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Synthesis of Novel Chiral Diamino Alcohols and Their Application in Copper-Catalyzed Asymmetric Allylic Oxidation of Cycloolefins

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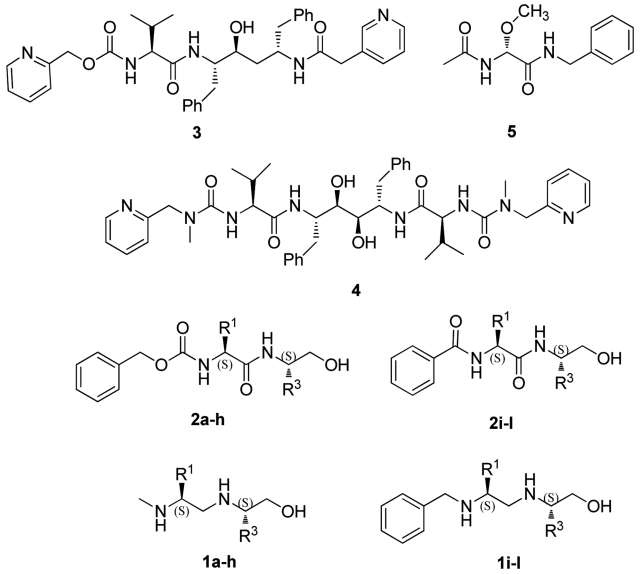
The small library of new enantiomerically pure (*S*,*S*)-diamino alcohols **1** and their hydroxyldiamide precursors **2** were conveniently synthesized on a gram scale from inexpensive and commercially chiral pool amino acids. The catalytic and induced asymmetric effects of the chiral ligands **1** in the asymmetric allylic oxidation of cycloolefins were investigated.

Key Words : Chiral diamino alcohols, Chiral hydroxyldiamides, Asymmetric allylic oxidation, Small chiral libraries, Chiral pool amino acids

Introduction

Optically active amino alcohols are one of the important classes of compounds because of their presence in the natural products.[1] They have also found applications as chiral ligands and auxiliaries for a variety of asymmetric reactions.[2,3] Furthermore, diamino alcohols[4] and their hydroxyldiamide[5] precursors, in particular, are core units in many medicinal compounds such as HIV protease inhibitors A80987 (**3**),[5f] A77003 (**4**)[5g-i] and lacosamide (**5**)[5j] (Scheme 1). Due to the importance and high efficiency of chiral hydroxyldiamide, chiral amino alcohols[4g] and their methoxy analogy, our attention was focused on the development of a simple and efficient method to produce a small library of enantiomerically pure diamino alcohols **1** and their hydroxyldiamide precursors **2** from readily available starting materials. Although the asymmetric synthesis of vicinal amino alcohols has been extensively studied, however, there have been a few reports of asymmetric synthesis to diamino alcohols, which may become precursors of new kinds of amino alcohol compounds.[4d-g] The chiral hydroxyldiamides **2**, which appear structurally similar to molecules **3-5**, can be expected to provide more opportunities for the development of biologically active compounds.[5] Moreover, the chiral diamino alcohols, **1**, can be used in the asymmetrical reactions as a catalyst to increase reaction rate and as a chiral auxiliary or chiral ligand to induce the chirality in the synthesis of chiral products.[2,3] Enantioselective allylic oxidation of olefins using copper chiral complexes have been the subject of great interest during the last decade. This reaction provides an access to chiral allylic alcohols, which are the key intermediates in natural products synthesis.[6,7] Since the use of chiral amino alcohol ligands has been less studied on asymmetric Kharasch reaction, our increasing interest[8] was concentered on the demonstration of catalytic and asymmetric effects of the chiral tridentate diamino alcohols **1** in the asymmetric copper-catalyzed allylic oxidation of cycloolefins.[9] To the best of our knowledge, all the reported allylic oxidations suffer from at least one disadvantage in terms of long reaction times, unsatisfactory yields, or low enantioselectivities. Apparently, yields and ees achieved in this work are superior for the allylic oxidation of cycloolefins in comparison with other works that used chiral amino alcohols as ligands.



Scheme 1

Experimental

General Information. Melting points were measured on an Elecrtothermal 9100 apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 341 polarimeter at 589 nm. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER DRX-300 AVANCE spectrometer at 300.13 and 75.47 MHz in $CDCl_3$ and DMSO-d_6 using TMS (δ = 0.0 ppm) as internal standard. IR spectra were recorded on a Bomen FT-IR-MB-series instrument. Mass spectra were recorded on a FINNIGAN-MAT 8430 spectrometer operating at an ionization potential of 70 eV. Enantiomeric excess (ee) of the allylic esters **9** were determined by HPLC analysis

using EC 250/4.6 Nucleocel Alpha S column. All reactions were performed under an atmosphere of dry, oxygen-free nitrogen. All reagents were purchased from Aldrich, Merk, Alfa Acer or Acros. *N*-protected amino acids **7** and amino alcohols **8** were prepared according to literature procedure.[10, 11] Olefins were distilled from calcium hydride before use. All solvents were of reagent grade and were dried and distilled immediately before use as follows: acetonitrile and acetone from P_2O_5, methylene chloride from calcium hydride, tetrahydrofuran and diethyl ether from sodium and methanol from magnesium. Column chromatography was performed using silica gel 60 (230 ± 400 mesh) eluting with ethyl acetate: *n*-hexane. TLC was performed using silica gel 60 F256 plates with visualization by UV.

General Procedure for the Synthesis of Chiral Hydroxyldiamide 2. To a cold solution of *N*-protected amino acid **7** (3 mmol) in dry THF (10 mL) at −15 ºC under N_2 were added 4-methylmorpholine (0.33 mL, 3 mmol) followed by addition of isobutyl chloroformate (0.39 mL, 3 mmol). The reaction mixture was allowed to stir for 5 minutes and then, a THF solution of chiral amino alcohol **8** (3 mmol) was added to the reaction flask at −15 ºC. The reaction was warmed to room temperature and stirred for 16 h at rt. The reaction mixture was concentered and dissolved in 15 mL of ethyl acetate and 3 mL of water. After separation of layers, The ethyl acetate layer was washed with 1 N HCl (12 mL), water (3 mL), 5% $NaHCO_3$ (12 mL), water (6 mL), and then with saturated NaCl. The organic layer was concerted to afford chiral hydroxyldiamide **2** as a white solid after crystallization in ethylacetate/hexane.

