Chapter 2

Direct and Enantioselective Conversion of Aliphatic Aldehydes to Terminal Epoxides

Introduction

Epoxides constitute one of the most powerful synthons in synthetic organic chemistry. Their ability to react with a wide range of nucleophiles stereospecifically to generate alcohol stereocenters has made epoxides a common intermediate in both organic synthesis[1] and nature.[2] Over the past few decades, a host of catalytic methodologies have been developed towards the asymmetric construction of epoxides[3] and excellent selectivities have been achieved for a broad range of substrates including allylic alcohols,[4] α,β-unsaturated carbonyls,[5] and styrene derivatives.[6] However, at the time of this work, there were surprisingly few methods for the catalytic enantioselective construction of terminal aliphatic epoxides. For the past ten years, the state of the art for

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[1] (a) Nicolaou, K. C.; Sorensen, E. J. *Classics in Total Synthesis*; VCH: Weinheim, 1996; pp 293–315. (b) Nicolaou, K. C.; Snyder, S. A. *Classics in Total Synthesis II*; Wiley-VCH; Weinheim, 2003; pp 137–159.

[2] Stryer, L. *Biochemistry*; W. H. Freeman and Company; New York, 1995; pp 695.

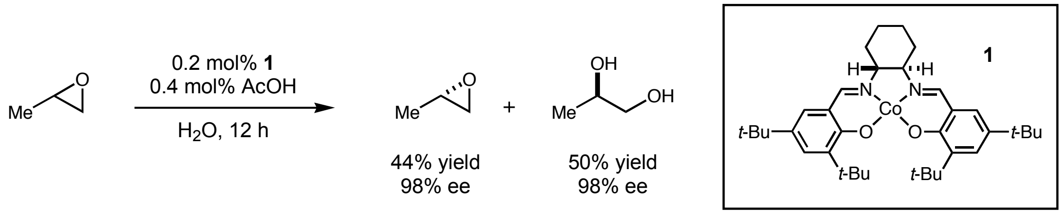
[3] Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*; Springer; Berlin, 1999; Vol. 2.

[4] (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

[5] Berkessel, A. in *Asymmetric Synthesis: the Essentials*; Christmann, M.; Braese, S., Eds.; Wiley-VCH; Weinheim, 2007; pp 176–180.

[6] See reference 3 and (a) Rose, E.; Ren Q.-Z.; Andrioletti, B. *Chem. Eur. J.* **2004**, *10*, 224. (b) Hickey, M.; Goeddel, D.; Crane, Z.; Shi, Y. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5794. (c) Bulman Page, P. C.; Buckley, B. R.; Blacker, A. J. *Org. Lett.* **2004**, *6*, 1543.

directly obtaining terminal epoxides in an enantioenriched form has been the cobalt(III)-salen catalyzed kinetic resolution developed by Jacobsen (equation 1).[7] With catalyst loadings as low as 0.2 mol%, epoxides can be obtained in exceedingly high enantioselectivities (98-99% ee) and isolated yields up to 46%.



(1)

Alternatively, Shi and coworkers have developed a two-step process for generating terminal epoxides via the ketone-catalyzed asymmetric epoxidation of vinylsilanes, which may be secondarily treated with tetrabutylammonium fluoride (TBAF) to reveal the terminal epoxide (equation 2).[8] Excellent selectivities (up to 92% ee) in good-to-moderate yields were obtained but required catalyst loadings of 65 mol%. Subsequent to this work, Shi reported a single example of a direct enantioselective epoxidation of a terminal aliphatic olefin, vinylcyclohexanone, which was converted to the terminal epoxide in 93% yield and 71% ee (equation 3).[9] However, this was the only aliphatic terminal epoxide the authors reported.[10]

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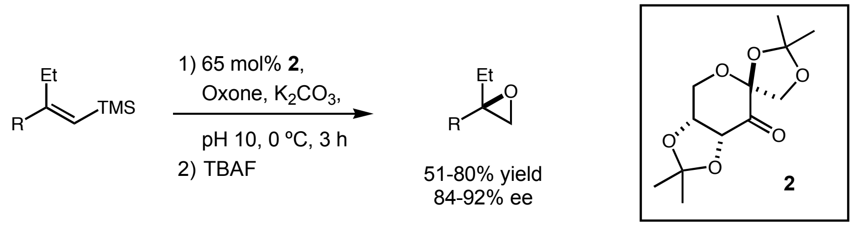
[7] (a) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936. (b) Larrow, J. F.; Schaus, S. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1996**, *118*, 7420. (c) Robinson, D. E. J. E.; Bull, S. D. *Tetrahedron Asymmetry* **2003**, *14*, 1407.

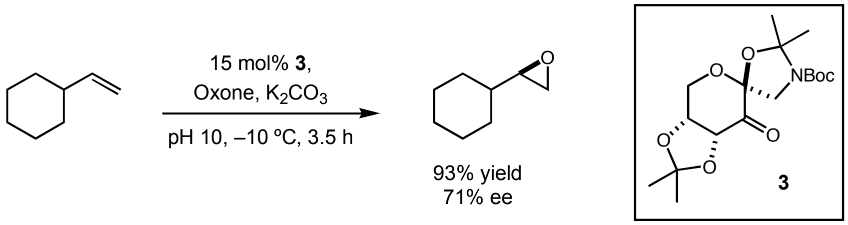
[8] Warren, J. D.; Shi, Y. *J. Org. Chem.* **1999**, *64*, 7675.

[9] (a) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem.* **2002**, *67*, 2435. (b) Tian, H.; She, X.; Xu, J.; Shi, Y. *Org. Lett.* **2001**, *3*, 1929.

[10] Asymmetric epoxidation of terminal aliphatic olefins catalyzed by transition metals has recently been accomplished: (a) Calladon, M.; Scarso, A.; Sgarbossa, P.; Michelin, R. A.; Strukul, G. *J. Am. Chem. Soc.* **2006**, *128*, 14006. (b) Sawada, Y.; Matsumoto, K.; Katsuki, T. *Angew. Chem. Int. Ed.* **2007**, *46*, 4559.

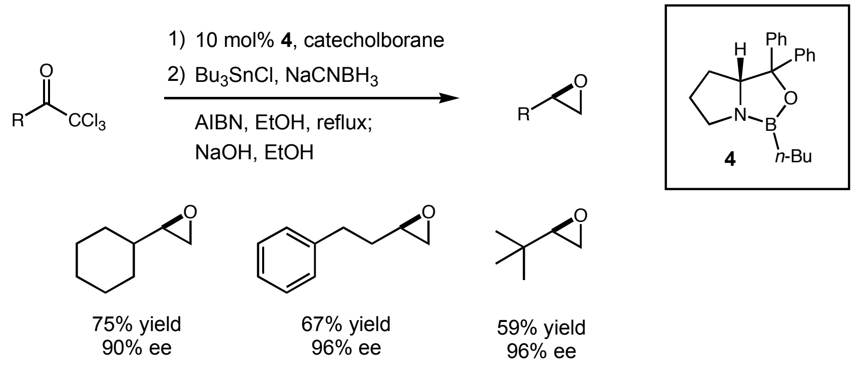


(2)



(3)

An alternative strategy for preparing unfunctionalized terminal epoxides is the base-induced cyclization of chiral halohydrins. Corey and Helal developed a two-step process for the asymmetric synthesis of chiral halohydrins with subsequent cyclization to the oxirane under basic conditions (equation 4).[11] The authors employed a catalytic oxazaborilidine reduction of trichloromethyl ketones to generate chiral trichlorohydrins that were subsequently dechlorinated under tin-mediated conditions to the chlorohydrin. After base-induced cyclization, three aliphatic terminal epoxides were prepared using this three-step, two-pot process in good-to-moderate yield (59–75% yield) and excellent stereoselectivity (90–96% ee).



