Tetrahedron: *Asymmetry* 19 (2008) 2159–2163

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Synthesis of novel C_3 symmetric tris(thiazoline) ligands and their application in the allylic oxidation reaction

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ARTICLE INFO

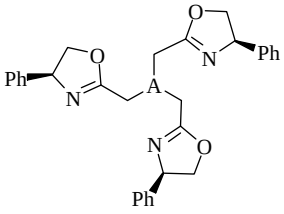
Article history:
Received 21 July 2008
Accepted 27 August 2008
Available online 1 October 2008

ABSTRACT

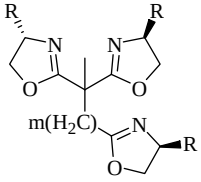
A series of novel C_3 symmetric tris(thiazoline) ligands were synthesized from trimethyl nitrilotriacetate and an enantiomerically pure amino alcohol via an efficient route. Compound **7a** showed moderate to good catalytic enantioselectivity for the asymmetric allylic oxidation of cycloalkenes.

1. Introduction

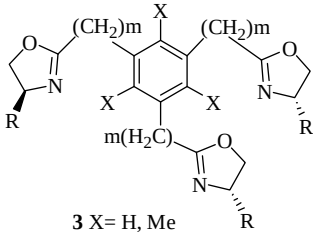
Over the past two decades, a plethora of mono- and bis(oxazoline) ligands have been synthesized and applied in a large variety of catalytic asymmetric reactions.[1] In order to find better chiral ligands for asymmetric transformations, researchers have also designed and prepared some tris(oxazoline) ligands such as **1**,[2] **2**[3] and **3**.[4] These ligands showed interesting catalytic reactivity and selectivity comparable or even better than their bidentate analogues in some reactions. Ligands such as **3** can also be used as host molecules in the area of molecular recognition.



1 A = N or CH



2 m = 0 or 1



3 X= H, Me
m = 0 or 1

For further tuning of the coordination ability and the catalytic activity, some chiral thiazoline ligands have been synthesized in recent years. However, the application of chiral thiazoline ligands in asymmetric catalysis is still limited. The investigations on the comparison between thiazolines and oxazolines in asymmetric catalysis were reported by Masson[5] and Du.[6] Thiazoline ligands gave better results in some cases, while the corresponding oxazoline ligands were superior in others. These results prompt us to explore the synthesis of novel thiazoline ligands and their application in asymmetric catalytic transformations.

Considering that a series of C_3 symmetric chiral ligands have been developed and showed interesting properties,[7] we designed tris(thiazolines) **7a–d** derived from a trimethyl nitrilotriacetate scaffold. To the best of our knowledge, the preparation and catalytic activity of C_3 symmetric tris(thiazoline) ligand have not been reported. Although several mono(thiazoline) and bis(thiazoline) ligands have been prepared and some methods for the construction of the thiazoline ring have been developed, the already existing methods may not be efficient in the synthesis of tris(thiazoline) ligands. Herein, we report the development of an efficient route for the synthesis of tris(thiazoline) ligands and an investigation of their catalytic activity in the asymmetric allylic oxidation of cycloalkenes.

2. Results and discussion

Trimethyl nitrilotriacetate **4**, which was easily prepared from commercially available nitrilotriacitic acid,[2c] was condensed with chiral aminoalcohol at 80 °C for 72 h to furnish the corresponding tris(β-hydroxyamide) **5a–d** in good yields. With these intermediates in hand, we turned to the simultaneous thio-substitution and dehydrative cyclization step. However, when **5a** was treated with phosphorus pentasulfide (P_2S_5) or Lawesson reagent (LR) under various conditions, as described by Du [6] and Molina,[8]

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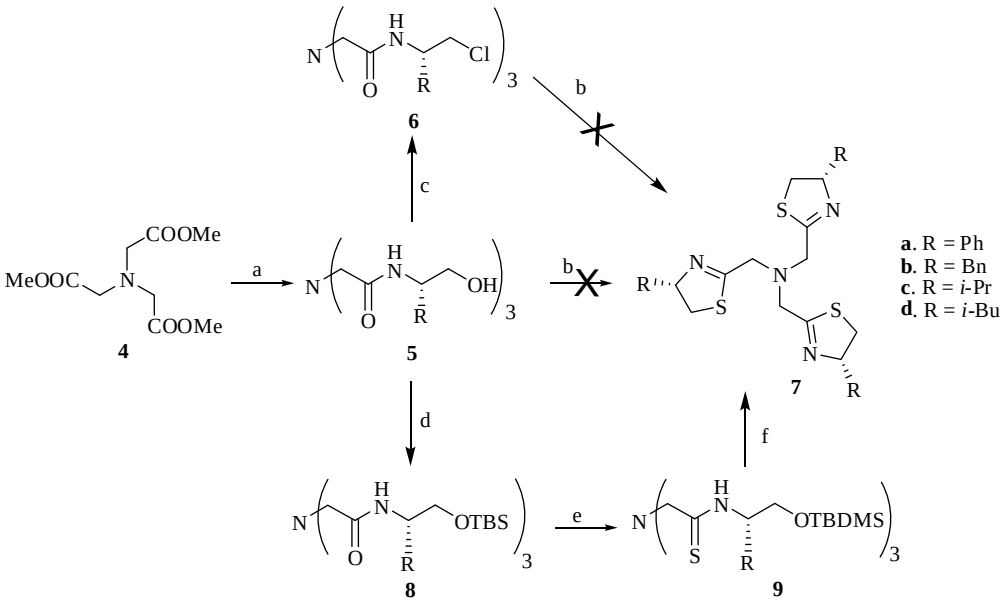
doi:10.1016/j.tetasy.2008.08.028



Scheme 1. Reagents and conditions: (a) L-aminoalcohol, 80 °C; (b) P_2S_5, or LR, toluene, reflux; (c) $SOCl_2$; (d) TBDMSCl, imidazole; (e) LR, benzene, (f) (i) TBAF, THF; (ii) MsCl, TEA.