Benzyl ((*S*)-2-(((*S*)-2-Hydroxy-1-phenylethyl)amino)-2-oxo-1-phenylethyl)carbamate (2a): White solid (1.077 g, 89% yield). mp 206 ºC. $[\alpha]_D^{20}$ = –23.52 (c = 0.42, DMSO). ^{1}H NMR (300 MHz, DMSO) δ_H 3.47-3.54 (br dd, 2H), 4.74-4.81 (dd, 1H), 4.86 (t, *J* = 5.4 Hz, 1H), 5.02 (s, 2H), 5.36 (d, *J* = 8.7 Hz, 1H), 7.22-7.33 (m, 13H), 7.44 (d, 2H), 7.91 (d, *J* = 8.5 Hz, 1H), 8.62 (d, *J* = 7.9 Hz, 1H). ^{13}C NMR (75.46 MHz, DMSO) δ_C 31.1, 55.6, 64.9, 66.0, 127.3, 127.4, 127.6, 128.0, 128.1, 128.2, 128.5, 128.7, 128.8, 137.3, 139.2, 141.3, 156.6, 169.9. FT-IR (KBr, cm^{-1}) 3306, 2966, 1694, 1651, 1561, 1529, 1250, 1048, 748, 700. MS (*m/z*) = 404 (M^+); Anal. calcd for $C_{24}H_{24}N_2O_4$: C 71.27, H 5.98, N 6.93; found C 71.35, H 6.08, N 6.90.

Benzyl ((*S*)-2-(((*S*)-1-Hydroxy-3-methylbutan-2-yl)amino)-2-oxo-1-phenylethyl)carbamate (2b): White solid (1.032 g, 93%). mp 130 ºC. $[\alpha]_D^{20}$ = +360 (c = 0.1, DMSO). ^{1}H NMR (300 MHz, DMSO) δ_H 0.82 (t, 6H), 1.73-1.87 (m, 1H), 3.48-3.53 (m , 2H), 4.6 (br t, 1H), 5.04 (s, 2H), 5.31 (d, *J* = 8.7 Hz, 1H), 7.25-7.34 (m, 10H), 7.91 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR (75.46 MHz, DMSO) δ_C 18.5, 20.0, 28.6, 56.2, 58.8, 61.5, 66.0, 127.5, 127.8, 128.1, 128.2, 128.6, 128.8, 137.4, 139.3, 156.1, 170.2. FT-IR (KBr, cm^{-1}) 3318, 2954, 2856, 1690, 1650, 1529, 1250, 1226, 1050, 854, 699. MS (*m/z*) = 370 (M^+); Anal. calcd for $C_{21}H_{26}N_2O_4$: C 68.09, H 7.07, N 7.56; found C 68.3, H 7.14, N 7.49.

Benzyl ((*S*)-2-(((*S*)-1-Hydroxy-4-methylpentan-2-yl)amino)-2-oxo-1-phenylethyl)carbamate (2c): White solid (921 mg, 80%). mp 78 ºC. $[\alpha]_D^{20}$ = +250 (c = 0.04, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.87 (d, 6H), 1.18-1.46 (m, 2H), 1.46-1.62 (m, 1H), 2.85 (br s, 1H), 3.38-3.47 (br dd, 2H), 3.91-4.09 (br s, 1H), 5.07 (s, 2H), 5.11-5.29 (br s, 1H), 6.28-6.43 (m, 2H) 7.32 (br s, 10H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 22.2, 23.0, 24.8, 39.8, 50.3, 59.0, 65.0, 67.1, 127.1, 128.1, 128.2, 128.4, 128.5, 129.0, 136.1, 137.9, 156.0, 170.4. FT-IR (KBr, cm^{-1}) 3316, 2960, 2905, 1720, 1659, 1521, 1237, 1050, 733, 698. MS (*m/z*) = 384 (M^+); Anal. calcd for $C_{22}H_{28}N_2O_4$: C 68.73, H 7.34, N 7.29; found C 68.84, H 7.40, N 7.23.

Benzyl ((*S*)-2-(((*S*)-1-Hydroxy-3-phenylpropan-2-yl)-amino)-2-oxo-1-phenylethyl)carbamate (2d): White solid (1.152 g, 92%). mp 156 ºC. $[\alpha]_D^{20}$ = +30 (c = 0.5, DMSO). ^{1}H NMR (300 MHz, DMSO) δ_H 2.61-2.68 (dd, ^2J = 13.2 Hz, ^3J = 8.3 Hz, 1H), 2.82-2.88 (dd, ^2J = 13.2 Hz, ^3J = 5.3 Hz, 1H), 3.21-3.31 (m, 2H), 3.79- 3.90 (m, 1H), 4.83 (t, *J* = 5.3 Hz, 1H), 5.03 (s, 2H), 5.22 (d, *J* = 8.6 Hz, 1H), 7.26-7.35 (m, 15H), 7.82 (d, *J* = 8.7 Hz, 1H), 8.10 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (75.46 MHz, DMSO) δ_C 36.8, 53.3, 62.2, 63.4, 67.2, 126.7, 127.2, 128.2, 128.3, 128.6, 128.6, 128.7, 128.8, 129.2, 136.0, 137.4, 137.6, 155.8, 170.0. FT-IR (KBr, cm^{-1}) 3379, 2881, 1694, 1663, 1468, 1278, 1189, 1108, 892, 863. MS (*m/z*) = 418 (M^+); Anal. calcd for $C_{25}H_{26}N_2O_4$: C 71.75, H 6.26, N 6.69; found C 71.79, H 6.31, N 7.09.

Benzyl ((*S*)-1-(((*S*)-1-Hydroxy-3-phenylpropan-2-yl)-amino)-1-oxo-3-phenylpropan-2-yl)carbamate (2e): White solid (1.242 g, 96%). mp 160 ºC. $[\alpha]_D^{20}$ = +12.76 (c = 0.4, CH_2Cl_2). ^{1}H NMR (300 MHz, DMSO) δ_H 2.61-2.73 (br dd, 2H), 2.82-2.93 (m, 2H), 3.20-3.36 (br s, 3H), 3.78-3.88 (br dd, 1H), 4.17-4.24 (m, 1H), 4.93 (s, 2H), 7.15-7.32 (m, 15H), 7.44 (d, *J* = 8.7 Hz, 1H), 7.92 (br s, 1H). ^{13}C NMR (75.46 MHz, DMSO) δ_C 36.7, 36.9, 53.4, 62.8, 63.4, 67.5, 126.8, 127.4, 128.2, 128.3, 128.4, 128.6, 128.8, 128.9, 129.1, 136.1, 137.4, 137.6, 156.1, 170.2. FT-IR (KBr, cm^{-1}) 3281, 2937, 1690, 1653, 1534, 1286, 1247, 1041, 747, 697. MS (*m/z*) = 432 (M^+); Anal. calcd for $C_{26}H_{28}N_2O_4$: C 72.20, H 6.53, N 6.48; found C 72.28, H 6.57, N 6.50.