(4)

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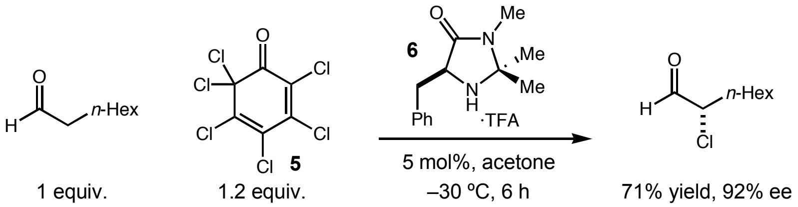
[11] Corey, E. J.; Helal, C. J. *Tetrahedron Lett.* **1993**, *34*, 5227.



(5)

Recently, our lab developed a direct organocatalytic α-chlorination of aldehydes using 5 mol% of imidazolidinone catalyst **6** and hexachlorocyclohexadieneone **5** as the chlorine source (equation 5).[12] Like Corey's trichloromethyl carbinols, we also saw our chiral chloroaldehydes as potential intermediates for the synthesis of important chiral synthons. While most asymmetric processes are capable of synthesizing a single structure class, we envisioned the α-chloroaldehyde to be a modular platform from which a variety of asymmetric motifs could be constructed *in situ* (Figure 1). We felt that the catalytic production of α-chloroaldehydes as intermediates during the synthesis of chiral motifs would be a viable alternative to the development of separate methodologies for each structure class. In this manner, a variety of important chiral synthons could be produced from simple achiral aldehydes in a single transformation simply by changing the reaction conditions of the second step.

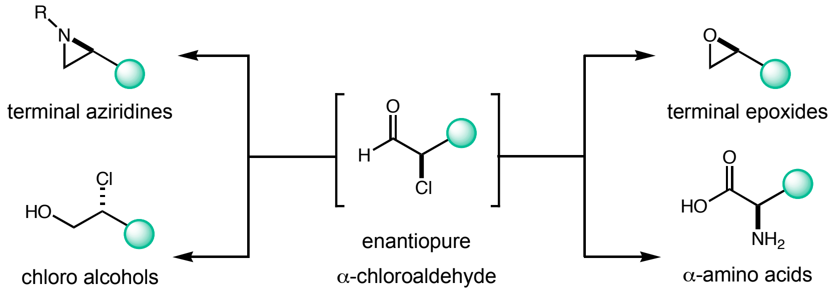


Figure 1. The α-chloroaldehyde as a platform for chiral structural diversity.

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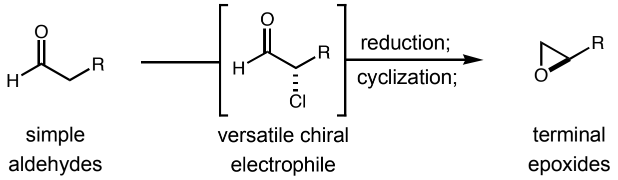
[12] (a) Brochu, M. P.; Brown, S. P.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2004**, *126*, 4108. (b) Simultaneously developed by: Halland, N.; Braunton, A.; Bachmann, S.; Marigo, M.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 4790.

Initial Strategy

Initially, our efforts towards the asymmetric conversion of simple achiral aldehydes into valuable chiral structural classes began with the synthesis of terminal aliphatic epoxides. We envisioned that terminal epoxides might be accessed by a rapid three-step single transformation comprising a simple aldehyde reduction followed by base-induced cyclization, and that these chemical steps could be performed *in situ* without epimerization of the α-chloroaldehyde intermediate (equation 6) or the need for laborious chemical isolations and purifications.



(6)

Initially, we pursued a procedure using our published reaction conditions for the α-chlorination using catalyst **6** at sub-ambient temperatures. However, the optimal reaction medium for the α-chlorination is acetone, which itself can react with sodium borohydride ($NaBH_4$) and other reducing agents used to convert the α-chloroaldehyde to the corresponding chlorohydrin. As shown in Table 1,[13] acetone and chloroform ($CHCl_3$) are both optimal solvents for the α-chlorination reaction (entries 5–6) but both are unsuitable solvents for subsequent hydride reduction and basic conditions required for oxirane formation. Dichloromethane (CH_2Cl_2) provides slightly lower conversion and enantioselectivity than acetone and $CHCl_3$ (entry 4); however, its compatibility with the conditions for subsequent epoxide formation led us to select it as the reaction medium.

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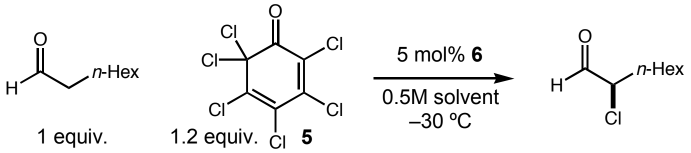
[13] Reproduced from: *Iminium and Enamine Activation: Methods for Enantioselective Organocatalysis.* Brown, S. P., Ph.D. Thesis: California Institute of Technology, Pasadena, CA, 2005.

Table 1. Survey of Solvents with Catalyst **6**[13]

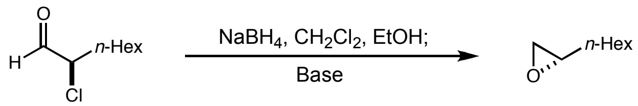


entry	solvent	time (h)	% conversion[a]	% ee[b]
1	EtOAc	12	93	87
2	THF	18	56	89
3	toluene	18	83	89
4	CH_2Cl_2	8	86	90
5	$CHCl_3$	8	91	92
6	acetone	7	93	92

(a) Conversion determined by GLC analysis relative to an internal standard (benzyl methyl ether). (b) Enantiomeric excess determined by GLC analysis (Bodman G-TA).

Next, a sampling of bases for affecting the epoxidation from the halohydrin was studied to determine conditions that could be successfully applied *in situ* after a $NaBH_4$ reduction (Table 2). A 50% solution of potassium hydroxide (KOH) was found to give the highest levels of conversion (entry 1) and a time study of the reduction and cyclization steps found that they were each completed in 30 min at ambient temperature. Longer cyclization reaction times resulted in reduced conversions due to unwanted epoxide opening and diol formation. While adequate levels of conversion to the desired terminal

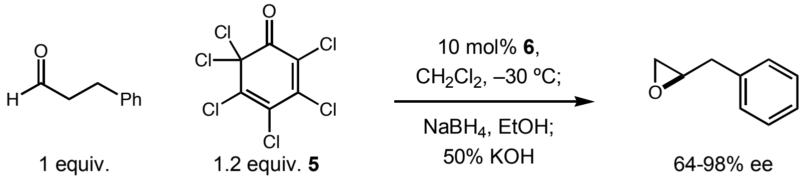
Table 2. Comparison of Bases for Oxirane Formation



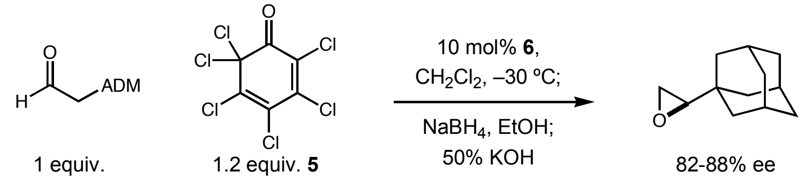
entry	base	% conversion[a]
1	50% aq. KOH	89
2	50% aq. NaOH	81
3	25% NaOMe in MeOH	59
4	21% NaOEt in EtOH	71

(a) Conversion determined by GLC analysis with tridecane as an internal standard.

epoxide from the chloroaldehyde intermediate could now be achieved, the α-chlorinations were necessarily conducted at or below –30 ºC to obtain adequate levels of enantioselectivity; at warmer temperatures catalyst **6** readily epimerizes the α-chloro stereocenter, and complete racemization occurs in only a few hours.[13] However, the necessary warming of the reactions during the reduction of the chloroaldehyde to the chlorohydrin resulted in a decrease in enantioselectivity. To maintain high levels of selectivity during the reduction step, it was necessary to use pre-cooled ethanol (EtOH) and the reactions were slowly warmed to 0 ºC over a period of an hour to maintain the desired enantiopurities of the final epoxides. After base-induced oxirane formation, aqueous workup and purification, terminal epoxides were isolated in good yields and high selectivities. While enantioselectivities for the octanal-derived oxirane were consistently high at 90% ee, expansion of the substrate scope to include a variety of functionalized oxiranes led to difficulties with reproducibility and often inconsistent results (equations 7 and 8).