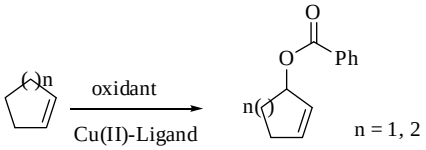
respectively, no desired product was formed. We also tried to prepare **6a** by treatment of **5a** with $SOCl_2$ and then cyclize with P_2S_5 or Lawesson reagent following Nishio's[9] procedure, which was successfully used in the cyclization of mono β-halogen substituted amides, but the tris(thiazoline) was not obtained.

In view of these negative results, some modification must be made for the route (Scheme 1). Since that the three hydroxyl groups can interact with each other and make the reaction complex, **5a** was protected by use of TBDMSCl (3.50 equiv) under the catalysis of imidazole, the hydroxyl-protected compound **8a** was obtained in 98% yield. When compound **8a** was treated with Lawesson's reagent (1.6 equiv) in benzene, the tris(β-siloxythioamide) **9a** was afforded in 81% yield.[10] After removing the TBDMS-group by TBAF, the tris(β-hydroxythioamide) intermediate was directly cyclized by treating with MsCl/Et_3N in CH_2Cl_2 at room temperature. The desired tris(thiazoline) **7a** was obtained in good yield (88% for two steps). Other dehydrating reagents, such as Burgess reagent[11] and DAST,[12] were also screened in this step; however lower yields (41% and 64%, respectively) were obtained. Ligands **7b, 7c** and **7d** could also be synthesized following the same route with comparable yields as listed in Table 1. In this synthetic route, every step proceeded smoothly under mild conditions and gave good to high yields.

With these new ligands in hand, we evaluated their catalytic activity in the Cu(II) catalyzed allylic oxidation of cycloalkene according to Katsuki's procedure[2] (Scheme 2). The asymmetric allylic oxidation of olefins with peresters represents an efficient methodology to prepare chiral allylic alcohols and their derivates, which are useful building blocks in organic syntheses. The oxidation reaction was performed in acetone by employing *t*-butyl perbenzoate as the oxidant and Cu(OTf)$_2$-tris(thiazoline) complexes

Table 1
The yields for the intermediates and tris(thiazoline) ligands

Entry	R	**5** (%)	**8** (%)	**9** (%)	**7** (%)
1	Ph	62	98	81	88
2	Bn	74	92	84	91
3	*i*-Pr	68	95	75	85
4	*i*-Bu	71	90	78	83



Scheme 2.

7a–d (5 mol %) as the catalyst in the presence of 4 Å MS at room temperature. The experimental results are outlined in Table 2. Compound **7a** showed the best enantioselectivity (77% ee) among the four Cu(II)–ligand complexes, while **7b** had no catalytic activity (entry 2). Compounds **7c** and **7d** showed low catalytic activity (entries 3 and 4). When other solvents were used in this catalytic reaction, catalytic activity or enantioselectivity become lower (entries 5–8). Reducing the reaction temperature to 0 °C enhanced the enantioselectivity, while the yield decreased dramatically even after prolonged reaction time (entry 9, 81% ee and 17% yield). These results were in accordance with Katsuki's report.[2] Next, under the optimized conditions, we performed the allylic oxidation of cyclohexene (entries 10–14), at room temperature four ligand–Cu(II) complexes showed better catalytic activity (51–87% yield) than that for cyclopentene; however the enantioselectivities were very low (11–35% ee); when lowering the temperature to 0 °C the ee's value rose to a moderate level (44%), while the chemical yield also dropped (68%).

In order to get a direct insight of the structure of new tris(thiazoline) ligands, we obtained the single crystal of **7c** from its solution in hexane-ethyl acetate (v/v 7:3) and conducted X-ray crystal diffraction analysis. The perspective view showed the typical C_3-symmetrical structure as illustrated in Figure 1.[13] Due to the presence of the three $-CH_2-$ units between the thiazoline cycle and the central nitrogen atom, the molecular structure is flexible to some extent. Although the distance between the three sulfur atoms is smaller than that between the three nitrogen atoms on the thiazoline ring, we believe it is more plausible that the three nitrogen atoms coordinate to the Cu(II) in the catalyst structure. We also attempted to prepare a single crystal of the Cu(OTf)$_2$–tris(thiazoline) **7c** complex in order to understand the real

Table 2
Asymmetric catalytic allylic oxidation of cyclopentene or cyclohexene[a]