Benzyl ((*S*)-1-(((*S*)-1-Hydroxy-3-methylbutan-2-yl)amino)-3-methyl-1-oxobutan-2- yl)carbamate (2f): White solid (816 mg, 81%). mp 160 ºC. $[\alpha]_D^{20}$ = +81.8 (c = 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, DMSO) δ_H 0.80-0.86 (m, 12H), 1.79-1.88 (m, 1H), 1.88-1.97 (m, 1H), 3.35-3.43 (br s, 2H), 3.54-3.60 (m, 1H), 3.84 (t, 1H), 4.59 (br t, 1H), 5.03 (s, 2H), 7.27-7.30 (br d, 1H), 7.30-7.38 (m, 5H), 7.50 (d, *J* = 8.9 Hz, 1H). ^{13}C NMR (75.46 MHz, DMSO) δ_C 18.6, 18.8, 20.0, 20.1, 28.7, 28.9, 56.4, 58.9, 61.4, 66.0, 127.5, 128.2, 128.8, 137.4, 156.09, 170.11. FT-IR (KBr, cm^{-1}) 3284, 2977, 2875, 1691, 1646, 1532, 1247, 1043, 1024, 746, 699. MS (*m/z*) = 336 (M^+); Anal. calcd for $C_{18}H_{28}N_2O_4$: C 64.26, H 8.39, N 8.33; found C 64.35, H 8.42, N 8.29.

Benzyl ((*S*)-1-(((*S*)-1-Hydroxy-4-methylpentan-2-yl)-amino)-4-methyl-1-oxopentan-2-yl)carbamate (2g): White solid (939 mg, 86%). mp 101 ºC. $[\alpha]_D^{20}$ = +41.25 (c = 1.4 CH_2Cl_2). ^{1}H NMR (300 MHz, DMSO) δ_H 0.80-0.87 (m, 12H), 1.28-1.35 (m, 2H), 1.35-1.44 (m, 2H), 1.55-1.61 (m, 2H), 3.17-3.20 (m, 1H), 3.28-3.31 (m, 1H), 3.71- 3.78 (m,

1H), 3.97-4.04 (m, 1H), 4.65 (t, 1H), 5.02 (s, 2H), 7.34-7.37 (m, 6H), 7.50 (d, J = 8.6 Hz, 1H). ^{13}C NMR (62.89 MHz, DMSO) δ_C 26.8, 27.1, 27.3, 28.0, 28.2, 28.7, 29.3, 29.5, 53.8, 58.5, 68.1, 69.0, 132.8, 133.0, 133.6, 142.4, 161.1, 177.1. FT-IR (KBr, cm^{-1}) 3304, 2967, 2864, 1691, 1653, 1552, 1235, 1118, 1035, 751, 737. MS (*m/z*) = 364 (M^+, 100). Anal. calcd for $C_{20}H_{32}N_2O_4$: C 65.91, H 8.85, N 7.69; found C 66.04, H 8.89, N 7.75.

Benzyl ((*S*)-1-(((*S*)-1-Hydroxy-3-phenylpropan-2-yl)-amino)-4-methyl-1-oxopentan-2-yl)carbamate (2h): White solid (979 mg, 82%). mp 130 °C. $[\alpha]_D^{20}$ = –25.71 (c = 1.1, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.89 (br s, 6H), 1.41-1.51 (m, 1H), 1.60-1.75 (m, 2H), 2.86 (d, J = 6 Hz, 2H), 3.49-3.72 (m, 2H), 4.15 (br s, 2H), 5.09 (s, 2H), 5.41 (br s, 1H), 6.70 (br s, 1H), 7.21-7.35 (m, 10H). ^{13}C NMR (62.89 MHz, $CDCl_3$) δ_C 20.6, 21.4, 23.2, 35.4, 39.7, 51.5, 52.4, 62.0, 65.7, 125.1, 126.6, 126.8, 127.1, 127.1, 127.8, 134.6, 136.3, 155.0, 171.2. FT-IR (KBr, cm^{-1}) 3451, 2958, 2925, 2870, 1712, 1652, 1541, 1273, 1163, 1114, 717, 690. MS (*m/z*) = 398 (M^+); Anal. calcd for $C_{23}H_{30}N_2O_4$: C 69.32, H 7.59, N 7.03; found C 69.28, H 7.65, N 7.11.

***N*-((*S*)-1-(((*S*)-1-Hydroxy-3-phenylpropan-2-yl)amino)-4-methyl-1-oxopentan-2-yl)benzamide (2i):** White solid (883 mg, 80%). mp 148 °C. $[\alpha]_D^{20}$ = –123.5.0 (c = 0.3, C_2H_5OH). ^{1}H NMR (300 MHz, DMSO) δ_H 0.82-0.88 (m, 6H), 1.38-1.50 (m, 1H), 1.50-1.69 (m, 2H), 2.61-2.68 (dd, ^2J = 13.5 Hz, ^3J = 8.1 Hz, 1H), 2.80-2.86 (dd, ^2J = 13.5Hz, ^3J = 4.9 Hz, 1H), 3.30-3.36 (dd, 2H), 3.89 (br d, 1H), 4.48 (br s, 1H), 4.87 (t, 1H), 7.11-7.25 (m, 5H), 7.44-7.54 (m, 3H), 7.75 (d, J = 8.1Hz, 1H), 7.86 (d, J = 6.9 Hz, 2H), 8.38 (d, J = 8.2 Hz, 1H). ^{13}C NMR (75.46 MHz, DMSO) δ_C 20.3, 21.4, 23.1, 35.3, 39.6, 51.40, 52.3, 61.8, 127.1, 128.1, 128.2, 128.4, 128.6, 128.9, 136.2, 137.6, 167.01, 171.19. FT-IR (KBr, cm^{-1}) 3308, 2951, 2867, 1655, 1632, 1536, 1288, 1150, 1042, 679. MS (*m/z*) = 368 (M^+); Anal. calcd for $C_{22}H_{28}N_2O_3$: C 71.71, H 7.66, N 7.60; found C 71.79, H 7.71, N 7.52.

***N*-((*S*)-1-(((*S*)-2-Hydroxy-1-phenylethyl)amino)-4-methyl-1-oxopentan-2-yl)benzamide (2j):** White solid (849 mg, 80%). mp 174 °C. $[\alpha]_D^{20}$ = –60 (c = 0.1, CH_2Cl_2). ^{1}H NMR (300 MHz, DMSO) δ_H 0.88 (d, J = 5.7 Hz, 6H), 1.48-1.80 (m, 3H), 3.68 (m, 2H), 4.51-4.66 (br s, 1H), 4.81 (br d, 1H), 4.92 (t, 1H), 7.22-7.30 (m, 5H), 7.45-7.47 (m, 3H), 7.86 (d, J = 6.6 Hz, 2H), 8.27 (d, J = 7.9 Hz, 1H), 8.47 (d, J = 8.1 Hz, 1H). ^{13}C NMR (75.46 MHz, DMSO) δ_C 20.3, 21.4, 23.1, 35.3, 51.4, 52.3, 61.8, 127.1, 128.1, 128.2, 128.4, 128.6, 128.9, 136.2, 137.6, 167.0, 171.2. FT-IR (KBr, cm^{-1}) 3303, 2966, 2941, 2881, 1659, 1633, 1539, 1275, 1078, 1036, 698. MS (*m/z*) = 354 (M^+); Anal. calcd for $C_{21}H_{26}N_2O_3$: C 71.16, H 7.39, N 7.90; found C 71.12, H 7.48, N 7.99.

