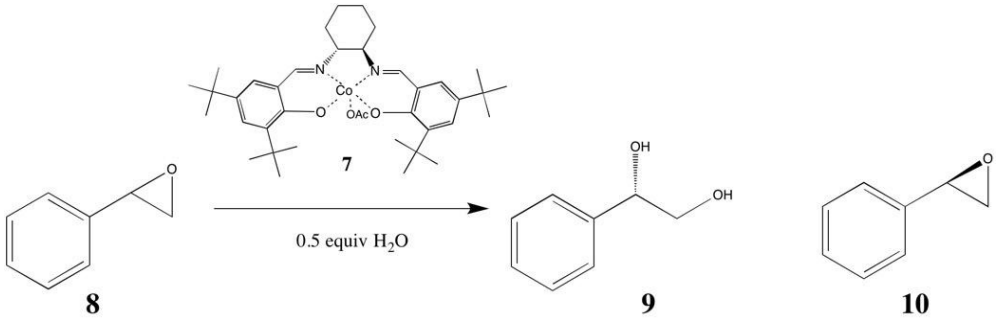
Enantioselective Epoxide Ring Opening of Styrene Oxide with Jacobsen's Salen(Co) Catalyst

Matthew Moreno and Mariah Seller

Wednesday Evening Chem 250 Laboratory, Fall 2014

Abstract



A synthesis of (*R,R*)-Jacobsen's Salen(Co) catalyst **7** is presented. Racemic styrene oxide **8** is treated with water, undergoing an epoxide-opening reaction catalyzed by complex **7**. The enantioselective catalytic properties of complex **7** favor the consumption of (*S*)-styrene oxide to form (*S*)-1-phenyl-1,2-ethanediol **9**, resolving (*R*)-styrene oxide **10**. Chiral gas chromatography analysis verifies and quantifies the enantioselectivity of this hydrokinetic resolution reaction. The enantioresolution achieved is compared to the results of other lab groups working with (*R,R*) and (*S,S*) species of Jacobsen's Salen(Co) catalyst.

Introduction

In asymmetric synthesis, specificity of chiral sites is often achieved through assembly of enantiopure reagents. These enantiopure reagents serve as building blocks in the asymmetric synthesis toolkit. Expansion of the diversity and accessibility of enantiopure chiral compounds

can broadly impact research and industry, as chemists further their own work by adopting new techniques and reagents. The development of Jacobsen's catalyst, a metal-coordinated complex that promotes the stereospecific ring opening of epoxides, marked one such advance, allowing for the hydrokinetic resolution of virtually any terminal epoxide.[1] Due to their sp^3 chiral center, structural properties, and utility in synthesizing a variety of functional groups and carbon-carbon bonds via ring opening reactions, terminal epoxides constitute an essential building block of asymmetric synthesis.[1] Before the introduction of Jacobsen's catalyst, the somewhat restricted pool of readily available chiral epoxides were obtained through olefin oxidation methods, Sharpless epoxidation reactions, biocatalysis, and catalytic action of chiral (salen) Mn^{III} complexes.[1] Nonetheless, these compounds found extensive and sundry roles as reagents in asymmetric synthesis, subjected to reactions with nucleophiles, Lewis acids, radicals, reducing agents, oxidizing agents, acids, and bases.[1] The variety and affordability of terminal, enantiospecific epoxides made possible by Jacobsen's catalyst has directly impacted the manufacture of industrially important epoxides.[2] In addition, pharmaceutical research and manufacture, which is highly sensitive to enantiomeric configuration because the biological activity of chiral compounds often differs greatly between enantiomers, benefits from expansion of the asymmetric synthesis toolkit.[3] Enantiospecific epoxide opening reactions, in particular, are known to play direct roles in pharmaceutical development. HIV protease inhibitors DMP 323 and

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[1] Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. Highly Selective Hydrolytic Kinetic Resolution of Terminal Epoxides Catalyzed by Chiral (salen)Co ^{III} Complexes. Practical Synthesis of Enantioenriched Terminal Epoxides and 1,2-Diols. *Journal of the American Chemical Society* **2002**, *124*, 1307–1315.

[2] Scharrer, E. Comments on Jacobsen's Catalyst, 2014.

