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Chiral Polyamino Alcohols *via* Hydroaminomethylation: A New Class of Polyamines for Dendritic Cores and Ligand Precursors

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Abstract: In this contribution, the synthesis of a new class of chiral polyamino alcohols (PAA) *via* a two-step hydroaminomethylation/hydrolysis procedure is reported. The chiral polyamines are obtained by hydroaminomethylation of *N*-olefinic oxazolidinones with different amines in first step followed by hydrolysis of the resulting polyamines to give the chiral PAA in the second step. The dendritic chiral PAA ($Mw = 1300$–$1400\ g\,mol^{-1}$) are also synthesized efficiently through a multifold hydroaminomethylation/hydrolysis procedure. Furthermore, chiral PAA are investigated as ligands in ruthenium-catalyzed asymmetric hydrogen transfer reduction of acetophenone to 1-phenyl alcohol.

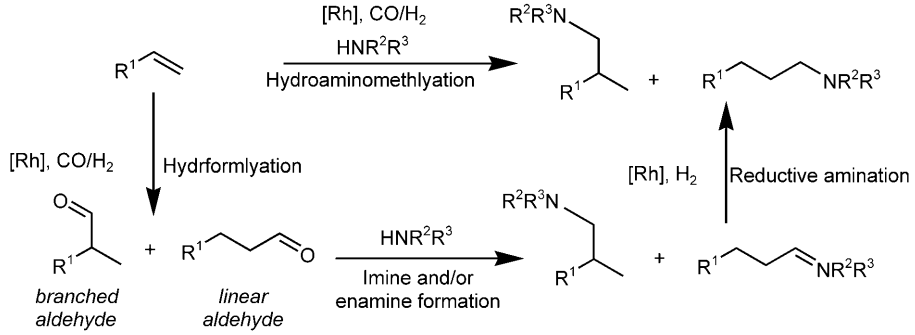
Keywords: amino alcohols; hydroaminomethylation; hydroformylation; hydrolysis; polyamines; polyamino alcohols

Introduction

Chiral amino alcohols are important building blocks of many natural products and an important functional feature in the design of a number of enzyme inhibitors.[1,2] Chiral amino alcohols are also versatile chiral auxiliaries and ligands for the introduction of chirality in asymmetric catalysis of C–C, C–O and C–H bond-forming reactions.[3–5] Asymmetric addition of dialkylzinc to carbonyl compounds and imines,[6] asymmetric cyanosilylation of aldehydes[7] and asymmetric hydrogen transfer reduction of ketones[8] are some recent examples in the literature where amino alcohols are employed as chiral ligands. The presence of N–O functional groups makes chiral amino alcohols suitable for chiral recognition and for a combinatorial approach to catalysis.

In the last decade, hydroaminomethylation has been used as a powerful tool in the synthesis of many organic compounds of great importance.[9,10] Hydroaminomethylation combines hydroformylation[11] and reductive amination to a synthetically versatile one-pot procedure for the synthesis of secondary and tertiary amines (Scheme 1). Syntheses of linear and cyclic polyfunctionalized amines,[12] azamacro hetrocycles as complexing agents for metal ions,[13] polyamine derivatives of putrescine and spermidine from *N*-olefinic phthalimide,[14] dendritic polyamine from polyallyl ethers[15] and selective synthesis of tertiary amines from olefins and urea[16] *via* hydroaminomethylation are some recent examples.

Herein we report an efficient preparation of chiral polyamino alcohols (PAA) by hydroaminomethylation of chiral *N*-olefinic oxazolidinones **1a–c** with dif-



Scheme 1. Hydroaminomethylation.

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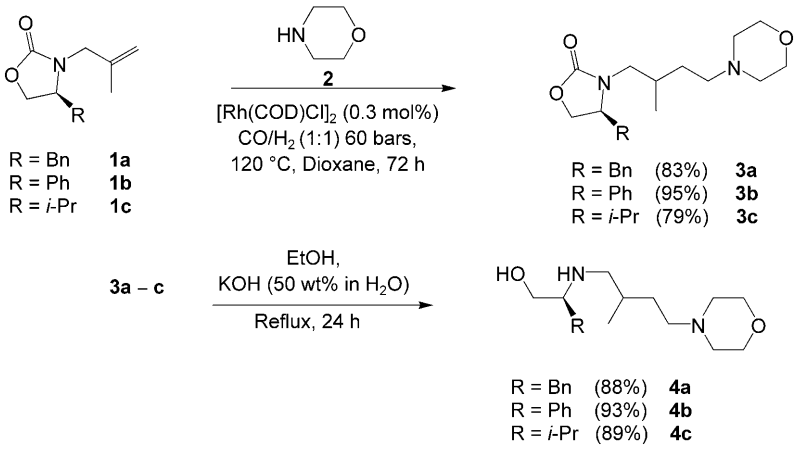

Scheme 2. Synthesis of chiral amino alcohols *via* hydroaminomethylation/hydrolysis.

ferent amines (e.g., **2**, **5**, **8** and **11**). In this synthetic strategy chiral *N*-olefinic oxazolidinones are used as chiral amino alcohol masked functional groups. The carbamate ring of the oxazolidinones can be hydrolyzed with KOH (50 wt% in H_2O) in ethanol to give the respective chiral amino alcohols. Subsequently, chiral PAA are used as ligand in the Ru-catalyzed asymmetric hydrogen transfer reduction of acetophenone.

Results and Discussion

In initial studies, chiral *N*-olefinic oxazolidinones **1a–c** were hydroaminomethylated with morpholine **2** as amine component to give corresponding chiral amines **3a–c** in excellent yields (Scheme 2). The optimized hydroaminomethylation conditions {CO/H_2 (1:1) 60 bar, $[Rh(COD)Cl]_2$ (0.3 mol%), 120 °C, 48 h} were used for all reactions. No hydrogenation product of an aldehyde was observed, because primary and secondary amines immediately condense with the aldehyde generated *in situ* and the resulting imines and/or enamines are usually reduced under the harsh conditions. The chiral oxazolidinones, also known as Evan's auxiliaries, are well known for their use as chiral auxiliaries for chiral induction.[17] But in this case, we did not observe any chiral induction during hydroformylation or reduction of imines. In the following step chiral amines **3a–c** were hydrolyzed with KOH (50 wt% in H_2O) in ethanol to give the corresponding chiral amino alcohols **4a–c** in good to excellent yield (Scheme 2).

Next, multi-fold hydroaminomethylation/hydrolysis was carried out for the synthesis of dendritic chiral PAA. This was achieved on use of multifunctional polyamine core molecules, for example, piperazine **5** for 2-fold, urea[16] **8** as ammonia equivalent for 3-fold and tris(aminoethyl)amine **11** for 6-fold hydroaminomethylation were used. As shown in Scheme 3 two-fold hydroaminomethylation of **1a–c** with piprazine **5** gave chiral polyamines **6a–c** in high yields. Subsequently chiral PAA **7a–c** were obtained on hydrolysis of polyamines **6a–c** (Scheme 3).

Recently, we envisaged urea as an ammonia source,[16,18] since it generates ammonia on hydrolysis and simultaneously acts as a scavenger for aldehydes to protect them against reduction to alcohols. Following these lines, tertiary polyamines **9a–c** were synthesized starting from **1a–c** and urea **8** *via* hydroaminomethylation. The desired symmetric polyamines **9a–c** were obtained selectively and in good to excellent yields and subsequently were hydrolyzed to give chiral polyamino alcohols **10a–c** (Scheme 3).