***N*-((*S*)-1-(((*S*)-1-Hydroxy-4-methylpentan-2-yl)amino)-4-methyl-1-oxopentan-2-yl)benzamide (2k):** White solid (821 mg, 82%). mp 134 °C. $[\alpha]_D^{20}$ = –115.40 (c = 0.12, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.83-0.91 (m, 12H), 1.31-1.44 (m, 2H), 1.51-1.76 (m, 4H), 3.52-3.72 (m, 2H), 3.92-4.19 (br s, 1H), 4.67-4.88 (br s, 1H), 7.22-7.57 (m, 5H), 7.79 (d, 2H). ^{13}C NMR (62.89 MHz, $CDCl_3$) δ_C 22.4, 23.0, 24.9, 39.9, 50.2, 52.4, 65.7, 127.3, 128.6, 131.9, 133.8, 163.4, 172.9. FT-IR (KBr, cm^{-1}) 3294, 2958, 2844, 1662, 1636, 1538, 1266, 1073, 1031, 695. MS (*m/z*) = 334 (M^+); Anal. calcd for $C_{19}H_{30}N_2O_3$: C 68.23, H 9.04, N 8.38; found C 68.29, H 9.09, N 8.32.

***N*-((*S*)-1-(((*S*)-1-Hydroxy-3-methylbutan-2-yl)amino)-4-methyl-1-oxopentan-2-yl)benzamide (2l):** White solid (797 mg, 83%). mp 242 °C. $[\alpha]_D^{20}$ = –100.26 (c = 0.08, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.83-0.86 (m, 12H), 1.31-1.44 (m, 2H), 1.51-1.76 (m, 2H), 3.50-3.68 (m, 2H), 3.89-4.10 (br s, 1H), 4.63-4.79 (br s, 1H), 7.25-7.60 (m, 5H), 7.81 (d, J = 6.6 Hz, 2H). ^{13}C NMR (62.89 MHz, $CDCl_3$) δ_C 26.8, 27.2, 27.3, 28.1, 28.2, 29.4, 29.5, 50.1, 52.3, 65.5, 127.4, 128.6, 131.8, 133.6, 163.9, 172.6. FT-IR (KBr, cm^{-1}) 3298, 2960, 2873, 1638, 1582, 1295, 1069, 695. MS (*m/z*) = 320 (M^+); Anal. calcd for $C_{18}H_{28}N_2O_3$: C 67.47, H 8.81, N 8.74; found C 67.52, H 8.85, N 8.70.

General Procedure for the Synthesis of Diamino Alcohol 1. To suspension of $LiAlH_4$ (263 mg, 7 mmol) in THF (15 mL) at 0 °C under N_2 atmosphere was added **2** (1 mmol). The suspension was reflux for 24 h, cooled to 0 °C and treated with 5 mL THF and 1 mL water. After filtration of the resulting suspension, the water layer was extracted with CH_2Cl_2, dried over $MgSO_4$. After removal of the solvent, the residue was chromatographed on silica gel (hexane/ethyl acetate = 30:3 to 1:30) to afford the product as a pale yellow oil (78-95%).

(*S*)-2-(((*S*)-2-(Methylamino)-2-phenylethyl)amino)-2-phenylethanol (1a): Light yellow oil (216 mg, 80%). $[\alpha]_D^{20}$ = +102 (c = 0.9, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 2.28 (s, 3H), 1.94-2.61 (br s, 3H), 2.69 (d, 2H), 3.50-3.90 (m, 4H), 7.24-7.38 (m, 10H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 34.2, 53.6, 64.4, 64.9, 67.0, 127.0, 127.2, 127.4, 127.6, 128.5, 128.5, 140.6, 141.6. FT-IR (KBr, cm^{-1}) 3340, 3063, 2936, 1649, 1547, 1278, 1111, 1073, 759, 701. MS (*m/z*) = 270 (M^+); Anal. calcd for $C_{17}H_{22}N_2O$: C 75.52, H 8.20, N 10.36; found C 75.59, H 8.28, N 10.34.

(*S*)-3-Methyl-2-(((*S*)-2-(methylamino)-2-phenylethyl) amino)butan-1-ol (1b): Yellow oil (210 mg, 89%). $[\alpha]_D^{20}$ = +38.75 (c = 4, CH_2H_5OH). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.85 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H), 1.67-1.78 (m, 1H), 2.28 (s, 3H), 2.32-2.38 (m, 1H), 2.69 (br s, 3H), 3.30-3.64 (dd, 1H), 3.56-3.61 (m, 2H), 7.22-7.35 (m, 5H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 18.6, 19.3, 29.3, 34.0, 53.9, 61.4, 64.7, 65.1, 127.2, 127.4, 128.5, 141.5. FT-IR (KBr, cm^{-1}) 3330, 2957, 2872, 2793, 1142, 1109, 1036, 759, 701. MS (*m/z*) = 236 (M^+); Anal. calcd for $C_{14}H_{24}N_2O$: C 71.14, H 10.23, N 11.85; found C 71.22, H 10.40, N 11.79.

(*S*)-4-Methyl-2-(((*S*)-2-(methylamino)-2-phenylethyl) amino)pentan-1-ol (1c): Light yellow oil (237 mg, 95%). $[\alpha]_D^{20}$ = +75 (c = 0.13, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.87 (d, J = 6.5 Hz, 6H), 1.21-1.31 (m, 2H), 1.56-1.63 (m, 1H), 2.33 (s, 3H), 2.73-2.77 (m, 1H), 2.87-2.92 (dd, ^2J = 12.7 Hz, ^3J = 4.3 Hz, 1H), 2.98-3.03 (dd, ^2J = 12.7 Hz, ^3J = 9.2 Hz = 1H), 3.31-3.37 (dd, ^2J = 11.1Hz, ^3J = 7.6 Hz, 1H), 3.60-3.65 (dd, ^2J = 11.2 Hz, ^3J = 3.4 Hz , 1H), 3.75-3.82 (dd, 1H), 7.27-7.39 (m, 5H). ^{13}C NMR (75.46 MHz, DMSO) δ_C 21.7, 23.7, 24.6, 30.6, 31.2, 47.4, 58.3, 58.9, 59.5, 129.4,

129.6, 130.2, 132.6. FT-IR (KBr, cm^{-1}) 3403, 2956, 2859, 1564, 1364, 1144, 1056, 759, 701. MS (*m/z*) = 250 (M^+); Anal. calcd for $C_{15}H_{26}N_2O$: C 71.95, H 10.47, N 11.19; found C 71.99, H 10.44, N 11.26.