[3] Woo, J.-H.; Lee, E. Y. Enantioselective Hydrolysis of Racemic Styrene Oxide and Its Substituted Derivatives Using Newly-Isolated Sphingopyxis Sp. Exhibiting a Novel Epoxide Hydrolase Activity. *Biotechnology Letters* **2014**, *36*, 357–362.

DMP 450, developed by Du Pont Merk, required careful enantiospecific engineering of a diol site to maximize the compounds' affinity for their target, the active site of HIV protease.[4] Additionally, (*R*)-1-phenyl-1,2-ethanediol, the product of an enantiospecific epoxide-opening reaction of styrene oxide, is a precursor of b-lactam antibiotics.[5] In light of the practical utility of enantiopure epoxides and active research effortson stereospecific epoxide opening reactions, we prepared Jacobsen's Salen(Co) catalyst and tested its efficacy in the hydrokinetic resolution of (*R*)-styrene oxide **10** from racemic styrene oxide.

Results and Discussion

Preparation of Jacobsen's Salen(Co) Catalyst (7)

Synthesis of Jacobsen's *(R,R)*-Salen(Co) Catalyst (**7**), presented in Scheme 1, began with the preparation of a salt from racemic 1,2-diaminocyclohexane (**1**) and L-(+)-Tartaric acid (**2**), commercially available reagents. Selective crystallization yielded tartrate salt **3**, which contained enantiopure *(R,R)*-1,2-Diammoniumcyclohexane. Salt **3** and 3,5 di-*tert*-butylsalicylaldehyde (**4**) were reacted under basic conditions to form (*R*,*R*)-*N*,*N*'-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine (**5**). The identity of product was confirmed by melting point measurement and IR analysis. The product was observed to melt between 208 and 209 °C, which matches the literature value of the melting point of ligand **5**, between 205 and 207 °C, reasonably well.[6] The product's IR spectrum, shown in Figure 1, exhibits absorbance at 1630 cm^{-1} that evidences the presence of carbon-nitrogen double bonds, indicating the successful joining of aldehyde **4** and

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[4] Gadamasetti, K. *Process Chemistry in the Pharmaceutical Industry*; CRC Press, 1999; p 205.

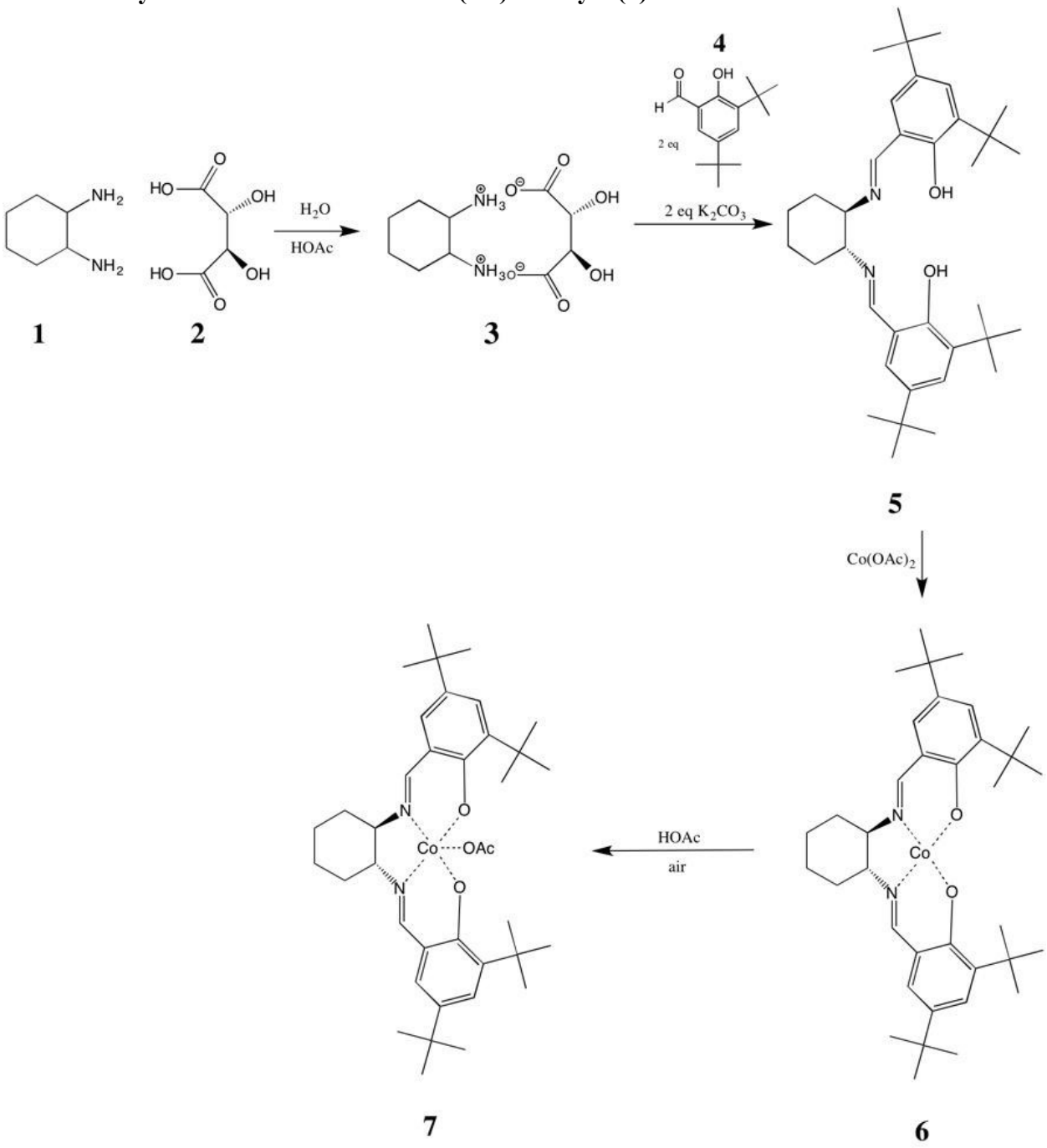
[5] Rui, L.; Cao, L.; Chen, W.; Reardon, K. F.; Wood, T. K. Protein Engineering of Epoxide Hydrolase from Agrobacterium Radiobacter AD1 for Enhanced Activity and Enantioselective Production of (R)-1-Phenylethane-1,2-Diol. *Applied and Environmental Microbiology* **2005**, *71*, 3995–4003.