Entry	$(CH_2)_n$	Catalyst	Solvent	Temperature (°C)	Time (h)	Yield[b] (%)	ee[c] (%)	Config.[d]
1	1	**7a**	Acetone	25	72	43	77	(*R*)
2	1	**7b**	Acetone	25	72	0	—	—
3	1	**7c**	Acetone	25	72	10	23	(*R*)
4	1	**7d**	Acetone	25	72	12	17	(*R*)
5	1	**7a**	$(CH_2Cl)_2$	25	72	28	55	(*R*)
6	1	**7a**	CH_2Cl_2	25	72	20	32	(*R*)
7	1	**7a**	AcOEt	25	96	0	—	—
8	1	**7a**	CH_3CN	25	72	25	17	(*R*)
9	1	**7a**	Acetone	0	96	17	81	(*R*)
10	2	**7a**	Acetone	25	72	87	35	(*R*)
11	2	**7b**	Acetone	25	72	51	22	(*R*)
12	2	**7c**	Acetone	25	72	71	14	(*R*)
13	2	**7d**	Acetone	25	72	66	11	(*R*)
14	2	**7a**	Acetone	0	72	68	44	(*R*)

[a] All reactions were conducted with *t*-butyl perbenzoate as oxidant and ligand–$Cu(OTf)_2$ (5 mol %) as catalyst in the presence of MS-4 Å.
[b] Isolated yield by column chromatography.
[c] Determined by HPLC (DAICEL CHIRACEL OD-H, *n*-hexane–*i*-PrOH = 99.9:0.1).
[d] By comparison with the literature rotation.[2]

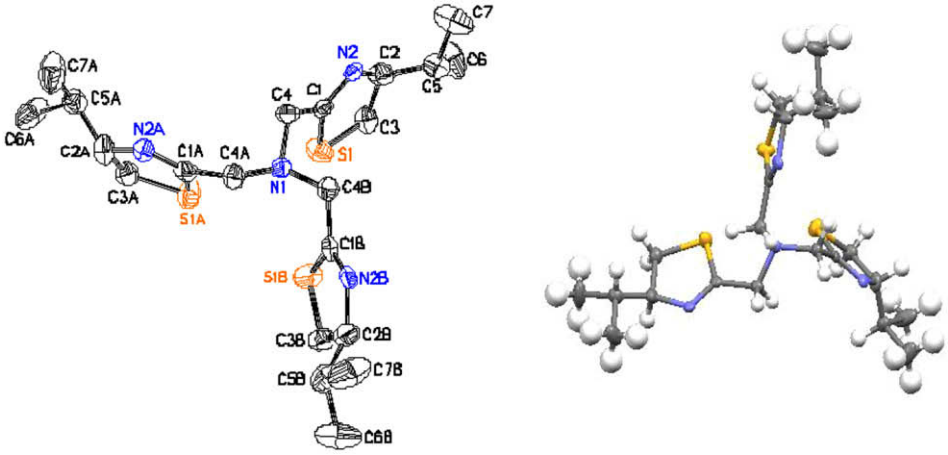


Figure 1. The molecular structure of compound (*S*)-**7c** from different side view.

structure of the active catalytic species. Unfortunately, no satisfactory crystals were obtained under a variety of conditions.

3. Conclusion

In conclusion, novel C_3-symmetric tris(thiazoline) ligands were synthesized from trimethyl nitrilotriacetate and chiral amino alcohols in good yields, this route may act as a general method for the preparation of complex thiazoline compounds. Their application in the catalytic allylic oxidation of cycloalkene was examined. Complex **7a**–Cu(II) showed moderate to good asymmetric catalytic activity and enantioselectivity. Further applications to extend the scope of these catalysts are currently in progress in our laboratory.

4. Experimental

Melting points were measured on an XT-4 melting point apparatus and are uncorrected. NMR spectra were recorded with a Bruker Avance DPX300 spectrometer with tetramethylsilane as the internal standard. Infrared spectra were obtained on a Nicolet AVATAR 330 FT-IR spectrometer.

Mass spectra were obtained on Bruker APEX II FT-ICRMS mass spectrometer. Optical rotations were measured on a Perkin–Elmer 341 LC polarimeter. Elemental analyses were carried out on an Elementar Vario EL instrument. The enantiomeric excesses of (*R*)- and (*S*)-cycloalkene ester were determined by HPLC analysis over a chiral column (Daicel Chiralcel OD-H; eluted with hexane–isopropyl alcohol; UV detector, 254 nm). The absolute configuration of the major enantiomer was assigned according to the sign of the specific rotation. Solvents were purified and dried by standard procedures.

4.1. *N,N′,N″*-Tris[(1*S*)-(2-hydroxy-1-phenylethyl-)]-nitrilotriacetamide 5a

The procedure was performed according to Katsuki's report.[2c] A mixture of (*S*)-phenylglycinol and trimethyl nitrilotriacetate was heated at 80 °C for 72 h. The mixture was purified by silica gel column chromatography (CH_3OH/AcOEt = 4:6) to give **5a** (62% yield). In a similar procedure, **5b**, **5c**, and **5d** were prepared from trimethyl nitrilotriacetate and the corresponding L-amino alcohols.