(7)



(8)

Improved Strategy

During the course of this work, graduate student Sean Brown began work on developing a new imidazolidinone catalyst that would be capable of maintaining high levels of enantioselectivity while being less apt to epimerize products after their formation. It was proposed that increasing the steric bulk of the catalyst would decrease the nucleophilicity of the amine, thereby reducing the propensity to reform enamine with the α-chloroaldehyde product. Catalyst **7** was developed as a pseudo C_2-symmetric catalyst in which the nitrogen lone pair is less accessible due to the bulky *tert*-butyl group (Figure 2).

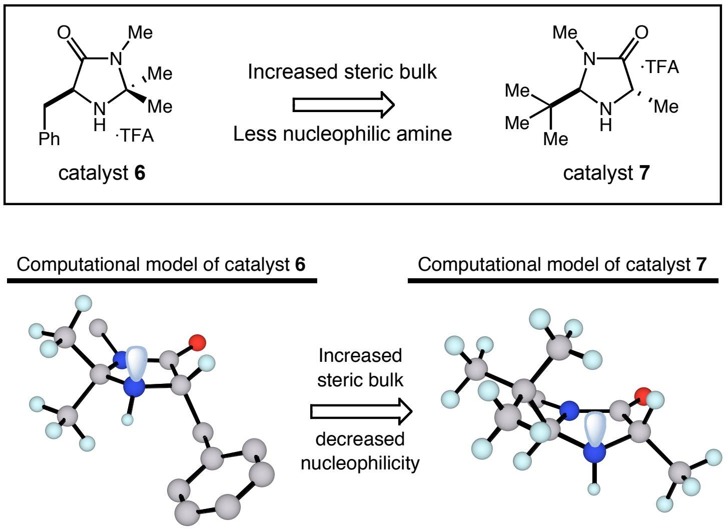
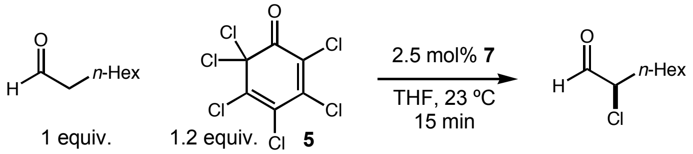


Figure 2. 3D models showing increased coverage of the nitrogen lone pair in catalyst **7** compared to catalyst **6**.

Notably, catalyst **7** was found to successfully affect the α-chlorination of aldehydes with excellent enantioselectivities, at ambient temperature.[13] In addition, the α-chloro stereocenter was stable for at least 2 hours at room temperature in the presence of catalyst **7**, as opposed to the rapid epimerization observed with catalyst **6**. Additionally, optimal solvents for the α-chlorination reaction with catalyst **6** were acetone and $CHCl_3$; however, neither solvent is compatible with the single transformation procedure for terminal epoxides and a less optimal solvent providing lower enantioselectivities was chosen for the three-step process. In contrast, reactions using catalyst **7** were found to work exceedingly well in tetrahydrofuran (THF), diethyl ether (Et_2O), and ethyl acetate (EtOAc).[13]

In order to reduce the overall time needed for the three-step construction of terminal epoxides, the effect of concentration on the α-chlorination was evaluated and showed that complete conversion to the α-chloroaldehyde was obtained in 15 minutes using only 2.5 mol% of catalyst **7** without affecting the enantioselectivity of the reaction (Table 3). Notably, the use of catalyst **7** in THF achieved 96% ee for octanal, as opposed to 89% ee with catalyst **6** in THF and 90% ee in CH_2Cl_2. Also, since the reaction was now performed at ambient temperature, the reduction step could now be conducted in only 30 minutes as the slow warming process was no longer necessary to prevent epimerization. Using these new conditions, reaction times were reduced to a 15 minute α-chlorination, 30 minute $NaBH_4$, reduction and 30 minute cyclization for a total overall reaction time of 75 minutes.

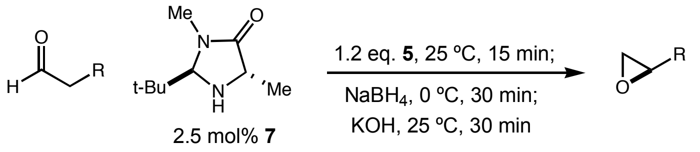
Table 3. Effect of Concentration using Catalyst **7**

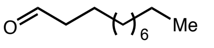
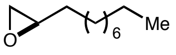
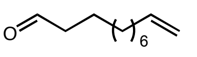
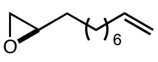
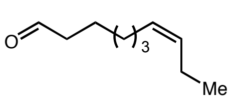
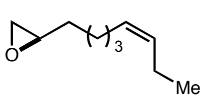
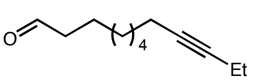
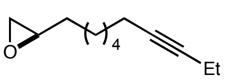
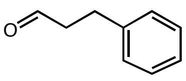
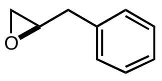
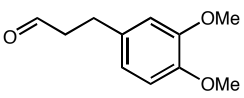
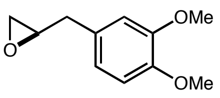
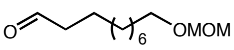
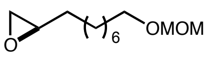
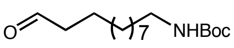
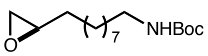
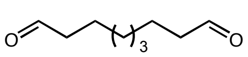
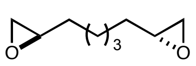
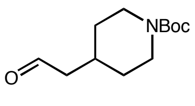
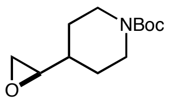
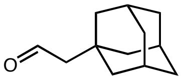
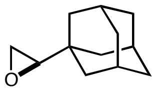


entry	concentration	% conversion[a]	% ee[b]
1	0.5 M	82	96
2	0.75 M	89	96
3	1 M	93	96
4	1.5 M	96	96
5	2 M	97	96
6	2.5 M	97	96

(a) Conversion determined by GLC analysis relative to an internal standard (benzyl methyl ether). (b) Enantiomeric excess determined by GLC analysis (Bodman Γ-TA).

Table 4. Enantioenriched Terminal Epoxides: Substrate Scope



entry	reactant	product	% yield	% ee
1			83	94
2			82	92
3			78	94
4			76	95
5			77	93
6			96^{a}	94
7			75	93
8			83	95
9			81	>99^{b}
10			86^{a}	96
11			50^{c}	89

(a) Total reaction time of 90 min. (b) 10:1 dr. (c) α-Chlorination using 20 mol% catalyst **6**, –40 °C for 12 hr.

