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Hydrolytic and Aminolytic Kinetic Resolution of Terminal Bis-Epoxides

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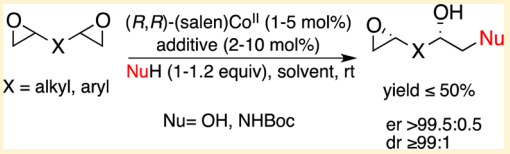
Supporting Information

ABSTRACT: Hydrolytic and aminolytic kinetic resolution of terminal bis-epoxides catalyzed by (salen)Co^{III} complexes affords epoxy-diols and N-protected epoxy-amino alcohols with excellent enantio- and diastereoselectivity and good yields. An operationally simple procedure gives instant access to valuable building blocks containing two remote stereocenters in highly enantioenriched form.



INTRODUCTION

Asymmetric construction of vicinal amino alcohols and diols is an important task due to the regular occurrence of such motifs in biologically active compounds.[1] Among the methods available, the highly selective kinetic resolution of racemic terminal epoxides catalyzed by Jacobsen's (salen)Co^{III} catalyst is frequently used both hydrolytically[2] and aminolytically.[3]

Despite the progress with such methods, the construction of secondary hydroxyl groups with a distal stereocenter is not trivial to achieve with both high enantio- and diastereoselectivity in a controlled manner. For instance, many representatives of the bioactive Annonaceous acetogenins contain such motifs (highlighted in Figure 1). Synthetic strategies for the assembly of such aliphatic units typically involve the synthesis of two separate building blocks, each with the appropriate chiral center, followed by the coupling of these two fragments.[4]

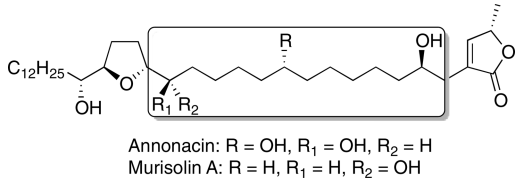
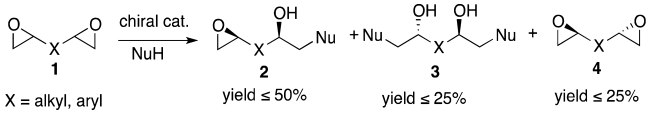


Figure 1. Acetogenins bearing remote hydroxy functionalities.

The hydrolytic and aminolytic kinetic resolution of terminal epoxides is a highly stereoselective method for the formation of 1,2-diols and 1,2-amino alcohols in which up to half of the material can be converted to the product with the desired stereochemistry; in addition, the unreacted epoxide can be recovered in enantioenriched form.[5] In the case of terminal bis-epoxides (**1**; Scheme 1) the situation is slightly different, as it consists of three isomers: *RS* (meso), *RR*, and *SS*. The meso isomer is expected to be resolved to afford **2** in up to 50% yield, while the other two isomers yield diol **3** and unreacted bis-epoxide **4**, respectively. It was envisioned that epoxy-diols and epoxy-amino alcohols of the type **2** would enable further two-directional derivatization, rendering these building blocks important and versatile intermediates.

Scheme 1. Kinetic Resolution of Bis-Epoxides



Surprisingly, very limited attention has been paid to bis-epoxides as substrates in kinetic resolution reactions. Jacobsen and co-workers have resolved D,L-butadiene diepoxide[6] with high ee using water as a nucleophile,[2c] Chow and Kitching have applied a similar strategy in the synthesis of insect pheromones,[7,8] although without directly measuring the ee of the products, and dianhydro sugars have been used as substrates by Yakota and Kakuchi.[9] Furthermore, to date the aminolytic kinetic resolution of terminal bis-epoxides has not been explored.

Herein, we report the first hydrolytic kinetic resolution (HKR) of aromatic bis-epoxides and the aminolytic kinetic resolution (AKR) of bis-epoxides catalyzed by chiral (salen)-Co^{III} complexes.

RESULTS AND DISCUSSION

We began our investigation with *p*- and *m*-bis(epoxyethyl)-benzenes (Table 1), since the products could be easily converted into useful building blocks and we expected that the analysis of the resulting isomer composition would be possible without further derivatizations.

Addition of 1.0 equiv of H_2O together with Jacobsen's catalyst (*R*,*R*)-**5** (5 mol %) and AcOH (10 mol %) as an oxidizing additive to *p*-bis(epoxyethyl)benzene **6** afforded the desired epoxy-diol (*R*,*S*)-**8a** as a major product with essentially complete enantioselectivity (Table 1, entry 1) along with the (*S*,*S*)-tetrol and unreacted (*R*,*R*)-bis-epoxide. However, in addition to compound **8a**, a fair amount of diastereomer **8b**

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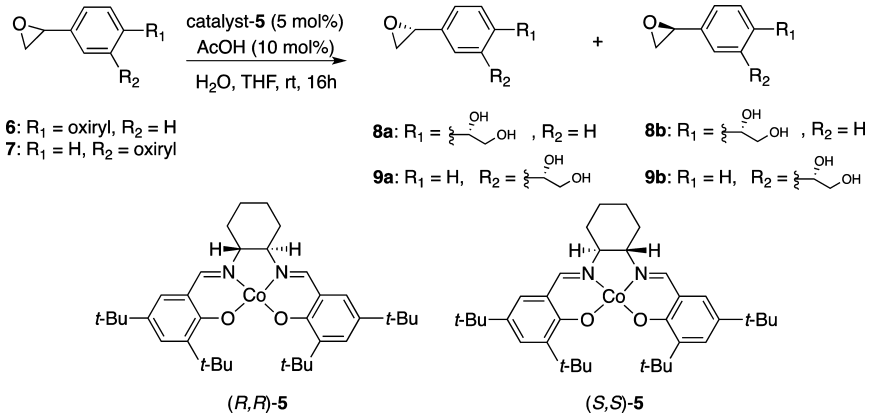
Table 1. Kinetic Resolution of Bis-Epoxides 6 and 7[a]



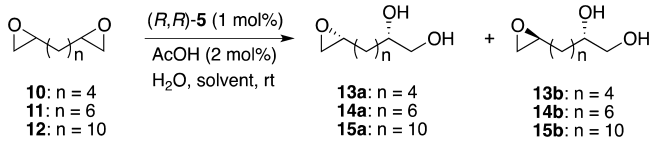
entry	product	cat. 5 confign	H_2O (equiv)[b]	yield[c] (%)	er[d]	dr[e]
1	**8**	*R,R*	1.0	47	>99.9:0.1	82.3:17.7
2[f]	**8**	*S,S*	1.1	37	<0.1:99.9	10.7:89.3
3	**8**	*R,R*	1.2	35	>99.9:0.1	96.2:3.8
4	**8**	*R,R*	1.0	36[g]	>99.9:0.1	95.3:4.7
5	**8**	*R,R*	1 + 0.4[h]	28	>99.9:0.1	98.8:1.2
6[f]	**9**	*S,S*	1.0	47	<0.1:99.9	14:86[i]