[6] (R,R)-(−)-N,N′-Bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediamine 98% | Sigma-Aldrich http://www.sigmaaldrich.com/catalog/product/aldrich/404411?lang=en&region=US (accessed Dec 4, 2014).

the hexane component of salt **3**. Characteristic arene IR absorbances further confirmed the products' identity as ligand **5**. The enantiopurity of the product was assessed by polarimetry. The ligand's specific rotation in dichloromethane was observed to be -378.6°, significantly higher than the literature value of -315°.[7] Calculation of percent enantiomeric excess from this measurement yields a value of 120%, a clear impossibility. Likely, inaccurate dilution of the sample in dichloromethane led to an errantly high specific rotation reading. Stereospecificity of an epoxide opening reaction catalyzed by a derivative of the ligand, which depends directly on the enantiopurity of the ligand itself, strongly suggests that the ligand was highly enantiopure at this stage of the synthesis. Having synthesized and confirmed the identity of ligand **5**, it was treated with cobalt(II) acetate tetrahydrate, yielding Jacobsen's Salen(Co) Complex **6**. Finally, by reaction with acetic acid and exposure to air, coordinated complex **6** was converted to the active Jacobsen's Salen(Co) Catalyst **7**. Although the catalyst was expected to have a melting point too high for ready observation, its identity was confirmed by IR analysis. The diagnostic carbon-nitrogen double bond absorbance appears in its spectra, shown in Figure 2.

[7] Hanson, J. Journal of Chemical Education • Vol. 78 No. 9 September 2001. *Journal of Chemical Education* **2001**, *24*, 1266–1268.