Polyamines and synthetic analogues have been investigated as potential therapeutic agents in various biological disorders and have attracted considerable attention in organic chemistry.[19–20] The chiral amino alcohols **4a–c** and chiral PAA **7a–c** and **10a–c** having a chiral ethylhydroxy functional group at the nitrogen atom are similar to the derivatives of naturally occurring polyamines such as putrescines and spermidine. Putrescines and spermidine are important biological polyamines which are present in all living cells and play important physiological functions.[21] Purescine derivatives have been used as antimalaria[22] and antiplasmodic agents.[23] This kind of polyamines has also been found to be important in other fields of current research, for example, metabolism[24] and biogenesis,[25] antibiotics,[26] coagulation inhibitors,[27] antidiarrhoics[28] and cytostatics.[29]

The two-step hydroaminomethylation/hydrolysis procedure has been used so far to synthesize chiral amino alcohols with low *Mw* (Scheme 2 and Scheme 3). The use of an amine core with a high degree of active sites available for hydroaminomethylation will lead to dendritic chiral PAA. The tris(aminoethyl)amine **11** core molecule with three primary

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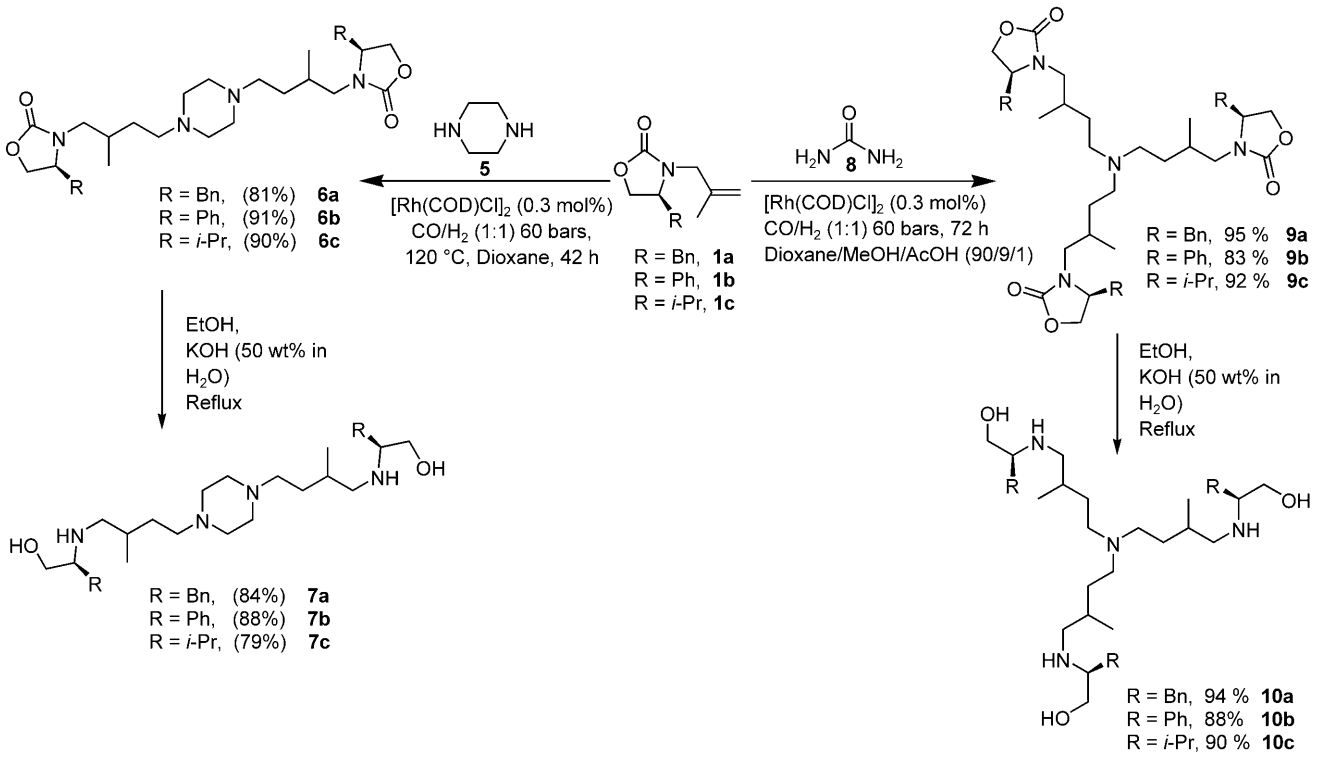

Scheme 3. Synthesis of chiral PAA *via* hydroaminomethylation/hydrolysis.

amine groups gives access to a 6-fold hydroaminomethylation that leads directly to higher *Mw* dendritic polyamines in one step. Hydroaminomethylation of chiral *N*-methylallyloxazolidinones **1a–c** with tris(aminoethyl)amine **11** was carried out under standard hydroaminomethylation conditions (*vide supra*) in dioxane with a reaction time extended from 72 h to 120 h. The dendritic chiral PAA **12a-c** ($Mw = 1300–1400\ g\,mol^{-1}$) were obtained in moderate to good yields (Scheme 4). Dialysis was used as a membrane ultrafiltration method for the purification of these chiral polyamines **12a–c** due to their higher *Mw*.[30]

In our initial studies, *N*-methylallyloxazolidinone had been used as a model system to prove the principle and to avoid the linear (*n*) to branched (*iso*) selectivity problem in the initial hydroformylation step. But the use of the *N*-methylallyl system leads to the generation of an extra stereogenic centre on each branch of the dendritic polyamines which is usually not desired (Scheme 2, Scheme 3, and Scheme 4). This problem can be avoided by the use of an *N*-allyl system instead of *N*-methylallyl, but regioselectivity is a major problem in the initial hydroformylation step of such terminal olefins when Rh or Rh salts with triphenylphosphine are used as catalysts for these reactions. Generally, the basic requirement to achieve high selectivity in hydroaminomethylation is to use a catalyst with a combination of a phosphine or phosphite ligand in the initial hydroformylation step. The influence of different phosphine and phosphite ligands in the regioselectivity of hydroformylation is well known.[31,32] It is also known that the presence of amines influences the *n/iso* selectivity of the hydroformylation step because amines compete with phosphines as ligands for the metal centre and thereby influence the regioselectivity. Therefore, for a highly regioselective hydroaminomethylation, the BIPHEPHOS **21** modified $Rh(acac)CO_2$ catalysts was used in 1:5 ratio under optimized conditions [CO/H_2 (10/10 bar), 50 °C, 48 h] for hydroformylation of **1a** in the first step. The aldehydes **14** were obtained in an *n:iso* ratio of (87:13) and in full conversion (Scheme 5) that was determined by ^1H NMR spectroscopy. To the same pot (autoclave), amine cores **14** and/or **17** were added and set under reductive amination conditions [CO/H_2 (10/50 bar)] to get dendritic polyamines **16** and **19** that were hydrolyzed to give dendritic PAA **17** and **20**, respectively, in excellent yields (Scheme 5).

We chose the ruthenium-catalyzed asymmetric hydrogen transfer reduction of acetophenone to 1-phenylethanol as model reaction to investigate the initial applications of these dendritic chiral polyamino alcohols.[3c,8,33] Several ruthenium complexes were prepared *in situ* from $[RuCl_2(p\text{-cymene})]_2$ (2 mol%) and chiral PAA (4 mol%) in isopropyl alcohol and were employed in the asymmetric hydrogen transfer reduction of acetophenone in the presence of KOH (10 mol%). The isopropyl alcohol was used as hydrogen donor which have favourable properties such that it is stable, easy to handle (bp 82 °C), non-toxic, envi-