4.1.1. *N,N′,N″*-Tris[(1*S*)-(2-TBDMSO-1-phenylethyl-)]-nitrilotriacetamide 8a

To a solution of trihydroxy triamide **5a** (1.37 g, 2.50 mmol) in CH_2Cl_2 (15.0 mL) was added imidazole (0.61 g, 9.0 mmol) at 0 °C, followed by TBDMSCl (1.20 g, 8.0 mmol). The mixture was stirred at room temperature for 12 h, then filtered through sintered glass to remove the salts after which brine was added. The organic phase was separated and dried over anhydrous Na_2SO_4, filtered

and evaporated in vacuo. Purification by silica gel column chromatography (petroleum ether/AcOEt, 6:4) gave **8a** (2.20 g, 98%) as a colourless oil. $[\alpha]_D^{25} = +30.0$ (c 0.50, CH_2Cl_2).

IR (cm^{-1}): 2929, 2953, 2856, 1653, 1541, 1471, 1254, 1122, 836, 777, 698. ^1H NMR ($CDCl_3$): δ 7.53 (d, J = 8.1 Hz, 3H, NH), 7.37–7.29 (m, 15H, ArH), 5.17–5.10 (m, 3H, CHNH), 3.91–3.79 (m, 6H, CH_2O), 3.47 (s, 6H, CH_2N), 0.91 (s, 27H, $C(CH_3)_3$), 0.01 (s, 18H, $Si(CH_3)_2$). ^{13}C NMR (75 MHz): δ 169.8, 139.7, 128.2, 127.2, 126.9, 66.1, 58.9, 54.9, 25.7, 18.1, −5.65, −5.70. HRMS (ESI): m/z calcd for $C_{48}H_{79}N_4O_6Si_3$ ($M+H^+$): 891.53019; found: 891.53093.

4.1.2. *N,N′,N″*-Tris[(1*S*)-(2-TBDMSO-1-benzylethyl-)]-nitrilotriacetamide 8b

Prepared according to the procedure mentioned in Section 4.1.1 starting from trihydroxy triamide **5b** (1.48 g, 2.50 mmol), imidazole (0.61 g, 9.0 mmol) and TBDMSCl (1.20 g, 8.0 mmol); colourless oil, 2.14 g (92%). $[\alpha]_D^{25} = +74.4$ (c 0.67, CH_2Cl_2). IR (cm^{-1}): 2953, 2928, 2857, 1654, 1537, 1253, 1116, 836, 776, 745, 699. ^1H NMR (300 MHz, $CDCl_3$): δ 7.28–7.14 (m, 15H, ArH), 6.82 (d, J = 9.0 Hz, 3H, NH), 4.27–4.19 (m, 3H, CHNH), 3.58 (dd, J = 3.6, 9.9 Hz, 3H, CH_2O), 3.53 (dd, J = 4.8, 9.9 Hz, 3H, CH_2O), 3.00 (s, CH_2, 6H, NCH_2), 2.95 (dd, J = 7.2, 13.5 Hz, 3H, one of CH_2Ph), 2.77(dd, J = 7.2, 13.5 Hz, 3H, one of CH_2Ph), 0.92 (s, 27H), 0.06 (s, 27H), 0.05 (s, 18H). ^{13}C NMR (75MHz): δ 169.4, 138.0, 129.1, 128.1, 126.1, 63.3, 58.1, 51.7, 36.8, 25.7, 18.0, −5.6 HRMS (ESI): m/z calcd for $C_{51}H_{85}N_4O_6Si_3$ ($M+H^+$): 933.57714; found: 933.57811.

4.1.3. *N,N′,N″*-Tris[(1*S*)-(2-TBDMSO-1-*iso*-propylethyl-)]-nitrilotriacetamide 8c

Prepared according to the procedure mentioned in Section 4.1.1 starting from trihydroxy triamide **5c** (1.12 g, 2.50 mmol), imidazole (9.0 mmol), TBDMSCl (1.20 g, 8.0 mmol); colourless oil, 1.87 g (95%). $[\alpha]_D^{25} = -38.1$ (c 1.50, CH_2Cl_2). IR (cm^{-1}): 2957, 2929, 2857, 1655, 1540, 1471, 1255, 1109, 937, 775. ^1H NMR (300 MHz, $CDCl_3$): δ 6.84–6.81 (d, J = 9.30 Hz, 3H, NH), 3.80–3.73 (m, 3H, CHNH), 3.62 (dd, J = 4.50, 9.90 Hz, 3H, CH_2O), 3.25 (s, 6H, NCH_2), 1.92–1.86 (m, 3H, $CHMe_2$), 0.89 (d, J = 6.60 Hz, 9H), 0.84 (d, J = 6.60 Hz, 9H), 0.02 (s, 18H, $SiMe_2$). ^{13}C NMR (75 MHz): δ 169.6, 62.7, 58.8, 55.5, 28.2, 25.7, 19.5, 18.1, 18.0, −5.6. HRMS (ESI): m/z calcd for $C_{39}H_{85}N_4O_6Si_3$ ($M+H^+$): 789.57714; found: 789.57875.