Finally, reactions were performed using a variety of structurally diverse aldehydes to determine the generality of this new protocol. As shown in Table 4, the reaction was found to be general for a broad range of functionalities including protected amines (entries 8 and 10), labile ethers (entry 7), and alkynes (entry 4). Sterically hindered substrates were also provided in excellent selectivities (entries 10 and 11), although the adamantyl substrate was a poor substrate for catalyst **7** and the initial protocol using catalyst **6** was used to provide the desired adamantyl epoxide. A bis-terminal epoxide was successfully synthesized using this new method in high yield and excellent selectivity (entry 9) and aromatic substrates were also obtained, with no evidence of electrophilic aromatic substitution on even highly electron-rich benzene rings (entries 5–6). Notably, while the generation of olefinic epoxides using typical olefin epoxidation methods is difficult to achieve due to regioselectivity requirements, such substrates are easily prepared using this new technology, which showed no evidence of olefin isomerization under the reaction conditions (entries 2 and 3).

Conclusion

In summary, the rapid enantioselective synthesis of chiral terminal epoxides from simple achiral aldehydes in a single transformation has been accomplished, providing the first example of the α-chloroaldehyde intermediate as a valuable chiral synthon. The use of a *trans*-imidazolidinone catalyst enabled the asymmetric chlorination of aldehydes at ambient temperatures in only fifteen minutes without product epimerization and allowed the development of a rapid, 75-minute one-pot protocol for constructing terminal aliphatic epoxides. Using this new protocol, terminal epoxides containing a wide variety of functionalities including olefins, alkynes, and aromatic rings were easily prepared in good yields and excellent enantioselectivities.[14]

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[14] Recently and subsequent to the completion of this work, a three-step synthesis of *trans*-epoxides was reported employing chlorohydrins as intermediates: Kang, B.; Britton, R. *Org. Lett.* **2007**, *9*, 5083.

Supporting Information

General Information. Commercial reagents were distilled prior to use following the guidelines of Perrin and Armarego.[15] Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished using forced-flow chromatography on EMD Silica Gel 60 230-400 mesh or Iatrobeads 6RS–8060 according to the method of Still.[16] Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization of the developed chromatogram was performed by fluorescence quenching, ceric ammonium molybdate, or anisaldehyde stain. High performance liquid chromatography (HPLC) and gas liquid chromatography (GLC) assays to determine enantiometric excess were developed using racemic samples.

^{1}H and ^{13}C NMR spectra were recorded on Varian Mercury 300 (300 MHz and 75 MHz respectively) as noted, and are internally referenced to residual protio solvent signals. Data for ^{1}H are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz), and assignment. Data for ^{13}C NMR are reported in terms of chemical shift. IR spectra were recorded on a Perkin Elmer Spectrum BX FT-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Mass spectra were obtained from the California Institute of Technology Mass Spectral Facility. Gas liquid chromatography (GLC) was performed on a Hewlett-Packard 6850 Series gas chromatograph equipped

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[15] Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd edition; Pergamon Press; Oxford, 1988.

[16] Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

with a split-mode capillary injection system and flame ionization detectors using a Bodman Chiraldex Γ-TA (30 m 0.25 mm) column. High performance liquid chromatography (HPLC) was performed on a Hewlett Packard 1100 Series chromatograph using a Chiralcel®OD-H, Chiralcel®OJ or Chiralpak®AD column (25 cm, 5 cm guard), as noted.

Starting Materials

10-(Methoxymethoxy)decanol: To a flask containing 1,10-decanediol (5.00 g, 28.7 mmol) and diisopropylethylamine (6.00 mL, 17.2 mmol) in CH_2Cl_2 (30 mL) was slowly added chloromethyl methyl ether (1.09 ml, 14.3 mmol) at 0 °C. The solution was warmed to room temperature and stirred for 12 h. The reaction was then treated with saturated aqueous NH_4Cl, extracted with CH_2Cl_2 (3 × 100 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by silica gel chromatography (20–40% EtOAc/hexanes) to provide 10-(methoxymethoxy)decan-1-ol. IR (film) 3435, 2929, 2855, 2360, 1466, 1385, 1214, 1148, 1112, 1045, 920.5, 722.1 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.61 (s, 2H, $C\mathbf{H_2}OMe$), 3.62 (t, 2H, $J = 6.7$ Hz, $C\mathbf{H_2}OH$), 3.50 (t, 2H, $J = 6.7$ Hz, $CH_2C\mathbf{H_2}O$), 3.35 (s, 3H, $C\mathbf{H_3}$), 1.65–1.21 (m, 16H, $(C\mathbf{H_2})_8CH_2OH$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 96.35, 67.85, 55.05, 32.76, 29.70, 29.49, 29.47, 29.37, 26.16, 25.69; HRMS (FAB+) exact mass calculated for $(C_{12}H_{25}O_3)$ $[(M+H)-H_2]^+$ requires *m/z* 217.1804, found *m/z* 217.1796.

10-(Methoxymethoxy)decanal: To a flask containing 10-(methoxymethoxy)decan-1-ol (1.46 g, 6.70 mmol) in CH_2Cl_2 (7.0 mL) was added TEMPO (105 mg, 0.670 mmol) followed by iodobenzene diacetate (2.36 g, 7.30 mmol). The reaction was stirred for 1 h and then diluted with CH_2Cl_2 (50 mL). Saturated aqueous solution of $Na_2S_2O_3$ (50 mL) was added and extracted with CH_2Cl_2 (3 × 25 mL). The combined organics were washed with saturated aqueous $NaHCO_3$ (75 mL) and brine (75 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by silica gel chromatography (15% EtOAc/hexanes) to provide the title compound. IR (film) 2929, 2856, 2718, 2360, 1726, 1466, 1389, 1214, 1147, 1111, 1044, 919.3, 723.1, 668.1 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.76 (t, 1H, J = 1.9 Hz, C**H**O), 4.62 (s, 2H, C$\mathbf{H_2}$OMe), 3.51 (t, 2H, J = 6.6 Hz, $CH_2C\mathbf{H_2}O$), 3.36 (s, 3H, C$\mathbf{H_3}$), 2.42 (dt, 2H, J = 1.9, 7.2 Hz C$\mathbf{H_2}$CHO), 1.68–1.54 (m, 4H, $C\mathbf{H_2}CH_2CHO$, $C\mathbf{H_2}CH_2O$), 1.40–1.24 (m, 10H, $(C\mathbf{H_2})_5CH_2CH_2O$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.8, 96.34, 67.79, 55.02, 43.84, 29.67, 29.29, 29.23, 29.08, 26.13, 22.01; HRMS (EI+) exact mass calculated for $[M+\bullet]^+$ ($C_{12}H_{24}O_3$) requires *m/z* 216.1726, found *m/z* 216.1716.

Dodec-9-ynal: To a flask containing dodec-9-yn-1-ol (4.56 g, 25.0 mmol) in CH_2Cl_2 (25 mL) was added TEMPO (390 mg, 2.50 mmol) followed by iodobenzene diacetate (8.86 g, 27.5 mmol). The reaction was stirred 1 h and then diluted with CH_2Cl_2 (100 mL). Saturated aqueous solution of $Na_2S_2O_3$ (100 mL) was added and extracted with CH_2Cl_2 (3 × 50 mL). The combined organics were washed with saturated aqueous $NaHCO_3$ (150 mL) and brine (150 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by silica gel chromatography (5% Et_2O/pentanes) to provide the title compound. IR (CH_2Cl_2) 3052, 2978, 2937, 2859, 1710, 1435, 1266, 896.4, 747.2, 735.7, 705.3 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (t, 1H, *J* = 1.9 Hz, C**H**O), 2.42 (dt, 2H, *J* = 1.9, 7.2 Hz, C**H₂**CHO), 2.20–2.09 (m, 4H, $CH_2C\mathbf{H_2}CC$, $C\mathbf{H_2}CH_3$), 1.68–1.26 (m, 10H, $(C\mathbf{H_2})_5CH_2CHO$), 1.11 (t, 3H, *J* = 7.1 Hz, $C\mathbf{H_3}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.8, 81.64, 79.33, 43.82, 28.99, 28.96, 28.81, 28.53, 21.97, 18.63, 14.32, 12.35; HRMS (EI+) exact mass calculated for $[M+\bullet]^+$ ($C_{12}H_{20}O$) requires *m/z* 180.1514, found *m/z* 180.1507.