Scheme 1. Synthesis of Jacobsen's Salen(Co) Catalyst (7)

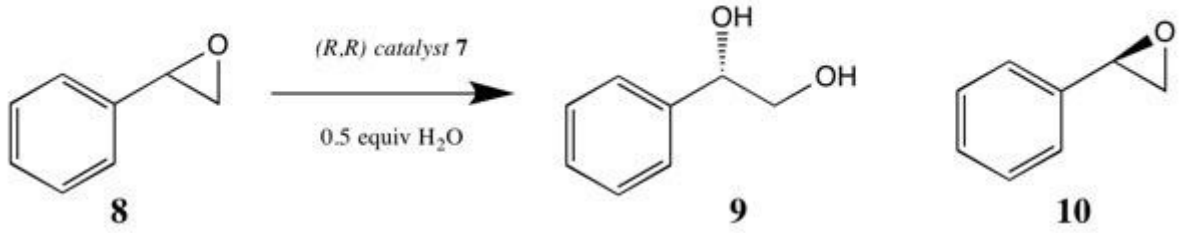


Hydrokinetic Resolution of (*R*)-Styrene Oxide 8

An enantiospecific epoxide ring opening reaction, overviewed in Scheme 2, was performed to characterize the enantioselective catalytic activity of complex **7**. A racemic mixture of styrene oxide (**8**) was treated with water and a catalytic amount of complex **7**, opening the epoxide ring

of the (*S*)-styrene oxide to form (*S*)-1-phenyl-1,2-ethanediol (**9**) while leaving the (*R*)-styrene oxide **10** unreacted. A half equivalence of water was used to maximize the enantiospecificity of the reaction. The epoxide and diol components of the product were subsequently separated by flash chromatography.

Scheme 2. Epoxide Opening of Styrene Oxide



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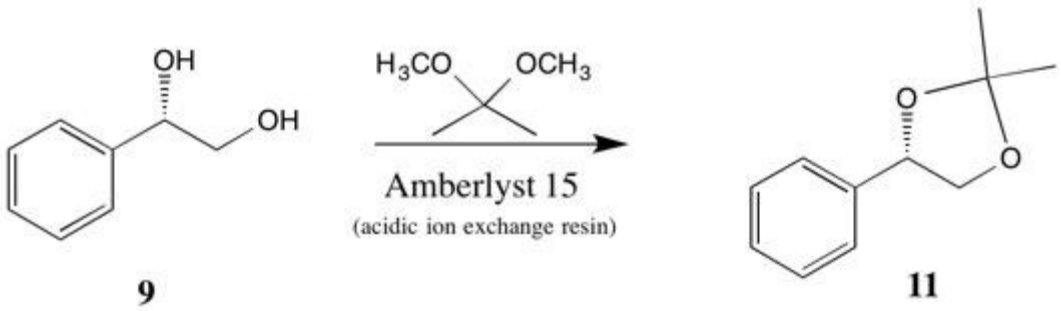
The epoxide opening reaction's structural outcome was confirmed by H-NMR and IR analysis of products **9** and **10**. H-NMR and IR spectra of both species **9** and **10**, as expected, evidence the presence of arene functionality. The IR spectra of species **9** and **10**, provided in Figures 5 and 6, contain a set of peaks between 3060 to 2900 cm^{-1}, a wavenumber range characteristic of absorbance by arene bonds. Likewise, evidence of arene functionality, a multiplet signal with an integration of 5 hydrogens and a chemical shift of around 7 ppm, can be found on H-NMR spectra obtained from both species **9** and **10**, provided in Figures 4 and 3. The H-NMR and IR spectra obtained from diol **9** exhibit signals characteristic of two alcohol groups—two overlapping IR absorbances around 3340 cm^{-1} and two broad singlet H-NMR signals with single hydrogen integrations and chemical shifts of 3.26 ppm and 2.85 ppm—that confirm its identity as a diol. In contrast, the H-NMR and IR spectra obtained from epoxide **10** lack signals characteristic of alcohol functionality, indicating that it was not reacted to form a diol. Three H-NMR doublet of doublets signals with single hydrogen integrations and chemical shifts of 3.26 ppm, 3.15 ppm, and 2.80 ppm corroborate the integrity of epoxide functionality in species **10**.

The enantioselectivity of the epoxide-opening reaction was evaluated by chiral gas chromatographic analysis, shown in Figure 6, of the isolated diol fraction **9** (and any enantiomer present) obtained by flash chromatography. Diol **9** was prepared through a ketalization reaction, shown in Scheme 3, which ensured adequate volatility for analysis by chiral gas chromatography while preserving the enantiomeric integrity of the sample.

Scheme 3. Ketalization of (*S*)-1-Phenyl-1,2-ethanediol



The enantiomeric composition of the diol product, calculated from chiral gas chromatography results, achieved by this lab group and by other lab groups is presented out in Table 1.