[a]Experimental conditions: reactions were run on a 1.2 mmol scale in THF (4 M) at room temperature with 5 mol % of catalyst and 10 mol % of AcOH. [b]Amount (in equiv) of H_2O used relative to bis-epoxide. [c]Yield of isolated product based on bis-epoxide. [d]Determined by chiral HPLC. [e]Determined by chiral HPLC. [f]The opposite stereoisomeric series was obtained. [g]Reaction time 96 h. [h]After 16 h the product was isolated and resubmitted to HKR conditions with an additional 0.4 equiv of H_2O for another 16 h. [i]Determined by NMR.

was formed. We speculated that **8b** results from the incomplete conversion of this particular isomer to the corresponding (*S,S*)-tetrol and therefore expected that prolonged reaction time and/or a small excess of water would improve the dr. Gratifyingly, when 1.1 equiv of H_2O was used the dr improved, while the enantiomeric purity of epoxy-diol **8** remained unchanged (entry 2), and increasing the amount of water to 1.2 equiv further improved the dr (entry 3). This observation is in accordance with the model, developed by Schreiber et al. in 1987, which estimates the effect of substrate and reagent concentrations of group and face selective addition reactions leading to terminus differentiation in a two-directional chain synthesis strategy.[10] Running the reaction for 4 days with 1.0 equiv of H_2O afforded dr and er values similar to those obtained using excess water (compare entries 4 and 3). After resubmitting the product from entry 1 to the kinetic resolution conditions with 0.4 equiv of water, the dr was improved up to 98.8:1.2, although at the cost of the yield (entry 5). Similarly, when *m*-bis(epoxyethyl)-benzene (**7**) was used as a substrate, epoxy-diol **9** was obtained in excellent er and with high dr (entry 6).

Next we applied the HKR strategy to aliphatic substrates (Table 2). The resolution of bis-epoxides **10**–**12** with 0.95–1.15 equiv of water in the presence of Jacobsen's catalyst **5** afforded the epoxy-diols **13a**–**15a**, respectively, in good yields (37–47%)[11] and excellent enantio- and diastereoselectivity (entries 1–4). In comparison to the aromatic bis-epoxides the aliphatic substrates were more reactive, leading to shorter reaction times and affording only a negligible amount of the undesired diastereomer (**13b**–**15b**, respectively). It should be noted that bis-epoxide **12** afforded the epoxy-diol **15a** in slightly lower enantioselectivity, but neither changing the solvent to THF (entry 5) nor using TsOH as a catalyst activator[12] (entry 6) improved the situation. In addition, to measure the mass balance of the reaction, for entry 5 we isolated the unreacted enantiomerically enriched bis-epoxide **12**

Table 2. HKR of Aliphatic Bis-Epoxides[a]



entry	product	H_2O (equiv)	solvent	yield[b] (%)	er[c]	dr[d]
1	**13**	1.0	*i*PrOH	39	99.9:0.1	99.8:0.2
2	**14**	1.0	*i*PrOH	37	99.5:0.5	99.4:0.6
3	**15**	0.95	*i*PrOH	47	97:3	98.4:1.6
4[e]	**15**	1.15	*i*PrOH	46	3:97	0.3:99.7
5[f]	**15**	1.05	THF	44	97:3	99.2:0.8
6[g]	**15**	1.05	THF	41	7:93	nd[h]

[a]Experimental conditions: reactions were typically run on a 1 mmol scale in the appropriate solvent (2 M) with 1–2 mol % of catalyst and 2–4 mol % of additive. [b]Isolated yield of epoxy-diol based on bis-epoxide. [c]Determined by chiral HPLC. [d]Determined by chiral HPLC. [e](*S,S*)-**5** was used. [f]2 mol % of (*R,R*)-**5** and 4 mol % of additive were used. [g]4 mol % TsOH was used as an additive together with 2 mol % of (*S,S*)-**5**. [h]Not determined.

in 16% yield and the corresponding tetradecane-1,2,13,14-tetrol in 22% yield. In general, both *i*PrOH and THF performed well as solvents and a high initial concentration of bis-epoxide (2 M) was crucial for the success of the reaction.

Finally we investigated the AKR of aliphatic bis-epoxides. Subjecting **10** to NH_2Cbz, catalyst (*R,R*)-**5**, and AcOH gave amino alcohol **16a** in excellent er and good dr (Table 3, entry 1). However, the reaction was rather slow and required 5 days to reach completion. As was the case in the HKR discussed above, it is speculated that diastereomer **16b** originates from incomplete conversion into the corresponding (*S,S*)-bis-amino alcohol. Bis-epoxide **11** afforded similar results with NH_2Cbz as the nucleophile (entry 2). Surprisingly, increasing the amount

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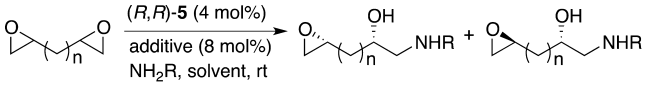
Table 3. AKR of Aliphatic Bis-Epoxides[a]



entry	product	NH_2R (equiv)	time (h)	yield[b] (%)	er[c]	dr[d]
1	**16**	NH_2Cbz[f] (1.0)	120	37	>99.9:0.1	88:12
2	**17**	NH_2Cbz[f] (1.0)	120	38	99.9:0.1	91:9
3	**17**	NH_2Cbz[f] (1.3)	120	37	99.9:0.1	88:12
4	**18**	NH_2Boc[g] (1.05)	16	39	99.2:0.8	99.3:0.7
5[e]	**18**	NH_2Boc[g] (1.05)	16	45	0.2:99.8	1:99
6[e]	**18**	NH_2Boc[g] (1.3)	16	39	0.3:99.7	0.9:99.1

[a]Experimental conditions: reactions were typically run on a 1 mmol scale in THF or MTBE (ca. 2 M) with 4 mol % of catalyst and 8 mol % of additive. [b]Isolated yield of N-protected epoxy-amino alcohol. [c]Determined by chiral HPLC. [d]Determined by chiral HPLC. [e](*S,S*)-**5** was used. [f]AcOH was used as an additive. [g]*p*-Nitrobenzoic acid was used as an additive.

of NH_2Cbz did not improve the outcome, as had been seen in HKR (entry 3).