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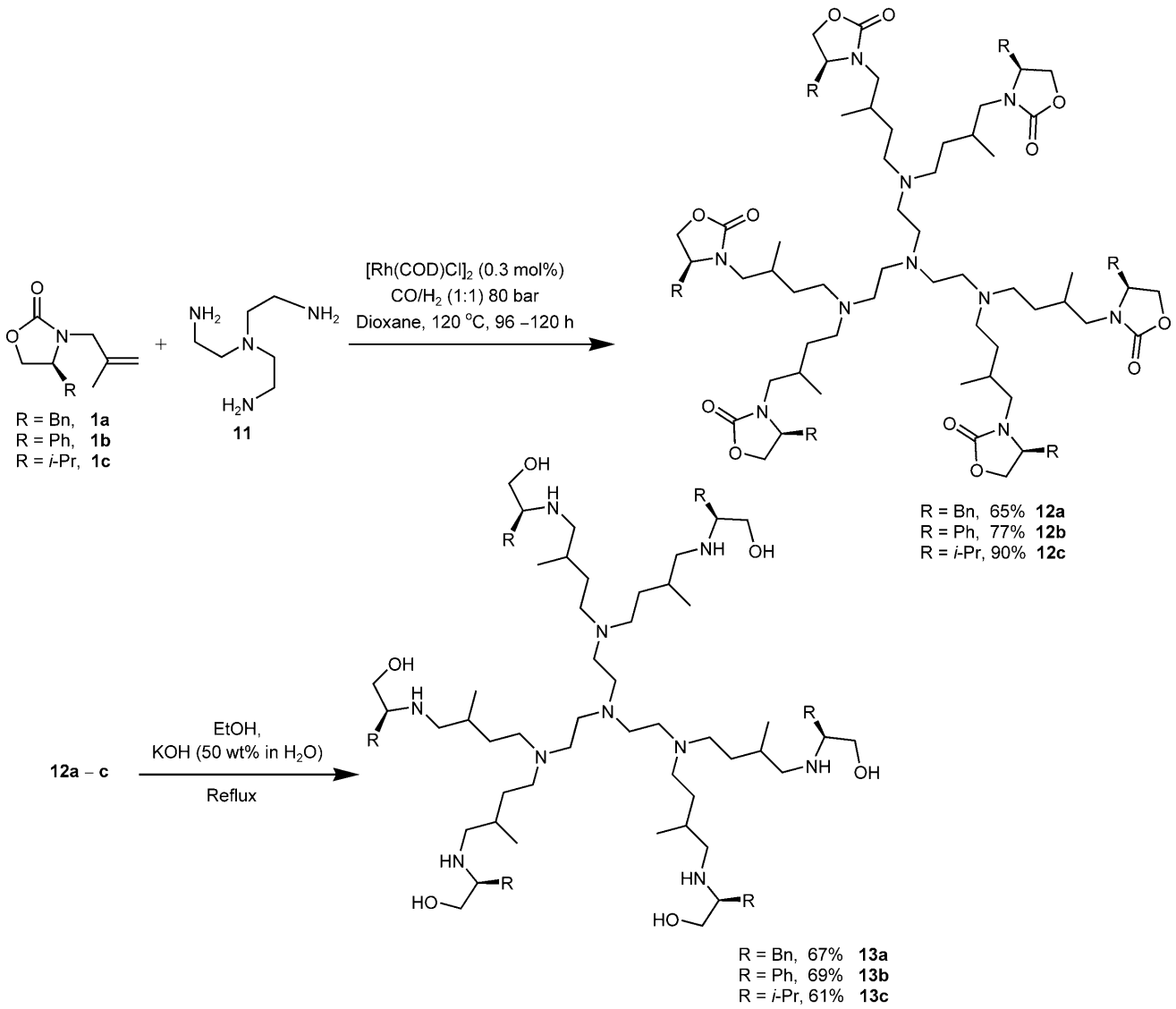

Scheme 4. Synthesis of dendritic chiral PAA *via* hydroaminomethylation/hydrolysis.

ronmentally friendly, inexpensive and dissolves in many organic compounds. In addition, this reaction is an attractive route as it avoids the use of pressurized hydrogen and/or use of the hazardous reducing agents. Initially, all of the chiral amino alcohol ligands were screened in the transfer hydrogenation of acetophenone and results are summarized in Table 1.

In general the catalytic reactions proceeded smoothly at room temperature and good to excellent conversions (76–91%) and moderate to good *ee* (22–71%) were observed (Table 1). The best *ee* (71%) was obtained when monoamino alcohol **4a** was used as ligand (Table 1, entry 1). However, a small decrease in enantioselectivity was observed with increased number of amino alcohol functionalities and increase in *Mw* of chiral PAA which can be attributed to the dendritic effect.[34] The larger polyamino alcohols such as **13a–c** and **20** have multiple sites available for catalyst interaction that can be the reason for lower enantioselectivities. (Table 1, entries 10–12, 14). Furthermore, the better *ee*s were obtained when chiral amino alcohols and chiral PAA derived from **1a** were used as ligands (Table 1, entries 1, 4, 7, 10 , 13 and 14) as compared to the chiral amino alcohols and chiral PAA derived from **1b** and **1c**, respectively (Table 1).

Conclusions

The chiral amino alcohols and chiral PAA were synthesized in good to excellent yields *via* a two step hydroaminomethylation/hydrolysis procedure. Our approach relies on use of chiral *N*-olefinic oxazolidinones which are easily accessible from chiral pool of

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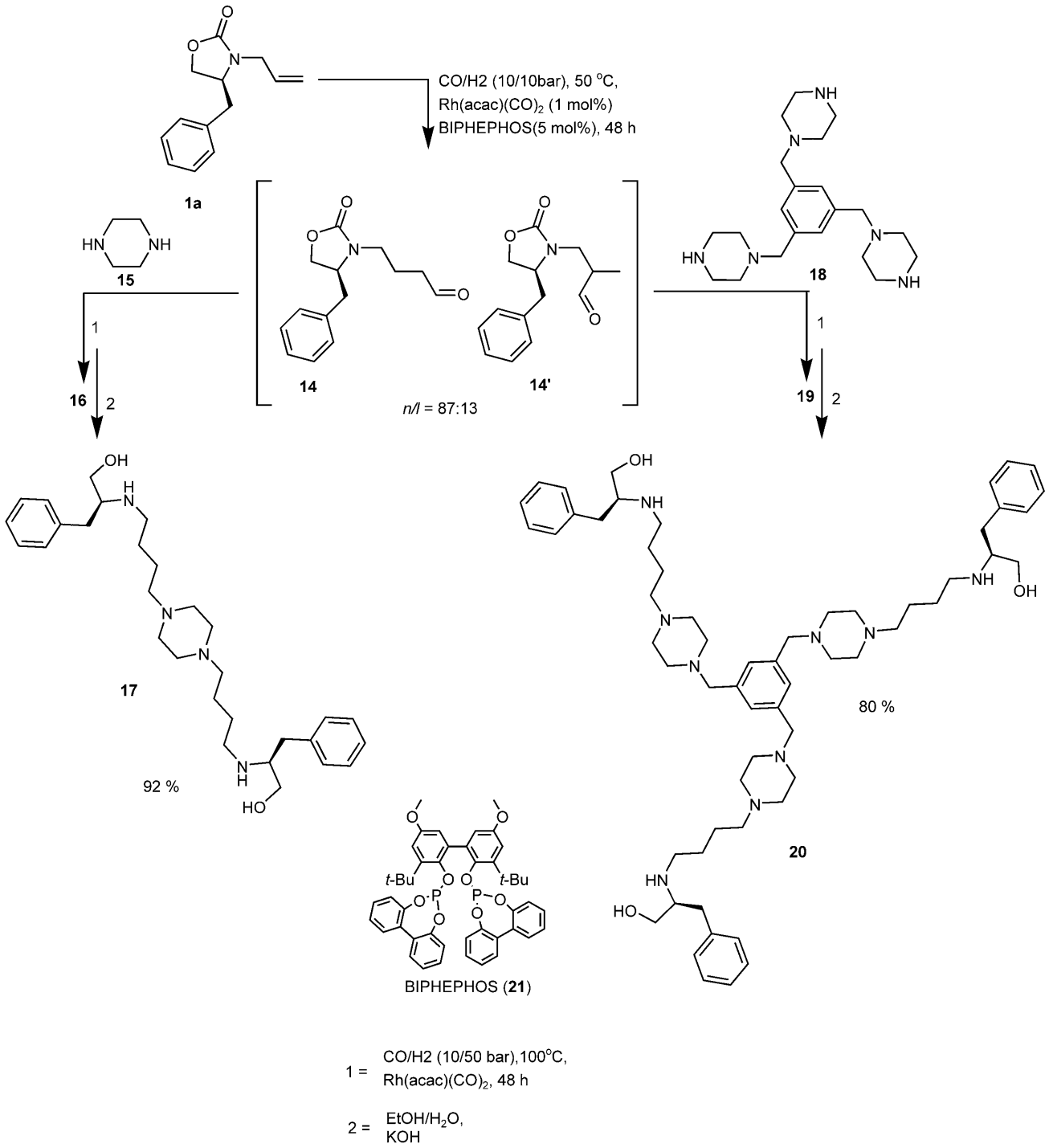

Scheme 5. Regioselective hydroaminomethylation.

amino acids. The chiral oxazolidinone are used as chiral amino alcohol masked functionalities. To the best of our knowledge, this is a new class of polyamines with terminal chiral amino alcohol groups. This method is an efficient tool for the synthesis of new derivatives of highly biological active polyamines such as putrescines and spermidine. The chiral amino alcohols and chiral PAA have also been employed as ligands in the Ru-catalyzed asymmetric hydrogen transfer reduction of acetophenone. Good to excellent conversion (76–91%) and moderate to good enantioselectivity (22–71%) were observed. The best results were obtained when chiral amino alcohols and chiral PAA derived from (*S*)-4-benzyl-3-(2-methylallyl)oxa-

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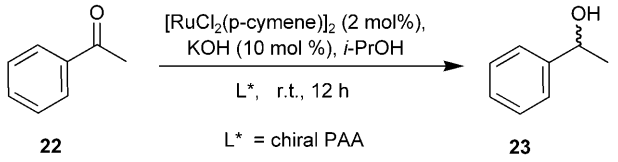
Table 1. Ruthenium catalyzed asymmetric hydrogen transfer reduction of acetophenone.