***tert*-Butyl 10-Formyldecylcarbamate:** To a flask containing 11-*tert*-butoxycarbonylamino-undecanoic acid (3.60 g, 12.0 mmol) in CH_2Cl_2 (120 mL) was added N,O-dimethylhydroxylamine hydrochloride (1.30 g, 13.2 mmol) followed by 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (2.30 g, 12.0 mmol), 4-dimethylaminopyridine (59.0 mg, 0.480 mmol), and diisopropylethylamine (2.30 mL, 13.2 mmol). The reaction was stirred 12 h and then diluted with CH_2Cl_2 (300 mL). The reaction was washed with water (2 × 100 mL), saturated aqueous citric acid solution (100 mL) and brine (100 mL), dried over Na_2SO_4, and concentrated *in vacuo* to obtain an oily residue. THF (60 mL) was added and the solution cooled to 0 °C. $LiAlH_4$ (1.03 g, 27.1 mmol) was added in portions and stirred 2 h. 20% aqueous citric acid solution was added slowly (300 mL) and stirred vigorously for 30 min. The reaction was diluted with 20% aqueous citric acid solution (200 mL) and extracted with Et_2O (3 × 150 mL). The combined organics were washed with saturated $NaHCO_3$ solution (150 mL), brine (150 mL), dried over Na_2SO_4, and concentrated *in vacuo* to obtain the title compound. IR (film) 3374, 2978, 2918, 2850, 2361, 1720, 1681, 1517, 1463, 1390, 1366, 1250, 1172, 1042, 864.5, 783.1, 725.0, 666.4 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.78 (t, 1H, *J* = 1.9 Hz, C**H**O), 4.54 (s, 1H, N**H**), 3.13 (q, 2H, *J* = 6.7 Hz, C$\mathbf{H_2}$NH), 2.45 (dt, 2H, *J* = 1.9, 7.4 Hz, C$\mathbf{H_2}$CHO), 1.76–1.22 (m, 25H, (C$\mathbf{H_2}$)$_8$$CH_2$CHO, C(C$\mathbf{H_3}$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.8, 155.9, 78.91, 43.83, 40.56, 30.01, 29.38, 29.24, 29.18, 29.07, 28.37, 26.71, 22.00; HRMS (CI+) exact mass calculated for [M+•]$^+$ ($C_{16}H_{31}NO_3$) requires *m/z* 285.2304, found *m/z* 285.2312.

Nonanedial: To a flask containing nonane-1,9-diol (2.40 g, 15.0 mmol) in CH_2Cl_2 (30 mL) was added TEMPO (351 mg, 2.25 mmol) followed by iodobenzene diacetate (10.15 g, 31.5 mmol). The reaction was stirred for 2 h and then diluted with CH_2Cl_2 (100 mL). Saturated aqueous solution of $Na_2S_2O_3$ (100 mL) was added and extracted with CH_2Cl_2 (3 × 50 mL). The combined organics were washed with saturated aqueous $NaHCO_3$ (150 mL) and brine (150 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by silica gel chromatography (20–40% Et_2O/pentanes) to provide the title compound, which was identical to the known literature compound.[17]

***tert*-Butyl 4-(formylmethyl)piperidine-1-carboxylate:** To a flask containing *tert*-butyl 4-(2-hydroxyethyl)piperidine-1-carboxylate (4.40 g, 19.2 mmol) in CH_2Cl_2 (20 mL) was added TEMPO (300 mg, 1.92 mmol) followed by iodobenzene diacetate (6.80 g, 21.1 mmol). The reaction was stirred 3 h and then diluted with CH_2Cl_2 (100 mL). Saturated aqueous solution of $Na_2S_2O_3$ (100 mL) was added and extracted with CH_2Cl_2 (3

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[17] Roels, J.; Metz, P. *Syn. Lett.* **2001**, *6*, 789.

× 50 mL). The combined organics were washed with saturated aqueous $NaHCO_3$ (150 mL) and brine (150 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by silica gel chromatography (40–70% Et_2O/pentanes) to provide the title compound, which was identical to the reported literature compound.[18] ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.5, 154.7, 79.37, 50.31, 43.68, 31.86, 30.63, 28.39.

Terminal Epoxides

General Procedure for Epoxide Formation: To a 10 mL round-bottom flask equipped with a magnetic stir bar and charged with (2*R*,5*S*)-2-*tert*-butyl-5-methyl-3-methylimidazolidin-4-one **7** (8.6 mg, 0.05 mmol) and THF (0.8 mL) was added TFA (5.8 mg, 0.05 mmol) followed by 2,3,4,5,6,6-hexachloro-2,4-cyclohexadien-1-one **5** (722 mg, 2.4 mmol). The aldehyde substrate (2.0 mmol) was added and the reaction mixture stirred 15 min. The reaction was cooled to 0 °C and diluted with 0.4 mL THF and 0.8 mL EtOH. $NaBH_4$ (189 mg, 5.0 mmol) was added and after 5 min the resulting suspension warmed to 25 °C and stirred an additional 25 min. 50% aqueous KOH solution (5 mL) was added and stirred vigorously for 30 min, drawing the organic phase completely into the aqueous phase. The cloudy suspension was allowed to separate and 10 mL of H_2O was added. The solution was extracted 3 times with Et_2O (10 mL) and the combined organics dried over Na_2SO_4. Filtration was followed by concentration *in vacuo* to afford a yellow oil that was then purified by forced flow chromatography to afford the

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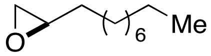
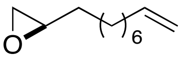
[18] Sato, T.; Okamoto, K.; Nakano, Y.; Uenishi, J.; Ikeda, M. *Heterocycles* **2001**, *54*, 747.

title compounds. The enantioselectivity was determined either by chiral GLC analysis, or chiral HPLC analysis after epoxide opening with naphthalene-2-thiol.

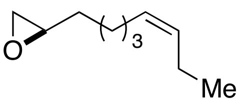


(*R*)-2-Nonyloxirane (Table 4, entry 1): Prepared according to the general procedure from undecanal (206 μL, 1.0 mmol) to afford a yellow oil. Purification on silica gel (5% Et_2O/pentanes) afforded (*R*)-2-nonyloxirane as a colorless liquid (142 mg, 83% yield, 94% ee). IR (film) 3043, 2956, 2926, 2855, 1466, 1410, 1378, 1259, 1129, 916.4, 836.9, 722.0 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.93–2.87 (m, 1H, OC**H**CH_2), δ 2.74 (dd, 1H, *J* = 4.1, 5.1 Hz, OCHC$\mathbf{H_2}$), δ 2.46 (dd, 1H, *J* = 2.8, 5.0 Hz, OCHC$\mathbf{H_2}$), δ 1.57–1.20 (m, 16H, $(C\mathbf{H_2})_8CH_3$), δ 0.88 (t, *J* = 7.2 Hz, 3H, C$\mathbf{H_3}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.40, 47.12, 32.49, 31.87, 29.55, 29.50, 29.44, 29.29, 25.96, 22.66, 14.09; HRMS (CI+) exact mass calculated for $[M+H]^+$ ($C_{11}H_{23}O$) requires *m/z* 171.1749, found *m/z* 171.1746. $[\alpha]_D$ = +5.88 (c = 1.0, $CHCl_3$). Enantiopurity was determined by chiral HPLC analysis of the 1-naphthyl-2-hydroxyundecane derivative (Chiralcel®OD-H Isocratic 5% IPA/hexanes). t_R(minor) = 11.9 min. t_R(major) = 14.2 min.