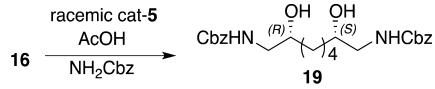
In order to improve the results, we then investigated the effect of the N-protecting group by switching to NH_2Boc as the nucleophile. To our delight, the reaction with NH_2Boc afforded the product **18** (entries 4–6) with equally high enantioselectivity and comparable yield. Notably, in this case, the diastereoselectivity was significantly improved. We also tested 1.3 equiv of NH_2Boc and varied the solvent, but these efforts did not provide any significant change in results. Furthermore, NH_2Boc reacted much faster with the aliphatic bis-epoxides in comparison to NH_2Cbz (overnight vs 5 days), making it the choice of nucleophile in AKR reactions.

To measure the er of aliphatic non-UV active products of HKR and AKR, these compounds were first converted into UV active derivatives via either tosylation (**20**–**22**, Scheme 3) or benzylation (**27**, Scheme 4) and the er was determined by HPLC on a chiral column by comparing with separately synthesized reference materials.

However, the direct measurement of dr of aliphatic products proved more complicated, and therefore a different strategy was used. We reasoned that due to the excellent er of HKR and AKR reactions the only diastereomer present in measurable amount is that possessing the same chirality at the alcohol center and opposite chirality at the epoxide center in comparison to the major KR product. This diastereomer results from the incomplete conversion to the corresponding tetrol or bis-amino alcohol.

To verify this, we opened Cbz-protected epoxy-amino alcohol **16** unselectively to yield **19** as a 88:12 mixture of two diasteromers (Scheme 2) and compared this to the *R,R* and *S,S* isomers of **19**, which were synthesized separately. The identity of the diastereomer detected in **16** was found to be *S,S*, thus being in agreement with our reasoning. The other aliphatic KR products were expected to show a similar diastereomeric preference. Therefore, for the dr analysis we eliminated the secondary hydroxyl center by oxidation to ketone. The

Scheme 2. Diastereomer Analysis for Cbz-Protected AKR Product 16



obtained enantiomers were analyzed by HPLC as a measure of dr for the KR product under scrutiny. In order to achieve a better separation on HPLC and to add UV activity when needed, the remaining keto epoxide was opened unselectively with 2-naphthalenethiol prior to analysis (compounds **23**–**25** in Scheme 3 and compounds **26** and **28** in Scheme 4).

CONCLUSION

We have demonstrated the efficient use of Jacobsen's catalyst for the highly enantio- and diastereoselective synthesis of epoxy-diols and N-protected epoxy-amino alcohols. This novel approach enables the construction of compounds with remote stereocenters in enantiomerically pure form. We are currently applying this methodology to the synthesis of biologically valuable targets.

EXPERIMENTAL SECTION

General Considerations. The ^1H and ^{13}C NMR spectra were recorded at 400.1 and 100.6 MHz, respectively. The chemical shifts for ^1H and ^{13}C are given in ppm relative to residual signals of solvents (for ^1H, $CDCl_3$ δ 7.27 ppm, DMSO-d_6 δ 2.50 ppm, and for ^{13}C, $CDCl_3$ δ 77.0 ppm, DMSO-d_6 δ 39.5 ppm). The following abbreviations are used for multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad singlet. Reactions were monitored by thin-layer chromatography (TLC) and visualized either by UV detection or by submerging into $KMnO_4$ or phosphomolybdic acid solution. Purification of reaction products was performed by flash chromatography using silica gel 60 (0.040–0.063 mm, 230–400 mesh ASTM). In HPLC analysis signals were detected by a diode-array detector. An LTQ Orbitrap analyzer was used in HRMS analysis.

All reagents and solvents were obtained from commercial sources and used without further purification. Aliphatic bis-epoxides were prepared by *m*-CPBA oxidation of the corresponding alkenes. 1,4-Bis(oxiran-2-yl)benzene and 1,3-bis(oxiran-2-yl)benzene were synthesized according to the literature procedure.[13] All HKR and AKR reactions were repeated at least twice, and both catalyst enantiomers ((*R,R*)-**5** and (*S,S*)-**5**) were used.

Determination of Absolute Configuration. We prepared Mosher's ester derivatives[14] from (*R*)-**23** and (*S*)-**23**, derived from HKR products **13a** and ***ent*-13a**, respectively, and from AKR products **18a** and ***ent*-18a**. Analysis of ^1H spectra indicated that the absolute configuration was in agreement with previously published enantiopreferences for HKR[2c] and AKR[3c] reactions. Other absolute configurations were assigned by analogy.

General Procedure for HKR of Terminal Bis-Epoxides. *Procedure for Aliphatic Substrates.* To a 0.05 M solution of the (*R,R*)- or (*S,S*)-(salen)Co^{II} complex (1–2 mol %) in CH_2Cl_2 was added AcOH (2–4 mol %). The mixture was stirred at room temperature open to air for 0.5–1 h, during which time the color turned from dark red to brown. Then the solution was concentrated to dryness in vacuo. The crude solid was resolvated in THF or *i*PrOH (see Table 2) and added to bis-epoxide (1.0 equiv). After the solution was cooled to 0 °C, H_2O was added (0.9–1.1 equiv; see Table 2). The reaction was stirred overnight at room temperature. Then the solvent was removed in vacuo and the residue purified by column chromatography.

Procedure for Aromatic Substrates. Under the same conditions as for aliphatic substrates, reagents used were as follows: (salen)Co^{II}

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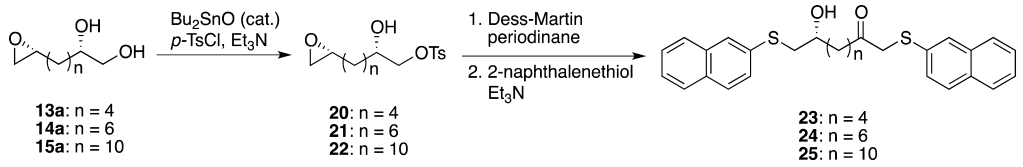
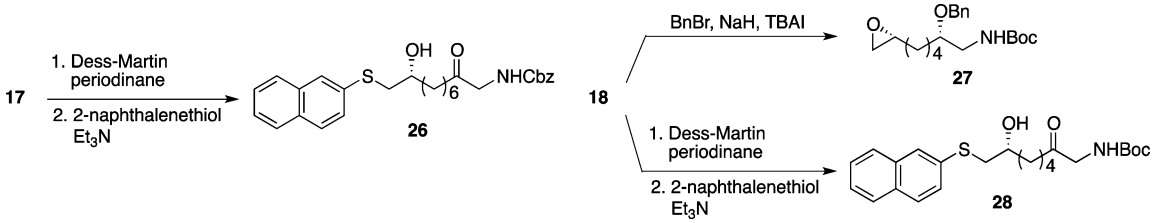
Scheme 3. Derivatization of Aliphatic HKR Products for Chiral HPLC Analysis



Scheme 4. Derivatization of AKR Products for Chiral HPLC Analysis



complex (5 mol %), additive AcOH (10 mol %), H_2O (1.0−1.4 equiv; see Table 1).