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Entry	Ligand [L*]	Conversion [%][a]	Yield [%][b]	*ee* [%][c] (Configuration)
1	**4a**	91	85	71 (*S*)
2	**4b**	89	84	68 (*S*)
3	**4c**	90	85	57 (*S*)
4	**7a**	88	84	69 (*S*)
5	**7b**	83	78	60 (*S*)
6	**7c**	76	72	40 (*S*)
7	**10a**	90	85	64 (*S*)
8	**10b**	92	86	41 (*S*)
9	**10c**	78	73	31 (*S*)
10	**13a**	85	81	59 (*S*)
11	**13b**	79	71	51 (*S*)
12	**13c**	81	74	22 (*S*)
13	**17**	92	85	63 (*S*)
14	**20**	89	82	57 (*S*)

[a] Determined by GC.
[b] Isolated yields.
[c] Determined by chiral GC.

zolidin-2-one (**1a**) were used as ligands. The chiral PAA can also be used as potential core molecules for higher generation dendrimer synthesis.

Experimental Section

All general chemicals were purchased and used as such. ^{1}H and ^{13}C NMR spectra were recorded at room temperature with Bruker DRX 400 and DRX 500 spectrometers using $CDCl_3$ as solvent and TMS as internal standard. Infrared spectroscopy was performed on a Nicolet Impact 400 D spectrometer using KBr palletss or as disks with KBr. GC analyses were performed on a Chromatograph MFS 800 (column: CHROMPACK DB-1701, 25 m × 0.32 mm × 1.0 m, detector: FID) by FISON instruments.

General Procedure A: Hydroaminomethylation of *N*-Methylallyloxazolidinones with Amines

In a typical hydroaminomethylation procedure, the *N*-methylallyloxazolidinone (10 mmol, 1 equiv.) and amine (10 mmol, 1 equiv.) were dissolved in 10 mL of dioxane, $[Rh(COD)Cl]_2$ (15 mg,0.3 mol%) was added and the mixture was placed in an pressure vessel (autoclave) and treated under typical hydroaminomethylation conditions [$CO:H_2$ (1:1) 60–80 bar, 100 °C, 48–72 h]. ***Caution!*** **CO is highly toxic.** The reaction vessel was cooled down to room temperature and the solvent was removed under reduced pressure. After evaporation of the solvent, the crude mixture was purified by column chromatography or bulb to bulb distillation if necessary.

General Procedure B: Hydrolysis of Oxazolidinone Functionalized Amines to Chiral Amino Alcohols

In a typical hydrolysis procedure, the oxazolidinone functionalized amine or polyamine (1 mmol) was dissolved in 20 mL of ethanol. To the reaction mixture 10 mL of aqueous KOH solution (50 wt%) were added and the mixture refluxed for 20 h. Ethanol was removed under reduced pressure and the aqueous phase was extracted with 15 mL of ethyl acetate three times. Organic fractions were combined, dried over $MgSO_4$ and the solvent was removed under reduced pressure to get chiral amino alcohol or chiral PAA alcohol without any further purification.

General Procedure C: Hydroaminomethylation *N*-Methylallyloxazolidinones with Urea

A solution of *N*-methylallyloxazolidinone (10 mmol), urea (10 mmol) and $[Rh(COD)Cl]_2$ (0.3 mol%) in 100 mL of dioxane:methanol:glacial acetic acid (90:9:1) solvent mixture was placed in an pressure vessel (autoclave) and treated under hydroaminomethylation conditions [40/40 bar (CO/H_2), at 100–120 °C for 72 h]. After cooling, the pressure was removed and the solvent was evaporated to dryness. The resulting mixture was treated with 10 mL of conc. sodium hydroxide solution and 10 mL of water. The mixture was extracted with 200 mL of ethyl acetate, the organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by column-chromatography on alumina (activity III) if necessary.

(*S*)-4-Benzyl-3-(2-methyl-4-morpholinobutyl)oxazolidin-2-one (3a): The general procedure **A** for hydroaminomethylation was followed with morpholine (189 mg, 2.16 mmol) and (*S*)-4-benzyl-3-(2-methylallyl)oxazolidin-2-one **1a** (500 mg, 2.16 mmol). The crude product was purified by flash chromatography on alumina activity III to get chiral amine **3a** as an oil; yield: 597 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.81$–1.02 (3H, m), 1.24–1.39 (2H, m), 1.84 (1H, m), 2.21–2.38 (6H, m), 2.81–2.94 (1H, m), 3.25–3.39 (1H, m), 3.01–3.11 (2H, m), 3.67–3.88 (4H, m), 4.13 (1H, m), 4.71–4.89 (2H, m), 7.11–7.27 (5H, m); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 17.2$, 28.1, 39.3, 48.8, 52.8, 53.2, 56.0, 56.5, 65.8, 128.6, 130.3, 130.5, 137.0, 159.7. IR (film, KBr): $\tilde{\nu} = 708$, 739, 768, 1011, 1053, 1135, 1248, 1396, 1462, 1501, 1606, 1741, 2810, 2926, 3026, 3534 cm^{-1}; LR-MS (FAB): $m/z = 333.2$ $[M+H]^+$; HR-MS (FAB): $m/z = 333.215$, calcd. for $C_{19}H_{28}N_2O_3$ $[M+H]^+$: 333.21.

(*S*)-3-(2-Methyl-4-morpholinobutyl)-4-phenyloxazolidin-2-one (3b): The general procedure **A** for hydroaminomethylation was followed with (*S*)-3-(2-methylallyl)-4-phenyloxazolidin-2-one **1b** (500 mg, 2.301 mmol) and morpholine (200 mg, 2.301 mmol). The crude product was purified by flash chromatography on alumina activity III to give chiral amine **3b** as an oil; yield: 695 mg (95%, 2.18 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.78$–0.96 (3H, dd, $J =$ 6.53 Hz, 7.03 Hz), 1.19–1.77 (3H, m), 2.17–2.49 (4H, m), 2.55–2.74 (1H, m), 3.19–3.35 (1H, m), 3.64–3.76 (4H, m), 4.13–4.19 (1H, m), 4.61–4.81 (2H, m), 7.26–7.48 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 17.5$, 29.4, 30.6, 47.9, 53.9,

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56.5, 60.4, 67.1, 69.8, 127.0, 129.2, 138.0, 158.7; IR (film, KBr): $\tilde{\nu}$ = 701, 759, 867, 1118, 1454, 1625, 1751, 2809, 2854, 2954, 3390 cm^{-1}; ESI-MS: m/z = 319.1 $[M+H]^+$; HR-MS (FAB): m/z = 319.1860, calcd. for $C_{18}H_{26}N_2O_3$ $[M+H]^+$: 319.1943.

(*S*)-4-Isopropyl-3-(2-methyl-4-morpholinobutyl)oxazolidin-2-one (3c): The general procedure **A** for hydroaminomethylation was followed with (*S*)-4-isopropyl-3-(2-methylallyl)oxazolidin-2-one **1c** (213 mg, 1.163 mmol) and morpholine (104 mg, 1.163 mmol). The crude product was purified by flash chromatography on alumina activity III to give chiral amine **3c** as an oil; yield: 265 mg (79%, 0.91 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79–1.01 (9H, m), 1.14–1.43 (2H, m), 1.69–1.94 (H, m), 2.02–2.16 (1H, m), 2.29–2.55 (4H, m), 2.78–2.94 (1H, m), 3.31–3.34 (1H, m), 3.62–3.77 (4H, m), 4.07–4.24 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5, 18.1, 27.3, 29.5, 30.6, 53.8, 56.7, 58.3, 62.6, 67.1, 68.6, 159. 8. IR (film, KBr): $\tilde{\nu}$ = 867, 914, 1118, 1286, 1373, 1461, 1621, 1741, 2884, 2956 cm^{-1}; ESI-MS: m/z = 285.3 $[M+H]^+$ HR-MS (FAB): m/z = 285.2025, calcd. for $C_{15}H_{25}N_3O_2$ $[M+H]^+$: 285.21.

