. Yield = 44%. ^{1}H NMR: (270 MHz, *d*$_6$-DMSO): δ 8.12 (d, 2H), 7.30–7.40 (m, 10H), 6.02 (d, 2H), 5.49 (d, 2H), 4.28 (d, 2H), 3.65 (s, 6H). ^{13}C NMR: (68 MHz, *d*$_6$-DMSO) δ 172.5, 170.8, 135.5, 129.2, 128.9, 127.4, 71.5, 56.7, 53.0. IR: (KBr): $\nu_{CO} = 1726\ cm^{-1}$ (ester), $1664\ cm^{-1}$ (amide). Elemental analysis: Calculated for $C_{22}H_{24}N_2O_8$: C, 59.45; H, 5.44; N, 6.30. Experimental: C, 59.50; H, 5.50; N 6.24. Compound **3b**: (Method 2) The product was purified by precipitation from methanol using diethyl ether. Yield = 47%, white solid. ^{1}H NMR: (270 MHz, $CDCl_3$): δ 7.88 (d, 2H), 7.12–7.28 (m, 20H), 5.41 (d, 2H), 5.17 (d, 2H), 5.11 (d, 2H), 4.82 (br s, 2H), 4.34 (s, 2H). ^{13}C NMR: (68 MHz, $CDCl_3$): δ 173.2, 169.7, 135.2, 135.0, 129.0, 128.8, 128.6, 128.6, 128.5, 128.0, 127.1, 70.5, 67.6, 56.4. Compound **3c**: (Method 2) The product was purified by precipitation from acetonitrile with diethyl ether. Yield = 61%. ^{1}H NMR: (270 MHz, $CDCl_3$): δ 7.88 (d, 2H), 7.15–7.30 (m, 20H), 5.36 (d, 2H), 4.79 (m, 2H), 4.36 (s, 2H), 1.23–1.90 (m, 22H). ^{13}C NMR: (68 MHz, $CDCl_3$): δ 173.2, 169.3, 135.8, 128.9, 128.5, 126.9, 74.5, 70.0, 56.5, 31.4, 30.8, 25.2, 23.4, 23.3. Compound **3d**: (Method 2) The product was purified by precipitation from methylene chloride with hexanes. Yield = 55%. ^{1}H NMR: (270 MHz, $CDCl_3$): δ 7.65 (d, 2H), 7.10–7.20 (m, 10H), 5.06 (m, 2H), 4.35 (s, 2H), 3.59–3.61 (m, 4H), 3.32 (s, 6H). ^{13}C NMR: (68 MHz, $CDCl_3$): δ 173.6, 138.4, 128.6, 127.6, 126.4, 74.9, 70.5, 59.2, 52.5. Compound **3e**: (Method 2) The product was purified by precipitation from acetonitrile and methanol with diethyl ether. Yield = 55%. ^{1}H NMR: (270 MHz, *d*$_6$-DMSO): δ 8.43 (t, 2H), 8.08 (d, 2H), 7.20–7.50 (m, 10H), 6.11 (d, 2H), 5.45 (d, 2H), 4.26 (d, 2H), 3.04 (m, 4H), 1.34 (m, 4H), 1.21 (m, 4H), 0.82 (t, 6H). ^{13}C NMR: (68 MHz, *d*$_6$-DMSO): δ 171.7, 169.8, 139.6, 128.7, 127.9, 127.0, 73.2, 56.0, 38.9, 31.4, 19.9, 14.1. Compound **3f**: (Method 2) The product was purified by precipitation from methylene chloride using hexane. Yield = 68.9%. ^{1}H NMR: (270 MHz, *d*$_6$-DMSO): δ 10.9 (s, 2H), 7.78 (d, 2H), 7.47 (d, 2H), 7.34 (d, 2H), 7.22 (s, 2H), 7.07 (dd, 2H), 6.98 (dd, 2H), 6.01 (d, 2H), 4.64 (m, 2H), 4.33 (d, 2H), 3.55 (s, 6H), 3.26 (dd, 2H), 3.14 (dd, 2H). ^{13}C NMR: (68 MHz, *d*$_6$-DMSO): δ 172.4, 172.3, 136.6, 127.6, 124.6, 121.6, 119.0, 118.6, 112.0, 109.0, 73.0, 52.9, 52.5, 27.8. Compound **3g**: (Method 1) The product was purified by column chromatography (ethyl acetate). Yield = 41% (from acetonide). ^{1}H NMR: (270 MHz, $CDCl_3$): δ 7.58 (d, 2H), 4.69 (d, 2H), 4.59 (m, 2H), 4.36 (d, 2H), 3.75 (s, 6H), 3.70 (s, 6H), 2.37 (m, 4H), 2.22 (m, 2H), 2.00 (m, 2H). ^{13}C NMR: (68 MHz, CDCl$_3$): δ 173.7, 173.2, 171.4, 71.0, 