(*S*)-2-(((*S*)-2-(Methylamino)-2-phenylethyl)amino)-3-phenylpropan-1-ol (1d): Light yellow iol (232 mg, 82%). $[\alpha]_D^{20}$ = +12.l5 (c = 4, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 2.25 (s, 3H), 2.68 (t, 2H), 2.81 (d, 2H), 2.93 (m, 4H), 3.31-3.37 (dd, 1H), 3.55-3.59 (m, 2H), 7.23-7.32 (m, 10H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 34.0, 38.1, 52.6, 63.1, 64.8, 65.0, 127.0, 127.2, 127.5, 127.6, 128.1, 128.5, 140.7, 141.2. FT-IR (KBr, cm^{-1}) 3389, 2958, 2920, 2851, 1262, 1035, 800, 701. MS (*m/z*) = 284 (M^+); Anal. calcd for $C_{18}H_{24}N_2O$: C 76.02, H 8.51, N 9.85; found C 76.11, H 8.59, N 9.79.

(*S*)-2-(((*S*)-2-(Methylamino)-3-phenylpropyl)amino)-3-phenylpropan-1-ol (1e): Light yellow oil (238 mg, 80%). $[\alpha]_D^{20}$ = +230.76 (c = 0.23, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 2.19 (d, *J* = 6 Hz, 2H), 2.37 (s, 3H), 2.55-2.93 (m, 7H), 3.31-3.37 (dd, ^2J = 10.5 Hz, ^3J = 6.5 Hz, 1H), 3.56-3.60 (dd, ^2J = 10.5 Hz, ^3J = 3.1 Hz, 1H), 7.09-7.29 (m, 10H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 28.6, 29.3, 33.8, 53.5, 61.5, 64.7, 65.0, 126.9, 127.2, 127.3, 127.5, 128.4, 128.6, 141.3, 141.4. FT-IR (KBr, cm^{-1}) 3337, 3025, 2932, 2846, 1564, 1135, 1033, 744, 701. MS (*m/z*) = 298 (M^+); Anal. calcd for $C_{19}H_{26}N_2O$: C 76.47, H 8.78, N 9.39; found C 76.57, H 8.85, N 9.36.

(*S*)-3-Methyl-2-(((*S*)-3-methyl-2-(methylamino)butyl)-amino)butan-1-ol (1f): Light yellow oil (158 mg, 78%). $[\alpha]_D^{20}$ = –107 (c = 0.23, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.85 (t, *J* = 5.8 Hz, 6H), 0.92 (d, *J* = 6.4 Hz, 6H), 1.67-1.79 (m, 1H) 1.79-1.89 (m, 1H), 2.33 (br s, 1H), 2.37 (s, 3H), 2.49 (t, 1H), 2.71 (br d, 1H), 3.35 (t, 1H), 3.58-3.61 (m, 4H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 18.8, 18.9, 19.5, 19.6, 29.3, 29.6, 33.9, 53.9, 61.6, 64.7, 65.4. FT-IR (KBr, cm^{-1}) 3359, 2959, 2874, 1567, 1048. MS (*m/z*) = 202 (M^+); Anal. calcd for $C_{11}H_{26}N_2O$: C 65.30, H 12.95, N 13.84; found C 65.28, H 12.98, N 13.90.

(*S*)-4-Methyl-2-(((*S*)-4-methyl-2-(methylamino)pentyl) amino)pentan-1-ol (1g): Light yellow oil (193 mg, 84%). $[\alpha]_D^{20}$ = +30 (c = 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.89 (d, *J* = 6.3 Hz, 12H), 1.08-1.46 (m, 4H), 1.46-1.66 (m, 2H), 2.39 (s, 3H), 2.51-2.70 (m, 3H), 3.23-3.33 (m, 3H), 3.54-3.59 (dd, 1H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 21.7, 21.9, 23.7, 23.8, 24.6, 24.5, 30.6, 31.2, 33.1, 54.5, 61.9, 65.3, 66.3. FT-IR (KBr, cm^{-1}) 3409, 2951, 2858, 2795, 1207, 1044. MS (*m/z*) = 230 (M^+); Anal. calcd for $C_{13}H_{30}N_2O$: C 67.77, H 13.12, N 12.16; found C 67.87, H 13.18, N 12.14.

(*S*)-2-(((*S*)-4-Methyl-2-(methylamino)pentyl)amino)-3-phenylpropan-1-ol (1h): Light yellow oil (205 mg, 78%). $[\alpha]_D^{20}$ = +85.71 (c = 0.1, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.88 (d, *J* = 6.5 Hz, 6H), 1.04-1.19 (m, 1H), 1.30-1.43 (m, 1H), 1.43-1.62 (m, 1H), 2.28 (t, 1H), 2.34 (s, 3H), 2.48 (t, 1H), 2.52-2.61 (m, 1H), 2.63-2.68 (dd, 1H), 2.70-2.73 (d, *J* = 6.9 Hz, 2H), 2.79-2.90 (m, 1H), 3.32-3.38 (dd, ^2J = 10.8 Hz, ^3J = 6.4 Hz, 1H), 3.57-3.62 (dd, ^2J = 10.8 Hz, ^3J = 3.6 Hz, 1H), 7.18-7.32 (m, 5H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 22.4, 23.2, 24.9, 31.7, 38.3, 39.8, 48.3, 58.7, 60.9, 63.3, 126.3, 128.6, 129.2, 138.8. FT-IR (KBr, cm^{-1}) 3367, 2956, 2927, 2860, 1564, 1139, 1040, 744, 700. MS (*m/z*) = 264 (M^+); Anal. calcd for $C_{16}H_{28}N_2O$: C 72.68, H 10.67, N 10.59; found C 72.75, H 10.71, N 10.54.

(*S*)-2-(((*S*)-2-(Benzylamino)-4-methylpentyl)amino)-3-phenylpropan-1-ol (1i): Light yellow oil (275 mg, 81%). $[\alpha]_D^{20}$ = +22 (c = 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.88 (t, *J* = 6.6 Hz, 6H), 1.10-1.21 (m, 1H), 1.31-1.46 (m, 1H), 1.51-1.68 (m, 1H), 2.41-2.49 (m, 1H), 2.66-2.76 (m, 4H), 2.83-2.87 (m, 1H), 3.33-3.38 (dd, ^2J = 10.7 Hz, ^3J = 5.6 Hz, 1H), 3.59-3.63 (dd, ^2J = 10.7 Hz, ^3J = 3.8 Hz, 1H), 3.63-3.72 (m, 2H), 7.19-7.35 (m, 10H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 18.5, 18.9, 20.7, 37.8, 38.5, 45.8, 46.6, 50.1, 60.4, 62.5, 122.7, 123.0, 133.2,124.0, 124.3, 124.9, 136.1, 136.7. FT-IR (KBr, cm^{-1}) 3336, 3031, 2998, 2945, 1458, 1035, 742, 700. MS (*m/z*) = 340 (M^+); Anal. calcd for $C_{22}H_{32}N_2O$: C 77.60, H 9.47, N 8.23; found C 77.65, H 9.45, N 8.28.