4.1.4. *N,N′,N″*-Tris[(1*S*)-(2-TBDMSO-1-*iso*-butylethyl-)]-nitrilotriacetamide 8d

Prepared according to the procedure mentioned in Section 4.1.1 starting from trihydroxy triamide **5d** (1.22 g, 2.50 mmol), imidazole (9.0 mmol), TBDMSCl (1.20 g, 8.0 mmol); colourless oil, 1.96 g (90%). $[\alpha]_D^{25} = -38.8$ (c 1.0, CH_2Cl_2). IR (cm^{-1}): 2956, 2918, 2850, 1653, 1538, 1253, 1096, 837, 776. ^1H NMR (300 MHz, $CDCl_3$): δ 6.77 (d, J = 8.7 Hz, 3H, NH), 4.10–4.00 (m, 3H, CHNH), 3.59 (dd, J = 3.90, 9.90 Hz, 3H, CH_2O), 3.52 (dd, J = 5.10, 10.20 Hz, 3H, CH_2O), 3.28 (s, 6H, NCH_2), 1.57–1.25 (m, 9H, CH_2CH), 0.91(t, J = 3.90 Hz, 18H), 0.88 (s, 27H), 0.05 (s, 9H), 0.04 (s, 9H). ^{13}C NMR (75 MHz): δ 169.4, 64.9, 58.9, 48.9, 40.4, 25.8, 24.8, 23.1, 22.2, 18.2, −5.5, −5.4. HRMS (ESI): m/z calcd for $C_{45}H_{97}N_4O_6Si_3$ ($M+H^+$): 873.67104; found: 873.67227.

4.1.5. *N,N′,N″*-Tris[(1*S*)-(2-TBDMSO-1-phenylethyl-)]-nitrilotri(thio-acetamide) 9a

To a solution of **8a** (1.07 g, 1.20 mmol) in benzene (15.0 mL) was added Lawesson's reagent (0.81 g, 2.0 mmol). The mixture was refluxed for 4 h under N_2, then the solvent was removed in vacuo. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 9:1) to afford 0.91 g (81%) **9a** as a pale oil. $[\alpha]_D^{25} = +35.6$ (c 0.50, CH_2Cl_2). IR (cm^{-1}): 2954, 2928, 2856, 1521, 1463, 1408, 1255, 1113, 1006, 836, 777, 697. ^1H NMR (300 MHz, $CDCl_3$): δ 9.23 (d, J = 8.10 Hz, 3H, NH), 7.33–7.23 (m, 15H, ArH), 5.67–5.61 (m, 3H, CHNH), 3.90 (dd, J = 5.10, 10.20 Hz, 3H, CH_2O), 3.83 (dd, J = 5.40, 10.50 Hz, 3H, CH_2O) 3.65 (s, 6H, NCH_2), 0.79 (s, 27H, $C(CH_3)_3$), 0.08 (s, 9H), 0.06 (s, 9H). ^{13}C NMR (75 MHz): δ 198.4, 137.9, 128.4, 127.7, 127.4, 65.0, 64.8, 60.6, 25.8, 18.1, −5.5, −5.6. HRMS (ESI): m/z calcd for $C_{48}H_{79}N_4O_3S_3Si_3$ ($M+H^+$): 939.46166; found: 939.46315.

4.1.6. *N,N′,N″*-Tris[(1*S*)-(2-TBDMSO-1-benzylethyl-)]-nitrilotri(thio-acetamide) 9b

Prepared according to the procedure mentioned in Section 4.1.5 starting from **8b** (1.12 g, 1.20 mmol) and Lawesson's reagent (0.81 g, 2.0 mmol) in toluene (15.0 mL); pale oil, 0.98 g (84.0%). $[\alpha]_D^{25} = +103.0$ (c 0.63, CH_2Cl_2). IR (cm^{-1}): 2953, 2927, 2856, 1524, 1470, 1113, 836, 813, 777, 699. ^1H NMR (300 MHz, $CDCl_3$): δ 8.80 (d, J = 8.40 Hz, 3H, NH), 7.28–7.17 (m, 15H, ArH), 4.89–4.86 (m, 3H, CHNH), 3.66 (d, J = 3.90 Hz, 6H, CH_2O) 3.40 (d, J = 3.30 Hz, 6H, NCH_2), 3.02 (d, J = 7.20 Hz, 6H, CH_2Ph), 0.92 (s, 27H, $C(CH_3)_3$), 0.06 (s, 9H), 0.05 (s, 9H). ^{13}C NMR (75 MHz): δ 198.2, 137.4, 128.1, 128.3, 126.5, 64.6, 61.8, 57.7, 35.7, 25.9, 18.2, −5.4. HRMS (ESI): m/z calcd for $C_{51}H_{85}N_4O_3S_3Si_3$ ($M+H^+$): 981.50861; found: 981.51054.

4.1.7. *N,N′,N″*-Tris[(1*S*)-(2-TBDMSO-1-i-propylethyl-)]-nitrilotri(thio-acetamide) 9c

Prepared according to the procedure mentioned in Section 4.1.5 starting from **8c** (0.95 g, 1.20 mmol) and Lawesson's reagent (0.81 g, 2.0 mmol) in toluene (15.0 mL); pale oil, 0.75 g (75.3%). $[\alpha]_D^{25} = -105.0$ (c 0.50, CH_2Cl_2). IR (cm^{-1}): 2957, 2928, 2856, 1525, 1463, 1411, 1389, 1256, 1103, 837, 802, 776. ^1H NMR (300 MHz, $CDCl_3$): δ 8.68 (d, J = 9.60 Hz, 3H, NH), 4.58–4.51 (m, 3H, CHNH), 3.67 (dd, J = 4.20, 10.20 Hz, 3H, CH_2O), 3.69 (dd, J = 5.10, 10.50 Hz, 3H, CH_2O), 3.56 (s, 6H, NCH_2), 2.17–2.08 (m, 3H, $CHMe_3$), 1.01 (d, J = 6.60 Hz, 9H), 0.93 (d, J = 6.30 Hz, 9H), 0.88 (s, 27H, $C(CH_3)_3$), 0.06 (s, 9H), 0.05 (s, 9H). ^{13}C NMR (75 MHz): δ 198.6, 65.2, 61.6, 60.3, 28.6, 25.9, 19.3, 19.0, 18.2, −5.38, −5.43. HRMS (ESI): m/z calcd for $C_{39}H_{85}N_4O_3S_3Si_3$ ($M+H^+$): 837.50861; found: 837.51043.