52.8, 52.0, 51.4, 29.9, 27.1. Compound **3h**: (Method 1) The product was purified by column chromatography (hexane/ethyl acetate, 1:4). Yield = 58% (from acetonide). ^{1}H NMR: (270 MHz, d_6-DMSO): δ 7.44 (d, 2H), 6.10 (d, 2H), 4.25 (d, 2H), 4.23 (d, 2H), 3.66 (s, 6H), 0.93 (s, 18H). ^{13}C NMR: (68 MHz, d_6-DMSO): 171.9, 171.7, 73.2, 60.0, 52.3, 34.9, 26.8. Compound **3i**: (Method 1) The product was purified by column chromatography (hexanes/ethyl acetate, 1:1). Yield = 74% (from acetonide). ^{1}H NMR: (270 MHz, d_6-DMSO): δ 7.52 (d, 2H), 5.87 (d, 2H), 4.30 (d, 2H), 4.25 (d, 2H), 3.65, (s, 6H), 0.91 (s, 18H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 172.0, 171.5, 72.8, 59.9, 52.2, 34.9, 26.7. Compound **3j**: (Method 2) The product was purified by recrystallization from methanol and diethyl ether. Yield = 62%. ^{1}H NMR: (300 MHz, d_6-DMSO): δ 8.07 (dd, 2H), 5.71 (d, 2H), 4.27 (d, 2H), 3.95 (dd, 2H), 3.79 (dd, 2H), 3.62 (s, 6H). ^{13}C NMR: (75 MHz, d_6-DMSO): δ 173.0, 170.7, 72.9, 52.3, 41.1. IR: (KBr): ν_{CO} = 1770 cm^{-1} (ester), 1740 cm^{-1} (ester), 1652 cm^{-1} (amide). Elemental Analysis: Calculated for $C_{10}H_{16}N_2O_8$: C, 41.10; H, 5.52; N, 9.59. Experimental: C, 40.83; H, 5.60; N, 9.51. Compound **3k**: (Method 2) The product was purified by precipitation from methanol and diethyl ether with hexanes. Yield = 58%. ^{1}H NMR: (270 MHz, CDCl$_3$): δ 7.86 (d, 2H), 7.35 (m, 10H), 5.50 (d, 2H), 4.77 (d, 2H), 4.40 (d, 2H), 3.71 (s, 6H). ^{13}C NMR: (68 MHz, CDCl$_3$): δ 172.0, 171.2, 137.0, 129.2, 128.8, 127.8, 73.3, 56.3, 53.1. IR: (KBr): ν_{CO} = 1754 cm^{-1} (ester), 1742 cm^{-1} (ester), 1662 cm^{-1} (amide), 1653 cm^{-1} (amide). Elemental Analysis: Calculated for $C_{22}H_{24}N_2O_8$: C, 59.45; H, 5.44; N, 6.30. Experimental: C, 59.52; H, 5.81; N, 6.24. Chiral HPLC analysis: ee >95%. Compound **3l**: (Method 1) The product was purified by column chromatography (hexane/ethyl acetate, 1:1). ^{1}H NMR: (270 MHz, CDCl$_3$): δ 7.40 (d, 2H), 4.72 (d, 2H), 4.47 (dd, 2H), 4.41 (d, 2H), 3.72 (s, 6H), 2.21 (m, 2H), 0.93 (d, 6H), 0.91 (d, 6H). ^{13}C NMR: (68 MHz, CDCl$_3$): δ 172.6, 171.8, 71.1, 57.3, 52.4, 30.8, 19.1, 17.8. Chiral HPLC analysis: ee >95%. Compound **3m**: (Method 1) The product was purified by column chromatography using ethyl acetate. Yield = 69% (from acetonide). ^{1}H NMR: (270 MHz, CDCl$_3$): δ 7.44 (d, 2H), 5.12 (d, 2H), 4.43 (dd, 2H), 4.31 (d, 2H), 3.72 (s, 6H), 2.15 (m, 2H), 0.90 (s, 6H), 0.87 (s, 6H). ^{13}C NMR: (68 MHz, CDCl$_3$): δ 174.0, 171.5, 70.7, 57.0, 52.3, 31.1, 19.0, 17.8. Compound **3n**: (Method 1) The product was purified by precipitation from methanol and diethyl ether using hexanes. Yield = 76%. ^{1}H NMR: (270 MHz, CDCl$_3$): δ 7.40 (d, 2H), 4.46 (dd, 2H), 4.42 (s, 2H), 3.72 (s, 6H), 2.21 (m, 2H), 0.93 (d, 6H), 0.91 (d, 6H). ^{13}C NMR: (68 MHz, CDCl$_3$): δ 172.6, 171.8, 71.2, 57.4, 52.4, 30.8, 19.1, 17.8. Compound **3o**: (Method 1) The product was precipitated from solution when water was added. Filtered and recrystallization from acetonitrile/methanol. Yield = 56% (from acetonide). ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.95 (d, 2H), 7.95 (d, 2H), 7.45 (d, 4H), 7.25–7.31 (m, 6H), 6.15 (d, 2H), 5.58 (d, 2H), 4.31 (m, 2H), 4.28 (d, 2H), 3.53 (s, 6H), 1.29 (d, 6H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 173.2, 171.8, 169.8, 138.9, 128.8, 128.1, 127.3, 73.4, 55.5, 52.5, 48.3, 17.6. Compound **3p**: (Method 1) The product was precipitated from solution when water was added. Filtered and recrystallized from acetonitrile. Yield = 80% (from acetonide). ^{1}H NMR: (270MHz, d_6-DMSO): δ 8.79 (d, 2H), 7.98 (d, 2H), 7.49 (d, 4H), 7.35 (m, 6H), 6.48 (br s, 2H), 5.74 (d, 2H), 4.30 (s, 2H), 4.20 (m, 2H), 3.55 (s, 6H), 2.08 (m, 2H), 0.92 (d, 6H), 0.89 (d, 2H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 171.9, 171.8, 170.3, 138.9, 128.6, 127.9, 127.1, 73.3, 58.2, 55.3, 52.2, 30.4, 19.5, 18.8. Compound **3q**: (Method 1) The product was purified by precipitation from a mixture of acetonitrile and methanol using diethyl ether. Yield = 83% (from acetonide). ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.99 (d, 2H), 7.94 (d, 2H), 7.15–7.42 (m, 20H), 6.12 (d, 2H), 5.56 (d, 2H), 4.47 (m, 2H), 4.26 (d, 2H), 3.51 (s, 6H), 3.05 (dd, 2H), 2.94 (dd, 2H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 171.9, 171.7, 170.0, 138.8, 137.5, 128.8, 128.7, 128.0, 127.4, 127.2, 127.1, 73.2, 55.5, 54.4, 52.3, 36.0. Compound **3r**: (Method 1) The product was purified by recrystallization from CH$_3$CN. Yield = 67% (from acetonide) ^{1}H NMR: (400 MHz, d_6-DMSO): δ 9.41 (d, 2H), 7.97 (d, 2H), 7.27–7.51 (m, 10H), 6.14 (br s, 2H), 5.72 (d, 2H), 5.44 (d, 2H), 4.24 (s, 2H), 3.54 (s, 6H). ^{13}C NMR: (100 MHz): δ 171.7, 171.0, 169.9, 138.9, 136.4, 129.3, 129.0, 128.7, 128.4, 128.0, 127.2, 73.3, 56.8, 55.2, 52.8. Compound **3s**: (Method 1) The product was purified by precipitation from CH$_3$CN with diethyl ether. Yield = 55% (from acetonide) ^{1}H NMR: (270 MHz, d_6-DMSO): δ 9.44 (d, 2H), 8.10 (d, 2H), 6.18 (br s, 2H), 5.77 (d, 2H), 5.43 (d, 2H), 4.29 (s, 2H), 3.64 (s, 6H). ^{13}C NMR: (MHz, d_6-DMSO): δ 171.7, 171.3, 170.2, 139.1, 136.2, 129.2, 128.9, 128.7, 128.1, 128.0, 127.1, 73.3, 56.7, 55.4, 53.0. Compound **3t**: (Method 1) Purified by precipitation from ethyl acetate with hexanes. Yield = 63% (from acetonide) ^{1}H NMR: (270 MHz, CDCl$_3$): δ 7.52 (d, 2H), 6.88 (d, 2H), 4.59 (s, 2H), 4.49 (d, 2H), 4.30 (d, 2H), 3.72 (s, 6H), 1.02 (s, 18H), 0.93 (s, 18H). ^{13}C NMR: (68 MHz, CDCl$_3$): δ 172.9, 171.9, 170.3, 73.2, 61.9, 60.1, 52.1, 34.7, 34.0, 27.0, 26.7.