(*S*)-1-(4-((*R*)-Oxiran-2-yl)phenyl)ethane-1,2-diol (8). This compound was synthesized according to the general procedure for HKR of bis-epoxides from **6** (413 mg, 2.54 mmol), (*R,R*)-**5** (60 mg, 99.3 μmol), AcOH (11 μL, 0.20 mmol), and H_2O (45 μL, 2.54 mmol). The product was isolated by flash chromatography (1:10 MeOH/CH_2Cl_2) as a beige solid (162 mg, yield 36%). The er >99.9:0.1 and dr 95.3:4.7 were determined by HPLC analysis (CHIRALPAK IB column, 90:10 *n*-hexane/*i*PrOH, 1.0 mL/min, *SR* isomer 19.1 min (major), *SS* isomer 17.4 min (minor)). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.38−7.29 (m, 4 H), 4.84 (d, *J* = 8.0 Hz, 1H), 3.88 (dd, *J* = 3.8, 2.7 Hz, 1H), 3.76−3.78 (m, 1H), 3.64−3.68 (m, 1H), 3.17 (dd, *J* = 5.4, 4.1 Hz, 1H), 2.80−2.83 (m, 1H), 2.73 (bs, 1H), 2.24 (bs, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 140.6, 137.4, 126.3, 125.7, 74.4, 68.0, 52.1, 51.1. IR (ATR) ν_{max} (cm^{-1}): 3377, 3238, 3043, 2965, 2918, 2870, 1464, 1421, 1383, 1335, 1308, 1267, 1080, 1051, 1019, 982, 897, 881, 831, 557. HRMS (ESI): calcd for $C_{10}H_{12}O_3$ $[M + H]^+$ 181.0859, found 181.0859. $[\alpha]^{25}_D$ +30.9 (*c* 1.25, MeOH). Mp: 53.2−54.4 °C.

(*R*)-1-(3-((*S*)-Oxiran-2-yl)phenyl)ethane-1,2-diol (9). This compound was synthesized according to the general procedure for HKR of bis-epoxides from **7** (276 mg, 1.70 mmol), (*S,S*)-**5** (41 mg, 68 μmol), AcOH (8 μL, 0.14 mmol) and H_2O (30 μL, 1.70 mmol). The product was isolated by flash chromatography (1:10 MeOH/CH_2Cl_2) as a yellow oil (146 mg, yield 47%). The er >99.9:0.1 was determined by HPLC analysis (CHIRALPAK IC column, 90:10 *n*-hexane/*i*PrOH, 1.0 mL/min; *RS* isomer 26.0 min). The dr 86:14 was determined by ^{13}C NMR analysis. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.20−7.36 (m, 4H), 4.79 (dd, *J* = 8.0, 3.1 Hz, 1H), 3.86 (dd, *J* = 4.1, 2.6 Hz, 1H), 3.73−3.76 (m, 1H), 3.60−3.65 (m, 1H), 3.15 (bs, 1H), 3.14 (dd, *J* = 5.4, 4.1 Hz, 1H), 2.80 (dd, *J* = 5.4, 2.6 Hz, 1H), 2.66 (bs, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 141.0, 137.9, 128.74 (major isomer), 128.72 (minor isomer), 125.98 (minor), 125.92 (major), 125.21 (minor), 125.16 (major), 123.17 (major), 123.09 (minor), 74.4, 68.0, 52.3, 51.1. IR (ATR) ν_{max} (cm^{-1}): 3352, 3055, 2924, 2874, 1447, 1377, 1323, 1231, 1161, 1072, 1030, 876, 853, 799, 702. HRMS (ESI): calcd for $C_{10}H_{12}O_3$ $[M + H]^+$ 181.0859, found 181.0852. $[\alpha]^{25}_D$ −35.8 (*c* 0.95, MeOH).

(*S*)-6-((*R*)-Oxiran-2-yl)hexane-1,2-diol (13). This compound was synthesized according to the general procedure for HKR of bis-epoxides from **10** (259 mg, 1.82 mmol), (*R,R*)-**5** (11 mg, 18 μmol), AcOH (4 μL, 72 μmol), and H_2O (33 μL, 1.82 mmol). The product **13** was isolated by flash chromatography (7:93 MeOH/CH_2Cl_2) as a pale yellow oil (118 mg, yield 39%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.70−3.59 (m, 2H), 3.43 (dd, *J* = 11.0, 7.4 Hz, 1H), 2.90 (m, 1H), 2.74 (dd, *J* = 5.0, 4.1 Hz, 1H), 2.46 (dd, *J* = 5.0, 2.7 Hz, 1H), 2.35 (bs, 1H), 2.19 (bs, 1H), 1.65−1.34 (m, 8H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 72.1, 66.7, 52.3, 47.0, 32.9, 32.3, 26.0, 25.3. IR (ATR) ν_{max} (cm^{-1}): 3368, 2930, 2859, 1462, 1410, 1257, 1049, 914, 831. HRMS (ESI): calcd for $C_8H_{16}O_3$ $[M + Na]^+$ 183.0992, found 183.0985. $[\alpha]^{25}_D$ −4.61 (*c* 0.76, MeOH).

(*S*)-8-((*R*)-Oxiran-2-yl)octane-1,2-diol (14). This compound was synthesized according to the general procedure for HKR of bis-epoxides from **11** (401 mg, 2.35 mmol), (*R,R*)-**5** (14.2 mg, 23 μmol), AcOH (5 μL, 94 μmol), and H_2O (42 μL, 2.35 mmol). Product **14** was isolated by flash chromatography (7:93 MeOH/CH_2Cl_2) as a pale yellow oil (161 mg, yield 37%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.58−3.66 (m, 2H), 3.39 (dd, *J* = 11.1, 7.6 Hz, 1H), 3.01 (bs, 2H), 2.87−2.91 (m, 1H), 2.73 (dd, *J* = 5.0, 4.1 Hz, 1H), 2.45 (dd, *J* = 5.0 2.7 Hz, 1H), 1.26−1.58 (m, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 72.2, 66.7, 52.4, 47.1, 33.0, 32.3, 29.4, 29.2, 25.8, 25.4. IR (ATR) ν_{max} (cm^{-1}): 3393, 2928, 2856, 1464, 1260, 1059, 914, 831, 733. HRMS (ESI): calcd for $C_{10}H_{20}O_3$ $[M + H]^+$ 189.1485, found 189.1481. $[\alpha]^{25}_D$ −1.88 (*c* 0.75, MeOH).