4.1.8. *N,N′,N″*-Tris[(1*S*)-(2-TBDMSO-1-*i*-butylethyl-)]-nitrilotri(thio-acetamide) 9d

Prepared according to the procedure mentioned in Section 4.1.5 starting from **8d** (1.05 g, 1.20 mmol) and Lawesson's reagent (0.81 g, 2.0 mmol) in toluene (15.0 mL); pale oil, 0.82 g (78.0%). $[\alpha]_D^{25} = -62.8$ (c 1.0, CH_2Cl_2). IR (cm^{-1}): 2955, 2929, 2857, 1528, 1470, 1254, 1102, 836, 776. ^1H NMR (300 MHz, $CDCl_3$): δ 8.78–8.75 (d, J = 8.40 Hz, 3H, NH), 4.74–4.69 (m, 3H, CHNH), 3.74 (dd, J = 3.90, 10.20 Hz, 3H, CH_2O), 3.62 (dd, J = 5.10, 10.20 Hz, 3H, CH_2O), 3.54 (s, 6H, NCH_2), 1.59–1.51 (m, 9H, CH_2CH), 0.95 (d, J = 3.30 Hz, 9H, CH_3), 0.92 (d, J = 3.0 Hz, 9H, CH_3), 0.89 (s, 27H, $C(CH_3)_3$), 0.07 (s, 9H), 0.06 (s, 9H). ^{13}C NMR (75 MHz): δ 197.7, 64.9, 63.2, 54.9, 39.4, 25.8, 24.9, 22.8, 22.3, 18.0, −5.43, −5.46. HRMS (ESI): m/z calcd for $C_{42}H_{91}N_4O_3S_3Si_3$ ($M+H^+$): 879.55556; found: 879.55738.

4.1.9. Tri{[2-(4*S*)-(4-phenyl-1,3-thiazolinyl)] methyl} amine 7a

To a solution of **9a** (0.938 g, 1.0 mmol) in THF (10 mL) was added TBAF (1.0 M solution in THF; 3.5 mL, 3.5 mmol) at 0 °C, The mixture was allowed to stir at room temperature overnight, after which a saturated solution of ammonium chloride (20 mL) was added. The aqueous layer was extracted CH_2Cl_2 (3 × 5 mL), the combined organic extracts were washed twice with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue obtained was not further purified, and directly dissolved in a solution of CH_2Cl_2 (15 mL) and Et_3N (1 mL, 7.5 mmol), and cooled to 0 °C, MsCl (0.35 g, 3.10 mmol) was added slowly. The mixture was allowed to warm to room temperature and then stirred for 1.5 h. The mixture

was washed with water (2 × 5 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo to give the crude product as yellow oil. Purification by silica gel column chromatography (petroleum ether/AcOEt, 1:1) afforded **7a** (0.48 g, 88%) as a colourless oil, $[\alpha]_D^{25} = +126.0$ (*c* 0.25, CH_2Cl_2). IR (cm^{-1}): 3025, 2926, 2360, 1622, 1492, 1453, 1161, 1027, 825, 772. ^1H NMR (300 MHz, $CDCl_3$): δ 7.38–7.25 (m, 15H, ArH), 5.55 (t, *J* = 9.30 Hz, 3H, CHN=), 3.83 (dd, *J* = 15.30, 24.0 Hz, 6H, NCH_2), 3.70 (dd, *J* = 9.0, 12.0 Hz, 3H, one of CH_2), 3.22 (t, *J* = 10.20, 10.50 Hz, 3H, one of CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.3, 141.6, 128.5, 127.5, 126.4, 80.2, 56.3, 40.1. HRMS (ESI): calcd for $C_{30}H_{30}N_4S_3H$ (MH^+): 543.1705; found: 543.1693.

4.1.10. Tri{[2-(4*S*)-(4-benzyl-1,3-thiazolinyl)] methyl} amine 7b

Prepared according to the procedure mentioned in Section 4.1.9 starting from **9b**; white solid, 0.53 g (91.0%). Compound **7b:** Mp 82–84 °C, $[\alpha]_D^{25} = +120.0$ (*c* 0.30, CH_2Cl_2). IR (cm^{-1}): 3025, 2921, 1622, 1495, 1453, 1166, 1030, 742. ^1H NMR (300 MHz, $CDCl_3$): δ 7.32–7.19 (m, 15H, ArH), 4.81–4.71 (m, 3H, CHN=), 3.58 (dd, *J* = 15.60, 18.10 Hz, 6H, CH_2N), 3.22–3.13 (m, 6H, one of CH_2S and one of CH_2Ph), 3.00 (dd, *J* = 7.20, 10.80 Hz, 3H, one of CH_2S), 2.75 (dd, *J* = 9.00, 10.50 Hz, one of CH_2Ph). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.1, 138.2, 129.2, 128.4, 126.4, 78.0, 56.0, 40.3, 36.3. Elemental Anal. Calcd for $C_{33}H_{36}N_4S_3$: C, 67.77; H, 6.20; N, 9.58. Found: C, 67.81; H, 6.36; N 9.51.