(*S*)-2-(2-Methyl-4-morpholinobutylamino)-3-phenylpropan-1-ol (4a): The general procedure **B** for hydrolysis was followed with **3a** (300 mg, 0.902 mmol), to get chiral amino alcohol **4a** as an oil; yield: 224 mg (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84–0.99 (3H, m), 1.29–1.41 (2H, m), 1.84–1.87 (1H, m), 2.21–2.31(2H, m), 2.36–2.45 (4H, m), 2.79–2.95 (1H, m), 3.21–3.32 (1H, m), 2.99–3.09 (2H, m), 3.63–3.78 (4H, m), 3.82 (1H, m), 4.31–4.45 (2H, m), 7.11–7.27 (5H, m); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 18.1, 30.1, 38.3, 50.8, 51.8, 53.5, 56.0, 57.5, 66.8, 128.6, 129.3, 131.5, 137.0; IR (film, KBr): $\tilde{\nu}$ = 698, 743, 771, 1001, 1044, 1139, 1251, 1389, 1459, 1505, 1611, 2810, 2933, 3042, 3521 cm^{-1}; LR-MS (FAB): m/z = 307.2 $[M+H]^+$; HR-MS (FAB): m/z = 307.2358, calcd. for $C_{18}H_{30}N_2O_2$ $[M+H]^+$: 307.2307.

(*S*)-2-(2-Methyl-4-morpholinobutylamino)-2-phenylethanol (4b): The general procedure **B** for hydrolysis was followed with (*S*)-3-(2-methyl-4-morpholinobutyl)-4-phenyloxazolidin-2-one (700 mg, 2.19 mmol) **3b** to get chiral amino alcohol **4b** as an oil; yield: 603 mg (93%, 2.03 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90–0.95 (3H, m), 1.26–1.30 (2H, m), 1.66–1.74 (1H, m), 2.35–2.51 (8H, m), 3.71–3.75 (6H, m), 7.21–7.39 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.5, 31.1, 36.6, 53.7, 57.0, 62.1, 66.6, 68.9. 69.7, 127.5, 129.7, 137.0; IR (film, KBr): $\tilde{\nu}$ = 701, 759, 867, 1118, 1454, 1625, 2809, 2854, 2954, 3390 cm^{-1}; ESI-MS: m/z = 293.2 $[M+H]^+$; HR-MS (FAB): m/z = 292.2226, calcd. for $C_{17}H_{28}N_2O_2$ $[M+H]^+$: 292.2151.

(*S*)-2-(2-Methyl-4-morpholinobutylamino)-3-methylbutan-1-ol (4c): The general procedure **B** for hydrolysis was followed with (*S*)-4-isopropyl-3-(2-methyl-4-morpholinobutyl)-oxazolidin-2-one **3c** (200 mg, 0.703 mmol) to get chiral amino alcohol **4c** as an oil; yield: 163 mg (89%, 0.62 mmol). ^{1}H NMR: (400 MHz, $CDCl_3$): δ = 0.87–1.01 (9H, m), 1.21–1.41 (2H, m), 1.56–1.73 (1H, m), 2.25.2.76 (8H, m),3.67–3.78 (6H, m); ^{13}C NMR: (100 MHz, $CDCl_3$): δ = 18.7, 20.0, 29.2, 31.9, 33.0, 53.8, 54.2, 57.4, 60.7, 62.1, 67.3; IR: (film, KBr): $\tilde{\nu}$ = 867, 914, 1118, 1286, 1373, 1461, 1621, 2884, 2956, 3380 cm^{-1}; ESI-MS: m/z = 259.3 $[M+H]^+$; HR-MS (FAB): m/z = 258.2218, calcd. for $C_{14}H_{30}N_2O_2$ $[M+H]^+$: 258.2307.

Chiral polyamine (6a): The general procedure **A** for hydroaminomethylation was followed with piperazine (93 mg, 1.08 mmol) and (*S*)-4-benzyl-3-(2-methylallyl)oxazolidin-2-one **1a** (500 mg, 2.16 mmol). The crude product was purified by flash chromatography on alumina activity III to get chiral polyamine **6a** as an oil; yield: 519 mg (84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86–0.90 (6H, m), 1.24 and 1.52 (4H, m), 1.84 (2H, m), 2.52–2.63 (8H, m), 2.88–2.90 (2H, m), 3.31–3.36 (2H, m), 3.05–3.08 (4H, m), 3.97 (4H, m), 4.13(2H, m), 7.14–7.25 (10H, m); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 17.7, 30.1, 38.3, 47.8, 48.3, 52.8, 53.2, 56.0, 56.5, 66.8, 128.6, 130.3, 130.5, 137.0, 159.7; IR (film, KBr): $\tilde{\nu}$ = 702, 743, 762, 1006, 1059, 1175, 1259, 1380, 1454, 1496, 1603, 1747, 2810, 2926, 3026, 3500 cm^{-1}; LR-MS (FAB): m/z = 577.7 $[M+H]^+$; HR-MS (FAB): m/z = 576.3734, calcd. for $C_{34}H_{48}N_4O_4$ $[M+H]^+$: 576.3676.

Chiral polyamine (6b): The general procedure **A** for hydroaminomethylation was followed with piperazine (158 mg, 1.84 mmol) and (*S*)-4-phenyloxazolidin-2-one **1b** (800 mg, 3:68 mmol). The crude product was purified by flash chromatography on alumina activity III to get chiral polyamine **6b** as an oil; yield: 898 mg (91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80–0.96 (6H, m), 1.21–1.34 (2H, m), 1.64–1.78 (2H, m), 1.36–1.34 (1H, m), 1.50–1.63 (2H, m), 2.13–2.56 (8H, m), 2.56–2.77 (2H, m), 3.20–3.37 (4H, m), 4.11–4.22 (2H, m), 4.59–4.71 (2H, m), 4.73–4.86 (2H, m), 7.25–7.48 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.3, 29.8, 36.0, 47.8, 52.9, 56.1, 59.7, 69.7, 127.0,129.0, 129.2, 137.8; IR (film, KBr): $\tilde{\nu}$ = 701, 761, 873, 1060, 1120, 1230, 1253, 1417, 1457, 1751, 2809, 2925, 2952, 3488 cm^{-1}; LR-MS (FAB): m/z = 549.0 $[M+H]^+$; HR-MS (FAB): m/z = 548.3390, calcd. for $C_{32}H_{44}N_4O_4$ $[M+H]^+$: 548.3363.

Chiral polyamine (6c): The general procedure **A** for hydroaminomethylation was followed with piperazine (117 mg, 1.36 mmol) and (*S*)-4-isopropyl-3-(2-methylallyl)oxazolidin-2-one **1c** (500 mg, 2.72 mmol). The crude product was purified by flash chromatography on alumina activity III to get chiral polyamine **6c** as an oil without any further purification; yield: 590 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79–0.98 (18H, m), 1.20–1.32 (1H, m), 1.34–1.44 (2H, m), 1.46–1.62 (4H, m), 1.74–1.89 and 2.00–2.15 (4H, m), 2.26–2.61 (8H, m), 2.74–2.94 and 3.26–3.41 (4H, m), 3.71–3.74 (2H, m), 4.05–4.24 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 17.6, 27.1, 29.7, 31.3, 47.2, 58.6, 59.2, 62.4, 68.3, 158.4; IR (film, KBr): $\tilde{\nu}$ = 769, 873, 1051, 1120, 1253, 1425, 1758, 2807, 2929, 2958, 3311 cm^{-1}; HR-MS (ESI-FT-MS): m/z = 481.3735, calcd. for $C_{26}H_{48}N_4O_4$ $[M+H]^+$: 481.3676.

Chiral polyamino alcohol (7a): The general procedure **B** for hydrolysis was followed with polyamine **6a** (350 mg, 0.61 mmol), to get chiral polyamino alcohol **7a** as an oil; yield: 259 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88–1.02 (6H, m), 1.31–1.49 (4H, m), 1.84 (2H, m), 2.52–2.63 (8H, m), 2.88–2.90 (2H, m), 3.31–3.36 (2H, m), 3.11–3.19 (4H, m), 3.86–4.01 (4H, m), 4.31(2H, m), 7.14–7.25 (10H, m); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 17.7, 29.1, 39.8, 50.0, 51.2, 52.6, 55.2, 56.0, 57.3, 69.1, 128.6, 130.3, 130.5, 135.0; IR (film, KBr): $\tilde{\nu}$ = 705, 743, 762, 1011, 1059, 1175, 1259, 1380, 1454, 1496, 1603, 2810, 2956, 3026, 3506 cm^{-1}; LR-MS (FAB): m/z = 525.4 $[M+H]^+$; HR-MS (FAB): m/z = 525.415, calcd. for $C_{32}H_{52}N_4O_2$ $[M+H]^+$: 525.409.