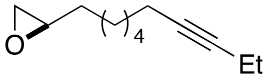


(*R*)-2-(Non-8-enyl)oxirane (Table 4, entry 2): Prepared according to the general procedure from undec-10-enal (416 *μ*L, 2.00 mmol) to afford a yellow oil. Purification on silica gel (5% Et_2O/pentanes) afforded (*R*)-2-(non-8-enyl)oxirane as a colorless liquid

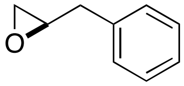
(277 mg, 82% yield, 92% ee). IR (film) 3584, 3077, 3044, 2977, 2928, 2856, 1641, 1465, 1411, 1259, 994.3, 909.8, 836.4, 665.8 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.81 (ddt, 1H, *J* = 6.7, 10.1, 17.3 Hz, CH$_2$**CH**=CH$_2$), δ 5.03–4.96 (m, 1H, CH=C**H$_2$**), δ 4.96–4.91 (m, 1H, CH=C**H$_2$**), δ 2.93–2.87 (m, 1H, OC**H**CH$_2$), δ 2.74 (dd, 1H, *J* = 2.9, 5.1 Hz, OCHC**H$_2$**), δ 2.46 (dd, 1H, *J* = 2.9, 5.1 Hz, OCHC**H$_2$**), δ 2.07–2.00 (m, 2H, **CH$_2$**CH=CH$_2$), δ 1.56–1.31 (m, 12H, OCH(C**H$_2$**)$_6$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 139.1, 114.1, 52.33, 47.06, 33.74, 32.45, 29.35, 28.97, 28.84, 25.92; HRMS (CI+) exact mass calculated for [M+H]$^+$ (C$_{11}$H$_{21}$O) requires *m/z* 169.1592, found *m/z* 169.1596. $[\alpha]_D$ = +7.12 (c = 1.0, CHCl$_3$). Enantiopurity was determined by chiral HPLC analysis of the 1-naphthyl-2-hydroxyundec-10-ene derivative (Chiralcel®OD-H Isocratic 5% IPA/hexanes). t_R(minor) = 14.1 min. t_R(major) = 17.5 min.



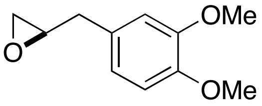
(*R*)-2-((*Z*)-Oct-5-enyl)oxirane (Table 4, entry 3): Prepared according to the general procedure from (*Z*)-dec-7-enal (366 μL, 2.00 mmol) to afford a yellow oil. Purification on silica gel (5% Et$_2$O/pentanes) afforded (*R*)-2-((*Z*)-oct-5-enyl)oxirane as a colorless liquid (240 mg, 78% yield, 94% ee). IR (film) 3369, 2932, 2861, 2360, 1461, 1413, 1373, 1260, 1137, 1066, 968.3, 915.0, 833.4, 668.0 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.42–5.27 (m, 2H, C**H**=C**H**Et), δ 2.93–2.87 (m, 1H, OC**H**CH$_2$), δ 2.75 (dd, 1H, *J* = 4.0, 5.1 Hz, OCHC**H$_2$**), δ 2.46 (dd, 1H, *J* = 2.9, 5.1 Hz, OCHC**H$_2$**), δ 2.08–1.99 (m, 4H, C**H$_2$**CH=CHC**H$_2$**), δ 1.58–1.35 (m, 6H, OCH(C**H$_2$**)$_3$), δ 0.95 (t, *J* = 7.4 Hz, 3H, C**H$_3$**); ^{13}C NMR (75 MHz, CDCl$_3$) δ 131.9, 128.8, 52.31, 47.11, 32.38, 29.51, 26.94, 25.56, 20.50, 14.35; HRMS (CI+) exact mass calculated for $[M+H]^+$ ($C_{10}H_{19}O$) requires *m/z* 155.1436, found *m/z* 155.1430. $[\alpha]_D = +7.95$ (c = 1.0, $CHCl_3$). Enantiopurity was determined by chiral HPLC analysis of the 1-naphthyl-2-hydroxyoct-5-ene derivative (Chiralcel®OD-H Isocratic 2% IPA/hexanes). t_R(minor) = 30.2 min. t_R(major) = 43.7 min.



(*R*)-2-(Dec-7-ynyl)oxirane (Table 4, entry 4): Prepared according to the general procedure from dodec-9-ynal (405 μL, 2.00 mmol) to afford a yellow oil. Purification on silica gel (5-10% Et_2O/pentanes) afforded (*R*)-2-(dec-7-ynyl)oxirane as a colorless liquid (275 mg, 76% yield, 95% ee). IR (film) 3044, 2975, 2934, 2858, 1462, 1410, 1320, 1260, 1131, 1063, 916.6, 834.6 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.93–2.87 (m, 1H, $OC\mathbf{H}CH_2$), δ 2.74 (dd, 1H, *J* = 4.0, 5.1 Hz, $OCHC\mathbf{H}_2$), δ 2.46 (dd, 1H, *J* = 2.7, 5.1 Hz, $OCHC\mathbf{H}_2$), δ 2.20–2.11 (m, 4H, $\mathbf{CH_2}CC\mathbf{CH_2}$), δ 1.59–1.30 (m, 10H, $OCH(C\mathbf{H_2})_5$), δ 1.11 (t, *J* = 7.2 Hz, 3H, $C\mathbf{H_3}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 81.68, 79.38, 52.35, 47.13, 32.41, 28.96, 28.93, 28.69, 25.84, 18.65, 14.36, 12.39; HRMS (CI+) exact mass calculated for $[M+H]^+$ ($C_{12}H_{21}O$) requires *m/z* 181.1592, found *m/z* 181.1589. $[\alpha]_D = +6.97$ (c = 1.0, $CHCl_3$). Enantiopurity was determined by chiral HPLC analysis of the 1-naphthyl-2-hydroxydodec-9-yne derivative (Chiralcel®OD-H Isocratic 5% IPA/hexanes). t_R(minor) = 31.9 min. t_R(major) = 47.0 min.



(*R*)-2-Benzyloxirane (Table 4, entry 5): Prepared according to the general procedure from hydrocinnamaldehyde (263 μL, 2.00 mmol) to afford a yellow oil. Purification on silica gel (5–8% Et_2O/pentanes) afforded (*R*)-2-benzyloxirane as a colorless liquid (207 mg, 77% yield, 93% ee) that matched literature data.[19] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.22 (m, 5H, Ph), δ 3.19–3.14 (m, 1H, OC**H**CH_2), δ 2.94 (dd, 1H, *J* = 5.6, 14.7 Hz, C**H**$_2$Ph), δ 2.86–2.79 (m, 2H, OC**H**$_2$CHC**H**$_2$Ph), δ 2.56 (dd, 1H, *J* = 2.7, 4.8 Hz, OCHC**H**$_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.2, 129.0, 128.5, 126.6, 52.42, 46.86, 38.75; HRMS (EI+) exact mass calculated for $[M+\bullet]^+$ ($C_9H_{10}O$) requires *m/z* 134.0732, found *m/z* 134.0734. $[\alpha]_D$ = +16.7 (c = 1.0, EtOH). Reported rotation for (*S*)-benzyl oxirane $[\alpha]_D$ = -17.3 (c = 1.94, EtOH). Enantiopurity was determined by GLC using a Bodman Chiraldex Γ-TA (30 m x 0.25 mm) column (70 °C isotherm); (*R*) isomer t_r = 52.4 min and (*S*) isomer t_r = 57.4 min.