(*S*)-12-((*R*)-Oxiran-2-yl)dodecane-1,2-diol (15). This compound was synthesized according to the general procedure for HKR of bis-epoxides from **12** (510 mg, 2.25 mmol), (*S,S*)-**5** (14 mg, 22 μmol), AcOH (5 μL, 90 μmol), and H_2O (38 μL, 2.14 mmol). The product **15** was isolated by flash chromatography (4:96 EtOAc/*n*-hexane) as a white solid (250 mg, yield 44%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.64−3.72 (m, 2H), 3.41−3.46 (m, 1H), 2.91 (tdd, *J* = 5.5, 3.9, 2.7 Hz, 1H), 2.76 (dd, *J* = 5.0, 4.1 Hz, 1H), 2.47 (dd, *J* = 5.0 2.7 Hz, 1H), 2.17 (bs, 1H), 2.06 (bs, 1H), 1.26−1.56 (m, 20H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 72.3, 66.8, 52.4, 47.1, 33.2, 32.5, 29.6, 29.5, 29.4, 25.9, 25.5. IR (ATR) ν_{max} (cm^{-1}): 3476, 3314, 2916, 2851, 1470, 1072, 849. HRMS (ESI): calcd for $C_{14}H_{28}O_3$ $[M + H]^+$ 245.2111, found 245.2106. $[\alpha]^{25}_D$ +6.0 (*c* 1.15, $CHCl_3$). Mp: 60.0−61.3 °C.

General Procedure for AKR of Terminal Bis-Epoxides. To a 0.05 M solution of the (*R,R*)- or (*S,S*)-(salen)Co^{II} complex (4 mol %) in CH_2Cl_2 was added AcOH (8 mol %) or *p*-nitrobenzoic acid (8 mol %) as additive (see Table 3). The mixture was stirred at room temperature open to air for 0.5−1 h, during which time the color changed from dark red to brown. Then the solution was concentrated to dryness in vacuo. The crude solid was resolvated in THF or MTBE and added to bis-epoxide (1.0 equiv). After the solution was cooled to 0 °C, NH_2Cbz or NH_2Boc was added (1.0−1.3 equiv, see Table 3). In the case of $BocNH_2$ as nucleophile, the reaction mixture was stirred 16 h at room temperature, and with $CbzNH_2$, 5 days. Then the mixture was concentrated in vacuo and purified by flash chromatography.

Benzyl((*S*)-2-hydroxy-6-((*R*)-oxiran-2-yl)hexyl)carbamate (16). This compound was synthesized according to the general procedure for AKR of bis-epoxides from **10** (200 mg, 1.40 mmol), (*R,R*)-**5** (37 mg, 61 μmol), AcOH (7 μL, 0.12 mmol), and NH_2Cbz (212 mg, 1.40 mmol). The product **16** was isolated by flash chromatography (1:1 *n*-hexane/EtOAc) as a beige solid (151 mg, yield 37%). The er >99.9:0.1 was determined by HPLC analysis (Phenomenex LUX Cellulose-1 column, 90:10 *n*-hexane/*i*PrOH, 1.5 mL/min, major isomer 20.6 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.30−7.36 (m, 5H), 5.26 (bs, 1H), 5.11 (s, 2H), 3.71 (bs, 1H), 3.34−

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3.40 (m, 1H), 3.04−3.11 (m, 1H), 2.90 (bs, 1H), 2.75 (dd, J = 4.9, 4.0 Hz, 1H), 2.46 (dd, J = 4.9, 2.7 Hz, 1H), 2.42−2.43 (m, 1H), 1.45−1.59 (m, 8H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 157.1, 136.4, 128.5, 128.1, 128.0, 71.1, 66.9, 52.2, 47.0, 34.5, 32.2, 26.0, 25.2. IR (ATR) ν_{max} (cm^{-1}): 3327, 3250, 3092, 3047, 3032, 2934, 2916, 2850, 1690, 1553, 1261, 1152, 1113, 1029, 972, 833, 756, 685. HRMS (ESI): calcd for $C_{16}H_{23}NO_4$ $[M + H]^+$ 294.1700, found 294.1696. $[\alpha]^{25}_D$ +12.08 (c 1.59, $CHCl_3$). Mp: 66.0−66.8 °C.

Benzyl((*S*)-2-hydroxy-8-((*R*)-oxiran-2-yl)octyl)carbamate (17). This compound was synthesized according to the general procedure for AKR of bis-epoxides from **11** (200 mg, 1.17 mmol), (*R*,*R*)-**5** (30 mg, 50 μmol), AcOH (5 μL, 94 μmol), and NH_2Cbz (177 mg, 1.17 mmol). The product was isolated by flash chromatography (1:1 *n*-hexane/EtOAc) as a white solid (143 mg, yield 38%). The er 99.9:0.1 was determined by HPLC analysis (Phenomenex LUX Cellulose-1 column, 90:10 *n*-hexane/*i*PrOH, 1.5 mL/min, major isomer 18.2 min, minor isomer 21.7 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.31−7.37 (m, 5H), 5.18 (bs, 1H), 5.12 (s, 2H), 3.71 (bs, 1H), 3.36−3.42 (m, 1H), 3.04−3.11 (m, 1H), 2.88−2.93 (m, 1H), 2,75 (dd, J = 5.0, 4.0 Hz, 1H), 2.47 (dd, J = 5.0, 2.8 Hz, 1H), 2,14 (bs, 1H), 1.26−1.56 (m, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 157.1, 136.4, 128.5, 128.1, 71.3, 66.9, 52.3, 47.1, 47.0, 34.7, 32.4, 29.4, 29.3, 25.9, 25.3. IR (ATR) ν_{max} (cm^{-1}): 3385, 3304, 3088, 3062, 3035, 2914, 2851, 1713, 1666, 1560, 1285, 1265, 1155, 1096, 1024, 914, 839, 743, 697, 583. HRMS (ESI): calcd for $C_{18}H_{27}NO_4$ $[M + H]^+$ 322.2013, found 322.2012. $[\alpha]^{25}_D$ +11.58 (c 1.33, $CHCl_3$). Mp: 51.9−52.9 °C.