2-(4-{4-[4-(2-Hydroxy-1-phenylethylamino)-3-methylbutyl]-piperazin-1-yl}-2-methylbutylamino)-2-phenylethanol (7b): The general procedure **B** for hydrolysis was followed with polyamine **6b** (347 mg, 0.265 mmol), to get chiral polya-

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mino alcohol **7b** as an oil; yield: 271 mg (88%); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.86$–0.88 (6H, m), 1.20–1.24 (4H, m), 1.45 (2H, m), 2.27–2.33 (16H, m), 3.39–3.66 (6H, m,), 7.24–7.30 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 18.6$, 31.8, 32.4, 53.3, 53.9, 56.6, 62.1, 66.7, 127.2, 127.6, 128.6, 141.0; IR (film, KBr): $\tilde{\nu} = 761$, 802, 1099, 1260, 1406, 1453, 1563, 1727, 2871, 2928, 2961, 3389 cm^{-1}; LR-MS (FAB): $m/z = 497.5$ $[M+H]^+$; HR-MS (FAB): $m/z = 497.3787$, calcd. for $C_{26}H_{48}N_4O_4$ $[M+H]^+$: 497.3777.

2-(4-{4-[4-(1-Hydroxymethyl-2-methylpropylamino)-3-methylbutyl]-piperazin-1-yl}-2-methylbutylamino)-3-methylbutan-1-ol (61): The general procedure B for hydrolysis was followed with polyamine 6c (347 mg, 0.265 mmol), to get chiral polyamino alcohol **7c** as an oil; yield: 271 mg (88%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.84$–1.03 (8H, m), 1.25–1.41 (4H, m), 1.59–1.61 (2H, m), 1.79–1.81 (2H, m), 2.33–2.37 (8H, m), 2.43–2.54 (8H, m), 3.24–3.35 (2H, m), 3.56–3.61 (18H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 18.7$, 20.0, 29.4, 32.2, 33.7, 53.7, 57.0, 64.9; IR (film, KBr): $\tilde{\nu} = 754$, 815, 1014, 1110, 1371, 1763, 1644, 2809, 2950, 3372 cm^{-1}; ESI-MS: $m/z = 429.5$ $[M+H]^+$; HR-MS (ESI-FT-MS): $m/z = 429.4152$, calcd. for $C_{24}H_{52}N_4O_2[M+H]^+$: 429.4163.

Chiral polyamine (9a): The general procedure **C** for hydroaminomethylation was followed with urea and (*S*)-4-benzyl-3-(2-methylallyl)oxazolidin-2-one **1a** (1.05 g, 4.54 mmol). The crude product was purified by flash chromatography on alumina activity III to give chiral polyamine **9a** as an oil; yield: 1.08 g (95%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.94$ (18H, m), 1.27 and 1.55 (12H, m), 1.87 (6H, m), 2.56 (12H, m), 2.66–2.68 (12H, m), 2.91–2.93 and 3.27–3.41 (12H, m), 3.09–3.14 (12H, m), 3.98–34.16 (18H, m), 7.18–7.32 (30H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm] = 18.4, 30.8, 48.6, 52.7, 57.2, 67.3, 127.8, 129.6, 129.8, 136.3, 159.1; IR (film, KBr): $\tilde{\nu} = 505$, 593, 664, 702, 761, 842, 937, 1061, 1255, 1380, 1453, 1525, 1603, 1731, 1954, 2454, 2832, 2882, 2972, 3060, 3478 cm^{-1}; LR-MS (FAB): $m/z = 753.8$ $[M^+ + H^+]$; HR-MS (FAB): $m/z = 753.4586$, calcd. for $C_{45}H_{60}N_4O_6$ $[M+H]^+$: 753.4513.

Chiral Polyamine (9b): The general procedure **C** for hydroaminomethylation was followed with urea and (*S*)-3-(2-methylallyl)-4-phenyloxazolidin-2-one **1b** (500 mg, 2.301 mmol). The crude product was purified by flash chromatography on alumina activity III to give chiral polyamine **9b** as an oil; yield: 449 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.75$–0.89 (9H, m,) 1.08–1.44 (6H, m), 1.62 (3H, m), 2.09–2.29 (6H, m), 2.52–2.65 and 3.17–3.32 (6H, m), 4.10–4.15 (3H, m), 4.60–4.65 and 4.72–4.84 (6H, m), 7.23–7.42 (15H, m); ^{13}C NMR: (100 MHz, $CDCl_3$): $\delta = 17.7$, 29.2, 31.2, 47.7, 51.3, 60.0, 69.6, 126.8, 128.9, 129.1, 137.7, 158.3;IR (flm, KBr): $\tilde{\nu} = 735$, 899, 1056, 1221, 1352, 1411, 1602, 1740, 2922, 2955, 3356 cm^{-1}; HR-MS (FAB): $m/z = 711.4159$, calcd. for $C_{42}H_{54}N_4O_6$ $[M+H]^+$: 711.4143.

Chiral polyamine (9c): The general procedure **C** for hydroaminomethylation was followed with urea and (*S*)-4-isopropyl-3-(2-methylallyl)oxazolidin-2-one **1c** (500 mg, 2.723 mmol), The crude product was purified by flash chromatography on alumina activity III to give chiral polyamine **9c** as an oil; yield: 508 mg (92%). ^{1}H NMR: (400 MHz, $CDCl_3$): $\delta = 0.83$–0.92 (27H, m), 1.22 (6H, m), 1.40 (6H, m), 1.48 (6H, m), 2.42 (6H, m), 2.73–2.87 & 3.29–3.24 (6H, m), 3.71 (3H, m), 4.06–4.22 (6H, m); ^{13}C NMR: (100 MHz, $CDCl_3$): $\delta = 14.6$, 18.0, 27.6,29.9, 47.9, 51.6, 59.8, 62.9, 68.8, 159.1; IR (film, KBr): $\tilde{\nu} = 766$, 873, 1051, 1120, 1258, 1425, 1758, 2807, 2933, 2958, 3324 cm^{-1}; HR-MS (FAB): $m/z = 609.4$ $[M+H]^+$; HR-MS (FAB): $m/z = 609.4526$, calcd. for $C_{33}H_{60}N_4O_6$ $[M+H]^+$: 609.4513.

2-(4-{Bis-[4-(1-benzyl-2-hydroxyethylamino)-3-methylbutyl]-amino}-2-methylbutylamino)-3-phenylpropan-1-ol (10a): The general procedure **B** for hydrolysis was followed with polyamine **9a** (200 mg, 0.265 mmol), to get chiral polyamino alcohol **10a** as an oil; yield: 168 mg (94%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.79$–0.98 (9H, m), 1.10–1.37 (6H, m), 1.43–1.63 (3H, m), 2.25–2.62 (12H, m), 2.70–3.00 (9H, m), 3.31–3.34 (3H, m), 3.60–363 (3H, m), 7.19–7.33 (15H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 18.4$, 30.8, 48.6, 52.7, 57.2, 67.3, 127.8, 129.6, 129.8, 136.3; IR (film, KBr): $\tilde{\nu} = 744$, 1041, 1114, 1376, 1454, 1621, 2867, 2925, 3372 cm^{-1}; ESI-MS: $m/z = 675.6$ $[M+H]^+$; HR-MS (ESI): $m/z = 675.5156$, calcd. for $C_{42}H_{66}N_4O_3$ $[M+H]^+$: 675.5166.

2-(4-{Bis-[4-(2-hydroxy-1-phenylethylamino)-3-methylbutyl]-amino}-2-methylbutylamino)-2-phenyl-ethanol (10b): The general procedure **B** for hydrolysis was followed with polyamine **9b** (347 mg, 0.265 mmol), to get chiral polyamino alcohol **10b** as an oil; yield: 271 mg (88%). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.90$–0.92 (9H, m), 1.26–1.30 (3H, m), 1.60–1.70 (6H, m), 2.36–2.48 (12H, m), 3.55–3.62 (3H, m), 3.70–3.78 (6H, m), 7.28–7.37 (15H, m); ^{13}C NMR (500 MHz, $CDCl_3$): $\delta = 19.0$, 31.8, 32.3, 51.8, 54.3, 65.7, 67.1, 127.6, 129.0, 141.0; IR (film, KBr): $\tilde{\nu} = 624$, 701, 800, 1025, 1089, 1261, 1454, 2809, 2869, 2923, 2960, 3355 cm^{-1}; LR-MS (FAB): $m/z = 631.7$ $[M+H]^+$; HR-MS (FAB): $m/z = 633.4679$, calcd. for $C_{39}H_{60}N_4O_3$ $[M+H]$: 633.4665.