4.1.11. Tri{[2-(4*S*)-(4-*iso*-propyl-1,3-thiazolinyl)] methyl} amine 7c

Prepared according to the procedure mentioned in Section 4.1.9 starting from **9c**; white solid, 0.37 g (85.1%).

Compound **7c**: Mp 94–95.5 °C, $[\alpha]_D^{25} = -65.0$ (*c* 0.30, CH_2Cl_2). IR (cm^{-1}): 2956, 2872, 1526, 1466, 1436, 1364, 1257, 1164, 967, 952. ^1H NMR ($CDCl_3$): δ 4.28–4.25 (m, 3H, CHN=), 3.56 (dd, *J* = 1.50, 3.60 Hz, 6H, CH_2N), 3.25 (dd, *J* = 4.50, 10.20 Hz, 3H, one of CH_2S), 2.98 (dd, *J* = 9.60, 10.80 Hz, 3H, one of CH_2S), 2.00 (m, 3H, $CHMe_2$), 1.03 (d, *J* = 6.60 Hz, 9H, CH_3), 0.95 (d, *J* = 4.50 Hz, 9H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.3, 83.5, 56.2, 34.3, 32.9, 19.6, 18.8. Elemental Anal. Calcd for $C_{21}H_{36}N_4S_3$: C, 57.23; H, 8.23; N, 12.71. Found: C, 57.35; H, 8.41; N, 12.74.

4.1.12. Tri{[2-(4*S*)-(4-*i*-butyl-1,3-thiazolinyl)] methyl} amine 7d

Prepared according to the procedure mentioned in Section 4.1.9 starting from **9c**; white solid, 0.40 g (83.0%). Compound **7d**: Mp. 84–85.5 °C, $[\alpha]_D^{25} = -95.0$ (*c* 0.20, CH_2Cl_2). IR (cm^{-1}): 2954, 2925, 2868, 1625, 1467, 1436, 1366, 1169, 832. ^1H NMR ($CDCl_3$): δ 4.51–4.46 (m, 3H, CHN=), 3.53 (s, 6H, CH_2N), 3.34 (dd, *J* = 8.10, 10.50 Hz, 3H, one of CH_2S), 2.88 (dd, *J* = 8.40, 10.80 Hz, 3H, one of CH_2S), 1.81–1.65 (m, 6H, CH_2), 1.43–1.33 (m, 3H, $CHMe_2$), 0.98 (d, *J* = 3.00 Hz, 9H, CH_3), 0.93 (d, *J* = 3.60 Hz, 9H, CH_3). ^{13}C NMR (75MHz, $CDCl_3$): δ 169.1, 75.5, 56.2, 44.2, 37.1, 25.7, 22.8, 22.5. Elemental Anal. Calcd for $C_{24}H_{42}N_4S_3$: C, 59.70; H, 8.77; N, 11.60. Found: C, 59.92; H, 8.90; N, 11.51.

4.2. Typical procedure for the asymmetric allylic oxidation of cyclopentene and cyclohexene

A mixture of $Cu(OTf)_2$ (4.0 mg, 11 μmol) and ligand **5a** (8.2 mg, 17 μmol) was stirred in dry CH_2Cl_2 (0.5 mL) under nitrogen for 1 h. The above solution was added to another flask containing acetone (0.40 mL) and cyclopentene (60 mg, 0.88 mmol) and molecular sieves 4 Å (85 mg). After being stirred for 30 min, the mixture was cooled to 0 °C, *tert*-butyl peroxybenzoate (42 mg, 0.22 mmol) was added dropwise and the reaction mixture was stirred at 25 °C for 3 days. The mixture was passed through a short silica gel column (petroleum ether/AcOEt = 9:1) to remove molecular sieves and copper catalyst. The filtrate was concentrated and purified by column chromatography (petroleum/AcOEt = 99:1) to give 2-cyclopentenyl benzoate as an oil (17.7 mg, 43% yield). The enantiomeric excess was determined by HPLC with a chiral column (Daicel Chiralcel OD-H; eluent, hexane–*iso*-propyl alcohol 99.9: 0.1; flow rate 0.5 mL/min). In a similar procedure, 2-cyclohexenyl benzoate was obtained.

Acknowledgements

We are grateful to the National Natural Science Foundation (Grant No. 20772151) and China Agricultural University for financial support. We thank Professor Da-ming Du for his valuable discussion and modifications of the manuscript, Tongling Liang is gratefully acknowledged for her careful determination of the X-ray crystal diffraction analysis.