***tert*-Butyl((*S*)-2-hydroxy-6-((*R*)-oxiran-2-yl)hexyl)carbamate (18).** This compound was synthesized according to the general procedure for AKR of bis-epoxides from **10** (159 mg, 1.12 mmol), (*S*,*S*)-**5** (20 mg, 33 μmol), *p*-nitrobenzoic acid (11 mg, 67 μmol), and NH_2Boc (138 mg, 1.18 mmol). The product was isolated by flash chromatography (7:93 MeOH/CH_2Cl_2) as a pale yellow oil (133 mg, yield 45%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 5.06 (bs, 1H), 3.65 (bs, 1H), 3.24−3.29 (m, 1H), 2.83−2.91 (m, 2H), 2.73 (dd, J = 5.0, 4.1 Hz, 1H), 2.44 (dd, J = 5.0 2.7 Hz, 1H), 1.35−1.58 (m, 17H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 156.8, 79.5, 71.3, 52.2, 47.0, 46.6, 34.5, 32.2, 28.3, 25.9, 25.2. IR (ATR) ν_{max} (cm^{-1}): 3385, 2934, 2860, 1717, 1452, 1274, 1177, 1113, 1070, 1025, 713. HRMS (ESI): calcd for $C_{13}H_{25}NO_4$ $[M + H]^+$ 260.1856, found 260.1852. $[\alpha]^{25}_D$ +16.0 (c 1.43, $CHCl_3$).

Dibenzyl((2*S*,7*R*)-2,7-dihydroxyoctane-1,8-diyl)dicarbamate (19). This compound was synthesized according to the general procedure for AKR of bis-epoxides from **16** (55 mg, 0.18 mmol), (*R*,*R*)-**5** (5 mg, 8 μmol), (*S*,*S*)-**5** (5 mg, 8 μmol), AcOH (1 μL, 17 μmol), and NH_2Cbz (30 mg, 0.19 mmol). The product **19** was isolated by flash chromatography (1:15 MeOH/CH_2Cl_2) with a yield of 34% (28.8 mg). The retention time of **19** in HPLC analysis was compared against the retention times of Cbz-protected (*S*,*S*)- and (*R*,*R*)-bis-amino alcohols retrieved from the AKR reactions. The dr 88:12 was determined by HPLC analysis (Phenomenex LUX Cellulose-1 column, 85:15 *n*-hexane/*i*PrOH, 1.5 mL/min, *RS* isomer 13.9 min (major), *SS* isomer 25.0 min (minor)). ^{1}H NMR (400.1 MHz, DMSO-d_6): δ 7.30−7.38 (m, 10H), 7.11 (dd, J = 5.7, 5.7 Hz, 2H), 5.01 (s, 4H), 4.53 (d, J = 5.1 Hz, 2H), 3.44 (bs, 2H), 2.90−3.01 (m, 4H), 1.17−1.40 (m, 8H). ^{13}C NMR (100.6 MHz, DMSO-d_6): δ 156.2, 137.2, 128.3, 127.7, 127.6, 69.0, 65.1, 46.9, 34.4, 25.2. HRMS (ESI): calcd for $C_{24}H_{32}N_2O_6$ $[M + H]^+$ 445.2333, found 445.2329.

General Procedure for Tosylation of Aliphatic Epoxy-Diols.[15] To a ∼0.35 M solution of epoxy-diol (1.0 equiv) in CH_2Cl_2 was added Bu_2SnO (0.02 − 0.04 equiv), Et_3N (1.0 equiv), and *p*-TsCl (1.0 equiv). The reaction was stirred overnight at room temperature. Then the mixture was diluted with CH_2Cl_2 and added $NaHCO_3$ (saturated aqueous). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2. The collected organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography.

(*S*)-2-Hydroxy-6-((*R*)-oxiran-2-yl)hexyl-4-methylbenzenesulfonate (20). This compound was synthesized according to the general procedure for tosylation of epoxy-diols from **13** (121 mg, 0.75 mmol), *p*-TsCl (144 mg, 0.75 mmol), Bu_2SnO (5 mg, 22 μmol), and Et_3N (105 μL, 0.75 mmol). The product **20** was purified by flash chromatography (1:15 MeOH/CH_2Cl_2) with a yield of 69% (164 mg). The er 99.9:0.1 was determined by HPLC analysis (CHIRALPAK IA column, 85:15 *n*-hexane/*i*PrOH, 1.5 mL/min; minor isomer 10.1 min, major isomer 14.9 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.79−7.82 (m, 2H), 7.36 (d, J = 8.0 Hz, 2H), 4.01−4.04 (m, 1H), 3.84−3.91 (m, 2H), 2.86−2.90 (m, 1H), 2.74 (dd, J = 5.0, 4.0 Hz, 1H), 2.44−2.45 (m, 4H), 2.24 (bs, 1H), 1.26−1.57 (m, 8H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 145.0, 132.6, 129.9, 127.8, 73.8, 69.1, 52.1, 46.9, 32.5, 32.1, 25.7, 24.9, 21.5. HRMS (ESI): calcd for $C_{15}H_{22}O_5S$ $[M + H]^+$ 315.1260, found 315.1258.

(*S*)-2-Hydroxy-8-((*R*)-oxiran-2-yl)octyl-4-methylbenzenesulfonate (21). This compound was synthesized according to the general procedure for tosylation of epoxy-diols from **14** (45 mg, 0.23 mmol), *p*-TsCl (45 mg, 0.23 mmol), Bu_2SnO (2 mg, 9 μmol), and Et_3N (33 μL, 0.23 mmol). The product **21** was purified by flash chromatography (1:15 MeOH/CH_2Cl_2) with a yield of 88% (71 mg). The er 99.5:0.5 was determined by HPLC analysis (Phenomenex LUX Cellulose-1 column, 90:10 *n*-hexane/*i*PrOH, 1.5 mL/min; minor isomer 15.2 min, major isomer 23.2 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.77−7.80 (m, 2H), 7.32−7.36 (m, 2H), 4.01 (dd, J = 10.0, 2.9 Hz, 1H), 3.81−3.89 (m, 2H), 2.86−2.90 (m, 1H), 2.72−2.74 (m, 1H), 2.43−2.46 (m, 4H), 2.30 (bs, 1H), 1.24−1.54 (m, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 145.0, 132.7, 129.9, 127.9, 73.9, 69.4, 52.3, 47.0, 32.6, 32.3, 29.4, 29.2, 25.8, 25.0, 21.6. HRMS (ESI): calcd for $C_{17}H_{26}O_5S$ $[M + H]^+$ 343.1574, found 343.1571.