(*R*)-2-(3,4-Dimethoxybenzyl)oxirane (Table 4, entry 6): The catalyst **7** (17.0 mg, 0.100 mmol) and 2,3,4,5,6,6-hexachloro-2,4-cyclohexadien-1-one **5** (361 mg, 1.20 mmol) in THF (2.0 mL) and TFA (11.4 mg, 0.100 mmol) was treated with 3-(3,4-dimethoxyphenyl)propanal (194 mg, 1.00 mmol) and stirred at rt for 30 min. The

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[19] Klunder, J. M.; Onami, T.; Sharpless, K. B. *J. Org. Chem.* **1989**, *54*, 1295.

reaction was cooled to 0 °C and diluted with EtOH (1.3 mL). $NaBH_4$ (95.0 mg, 2.50 mmol) was added and after 5 min the reaction was warmed to rt and stirred an additional 25 min. 50% aqueous KOH solution (6.0 mL) was added and the stirred vigorously for 30 min. 12 mL of H_2O was added and the solution extracted with Et_2O (3 × 12 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford a yellow oil. Purification on Iatrobeads (20–60% Et_2O/Pentanes) afforded (*R*)-2-(3,4-dimethoxybenzyl)oxirane as a colorless oil (186 mg, 96% yield, 94% ee) which matched literature data.[20] IR (film) 2996, 2936, 2836, 1608, 1590, 1517, 1464, 1420, 1335, 1262, 1237, 1157, 1141, 1028, 969.9, 833.6, 765.4 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.84–6.77 (m, 3H, Ph), δ 3.88 (s, 3H, PhOC**H₃**), δ 3.87 (s, 3H, PhOC**H₃**), δ 3.17–3.11 (m, 1H, OC**H**CH₂), δ 2.83–2.78 (m, 3H, C**H₂**Ph, OCHC**H₂**), δ 2.54 (dd, 1H, *J* = 2.7, 4.5 Hz, OCHC**H₂**); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.90, 147.81, 129.73, 120.90, 112.25, 111.25, 55.90, 55.84, 52.58, 46.77, 38.27; HRMS (EI+) exact mass calculated for $[M+\bullet]^+$ ($C_{11}H_{14}O_3$) requires *m/z* 194.0943, found *m/z* 194.0946. $[\alpha]_D$ = +9.2 (c = 1.0, $CHCl_3$). Reported rotation $[\alpha]_D$ = +9.7 (c = 0.5, $CHCl_3$). Enantiopurity was determined by chiral HPLC analysis (Chiralcel®OD-H Isocratic 4% IPA/hexanes). t_R(major) = 27.1 min. t_R(minor) = 32.1 min.

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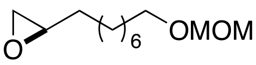
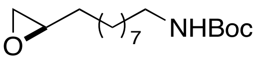
[20] Gooding, O. W.; Bansal, R. P. *Synth. Commun.* **1995**, *25*, 1155.

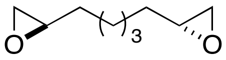


(*R*)-2-(8-(Methoxymethoxy)octyl)oxirane (Table 4, entry 7): Prepared according to the general procedure from 10-(methoxymethoxy)decanal (433 mg, 2.00 mmol) to afford a yellow oil. Purification on Iatrobeads (5–30% Et_2O/pentanes) afforded (*R*)-2-(8-(methoxymethoxy)octyl)oxirane as a colorless liquid (326 mg, 75% yield, 93% ee). IR (film) 3044, 2930, 2857, 1467, 1410, 1386, 1260, 1214, 1149, 1111, 1046, 918.6, 834.6, 723.9 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.62 (d, 2H, *J* = 0.8 Hz, $OC\mathbf{H_2}O$), δ 3.52 (t, 2H, *J* = 6.4 Hz, $CH_2C\mathbf{H_2}O$), δ 3.36 (d, 3H, *J* = 0.8 Hz, $OC\mathbf{H_3}$), δ 2.93–2.87 (m, 1H, $OC\mathbf{H}CH_2$), δ 2.74 (dd, 1H, *J* = 4.8, 4.5 Hz, $OCHC\mathbf{H}_2$), δ 2.46 (dd, 1H, *J* = 2.7, 5.1 Hz, $OCHC\mathbf{H}_2$), δ 1.63–1.32 (m, 14H, $OCH(C\mathbf{H_2})_7$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 96.39, 67.84, 55.08, 52.36, 47.11, 32.47, 29.72, 29.47, 29.36, 29.31, 26.17, 25.94; HRMS (CI+) exact mass calculated for $[M+H]^+$ ($C_{12}H_{25}O_3$) requires *m/z* 217.1804, found *m/z* 217.1798. $[\alpha]_D$ = +5.97 (c = 1.0, $CHCl_3$). Enantiopurity was determined by chiral HPLC analysis of the 1-naphthyl-2-hydroxy-8-(methoxymethoxy)octane derivative (Chiralpak®AD Isocratic 2% IPA/hexanes). t_R(minor) = 71.4 min. t_R(major) = 75.7 min.

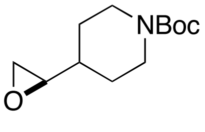


(*R*)-*tert*-Butyl 9-(oxiran-2-yl)nonylcarbamate (Table 4, entry 8): The catalyst **7** (4.30 mg, 25.0 μmol) and 2,3,4,5,6,6-hexachloro-2,4-cyclohexadien-1-one **5** (361 mg, 1.20 mmol) in THF (1.0 mL) and TFA (2.90 mg, 25.0 μmol) was treated with *tert*-butyl 10-formyldecylcarbamate (286 mg, 1.00 mmol) and stirred at rt for 15 min. The reaction was cooled to 0 °C and diluted with THF (0.50 mL) and EtOH (1.0 mL). $NaBH_4$ (95.0

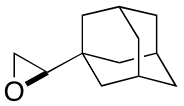
mg, 2.50 mmol) was added and after 5 min the reaction was warmed to rt and stirred an additional 25 min. 50% aqueous KOH solution (5.0 mL) was added and the stirred vigorously for 30 min. 10 mL of H_2O was added and the solution extracted with Et_2O (3 × 10 mL). The combined organics were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford a yellow oil. Purification on Iatrobeads (20–50% Et_2O/pentanes) afforded (*R*)-*tert*-butyl 9-(oxiran-2-yl)nonylcarbamate as a colorless oil (237 mg, 83% yield, 95% ee). IR (film) 3358, 3045, 2977, 2929, 2856, 2361, 1715, 1523, 1456, 1391, 1366, 1250, 1174, 1042, 996.4, 916.0, 835.6, 781.1, 722.9 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.50 (s, 1H, N**H**), δ 3.09 (app. q, 2H, *J* = 6.7 Hz, C$\mathbf{H_2}$NH), δ 2.93–2.87 (m, 1H, OC**H**CH_2), δ 2.74 (dd, 1H, *J* = 4.0, 5.1 Hz, OCHC$\mathbf{H}_2$), δ 2.46 (dd, 1H, *J* = 2.7, 5.1 Hz, OCHC$\mathbf{H}_2$), δ 1.57–1.34 (m, 16H, OCH(C$\mathbf{H_2}$)$_\mathbf{8}$), δ 1.28 (s, 9H, C(C$\mathbf{H_3}$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.6, 78.92, 52.33, 47.06, 40.57, 32.43, 30.01, 29.37, 29.34, 29.19, 28.39, 26.72, 25.90; HRMS (CI+) exact mass calculated for $[M+H]^+$ ($C_{16}H_{32}NO_3$) requires *m/z* 286.2382, found *m/z* 286.2372. $[\alpha]_D$ = +4.0 (c = 1.0, $CHCl_3$). Enantiopurity was determined by chiral HPLC analysis of the 1-naphthyl-2-hydroxyundecane derivative (Chiralcel®OJ Isocratic 10% IPA/hexanes). t_R(major) = 36.6 min. t_R(minor) = 41.4 min.