(*S*)-2-(((*S*)-2-(Benzylamino)-4-methylpentyl)amino)-2-phenylethanol (1j): Light yellow oil (283 mg, 87%). $[\alpha]_D^{20}$ = +56.07 (c = 0.9, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.85-0.90 (dd, 6H), 1.10-1.23 (m, 1H), 1.32-1.48 (m, 1H), 1.48-1.64 (m, 1H), 2.12-2.34 (br s, 3H), 2.38-2.45 (dd, ^2J = 11.7 Hz, ^3J = 7.7 Hz, 1H), 2.56-2.61 (dd, ^2J = 11.7 Hz, ^3J = 3.6 Hz, 1H), 2.63-2.78 (m, 2H), 3.49-3.63 (m, 1H), 3.63-3.82 (m, 3H), 7.19-7.36 (m, 10H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 18.4, 18.9, 20.7, 37.9, 45.9, 46.5, 50.2, 60.3, 62.6, 123.0, 133.2, 124.0, 124.2, 124.3, 124.9, 136.1, 136.7. FT-IR (KBr, cm^{-1}) 3350, 3016, 2958, 1458, 1374, 1208, 1031, 752, 700. MS (*m/z*) = 326 (M^+); Anal. calcd for $C_{21}H_{30}N_2O$: C 77.26, H 9.26, N 8.58; found C 77.33, H 9.29, N 8.51.

(*S*)-2-(((*S*)-2-(Benzylamino)-4-methylpentyl)amino)-4-methylpentan-1-ol (1k): Colorless oil (269 mg, 88%). $[\alpha]_D^{20}$ = –44 (c = 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.89 (d, *J* = 5.8 Hz, 12H), 1.10-1.30 (m, 4H), 1.56-1.78 (m, 2H), 2.39-2.75 (m, 6H), 3.20-3.30 (m, 1H), 3.54-3.58 (dd, 1H), 3.74-3.78 (dd, 2H), 7.23-7.31 (m, 5H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 18.4, 18.5, 18.7, 18.9, 20.6, 20.7, 35.6, 35.8, 37.9, 51.6, 50.7, 60.4, 62.3, 123.0, 133.2,124.0, 124.2. FT-IR (KBr, cm^{-1}) 3336, 3025, 2961, 2859, 1367, 1161, 1029, 740, 699. MS (*m/z*) = 306 (M^+); Anal. calcd for $C_{19}H_{34}N_2O$: C 74.46, H 11.18, N 9.14; found C 74.53, H 11.15, N 9.19.

(*S*)-2-(((*S*)-2-(Benzylamino)-4-methylpentyl)amino)-3-methylbutan-1-ol (1l): Colorless oil (248 mg, 85%). $[\alpha]_D^{20}$ = +90 (c = 0.8, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.88-0.99 (m, 12H), 1.24-1.28 (m, 1H), 1.40-1.50 (m, 1H), 1.63-1.65 (m, 1H), 1.75-1.91 (m, 1H), 2.33 (br s, 1H), 2.44-2.56 (m, 1H), 2.67-2.70 (br d, 2H), 3.25-3.49 (m, 1H), 3.59-3.67 (m, 1H), 3.78 (br s, 2H), 7.33 (br s, 5H). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ_C 18.3, 18.4, 18.7, 18.9, 20.5, 35.4, 35.5, 37.6, 51.4, 50.4, 60.3, 62.0, 123.2, 133.5, 124.5, 124.6. FT-IR (KBr, cm^{-1}) 3389, 3033, 2967, 2869, 1365, 1104, 1048, 740, 699. MS (*m/z*) = 292 (M^+); Anal. calcd for $C_{18}H_{32}N_2O$: C 73.92, H 11.03, N 9.58; found C 73.99, H 11.08, N 9.55.

Synthesis of (*S*)-N2-((*S*)-1-Hydroxy-3-methylbutan-2-yl)-N1-methyl-1-phenylethane-1,2-diaminium Chloride: To a solution of diamine **1b** (1 mmol) in dry diethyl ether (5

mL) was added dropwise, at 0 °C, a 1 N anhydrous HCl/methanol solution (2 mmol, 2 equiv). A white precipitate was immediately formed. After 10 min of stirring, the solvent was evaporated to afford the corresponding chlorhydrate of diamine in quantitative yield. $[\alpha]_D^{20}$ = +40.25 (c = 2.5, CH_2H_5OH). ^{1}H NMR (300 MHz, DMSO) δ_H 0.95 (d, *J* = 6.4 Hz, 6H), 2.14-2.20 (m, 1H), 2.31 (s, 3H), 2.96-3.08 (br s, 1H), 3.58-3.62 (m, 1H), 3.63-3.78 (br s, 2H), 3.87-4.03 (m, 1H), 4.68-4.93 (br s, 1H), 7.40-7.68 (m, 5H), 9.27-9.49 (br d, 1H), 10.23-10.44 (br d, 1H). ^{13}C NMR (75.46 MHz, DMSO) δ_C 17.5, 19.9, 27.8, 30.7, 49.1, 57.4, 59.6, 65.8, 129.3, 129.7, 130.3, 132.9. FT-IR (KBr, cm^{-1}) 3330, 2957, 2872, 2793, 1142, 1109, 1036, 759, 701. MS (*m/z*) = 236 (M-2Cl$^-$); Anal. calcd for $C_{14}H_{26}Cl_2N_2O$: C 54.37, H 8.47, N 9.06; found C 54.46, H 8.51, N 9.01.

Synthesis of *tert*-Butyl 4-Nitrobenzoperoxoate[6j]: *p*-Nitrobenzoyl chloride (3.2 g, 17.2 mmol) was dissolved in a 100 mL round bottom flask containing CH_2Cl_2 (35 mL). The solution was cooled to –20 ºC and stirred under nitrogen for 15 min. Pyridine (1.7 mL, 20.0 mmol) was added and the reaction mixture was stirred for 10 min. Next, *tert*-butyl hydroperoxide (3.5 mL, 20.0 mmol) was added dropwise to the reaction at –20 ºC, and stirred for 4 h. Then the reaction solution was diluted with CH_2Cl_2 (20 mL), and washed with water. The organic layer was separated, dried over $MgSO_4$, and evaporated to obtained crude yellow solid product. Purification using flash chromatography (*n*-hexane: EtOAc; 90:10) afforded the light yellow solid product. (3.9 g, 98% yield). mp 75-78 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.45 (s, 9H), 8.14-8.35 (m, 4H).

General Procedure for the Enantioselective Allylic Oxidation of Cycloolefins using *tert*-Butyl 4-Nitrobenzoperoxoate. To a flame-dried round bottom flask (25 mL), a light yellow solution of the diamino alcohol ligand **1** (0.065 mmol) and copper salt (0.55 mmol) were stirred in CH_3CN (4 mL) and stirred for 3 h at ambient temperature. After addition of phenyl hydrazine (6 μL, 0.06 mmol) color of the solution was changed from blue green to red. Then, 10 mg of 4 Å molecular sieves were added. After a few min, cycloolefin (5 mmol) was added. The reaction mixture was cooled to –10 ºC and then *tert*-butyl 4-nitrobenzoperoxoate (0.203 g, 0.85 mmol) was added dropwise to the reaction solution under nitrogen atmosphere. The mixture was kept at room temperature until TLC showed to complete disappearance of perester. The reaction mixture was dissolved in 10% NH_4OH, extracted with EtOAc and dried over $MgSO_4$. Removal of solvent *in vacuo* afforded a yellow residue that was chromatographed over silica gel to provide the pure white solid product.