2-(4-{Bis-[4-(1-hydroxymethyl-2-methylpropylamino)-3-methylbutyl]-amino}-2-methyl-butylamino)-3-methyl-butan-1-ol (10c): The general procedure **B** for hydrolysis was followed with polyamine 9c (347 mg, 0.265 mmol), to get chiral polyamino alcohol **10c** as an oil; yield: 271 mg (88%). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.90$–0.98 (27H, m), 1.26–1.28 (6H, m), 1.61–1.63 (3H, m), 1.81–1.84 (3H, m), 2.36–2.51 (12H, m), 2.55–2.63 (3H, m), 3.33–3.36 and 3.60–3.64 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 18.8$, 20.1, 29.2, 32.8, 35.0, 52.0, 53.8, 60.8, 64.8; IR (film, KBr): $\tilde{\nu} = 752$, 1045, 1105, 1232, 1380, 1463, 1621, 2869, 2960, 3372 cm^{-1}; LR-MS (FAB): $m/z = 531.6$ $[M+H]^+$; HR-MS (FAB): $m/z = 531.5231$, calcd. for $C_{30}H_{66}N_4O_3$ $[M+H]^+$: 531.5135.

Chiral polyamine (12a): The general procedure **A** for hydroaminomethylation was followed with tris(2-aminoethyl)-amine **11** (200 mg, 1.36 mmol, 1 equiv.), (*S*)-4-benzyl-3-(2-methylallyl)oxazolidin-2-one **1a** (1.9 g, 8.3 mmol, 6.1 equiv.) and $[Rh(COD)Cl_2]$ (14 mg, 0.3 mol%). The crude product was purified by dialysis in chloroform. The solvent was removed under reduced pressure to get polyamine **12a** as an oil; yield: 1.02 g (65%); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 0.94 (18H, m), 1.27 & 1.55 (12H, m), 1.87 (6H, m), 2.56 (12H, m), 2.66–2.68 (12H, m), 2.91–2.93 & 3.27–3.41 (12H, m), 3.09–3.14 (12H, m), 3.98–34.16 (18H, m), 7.18–7.32 (30H, m); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 18.4$, 30.8, 48.6, 52.7, 57.2, 67.3, 127.8, 129.6, 129.8, 136.3, 159.1; IR (Film, KBrl): $\tilde{\nu} = 505$, 593, 664, 702, 761, 842, 937, 1061, 1255, 1380, 1453, 1525, 1603, 1731, 1954, 2454, 2832, 2882, 2972, 3060, 3478 cm^{-1}; LR-MS (FAB): $m/z = 1619.16$ $[M^+ + H^+]$; HR-MS (ESI): $m/z = 1618.99872$, calcd. for $C_{96}H_{132}N_{10}O_{12}$ $[M+H]^+$: 1618.00990.

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Chiral polyamine (12b): The general procedure **A** for hydroaminomethylation was followed with tris(2-aminoethyl)-amine **11** (67 mg, 0.46 mmol, 1 equiv.), (*S*)-4-phenyl-3-(2-methylallyl)oxazolidin-2-one **1b** (1 g, 4.6 mmol, 10 equiv.) and $[Rh(COD)Cl_2]$ (7 mg, 0.3 mol%). The crude product was purified by dialysis in chloroform. The solvent was removed under reduced pressure to get polyamine **12b** as an oil; yield: 0.705 g (77%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 0.79–0.86 (18H, m), 1.12–1.66 (18H, m), 2.26–2.96 (36H, m), 4.09 (6H, m), 4.62–4.76 (12H, m), 7.26–7.37 (30H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 17.5$, 27.9, 29.5, 51.9, 59.9, 69.9, 127.4, 129.3, 138.0, 158.8; IR (film, KBr): $\tilde{\nu} = 730$, 910, 1062, 1133, 1234, 1382, 1382, 1417, 1747, 2825, 2958, 3475 cm^{-1}; ESI-MS: $m/z = 1534.1$ $[M+H]^+$; MS (MALDI-TOF): $m/z = 1534.253$ $[M+H]^+$.

Chiral polyamine (12c): The general procedure **A** for hydroaminomethylation was followed with tris(2-aminoethyl)-amine **11** (80 mg, 0.46 mmol, 1 equiv.), (*S*)-4-isopropyl-3-(2-methylallyl)oxazolidin-2-one **1c** (1 g, 5.45 mmol, 10 equiv.) and $[Rh(COD)Cl_2]$ (8 mg, 0.3 mol%). The crude product was purified by dialysis in chloroform. The solvent was removed under reduced pressure to get polyamine **12c** as an oil; yield: 0.751 g (90%); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 0.73–0.97 (54H, m), 1.12–1.34 (6H, m), 1.36–1.62 (6H, m), 1.67–1.87 (6H, m), 1.93–2.13 (6H, m), 2.28–2.93 (24H, m), 3.16–3.41 (6H, m), 3.60–3.85 (6H, m), 3.93–4.09 (6H, m), 4.12–4.32 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 14.2,17.7, 27.2, 29.8, 47.5, 52.1, 58.9, 62.6, 66.5, 160.1; IR (film, KBr): $\tilde{\nu} = 755$, 977, 1049, 1185, 1243, 1384, 1438, 2873, 2958, 3363 cm^{-1}; ES- MS: $m/z = 1330.2$ $[M+H]^+$.

Chiral polyamino alcohol (13a): The general procedure **B** for hydrolysis was followed with polyamine **12a** (200 mg, 0.123 mmol), to get chiral PAA **13a** as a colourless oil; yield: 120 mg (67%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 0.81–0.95 (18H, m), 1.12–1.28 (6H, m), 1.43–1.65 (6H, m), 1.95–2.15 (6H, m), 2.26–2.96 (48H, m), 3.24–3.44 (6H, m), 3.51–3.61 (6H, m), 7.07–7.38 (30H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 18.3, 23.5, 32.2, 38.1, 52.3, 60.3, 62.6, 126.4, 128.5, 129.2, 138.8; IR (film, KBr): $\tilde{\nu} = 700$, 744, 804, 1039, 1251, 1454, 1602, 2867, 2923, 3363 cm^{-1} (m); ESI MS: $m/z =$ 1462.1 $[M+H]^+$; LR-MS (FAB): $m/z = 1462.4$ $[M]^+$; HR-MS (ESI): $m/z = 1462.1343$, calcd. for $C_{90}H_{144}N_{10}O_6$ $[M+H]^+$: 1462.1270.

Chiral polyamino alcohol (13b): The general procedure **B** for hydrolysis was followed with polyamine **12b** (500 mg, 0.325 mmol), to get chiral PAA **13b** as a dark brown oil; yield: 310 mg (69%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 0.81–1.01 (18H, m), 1.11–1.38 (6H, m), 1.46–1.83 (12H, m), 2.13–2.86 (36H, m), 3.40–3.86 (18H, m), 7.15–7.53 (30H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 18.5, 29.9, 32.0, 52.0, 53.9, 60.4, 62.6, 127.4, 128.6, 141.0; IR (film, KBr): $\tilde{\nu} = 700$, 744, 804, 1039, 1251, 1454, 1602, 2867, 2923, 3363 cm^{-1} (m); ESI-MS: $m/z = 1379.4$ $[M+H]^+$; HR-MS (ESI): $m/z = 1377.0389$, calcd. for $C_{84}H_{132}N_{10}O_6$ $[M+H]^+$: 1377.0331.

Chiral polyamino alcohol (13c): The general procedure **B** for hydrolysis was followed with polyamine **12c** (300 mg, 0.225 mmol), to get chiral PAA **13c** as a brown oil; yield: 162 mg (61%); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 0.73–1.07 (54H, m), 1.19–1.33 (6H, m), 1.39–1.59 (6H, m), 1.67–1.79 (6H, m), 2.01–2.13 (6H, m), 2.31–2.93 (30H, m), 3.21–3.39 (6H, m), 3.56–3.91 (6H, m), 3.90–4.11 (6H, m), 4.06–4.29 (6H, m);^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 14.2,17.7, 27.2, 29.8, 47.5, 52.1, 58.9, 62.6, 68.2; IR (Film, KBr): $\tilde{\nu} = 723$, 1005, 1049, 1185, 1243, 1406, 1456, 2821, 2986, 3363 cm^{-1}; ESI-MS: $m/z = 1174.1$ $[M+H]^+$; HR-MS (ESI): $m/z =$ 1174.1293, calcd. for $C_{66}H_{144}N_{10}O_6$ $[M+H]^+$: 1174.1270.