References

1. (a) Desimoni, G.; Faita, G.; Jorgensen, K. A. *Chem. Rev.* **2006**, *106*, 3561–3651; (b) Mcmanus, H. A.; Guiry, P. J. *Chem. Rev.* **2004**, *104*, 4151–4202; (c) Ghosh, A. K.; Mathivannan, P.; Cappiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1–45.
2. (a) Kohmura, Y.; Katsuki, T. *Tetrahedron Lett.* **2000**, *41*, 3941–3945; (b) Kohmura, Y.; Katsuki, T. *Synlett* **1999**, 1231–1234; (c) Kawasaki, K.; Katsuki, T. *Tetrahedron* **1997**, *53*, 6337–6350.
3. (a) Zhou, J.; Tang, Y. *J. Am. Chem. Soc.* **2002**, *124*, 9030–9031; (b) Foltz, C.; Stecker, B.; Marconi, G.; Bellemin-Laponnaz, S.; Wadepohl, H.; Gade, L. H. *Chem. Commun.* **2005**, 5115–5117; (c) Bellemin, L. S.; Gade, L. H. *Angew. Chem.* **2002**, *41*, 3473–3475.
4. (a) Seong, H. R.; Kim, D. S.; Kim, S. G.; Choi, H. J.; Ahn, K. H. *Tetrahedron Lett.* **2004**, *45*, 723–727; (b) Kim, S. G.; Ahn, K. H. *Chem. Eur. J.* **2000**, *6*, 3399–3403; (c) Kim, H. J.; Moon, D.; Lah, M. S.; Hong, J. I. *Angew. Chem., Int. Ed.* **2002**, *41*, 3174–3177; (d) Kim, H. J.; Kim, Y. H.; Hong, J. I. *Tetrahedron Lett.* **2001**, *42*, 5049–5052; (e) Kim, S.-G.; Kim, K.-H.; Jung, J.; Shin, S. K.; Ann, K. H. *J. Am. Chem. Soc.* **2002**, *124*, 591–596; (f) Kim, S.-G.; Kim, K.-H.; Kim, Y. K.; Shin, S. K.; Ann, K. H. *J. Am. Chem. Soc.* **2003**, *125*, 13819–13824.
5. (a) LeMaux, P.; Abrunhosa, I.; Berchel, M.; Simonneaux, G.; Gulea, M.; Masson, S. *Tetrahedron: Asymmetry* **2004**, *15*, 2569–2573; (b) Abrunhosa, I.; Gulea, M.; Delain-Bioton, L.; Gaumont, A.-C.; Masson, S. *Tetrahedron: Asymmetry* **2004**, *60*, 9263–9272; (c) Abrunhosa, I.; Gulea, M.; Levillain, J.; Masson, S. *Tetrahedron: Asymmetry* **2001**, *12*, 2851–2859.
6. (a) Liu, H.; Xu, J. X.; Du, D. M. *Org. Lett.* **2007**, *9*, 4725–4728; (b) Lu, Sh.-F.; Du, D.-M.; Xu, J.-X.; Zhang, Sh. W. *J. Am. Chem. Soc.* **2006**, *128*, 7418–7419.
7. (a) Gibson, S. E.; Castaldi, M. P. *Angew. Chem., Int. Ed.* **2006**, *45*, 4718–4720; (b) Mosberg, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 4721–4723; (c) Zhou, J.; Tang, Y. *Chem. Soc. Rev.* **2005**, *34*, 664.
8. Tarrage, A.; Molina, P.; Curiel, D.; Bautista, D. *Tetrahedron: Asymmetry* **2002**, *13*, 1621–1628.
9. Kodama, Y.; Ori, M.; Nishio, T. *Helv. Chim. Acta* **2005**, *88*, 187–193.
10. (a) Markovic, R.; Baranac, M.; Jovetic, S. *Tetrahedron Lett.* **2003**, *44*, 7087–7090; (b) Soukara, S.; Wunschh, B. *Tetrahedron Lett.* **2001**, *57*, 4359–4363.
11. (a) Wagner, S.; Schumann, D.; Linne, U.; Koert, U.; Marahiel, M. A. *J. Am. Chem. Soc.* **2006**, *128*, 10513; (b) Nicolaou, K. C.; Kim, D. W.; Schlawe, D.; Lizos, D. E.; de Noronha, R. G.; Longbottom, D. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 4925–4929; (c) McKeever, B.; Pattenden, G. *Tetrahedron* **2003**, *59*, 2701–2712.
12. (a) McKeever, B.; Pattenden, G. *Tetrahedron* **2003**, *59*, 2713–2727; (b) Zarantonello, P.; Leslie, C. P.; Ferritto, R.; Kazmierski, W. M. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 561–565.
13. Crystal data for (*S*)-**7c**: $C_{21}H_{36}N_4S_3$–H_2O, *M* = 458.73, Hexagonal, space group *P*6(3)c, *a* = 15.568(2) Å, *b* = 15.568(2) Å, *c* = 6.3100(13) Å, $\alpha = \beta = 90°$, $\gamma = 120°$, *V* = 1324.4(4) $Å^3$, *Z* = 2, *D* = 1.150 mg/m^3, Mo Kα (λ = 0.71073 Å), *T* = 173(2) K, μ = 0.298 mm^{-1}, crystal size (mm) 0.38 × 0.38 × 0.31 mm. Area detector data collected on a Rigaka axis rapid IP diffractometer. A total of 1999 reflections were collected ($2.62 < \theta < 27.46$). Structure solution by direct method (SHELXS-97), refinement by full-matrix least-squares using all reflections, $R_1 = 0.0638$, $wR_2 = 0.1057$, GOF = 1.002. Crystallographic Data Centre as supplementary publication number CCDC 683616. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.