(*R*)-Cyclohex-2-en-1-yl 4-nitrobenzoate (9a)[6j]: mp 68-71 °C. $[\alpha]_D^{20}$ = +29° (*c* =1.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.76-2.14 (m, 6H), 5.54 (m, 1H), 5.84 (d, *J* = 9.8 Hz, 1H), 6.04 (d, *J* = 9.8 Hz, 1H), 8.21-8.31 (m, 4H). ^{13}C NMR (300 MHz, $CDCl_3$) δ_C 18.8, 25.0, 28.2, 69.8, 123.4, 125.0, 130.7, 133.6, 136.2. IR (KBr, cm^{-1}) 1107, 1278, 1525, 1713, 2928. The enantiomeric excess was determined by chiral HPLC (EC 250/4.6 Nucleocel Alpha S column, *iso*-propyl alcohol/hexanes; 99.5:0.5; flow rate 0.5 mL/min; t_R = 31.2 min (*R*), 33.8 min (*S*)) (maximum ee = 19% (*R*)).

(*R*)-Cyclopent-2-en-1-yl 4-nitrobenzoate (9b)[6j]: mp 77-79 °C. $[\alpha]_D^{20}$ = +10° (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.97-2.04 (m, 1H), 2.38-2.50 (m, 2H), 2.59-2.63 (m, 1H), 5.98 (m, 2H), 6.22 (m, 1H), 8.20 (d, *J*= 8.5 Hz, 2H), 8.28 (d, *J* = 8.5 Hz, 2H). IR (KBr, cm^{-1}) 1109, 1268, 1520, 1706, 2846. The enantiomeric excess was determined by chiral HPLC (EC 250/4.6 Nucleocel Alpha S column, *iso*-propyl alcohol/hexanes; 99.5:0.5; flow rate 0.4 mL/min; t_R = 36.5 min (*R*), 38.4 min (*S*)) (maximum ee = 8% (*R*)).

(*R*)-Cyclohept-2-en-1-yl 4-nitrobenzoate (9c)[6j]: mp 72-75 °C. $[\alpha]_D^{20}$ = +8° (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.66-1.72 (m, 4H), 2.02-2.12 (m, 2H), 2.07-2.40 (m, 2H), 5.58-5.64 (m, 1H), 5.75-5.82 (m, 1H), 5.92-5.98 (m, 1H), 8.22-8.28 (m, 4H). IR (KBr, cm^{-1}) 1106, 1273, 1528, 1709, 2893. The enantiomeric excess was determined by chiral HPLC (EC 250/4.6 Nucleocel Alpha S column, *iso*-propyl alcohol/hexanes; 99.5:0.5; flow rate 0.4 mL/min; t_R = 28.7 min (*R*), 32.6 min (*S*)) (maximum ee = 3% (*R*)).

(*R*)-Cyclooct-2-en-1-yl 4-nitrobenzoate (9d)[6j]: mp 71-74 °C. $[\alpha]_D^{20}$ = +13° (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.46-1.72 (m, 7H), 2.07-2.40 (m, 3H), 5.60-5.66 (m, 1H), 5.73-5.82 (m, 1H), 5.92-5.96 (m, 1H), 8.22-8.32 (m, 4H). IR (KBr, cm^{-1}) 1108, 1281, 1527, 1718, 2853. The enantiomeric excess was determined by chiral HPLC (EC 250/4.6 Nucleocel Alpha S column, *iso*-propyl alcohol/hexanes; 99.5:0.5; flow rate 0.4 mL/min; t_R = 20.9 min (*R*), 23.1 min (*S*)) (maximum ee = 15% (*R*)).

Results and Discussion

A series of (*S*,*S*)-diamino alcohol ligands **1** were conveniently prepared by a three-steps procedure with minimal purification of intermediates in high overall yields and excellent enantiomeric excess from the readily available (*S*)-amino acids. Table 1 describes a small library of novel ligands **1** and (*S*,*S*)-hydroxyldiamide precursors **2**. For synthesis of these molecules, at first, the amino acids were protected by one of the two kinds of protecting groups, the carbobenzoxy (Cbz) or benzoyl (Bz) groups.[10] Then, hydroxyldiamide precursors **2** were obtained in 80-96% yields from coupling of protected amino acids with chiral amino alcohols **8**, which were easily prepared from the reduction of amino acids.[11] Afterwards, the hydroxyldiamide **2** were reduced easily with lithium aluminum hydride to provide the chiral tridentate ligands **1** in the range of 78-95% yields. The diversity of chiral amino acids, chiral amino alcohols and the protecting groups make it possible to create a library of chiral diamido and diamino alcohols **2** and **1**.

The structures of products **1** and precursors **2** were assigned by their elemental and spectroscopic analysis including, IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. As expected, the ^{1}H NMR and ^{13}C NMR spectrum of the precursor **2**, and ligand **1** clearly showed the presence of only (*S*,*S*)-diastereomer. In order to confirm further that no racemization occurs, the diaminium chloride of **1b** was prepared and its

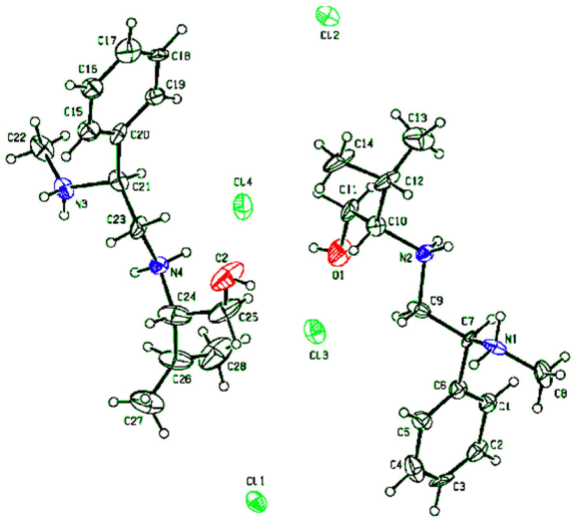


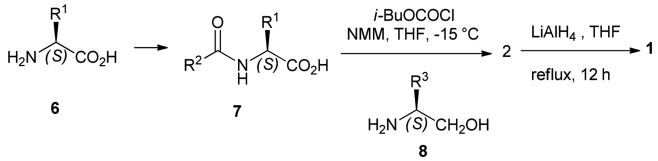
Figure 1. The ORTEP diagram of diaminium chloride of **1b**. Thermal ellipsoids are at 30% probability level.

absolute configuration was determined by single-crystal X-ray analysis (Figure 1).[12]

In order to evaluate the potential of new chiral diamino alcohols **1** in the catalytic asymmetric reaction, we tested chiral tridentate ligands **1** in the copper-catalyzed allylic oxidation of cycloolefins using *tert*-butyl *p*-nitroperbenzoate as an oxidant at room temperature in the presence of various copper complexes ($[Cu(CH_3CN)_4]PF_6$, CuOTf and $Cu(OTf)_2$) and in three different solvents. The reactions were monitored by TLC for consumption of the perester and stopped at the given time. The results are summarized in Table 2. The best results were achieved in oxidation of cyclohexene in acetonitrile with 10 mol % **1a**-$CuPF_6$ complex in the presence of molecular sieves, which afforded 2-cyclohexenyl-*p*-nitrobenzoate **9a** in 95% yield 19% ee (entry 1 in Table 2). To the best of our knowledge, this enantioselectivity and yield in entry **1** are the highest for the allylic oxidation of cycloolefins so far in contrast to 48% yield and 11% ee of products, which were obtained when chiral amines or other amino alcohols were used as ligands in this reaction.[9] Most likely, the presence of additional coordinating group might promote catalysis in this case.