(*S*)-2-Hydroxy-12-((*R*)-oxiran-2-yl)dodecyl-4-methylbenzenesulfonate (22). This compound was synthesized according to the general procedure for tosylation of epoxy-diols from **15** (178 mg, 0.72 mmol), *p*-TsCl (145 mg, 0.76 mmol), Bu_2SnO (3 mg, 14 μmol), and Et_3N (101 μL, 0.72 mmol). The product **22** was purified by flash chromatography (1:50 MeOH/CH_2Cl_2) with a yield of 87% (253 mg). The er 97:3 was determined by HPLC analysis (Phenomenex LUX Cellulose-1 column, 90:10 *n*-hexane/*i*PrOH, 1.5 mL/min, major isomer 8.83 min, minor isomer 9.94 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.79−7.82 (m, 2H), 7.37−7.33 (m, 2H), 4.04 (dd, J = 9.5, 2.6 1H), 3.80−3.90 (m, 2H), 2.91 (tdd, J = 5.5, 3.9, 2.6 Hz, 1H), 2.76 (dd, J = 5.1, 3.9 Hz, 1H), 2.46−2.48 (m, 4H), 2.09 (d, J = 4.7 Hz, 1H), 1.25−1.63 (m, 20H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 145.0, 132.7, 129.9, 127.9, 74.0, 69.5, 52.4, 47.1, 32.6, 32.5, 29.5, 29.4, 29.2, 25.9, 25.2, 21.6. HRMS (ESI): calcd for $C_{21}H_{34}O_5S$ $[M + H]^+$ 399.2199, found 399.2192.

General Procedure for Oxidation/Thiolation. To a 0.06 M solution of epoxy-alcohol (1.0 equiv) in CH_2Cl_2 was added Dess−Martin reagent (in excess, 1.5−6.0 equiv). The reaction was stirred overnight at room temperature under an argon atmosphere. Then the mixture was concentrated in vacuo and filtered through a silica plug. The oxidized compound was then subjected to a thiolation reaction, where to a 0.05 M solution of epoxide (1.0 equiv) and 2-naphthalenethiol (in excess, 1.5−6.0 equiv) in MeOH was added Et_3N (in excess, 1.5−6.0 equiv). After the reaction mixture was stirred overnight, it was concentrated in vacuo and purified by flash chromatography.

(*R*)-7-Hydroxy-1,8-bis(naphthalen-2-ylthio)octan-2-one (23). This compound was synthesized according to the general procedure for oxidation/thiolation from **20** (97 mg, 0.31 mmol) and Dess−Martin periodinane (196 mg, 0.46 mmol) and continued with oxidized product (82 mg, 0.26 mmol), 2-naphthalenethiol (255 mg, 1.59 mmol), and Et_3N (220 μL, 1.58 mmol). The product **23** was purified by flash chromatography (1:20 MeOH/CH_2Cl_2) with 75% yield (77 mg) over two steps. The er 99.8:0.2 was determined by HPLC analysis and is referred to as the dr of **13** in Table 2 (CHIRALPAK IA column, 90:10 *n*-hexane/*i*PrOH, 1.5 mL/min, major isomer 30.3 min, minor isomer 32.2 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.73−7.82 (m, 8H), 7.40−7.51 (m, 6H), 3.75 (s, 2H), 3.62−3.68 (m, 1H), 3.17 (dd, J = 13.7, 3.5 Hz, 1H), 2.87 (dd, J = 13.7, 8.6 Hz, 1H), 2.61 (t, J = 7.1 Hz, 2H), 1.23−1.63 (m, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 205.4, 133.7, 132.6, 132.2, 132.0, 128.7, 128.6, 128.2, 127.8, 127.7, 127.2, 127.1, 126.7, 126.6, 126.1, 126.0, 69.2, 43.7, 42.1, 40.3, 35.7,

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25.1, 23.6. HRMS (ESI): calcd for $C_{28}H_{28}O_2S_2$ $[M - H]^-$ 459.1458, found 459.1446.

(*R*)-9-Hydroxy-1,10-bis(naphthalen-2-ylthio)decan-2-one (24). This compound was synthesized according to the general procedure for oxidation/thiolation from **21** (22 mg, 66 μmol) and Dess–Martin periodinane (41 mg, 99 μmol) and continued with oxidized product (11 mg, 34 μmol), 2-naphthalenethiol (21 mg, 130 μmol), and Et_3N (10 μL, 130 μmol). The product **24** was purified by flash chromatography (2:3 EtOAc/*n*-hexanes) with 47% yield (7 mg) over two steps. The er 99.4:0.6 was determined by HPLC analysis and is referred to as the dr of **14** in Table 2 (Phenomenex LUX Cellulose-1 column, 70:30 *n*-hexane/*i*PrOH, 1.5 mL/min, major isomer 10.2 min, minor isomer 12.4 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.73–7.83 (m, 8H), 7.40–7.51 (m, 6H), 3.74–3.77 (m, 2H), 3.64–3.71 (m, 1H), 3.22 (dd, *J* = 13.7, 3.5 Hz, 1H), 2.91 (dd, *J* = 13.7, 8.6 Hz, 1H), 2.59 (t, *J* = 7.2 Hz, 2H), 1.22–1.58 (m, 10H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 205.7, 133.7, 132.7, 132.1, 132.0, 129.0, 128.7, 128.6, 128.3, 127.9, 127.7, 127.6, 127.5, 127.2, 127.1, 126.7, 126.6, 126.2, 126.0, 125.7, 69.4, 43.8, 42.2, 40.5, 36.0, 29.2, 28.9, 25.4, 23.6. MS (ESI) calcd for $C_{30}H_{32}O_2S_2$ $[M + H]^+$ 489.1917, found 489.1902.