(*R*)-2-(5-(Oxiran-2-yl)pentyl)oxirane (Table 4, entry 9): The catalyst **7** (8.60 mg, 50.0 μmol) and 2,3,4,5,6,6-hexachloro-2,4-cyclohexadien-1-one **5** (722 mg, 2.40 mmol) in THF (0.80 mL) and TFA (5.8 mg, 50.0 μmol) was treated with nonanedial (174 μL, 1.00 mmol) and stirred at rt for 15 min. The reaction was cooled to 0 °C and diluted with THF (0.40 mL) and EtOH (0.80 mL). $NaBH_4$ (132 mg, 3.50 mmol) was added and after 5 min the reaction was warmed to rt and stirred an additional 25 min. 50% aqueous KOH solution (5.0 mL) was added and the stirred vigorously for 30 min. 10 mL of H_2O was added and the solution extracted with Et_2O (3 × 10 mL). The combined organics were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford a yellow oil. Purification on Iatrobeads (15–40% Et_2O/pentanes) afforded (*R*)-2-(5-(oxiran-2-yl)pentyl)oxirane as a colorless liquid (126 mg, 81% yield, >99% ee, 10:1 dr). IR (film) 3046, 2982, 2932, 2859, 1483, 1464, 1410, 1260, 1132, 915.8, 837.1 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.93–2.87 (m, 2H, OC**H**CH_2), δ 2.74 (dd, 2H, *J* = 4.0, 4.8 Hz, OCHC**H**$_2$), δ 2.46 (dd, 2H, *J* = 2.9, 5.1 Hz, OCHC**H**$_2$), δ 1.58–1.34 (m, 10H, OCH(C**H**$_2$)$_5$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.29, 47.08, 32.33, 29.19, 25.89; HRMS (CI+) exact mass calculated for ($C_9H_{17}O_2$) $[M+H]^+$ requires *m/z* 157.1229, found *m/z* 157.1227. $[\alpha]_D$ = +18.1 (c = 1.0, $CHCl_3$). Enantiopurity was determined by chiral HPLC analysis of the 1,9-dinaphthyl-2,8-dihydroxynonane derivative (Chiralcel®OD-H Isocratic 10% EtOH/hexanes). t_R(minor) = 33.2 min. t_R(diastereomer) = 39.4 min t_R(major) = 44.9 min.



(*R*)-*tert*-Butyl 4-(oxiran-2-yl)piperidine-1-carboxylate (Table 4, entry 10): The catalyst **7** (17.0 mg, 0.100 mmol) and 2,3,4,5,6,6-hexachloro-2,4-cyclohexadien-1-one **5** (361 mg, 1.20 mmol) in THF (2.0 mL) and TFA (11.4 mg, 0.100 mmol) was treated with *tert*-butyl 4-(formylmethyl)piperidine-1-carboxylate (227 mg, 1.00 mmol) and stirred at rt for 30 min. The reaction was cooled to 0 °C and diluted with EtOH (1.3 mL). $NaBH_4$ (95.0 mg, 2.50 mmol) was added and after 5 min the reaction was warmed to rt and stirred an additional 25 min. 50% aqueous KOH solution (6.0 mL) was added and the stirred vigorously for 30 min. 12 mL of H_2O was added and the solution extracted with Et_2O (3 × 12 mL). The combined organics were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford a yellow oil. Purification on Iatrobeads (20–50% Et_2O/pentanes) afforded (*R*)-*tert*-butyl 4-(oxiran-2-yl)piperidine-1-carboxylate as a colorless oil (195 mg, 86% yield, 96% ee). IR (film) 2975, 2930, 2954, 1693, 1480, 1450, 1421, 1366, 1283, 1254, 1231, 1164, 1094, 1008, 976.7, 929.2, 872.4, 834.0, 809.9, 769.5 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.13 (d, 2H, *J* = 12.0 Hz, N(C**H**$_2$)$_2$), δ 2.78–2.60 (m, 4H, N(C**H**$_2$)$_2$, OC**H**C**H**$_2$), δ 2.55 (dd, 1H, *J* = 4.0, 3.3 Hz, OCHC**H**$_2$), δ 1.85–1.75 (m, 1H, C**H**(CH$_2$)$_2$), δ 1.63–1.57 (m, 2H, CH(C**H**$_2$)$_2$), δ 1.45 (s, 9H, C(C**H**$_3$)$_3$), δ 1.42–1.22 (m, 2H, CH(C**H**$_2$)$_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.76, 79.43, 77.20, 55.62, 45.81, 38.75, 28.68, 28.43, 27.81; HRMS (EI+) exact mass calculated for $[M+\bullet]^+$ ($C_{12}H_{21}NO_3$) requires *m/z* 227.1521, found *m/z* 157.1516. $[\alpha]_D = +1.23$ (c = 1.0, EtOH). Enantiopurity was determined by chiral HPLC analysis of the 1-naphthyl-2-hydroxypiperidine derivative (Chiralcel®OD-H Isocratic 5% IPA/hexanes). t_R(major) = 34.6 min. t_R(minor) = 39.8 min.



(*R*)-Tricyclo[3.3.1.1^{0,0}]dec-1-yl-oxirane (Table 4, entry 11): To a flask containing (5*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one **6** (66 mg, 0.2 mmol) and

2,3,4,5,6,6-hexachloro-2,4-cyclohexadien-1-one **5** (361 mg, 1.2 mmol) in CH_2Cl_2 (2 mL) at –40 °C was added tricyclo[3.3.1.1^{0,0}]dec-1-yl-acetaldehyde (169 μL, 1.00 mmol) and stirred for 24 h. The flask was cooled to –78 °C and diluted with cooled CH_2Cl_2 (4 mL) and EtOH (4 mL). $NaBH_4$ (95 mg, 2.5 mmol) was added and the reaction allowed to warm slowly to rt. After stirring 25 min at rt, 50% KOH solution (20 mL) was added and then stirred vigorously 6 hr. 20 mL of H_2O was added and the solution extracted with Et_2O (3 × 20 mL). The combined organics were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford a yellow oil. Purification on silica gel (5% Et_2O/Pentanes) afforded (*R*)-Tricyclo[3.3.1.1^{0,0}]dec-1-yl-oxirane as a colorless oil (90 mg, 50%, 89% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.67 (dd, 1H, *J* = 3.2, 4.5 Hz, OC**H**CH$_2$), δ 2.60 (dd, 2H, *J* = 4.0, 5.0 Hz, OCHC**H$_2$**), δ 2.02–1.95 (m, 3H), δ 1.77–1.51 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 60.48, 42.99, 38.40, 37.01, 32.20, 27.99; HRMS (EI) exact mass calculated for ($C_{12}H_{18}O$) requires *m/z* 178.1358, found *m/z* 178.1362. $[\alpha]_D$ = -9.42 (c = 1.0, EtOH). The enantiomeric ratio of the epoxide was determined by GLC using a Bodman Chiraldex Γ-TA (30 m x 0.25 mm) column (100 °C isotherm, 1 mL/min); (*S*) isomer t_r = 44.4 min and (*R*) isomer t_r = 46.4 min.