Chiral Polyamine *via n*-Selective Hydroaminomethylation (16)

(*S*)-4-Benzyl-3-(2-methylallyl)oxazolidin-2-one **1a** (500 mg, 2.31 mmol), $Rh(acac)(CO)_2$ (1 mol%) and BIPHEPHOS (4 mol%) were dissolved in 7–8 mL of dioxane in a glass vessel. This glass vessel was placed in an autoclave. The autoclave was pressurized with CO/H_2 (10/10 bar) and the reaction was run for 48 h at 50 °C. Solvent was removed under reduced pressure and the linear (*n*) to branch (*iso*) ratio (*n*:*iso* = 87:13) was determined by ^{1}H NMR spectroscopy. Then piperazine was dissolved in 5–8 mL of dioxane and added to the reaction vessel and autoclave was pressurized with CO/H_2 (10/40 bar) and the reaction was run for 48 h at 100 °C. The autoclave was cool down to room temperature and solvent was removed under reduce pressure to get polyamine **16** without any further purification; yield: 95%. ***Note!*** The reductive amination is done without separation of regoisomers. So the final product also contains 17% branched isomers. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 1.47–1.61 (8H, m), 2.32–2.35 (4H, t, $J = 7.53$ Hz), 2.46 (8H, m), 2.62–2.68 and 3.52–3.58 (4H, m), 3.07–3.12 (4H, dd, $J =$ 3.51 Hz), 3.51–4.02 and 4.12–4.16 (6H, m), 7.14–7.33 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.6$, 25.0, 38.2, 41.7, 52.9, 55.6, 57.7, 66.5, 126.9, 128.7, 128.8, 135.3, 157.8; IR (film, KBr): $\tilde{\nu} = 701$, 761, 873, 1060, 1120, 1230, 1253, 1417, 1457, 1751, 2809, 2925, 2952, 3488 cm^{-1}; LR-MS (FAB): $m/z = 549.2$ $[M+H]^+$; HR-MS (FAB): $m/z = 549.3410$, calcd. for $C_{32}H_{44}N_4O_4$ $[M+H]^+$: 549.3363.

2-(4-{4-[4-(1-Benzyl-2-hydroxyethylamino)-butyl]-piperazin-1-yl}-butylamino)-3-phenylpropan-1-ol (17)

The general procedure **B** for hydrolysis was followed with polyamine **16** (120 mg, 0.216 mmol), to get 2-(4-{4-[4-(1-benzyl-2-hydroxyethylamino)butyl]piperazin-1-yl}-butyl-amino)-3-phenylpropan-1-ol **17** as dark brown oil; yield: 100 mg (92%). ^{1}H NMR: (400 MHz, $CDCl_3$): $\delta =$ 1.45 1.46-(8H, m), 2.30 (4H, m), 2.45 (8H, m), 2.57–2.63 and 2.86–2.90 (4H, m), 2.72–2.79 (4H, m), 3.31–3.35 (2H, dd, $J =$ 5.52 Hz), 3.48–3.53 (2H, m), 3.59–3.63 (2H, dd, $J = 4.02$ Hz), 7.17–7.32 (10H, m); ^{13}C NMR: (100 MHz, $CDCl_3$): $\delta =$ 24.3, 27.9, 37.7, 46.6, 52.9, 58.2, 60.1, 62.1, 126.3, 128.4, 129.0, 138.4; IR: (film, KBr) $\tilde{\nu} = 701$, 734, 803, 910, 1031, 1094, 1261, 1454, 1601, 2819, 2933, 3363 cm^{-1} (s); LR-MS (FAB): $m/z = 497.1$ $[M+H]^+$. HR-MS (FAB): $m/z = 497.3865$, calcd. for $C_{30}H_{48}N_4O_2$ $[M+H]^+$: 497.3777.

2-{4-[4-(3,5-Bis-{4-[4-(2-hydroxy-1-phenylethylamino)-3-methyl-butyl]-piperazin-1-ylmethyl}-benzyl)-piperazin-1-yl]-2-methylbutylamino}-2-phenylethanol (19)

(*S*)-4-Benzyl-3-(2-methylallyl)oxazolidin-2-one **1a** (500 mg, 2.31 mmol), $Rh(acac)(CO)_2$ (1 mol%) and BIPHEPHOS (4 mol%) were dissolved in 7–8 mL of dioxane in a glass vessel. This glass vessel was placed in an autoclave and then

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pressurized with CO/H_2 (10/10 bar) and the reaction was run for 48 h at 50 °C. Solvent was removed under reduced pressure and linear (*n*) to branch (*iso*) ratio (*n:iso* = 87:13) was determined by ^1H NMR spectroscopy. Then amine core 1-(3,5-bis((piperazin-1-yl)methyl)benzyl)piperazine was dissolved in 5–8 mL of dioxane and added to the reaction vessel and autoclave was pressurized with CO/H_2 (10/40 bar) and the reaction was run for 48 h at 100 °C. The autoclave was cooled down to room temperature and thesolvent was removed under reduced pressure. The crude product was purified by running dialysis in cholorform overnight to get polyamine **19** without any further purification; yield: 66%. ***Note!*** Reductive amination is done without separation of regoisomers. So the final product also contains 17% branched isomers.^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.52$–1.65 (6H, m), 1.75–1.84 (6H, m), 2.64–2.68 (6H, m), 2.80–3.00 (12H, m), 3.05–3.20 (12H, m), 3.36–3.52 (6H, m), 3.58–3.72 (6H, m), 3.90–4.25 (9H, m), 7.11–7.35 (15H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 20.4$, 25.2, 30.6, 38.8, 41.5, 56.2, 56.4, 67.3, 127.6, 129.3, 129.4, 130.1, 135.7, 158.7; IR (film, KBr): $\tilde{\nu} = 703$, 742, 968, 1029, 1178, 1249, 1361, 1454, 1648, 1741, 2462, 2582, 2933, 3426 cm^{-1}; LR-MS (FAB): $m/z = 1066.10$ $[M+H]^+$.

2-{4-[4-(3,5-Bis-{4-[4-(1-benzyl-2-hydroxyethylamino)-butyl]-piperazin-1-ylmethyl}-benzyl)-piperazin-1-yl]-butylamino}-3-phenylpropan-1-ol (20)

The general procedure for hydrolysis was followed with polyamine **19** (190 mg, 0.178 mmol), to get **20** as an oil; yield: 140 mg (80%). ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.49$–1.52 (12H, m), 2.30–2.33 (6H, m), 2.44–2.48 (12H, m), 2.64–2.68 (12H, m), 2.72–2.79 (6H, m), 2.83–2.91 (6H, m), 3.51 (6H, s), 3.32–3.36 (6H, m), 3.51 (6H, s), 3.62–3.67 (3H, m), 7.15–7.32 (15H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.9$, 31.6, 38.1, 47.0, 49.7, 53.2, 53.5, 58.7, 60.0, 63.2, 126.8, 128.8, 128.9, 129.5, 138.7; IR (film, KBr): $\tilde{\nu} = 700$, 746, 804, 1029, 1095, 1261, 1373, 1454, 1602, 2809, 2871, 2933, 3378 cm^{-1}; LR-MS (FAB): $m/z = 988.2$ $[M+H]^+$.

General Procedure for Hydrogen Transfer Reduction of Acetophenone

To a solution of $[RuCl_2(p\text{-cymene})]_2$ (2 mol%) in 2 mL of dry isopropyl alcohol, chiral polyamino alcohol ligand (4 mol%) was added under an inert atmosphere. The suspension was stirred and heated at 80 °C for 30 min. Then reaction mixture was allowed to cool down to room temperature and 2 mL of KOH (0.1 M in isopropyl alcohol) solution was added followed by the addition of acetophenone (1 mmol). The conversion of acetophenone to 1-phenylethanol and *ee* were determined by gas chromatography. GC conditions; carrier gas 50 kPa He, temperature program of 100 °C for 5 min, then 4 °C min^{-1} to 160 °C and 20 °C min^{-1} to 200 °C; retention times: 11.30 min for (*S*)-1-phenylethanol and 11.50 min for (*R*)-1-phenylethanol. The major enantiomer was (*S*)-1-phenylethanol.

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