(*R*)-13-Hydroxy-1,14-bis(naphthalen-2-ylthio)tetradecan-2-one (25). This compound was synthesized according to the general procedure for oxidation/thiolation from **22** (10 mg, 25 μmol) and Dess–Martin periodinane (60 mg, 141 μmol) and continued with oxidized product (4 mg, 10 μmol) and 2-naphthalenethiol (10 mg, 62 μmol). The product **25** was purified by flash chromatography (1:10:10 EtOAc/CH_2Cl_2/petroleum ether) with 78% yield (5 mg) over two steps. The er 99.2:0.8 was determined by HPLC analysis and is referred to as the dr of **15** in Table 2 (Phenomenex LUX Cellulose-1 column, 80:20 *n*-hexane/*i*PrOH, 1.5 mL/min, minor isomer 14.5 min, major isomer 17.6 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.74–7.83 (m, 8H), 7.41–7.51 (m, 6H), 3.77 (s, 2H), 3.71 (m, 1H), 3.26 (dd, *J* = 13.7, 3.3 Hz, 1H), 2.94 (dd, *J* = 13.7, 8.7 Hz, 1H), 2.59–2.63 (m, 2H), 2.44 (d, *J* = 2.9 Hz, 1H), 1.20–1.59 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 205.8, 133.7, 132.7, 132.3, 132.0, 131.9, 128.7, 128.6, 128.2, 127.8, 127.7, 127.6, 127.2, 127.1, 126.7, 126.0, 125.9, 69.4, 43.8, 42.1, 40.7, 36.2, 29.5, 29.4, 29.3, 29.1, 25.6, 23.8. HRMS (ESI): calcd for $C_{34}H_{40}O_2S_2$ $[M - H]^-$ 543.2397, found 543.2389.

(*R*)-Benzyl(9-hydroxy-10-(naphthalen-2-ylthio)-2-oxodecyl)-carbamate (26). This compound was synthesized according to the general procedure for oxidation/thiolation from **17** (86 mg, 0.24 mmol) and Dess–Martin periodinane (171 mg, 0.37 mmol) and continued with oxidized product (53 mg, 0.16 mmol), 2-naphthalenethiol (40 mg, 0.25 mmol), and Et_3N (35 μL, 0.25 mmol). Product **26** was purified using flash chromatography (3:4 EtOAc/*n*-hexanes) with 88% yield over two steps (77 mg). The er 91.6:8.4 was determined by HPLC analysis and is referred to as the dr of **17** in Table 3 (CHIRALPAK IB column, 85:15 *n*-hexane/*i*PrOH, 1.5 mL/min, major isomer 26.3 min, minor isomer 33.4 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.75–7.84 (m, 4H), 7.44–7.51 (m, 3H), 7.31–7.37 (m, 5H), 5.48 (bs, 1H), 5.12 (s, 2H), 4.07 (d, *J* = 4.4 Hz, 2H), 3.71 (ddt, *J* = 8.7 5.9, 3.2 Hz, 1H), 3.25 (dd, *J* = 13.7, 3.2 Hz, 1H), 2.94 (dd, *J* = 13.7, 8.7 Hz, 1H), 2.4 (t, *J* = 7.5 Hz, 1H), 1.29–1.61 (m, 10H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 205.2, 156.1, 136,3, 133.7, 132.7, 132.0, 128.6, 128.5, 128.2, 128.1, 128.0, 127.8, 127.7, 127.1, 126.6, 125.9, 69.4, 67.0, 50.5, 42.1, 39.9, 36.0, 29.2, 28.9, 25.4, 23.5. HRMS (ESI): calcd for $C_{28}H_{33}NO_4S$ $[M + H]^+$ 480.2203, found 480.2184.

***(R)*-*tert*-Butyl(7-hydroxy-8-(naphthalen-2-ylthio)-2-oxooctyl)carbamate (28).** This compound was synthesized according to the general procedure for oxidation/thiolation from **18** (16 mg, 63 μmol) and Dess–Martin periodinane (40 mg, 94 μmol) and continued with oxidized product (7 mg, 27 μmol), 2-naphthalenethiol (6 mg, 41 μmol), and Et_3N (5 μL, 36 μmol). Product **28** was purified using flash chromatography (3:4 EtOAc/*n*-hexanes) with 63% yield over two steps (8 mg) (58% yield over two steps). The er 99.3:0.7 was determined by HPLC analysis and is referred to as the dr of **18** in Table 3 (Phenomenex LUX Cellulose-1 column, 85:15 *n*-hexane/*i*PrOH, 1.0 mL/min, minor isomer 17.3 min, major isomer 19.9 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.75–7.84 (m, 4H), 7.44–7.52 (m, 3H), 5.2 (bs, 1H), 3.98 (d, *J* = 4.4 Hz, 2 H), 3.68–3.74 (m, 1H), 3.22–3.26 (dd, *J* = 13.7, 3.4 Hz, 1H), 2.94 (dd, *J* = 13.7, 8.7 Hz, 1H), 2.41 (t, *J* = 7.3, 2H), 1.27–1.67 (m, 15H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 205.6, 155.6, 133.7, 132.6, 132.1, 128.7, 128.4, 127.9, 127.7, 127.2, 126.7, 126.0, 79.8, 69.2, 50.3, 42.2, 39.8, 35.7, 28.3, 25.2, 23.5. HRMS (ESI): calcd for $C_{23}H_{31}NO_4S$ $[M + Na]^+$ 440.1866, found 440.1858.

***tert*-Butyl((*S*)-2-(benzyloxy)-6-((*R*)-oxiran-2-yl)hexyl)-carbamate (27).** To a solution of epoxy-amino alcohol **18** (20 mg, 77 μmol) in THF (1.5 mL) were added NaH (4.6 mg, 115 μmol), benzyl bromide (12 μL, 100 μmol), and tetrabutylammonium iodide (5.7 mg, 15.4 μmol) under an argon atmosphere and stirred overnight. Then the reaction was quenched with $NaHCO_3$ (saturated aqueous) and washed with brine. The organic phase was dried over $MgSO_4$ and concentrated in vacuo. The obtained crude product was purified by flash chromatography (10:90 EtOAc/*n*-hexanes) to afford 14 mg of the benzylated product **27** with 52% yield. The er 99.8:0.2 was determined by HPLC analysis (CHIRALPAK IC column, 94:6 *n*-hexane/*i*PrOH, 1.0 mL/min, minor isomer 24.4 min, major isomer 27.8 min). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.27–7.38 (m, 5H), 4.81 (bs, 1H), 4.51–4.58 (m, 2H), 3.45–3.54 (m, 1H), 3.35–3.41 (m, 1H), 3.11–3.17 (m, 1H), 2.88–2.92 (m, 1H), 2.75 (dd, *J* = 5.0, 3.9 Hz, 1H), 2.46 (dd, *J* = 5.0 2.7 Hz, 1H), 1.26–1.66 (m, 17H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 156.1, 138.5, 128.4, 127.8, 127.7, 79.2, 77.9, 71.3, 52.2, 47.0, 43.2, 32.3, 31.8, 28.4, 26.1, 25.1. HRMS (ESI): calcd for $C_{20}H_{31}NO_4$ $[M + H]^+$ 350.2326, found 350.2320.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving ^{1}H and ^{13}C NMR spectra, ^{1}H data of Mosher ester derivatives, and chromatograms from chiral HPLC analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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