5.6. General procedure for the preparation of copper salts 5a–t

$H_2BBr\cdot SMe_2$ (1.0 M in dichloromethane, 300 µl, 0.300 mmol) was added to a suspension of diol **3a**–**t** (0.6 mmol) in CH$_2$Cl$_2$ (20 ml). A gas slowly evolved. The suspension was stirred overnight to provide a clear solution. The solvent was removed under vacuum and the resulting solid dissolved in CH$_3$CN (5 ml). This solution was then added in portions to a vigorously stirred suspension of Ag$_2$CO$_3$ (170 mg, 0.62 mmol) in CH$_3$CN (5 ml). The mixture was stirred for 10 min, filtered through Celite and pumped dry to provide **4a**–**t** as white solids. To a solution of CuCl (0.20 mmol) in 3 ml CH$_3$CN was added **4a**–**t** (0.20 mmol) in 3 ml CH$_3$CN. A white precipitate formed immediately. The mixture was stirred for 10 min and then filtered through Celite. The solvent was then reduced to approximately 0.5 ml and diethyl ether then added slowly as the product oiled from solution. The oily residue was pumped dry to give the copper borate salt **5a**–**t** as a white solid.

5a·2CH$_3$CN. Yield = 97%. ^{1}H NMR: (270 MHz, CD$_3$CN): δ 8.59 (d, 4H), 7.29–7.52 (m, 20H), 5.42 (d, 4H), 4.04 (s, 4H), 3.60 (s, 12H). ^{13}C NMR: (68 MHz, CD$_3$CN): δ 174.5, 171.0, 136.9, 128.8, 128.3, 127.5, 78.9, 56.7, 52.2. ^{11}B NMR: (87 MHz, CD$_3$CN): δ 11.87. IR: (KBr): ν_{CO} = 1740 cm^{-1} (ester), 1646 cm^{-1} (amide). LRMS: M$^+$ = 959. Elemental Analysis: Calculated for $C_{48}H_{50}BCuN_6O_{16}$: C, 55.36; H, 4.84; N, 8.07. Found: C, 55.40; H, 5.14; N, 7.78. **5b**·CH$_3$CN. Yield = 94%. ^{1}H NMR: (270 MHz, CD$_3$CN): δ 8.67 (d, 4H), 7.10–7.60 (m, 40H), 5.46 (d, 4H), 5.08 (d, 4H), 5.02 (d, 4H), 4.03 (s, 4H). ^{13}C NMR: (68 MHz, CD$_3$CN): 174.6, 170.4, 136.7, 136.0, 128.8, 128.4, 128.3, 128.1, 127.7, 127.6, 78.9, 66.6, 56.9. ^{11}B NMR: (87 MHz, CD$_3$CN): δ 12.09. **5c**·CH$_3$CN. Yield = 94%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.70 (d, 4H), 7.28–7.50 (m, 20H), 5.44 (d, 4H), 4.60 (m, 4H), 4.02 (s, 4H), 1.19–1.70 (m, 44H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 174.4 (br), 169.8, 137.6, 128.9, 128.4, 127.5, 78.9 (br), 73.4, 56.8, 31.0, 30.9, 25.1, 23.2, 23.1. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 12.7. **5d**·CH$_3$CN. Yield = 95%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.39 (d, 4H), 7.20–7.50 (m, 20H), 5.02 (m, 4H), 4.03 (s, 4H), 3.50–3.60 (m, 8H), 3.16 (s, 12H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 174.5 (br), 141.2, 128.6, 127.3, 127.3, 78.9 (br), 76.0, 58.6, 52.6. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 12.00 **5e**·2CH$_3$CN. Yield = 85%. ^{1}H NMR: (270 MHz, CD$_3$CN): δ 8.75 (d, 4H), 7.20–7.5 (m, 24H), 5.35 (d, 4H), 4.13 (s, 4H), 2.97 (m, 4H), 2.93 (m, 4H), 1.12–1.40 (m, 16H), 0.77 (t, 12H). ^{13}C NMR: (68 MHz, CD$_3$CN): δ 174.7, 170.5, 138.5, 128.5, 127.7, 127.0, 79.0, 57.9, 39.0, 31.2, 19.7, 13.1. ^{11}B NMR: (87 MHz, CD$_3$CN): δ 11.85 **5f**·2CH$_3$CN. Yield = 97%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 10.84 (s, 4H), 8.14 (d, 4H), 7.50 (d, 4H), 7.29–7.32 (m, 8H), 6.93–7.07 (m, 8H), 4.51 (m, 4H), 4.09 (s, 4H), 3.47 (s, 12H), 3.16 (m, 8H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 174.7, 172.6, 136.6, 127.6, 124.8, 121.3, 118.8, 118.4, 111.9, 109.5, 78.2, 53.6, 52.3, 28.0. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 11.80. **5g**·CH$_3$CN. Yield = 87%. ^{1}H NMR: (270 MHz, CD$_3$CN): δ 7.91 (br s, 4H), 4.43 (m, 4H), 4.13 (s, 4H), 3.66 (m, 12H), 3.58 (s, 12H), 2.41 (m, 8H), 2.10 (m, 4H), 1.94 (m, 4H). ^{13}C NMR: (68 MHz, CD$_3$CN): δ 175.0, 173.1, 172.4, 78.4, 51.9, 51.2, 51.2, 29.3, 26.8. ^{11}B NMR: (87 MHz, CD$_3$CN): δ 11.9. **5h**·CH$_3$CN. Yield = 97%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.91 (d, 4H), 4.20 (d, 4H), 4.02 (s, 4H), 3.56 (s, 12H), 0.91 (s, 36H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 174.3, 171.2, 80.2, 60.7, 51.8, 35.1, 26.7. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 12.10. **5i**·CH$_3$CN. Yield = 93%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.09 (br s, 4H), 4.03 (br s, 4H), 3.98 (br s, 4H), 3.60 (s, 12H), 0.92 (s, 36H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 174.7 (broad), 171.5, 78.2 (broad), 61.4, 51.8, 34.1, 27.0. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 11.86. **5j**·CH$_3$CN. Yield = 99%. ^{1}H NMR: (270 MHz, CD$_3$CN): δ 7.99 (br s, 4H), 4.17 (s, 4H), 3.98 (s, 4H), 3.96 (s, 4H), 3.67 (s, 12H). ^{13}C NMR: (68 MHz, CD$_3$CN): δ 175.5, 170.9, 77.6, 51.8, 40.7. ^{11}B NMR: (87 MHz, CD$_3$CN): δ 11.39. IR: (KBr): ν_{CO} = 1748 cm^{-1} (ester), ν_{CO} = 1656 cm^{-1} (amide). LRMS: M$^+$ = 655. Elemental Analysis: Calculated for $C_{22}H_{47}BCuN_5O_{16}$: C, 37.97; H, 4.49; N 10.06. Found: C, 37.97; H 4.45; N, 10.15. **5k**·CH$_3$CN. Yield = 88%. ^{1}H NMR: (270 MHz, CD$_3$CN): δ 8.54 (d, 4H), 7.28 (m, 20H), 5.18 (d, 4H), 4.20 (s, 4H), 3.59 (s, 12H). ^{13}C NMR: (68 MHz, CD$_3$CN): δ 174.9, 171.0, 136.6, 128.7, 128.2, 127.5, 78.5, 56.9, 52.1. ^{11}B NMR: (87 MHz, CD$_3$CN): δ 12.05. IR: (KBr): ν_{CO} = 1743 cm^{-1} (ester), 1673 (amide). LRMS: M$^+$ = 959. Elemental Analysis: Calculated for $C_{46}H_{47}BCuN_5O_{16}$: C, 55.24; H, 4.74; N, 7.00. Found: C, 55.01; H, 4.74; N, 7.17. **5l**·CH$_3$CN. Yield = 90%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.06 (d, 4H), 7.10–7.40 (m, 20H), 4.51 (m, 4H), 3.89 (s, 4H), 3.55 (s, 12H), 3.06 (dd, 4H), 2.91 (dd, 4H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 174.5 (br), 172.1, 137.5, 129.9, 128.6, 127.0, 78.2 (br), 53.8, 52.4, 38.1. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 11.83. **5m**·CH$_3$CN. Yield = 98%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 7.94 (d, 4H), 4.22 (dd, 4H), 4.03 (s, 4H), 3.59 (s, 12H), 2.09 (m, 4H), 0.89 (d, 12H), 0.85 (d, 12H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 174.8, 172.0, 79.4, 57.5, 52.2, 31.1, 19.2, 17.8. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 12.01. **5n**·CH$_3$CN. Yield = 90%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.06 (d, 4H), 7.18–7.40 (m, 20H), 4.51 (m, 4H), 3.89 (s, 4H), 3.55 (s, 12H), 3.06 (dd, 4H), 2.91 (dd, 4H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 174.5 (br), 172.1, 137.5, 129.9, 128.6, 127.0, 78.2 (br), 53.8, 52.4, 38.1. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 11.8 **5o**·2CH$_3$CN. Yield = 79%. ^{1}H NMR: (270 MHz, CD$_3$CN): δ 8.66 (d, 4H), 7.42 (d, 4H), 7.28–7.50 (m, 20H), 5.43 (d, 4H), 4.20 (m, 8H), 3.52 (s, 12H), 1.20 (d, 12H). ^{13}C NMR: (68 MHz, CD$_3$CN): 174.8, 172.6, 170.1, 137.9, 128.4, 127.8, 127.3, 78.6, 57.1, 51.7, 48.2, 16.6. ^{11}B NMR: (87 MHz, CD$_3$CN): 11.87 **5p**·4CH$_3$CN. Yield = 87%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.65 (d, 4H), 8.36 (d, 4H), 7.50 (m, 8H), 7.22 (m, 12H), 5.61 (d, 4H), 4.10 (m, 4H), 4.09 (s, 4H), 3.48 (s, 12H), 1.91 (m, 4H), 0.81 (d, 12H), 0.78 (d, 12H). ^{13}C NMR: (68 MHz, d_6-DMSO): δ 174.6, 172.0, 170.2, 138.8, 128.4, 127.6, 127.5, 78.6, 58.0, 56.3, 52.0, 30.3, 19.3, 18.8. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 11.70. **5q**·2CH$_3$CN. Yield = 80%. ^{1}H NMR: (270 MHz, d_6-DMSO): δ 8.58 (m, 8H), 7.0–7.45 (m, 40H), 5.51 (d, 4H), 4.41 (m, 4H), 4.09 (br s, 4H), 3.41 (s, 12H), 2.89 (s, 4H), 2.86 (s, 4H). ^{13}C NMR: (68 MHz, CD$_3$CN): δ 174.5 (br), 171.4, 170.2, 137.7, 136.9, 129.4, 128.5, 128.4, 127.8, 127.5, 126.7, 78.4, 57.2, 54.0, 51.7, 36.9. ^{11}B NMR: (87 MHz, d_6-DMSO): δ 11.75. IR: (KBr): ν_{CO} = 1743 cm^{-1} (ester), 1659 cm^{-1} (amides). Elemental Analysis: Calculated for $C_{84}H_{86}BcuN_{10}O_{20}$: C, 61.90; H, 5.32; N, 8.59. Found: C, 61.56; H, 5.34; N, 8.41. **5r**·2CH$_3$CN. Yield = 92%. ^{1}H NMR: (270 MHz, CD$_3$CN): δ 8.69 (d, 4H), 7.80 (d, 4H), 7.20–7.50 (m, 40H), 5.48 (d, 4H), 5.29 (d, 4H), 4.15 (s, 4H), 3.49 (s, 12H). ^{13}C NMR: (68 MHz, CD$_3$CN): δ 174.8, 170.7, 170.0, 137.7, 136.4, 128.9, 128.7, 128.4, 128.2, 127.5, 127.4, 78.5, 57.1, 56.5, 52.1. ^{11}B NMR: (87 MHz, CD$_3$CN): δ 11.62. **5s**·2CH$_3$CN. Yield = 87%. ^{1}H NMR: (270 MHz, CD$_3$CN): δ 8.57 (d, 4H), 7.78 (d, 4H), 7.14–7.50 (m, 40H), 5.47 (d, 4H), 5.40 (d, 4H), 4.06 (s, 4H), 3.58 (s, 12H). ^{13}C NMR: (68 MHz, CD$_3$CN): δ 174.8, 170.8, 170.0, 137.8, 136.4, 128.7, 128.5, 128.3, 127.8, 127.4, 127.3, 78.5, 57.3, 56.4, 52.3. ^{11}B NMR: (87 MHz, CD$_3$CN): δ 11.7. **5t**·2CH$_3$CN. Yield = 91%. ^{1}H NMR: (270 MHz, CD$_3$CN): 7.97 (d, 4H), 6.96 (d, 4H), 4.33 (d, 4H), 4.16 (d, 4H), 4.15 (s, 4H), 3.62 (s, 12H), 0.99 (s, 36H), 0.94 (s, 36H). ^{13}C NMR: (68 MHz, CD_3CN): δ 174.9, 171.5, 170.8, 77.8, 61.0, 60.8, 51.1, 34.3, 33.4, 26.6, 26.1. ^{11}B NMR: (87 MHz, CD_3CN): δ 11.2.

5.7. General cyclopropanation procedure

A solution of styrene (250 mg, 2.4 mmol), hexadecane (100 μl), and copper catalyst (0.0095 mmol) in 1.5 ml CH_2Cl_2 was cooled to 0 °C under N_2. Ethyl diazoacetate (100 μl, 0.95 mmol) in 1.0 ml of CH_2Cl_2 was then added via syringe pump over 8 h. The resulting solution was stirred overnight at 0 °C and then filtered through a short plug of silica using hexane/ethyl acetate (1:1). The crude mixture was then subjected to GC analysis to give the trans/cis ratio and yield relative to an internal standard, hexadecane.

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References

1. For reviews of amino acid libraries in asymmetric catalysis: (a) Gennari, C.; Piarulli, U. *Chem. Rev.* **2003**, *103*, 3071–3100; (b) Reetz, M. T. *Angew. Chem., Int. Ed.* **2001**, *40*, 284–310; (c) Traverse, J. F.; Snapper, M. L. *Drug Discovery Today* **2002**, *7*, 1002–1012; (d) Francis, M. B.; Jamison, T. F.; Jacobsen, E. N. *Curr. Opin. Chem. Biol.* **1998**, *2*, 422–428.