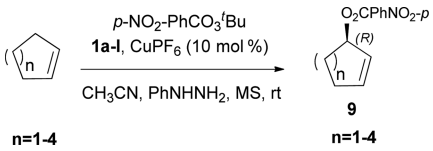
Increasing or decreasing the catalyst loading led to decrease of the enantioselectivity (entries 1 *vs.* 2 in Table 2). Reducing the reaction temperature resulted in a decrease in reactivity without any significant increase in enantioselectivity (entries 1 *vs.* 5 in Table 2). Higher enantioselectivity was observed in acetonitrile, and the reactivity was also found to be dependent on solvent. The reactions that carried out in acetonitrile proceed faster than those in dichloromethane and slightly better than those in acetone (entries 1 *vs.* 6-7 in Table 2). Finally, for comparison, the reaction was carried out in the absence of ligands and low yield of the desired product was obtained after 40 h.

Table 1. Synthesis of chiral diamino alcohols **1** from *N*-protected chiral amino acids



Entry	R^1	R^2	R^3	**2** (Yield%)	**1** (Yield%)
1	Ph	$PhCH_2O$	Ph	**2a** (89)	**1a** (80)
2	Ph	$PhCH_2O$	*i*-Pr	**2b** (93)	**1b** (89)
3	Ph	$PhCH_2O$	*i*-Bu	**2c** (80)	**1c** (95)
4	Ph	$PhCH_2O$	Bn	**2d** (92)	**1d** (82)
5	Bn	$PhCH_2O$	Bn	**2e** (96)	**1e** (80)
6	*i*-Pr	$PhCH_2O$	*i*-Pr	**2f** (81)	**1f** (78)
7	*i*-Bu	$PhCH_2O$	*i*-Bu	**2g** (86)	**1g** (84)
8	*i*-Bu	$PhCH_2O$	Bn	**2h** (82)	**1h** (78)
9	*i*-Bu	Ph	Bn	**2i** (80)	**1i** (81)
10	*i*-Bu	Ph	Ph	**2j** (80)	**1j** (87)
11	*i*-Bu	Ph	*i*-Bu	**2k** (82)	**1k** (88)
12	*i*-Bu	Ph	*i*-Pr	**2l** (83)	**1l** (85)

Table 2. Asymmetry allylic oxidation of cycloolefins in the present of chiral diamino alcohols **1**



Entry	n	Ligand	Time (h)	Yield (%)	ee[a] (%)
1	2	**1a**	40	**9a** (95)	19
2	2	**1a**	40	**9a** (95)	17[b]
3	2	**1a**	30	**9a** (70)	8[c]
4	2	**1a**	180	**9a** (50)	Trace[d]
5	2	**1a**	38	**9a** (80)	19[e]
6	2	**1a**	50	**9a** (80)	Trace[f]
7	2	**1a**	85	**9a** (60)	Trace[g]
8	1	**1a**	60	**9b** (90)	9
9	3	**1a**	40	**9c** (90)	3
10	4	**1a**	40	**9d** (90)	15
11	4	**1a**	40	**9d** (90)	10[b]
12	2	**1b**	75	**9a** (87)	Trace
13	2	**1c**	72	**9a** (90)	Trace
14	2	**1d**	64	**9a** (95)	17
15	2	**1e**	70	**9a** (90)	10
16	2	**1f**	84	**9a** (80)	5
17	2	**1g**	83	**9a** (75)	3
18	2	**1h**	60	**9a** (90)	12
19	2	**1i**	65	**9a** (85)	3
20	2	**1j**	63	**9a** (80)	5
21	2	**1k**	50	**9a** (92)	10
22	2	**1l**	63	**9a** (80)	5

[a]Enantiomeric excess (ee) of the allylic esters were determined by HPLC analysis using an EC 250/4.6 Nucleocel Alpha S column. [b]15% $CuPF_6$ as a source of Cu was used. [c]10 mol % $Cu(OTf)_2$ as a source of Cu was used. [d]CuOTf was used as a source of Cu. [e]The reaction was carried out at 0 °C. [f]Acetone was used as solvent. [g]CH_2Cl_2 was used as solvent

Conclusion

In summary, we have synthesized the small library of new enantiomerically pure (*S*,*S*)-diamino alcohols **1**, and their hydroxyldiamide precursors **2** derived from the commercially chiral pool amino acids. The applicability of the chiral tridentates diamino alcohols **1** as ligands to the copper-catalyzed asymmetric allylic oxidation reaction of cycloolefins were demonstrated. The best result in the oxidation of cyclohexene was achieved with **1a**-$CuPF_6$ complex in acetonitrile to afford the product in 95% yield and 19% ee. These values in ee and yields are the highest so far in the allylic oxidation of cycloolefins. Although the enantioselectivity of the reactions is still low, we are confident that improvements in the reaction condition will result in an increase of asymmetric induction that is in progress in our laboratory. Efforts to improve the enantioselectivity in this reaction and extend the scopes of the reaction using these ligands are in progress.

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12. X-ray data for diaminium chloride of **1b:** $C_{14}H_{26}N_2Cl_2O$, M = 309.27, triclinic system, space group $P1$, a = 7.1264(14), b = 10.864(2), c = 12.215(2) Å; α = 67.22(3), β = 81.67(3), γ = 76.53(3)º; V = 846.4(3) Å^3, Z = 2, Dcalcd = 1.214 g cm^{-3}, μ(Mo-Kα) = 0.379 mm^{-1}, crystal dimension of 0.35 × 0.2 × 0.17 mm. The X-ray diffraction measurement was made on a STOE IPDS-II diffractometer with graphite monochromated Mo-Kα radiation. The structure was solved by using SHELXS. The Data reduction and structure refinement was carried out with SHELXL using the X-STEP32 crystallographic software package.[13] The non-hydrogen atoms were refined anisotropically by full matrix least-squares on F^2 values to final R_1 = 0.1148, wR_2 = 0.2726 and S = 0.979 with 327 parameters using 4924 independent reflection (θ range = 2.94-25.00º). Hydrogen atoms were added in idealized positions. The crystallographic information file has been deposited with the Cambridge Data Centre, CCDC 928537.
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