2. Representative examples: (a) Cole, B. M.; Shimizu, K. D.; Krueger, C. A.; Harrity, J. P. A.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **1996**, *35*, 1668–1761; (b) Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901–4902; (c) Francis, M. B.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **1999**, *38*, 937–941; (d) Chataigner, I.; Gennari, C.; Piarulli, U.; Ceccarelli, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 916–918; (e) Luchaco-Cullis, C. A.; Mizutani, H.; Murphy, K. E.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 1456–1460; (f) Ongeri, S.; Piarulli, U.; Jackson, R. F.; Gennari, C. *Eur. J. Org. Chem.* **2001**, 803–807; (g) Gilbertson, S. R.; Wang, X. F. *Tetrahedron Lett.* **1996**, *37*, 6475–6478; (h) Gilbertson, S. R.; Collibee, S. E.; Agarkov, A. *J. Am. Chem. Soc.* **2000**, *122*, 6522–6523; (i) Greenfield, S. J.; Agarkov, A.; Gilbertson, S. R. *Org. Lett.* **2003**, *5*, 3069–3072; (j) Green, S. D.; Monti, C.; Jackson, R. F. W.; Anson, M. S.; Macdonald, S. J. F. *Chem. Commun.* **2001**, 2594–2595; (k) Dyker, G.; Breitenstein, K.; Henkel, G. *Tetrahedron: Asymmetry* **2002**, *13*, 1929–1936.
3. Llewellyn, D. B.; Adamson, D.; Arndtsen, B. A. *Org. Lett.* **2000**, *2*, 4165–4168.
4. For a recent review, see: (a) Lacour, J.; Hebbe-Viton, V. *Chem. Rev. Soc.* **2003**, *32*, 373–382; For representative examples of chiral counteranions: (b) Boeseken, J.; Mijs, J. A. *Recl. Trav. Chim. Pays-Bas.* **1925**, *44*, 758; (c) Lacour, J.; Gougon-Ginglinger, C.; Torche-Haldimann, S.; Jordy, J. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 3695; (d) Monchaud, D.; Jodry, J. J.; Pomeranc, D.; Heitz, V.; Chambron, J.-C.; Sauvage, J.-P.; Lacour, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 2317; (e) Green, S.; Nelson, A.; Warriner, S.; Whittaker, B. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4403; (f) Carter, C.; Fletcher, S.; Nelson, A. *Tetrahedron: Asymmetry* **2003**, *14*, 1995; (g) Ishihara, K.; Miyata, M.; Hattori, K.; Tada, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 10520; (h) Ishihara, K.; Kurihara, H.; Matsumoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1998**, *120*, 6920; (i) Graf, E.; Graff, R.; Hosseini, M. W.; Huguenard, C.; Taulelle, F. *Chem. Commun.* **1997**, 1459; (j) Owen, D. J.; VanDerveer, D.; Schuster, G. B. *J. Am. Chem. Soc.* **1998**, *120*, 1705(k) Fiedler, D.; Leung, D. H.;, Bergman, R. G.; Raymond, K. N., in preparation.
5. For examples of chiral phase transfer catalysts, see: (a) Dehmlow, E. V.; Dehmlow, S. S. *Phase Transfer Catalysis*, 3rd ed.; VCH: Weinheim, 1993; (b) Nelson, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 1583–1585; (c) Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414–12415; (d) Carter, C.; Fletcher, S.; Nelson, A. *Tetrahedron: Asymmetry* **2003**, *14*, 1995–2004; (e) Dolling, U. H.; Davis, P.; Grabowski, E. J. J. *J. Am. Chem. Soc.* **1984**, *106*, 446–447; (f) Ooi, T.; Doda, K.; Maruoka, K. *Org. Lett.* **2001**, *3*, 1273–1276; (g) Arai, S.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 2145–2148; (h) Chang, S.; Galvin, J. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 6937.
6. A portion of this work has been previously communicated: Llewellyn, D. B.; Arndtsen, B. A. *Organometallics* **2004**, *23*, 2838–2840.
7. Arnaud, N.; Picard, C.; Cazaux, L.; Tisnes, P. *Tetrahedron* **1997**, *53*, 13757–13768.
8. Chiral HPLC analysis of **3i** and **3k** showed no racemization.
9. For reviews: (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley & Sons: New York, 1998; (b) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977–1050; For representative examples of asymmetric copper catalyzed cyclopropanations: (c) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726–728; (d) Kanemasa, S.; Hamura, S.; Harada, E.; Yamamoto, H. *Tetrahedron Lett.* **1994**, *35*, 7985–7988; (e) Lo, W.-C.; Che, C.-M.; Cheng, K.-F.; Mak, T. C. W. *Chem. Commun.* **1997**, 1205–1206; (f) Galardon, E.; Roue, S.; Maux, O. L.; Simonneaux, G. *Tetrahedron Lett.* **1998**, *39*, 2333–2334; (g) Kwong, H.; Lee, W.; Ng, H.; Chiu, W.; Wong, W. *J. Chem. Soc., Dalton Trans.* **1998**, 1043–1046.
10. Low cyclopropane yields are the result of the nonpolar solvent employed: more polar solvents or elevated temperatures have been previously demonstrated to lead to higher yields.[6]
11. The yield under the reaction conditions employed (0 °C, benzene) was low at 3%. Changing the solvent from benzene to either methylene chloride or diethyl ether, at 0 °C, increased the yields to 40% and 22%, respectively, with only a slight drop in the selectivity of the reaction (29% trans ee in methylene chloride and 25% trans ee in diethyl ether).
12. Catalyst **3r** was insoluble in benzene.
13. For representative examples: (a) Lacour, J.; Ginglinger, C.; Favarger, F.; Torche-Haldimann, S. *Chem. Commun.* **1997**, *23*, 2285–2286; (b) Ginglinger, C.; Jeannerat, D.; Lacour, J.; Juge, S.; Uziel, J. *Tetrahedron Lett.* **1998**, *39*, 7495–7498; (c) Monchaud, D.; Lacour, J.; Coudret, C.; Fraysse, S. *J. Organomet. Chem.* **2001**, *624*, 388–391; (d) Planas, J. G.; Prim, D.; Rose, E.; Rose-Munch, F.; Monchaud, D.; Lacour, J. *Organometallics* **2001**, *20*, 4107–4110; (e) Desvergnes-Breuil, V.; Hebbe, V.; Dietrich-Buchecker, C.; Sauvage, J.-P.; Lacour, J. *Inorg.*

Chem. **2003**, *42*, 255–257; (f) Fiedler, D.; Pagliero, D.; Brumaghim, J. L.; Bergman, R. G.; Raymond, K. N. *Inorg. Chem.* **2004**, *43*, 846–848.

14. For examples: (a) Lacour, J.; Jordy, J. J.; Ginglinger, C.; Torche-Haldimann, S. *Angew. Chem., Int. Ed.* **1998**, *37*, 2379–2380; (b) Lacour, J.; Jodry, J. J.; Monchaud, D. *Chem. Commun.* **2001**, 2302; (c) Fiedler, D.; Leung, D. H.; Bergman, R. G.; Raymond, K. N. *J. Am. Chem. Soc.* **2004**, *126*, 3674–3675.
15. (a) Bellachioma, G.; Cardaci, G.; Macchioni, A.; Reichenbach, G.; Terenzi, S. *Organometallics* **1996**, *15*, 4349–4351; (b) Macchioni, A.; Bellachioma, G.; Cardaci, G.; Gramlich, V.; Ruegger, H.; Terenzi, S.; Venanzi, L. M. *Organometallics* **1997**, *16*, 2139–2145; (c) Bellachioma, G.; Cardaci, G.; Gramlich, V.; Macchioni, A.; Valentini, M.; Zuccaccia, C. *Organometallics* **1998**, *17*, 5025–5030; (d) Macchioni, A.; Bellachioma, G.; Cardaci, G.; Cruciani, G.; Foresti, E.; Sabatino, P.; Zuccaccia, C. *Organometallics* **1998**, *17*, 5549–5556; (e) Macchioni, A.; Bellachioma, G.; Cardaci, G.; Travaglia, M.; Zuccaccia, C. *Organometallics* **1999**, *18*, 3061–3069; (f) Zuccaccia, C.; Bellachioma, G.; Cardaci, G.; Macchioni, A. *Organometallics* **1999**, *18*, 1–3; (g) Macchioni, A.; Zuccaccia, C.; Clot, E.; Gruet, K.; Crabtree, R. H. *Organometallics* **2001**, *20*, 2367–2373; (h) Martinez-Vivente, E.; Pregosin, P. S.; Vial, L.; Herse, C. *Lacour J.* **2004**, *10*, 2912–2918.
16. Huntington, M.; Corley, E. G.; Thompson, A. S.; Shinkai, I. *Org. Synth.* **1998**, *75*, 19–30.
17. Braghiroli, D.; Di Bella, M. *Tetrahedron: Asymmetry* **1996**, *7*, 2145–2150.
18. Bodansky, M.; Bodansky, A. *The Practice of Peptide Synthesis*, 2nd ed.; Springer: New York, 1994.