Table 1: Enantiomeric Composition of Diol Product of Epoxide Opening of Styrene Oxide Catalyzed by Jacobsen's Salen(Co) Catalyst

	Our Results	Other Lab Groups' Results	
	D-Tartaric acid	D-Tartaric acid	R-Tartaric acid
(*R*)-1-Phenyl-1,2-ethanediol	4%	3%	93%
(*S*)-1-Phenyl-1,2-ethanediol	96%	97%	7%

Uniformly among all data sources, one diol enantiomer was obtained in much greater abundance than its mirror opposite, demonstrating the enantiospecific catalytic properties of Jacobsen's Salen(Co) catalyst. Our group achieved 92% enantiomeric excess of (*S*)-1-Phenyl-1,2-ethanediol, slightly lower than the 94% enantiomeric excess other groups working with *(R,R)* catalyst **7**

achieved. Groups working with the (*S,S*) enantiomer of Jacobsen's Salen(Co) catalyst achieved somewhat lower enantiomeric resolution, reporting only 86% enantiomeric excess of (*R*)-1-Phenyl-1,2-ethanediol. This discrepancy could be due to a difference in the enantiopurity of the tartaric acid reagents used in the synthesis of (*S,S*) and (*R,R*) species of Jacobsen's catalyst, on which depends the enantiopurity of the catalyst and—therefore—the enantiomeric outcome of the epoxide opening reaction. As expected, groups working with opposite enantiomers of tartaric acid—and, therefore, opposite chiral configurations of Jacobsen's catalyst—achieved opposite enantiomeric outcomes in the hydrokinetic resolution of styrene oxide. The *(R,R)* enantiomer of Jacobsen's ligand, in both our experiment and other groups' experiments, favored the production of (*S*)-1-Phenyl-1,2-ethanediol while the *(S,S)* enantiomer of Jacobsen's ligand favored the production of (*R*)-1-1-Phenyl-1,2-ethanediol. Due to stoichiometric constraint of the hydrokinetic resolution, only half of the racemic mix of styrene oxide reacted with water to form a diol. We can readily deduce the dominant enantiomeric configuration of the unreacted styrene oxide from the enantiomeric composition of the diol products. The (*R,R)* enantiomer of Jacobsen's catalyst resolved (*R*)-styrene oxide and the *(S,S)* enantiomer of Jacobsen's catalyst resolved (*S*)-styrene oxide. Chiral gas chromatographic analysis of the epoxide fraction obtained through flash chromatography, shown in Figure 7, confirms that (*R*)-styrene oxide was resolved with 90% enantiomeric excess in the epoxide opening reaction catalyzed by the (*R,R*) species of Jacobsen's catalyst.

Conclusions and Future Work

Our synthesis of Jacobsen's Salen(Co) catalyst **7** and successful hydrokinetic resolution of styrene oxide demonstrates that the is practical and affordable to obtain and that it exhibits

strongly enantioselective catalytic activity. These characteristics are corroborated by the work of other students and lab groups.[8] Investigation of the mechanisms behind the catalytic action of Jacobsen's Salen(Co) catalyst **7** might lead to new protocols and reactions to better exploit its catalytic properties.[9] To this end, the Jacobsen group at Harvard has carried out kinetic studies of monomeric, dimeric, and trimeric variations of the Jacobsen's Salen(Co) catalyst **7** to probe the mechanism by which it promotes epoxide opening reactions and the rate laws that it operates under.[8] In this vein, we propose a kinetic study of epoxide opening reactions of compounds containing multiple epoxide groups catalyzed by Jacobsen's Salen(Co) catalyst **7**. Procedures developed by the Jacobsen group would be used to investigate the rate laws governing various species of poly-epoxides. The distribution of diol functionality resulting from stoichiometrically limited epoxide-opening reactions on the poly-epoxide molecules would be assessed by quantitative chromatography and IR/NMR analysis of products. The generated diol functionality might be concentrated on a subset of the treated poly-epoxide molecules or evenly distributed across the treated poly-epoxide molecules. This investigation could shed further light on how the Jacobsen's Salen(Co) catalyst interacts with substituents.

Experimental Section

General. All reagents and solvents were obtained from commercial suppliers and used without further purification. Thin-layer chromatography was carried out on 0.2-mm silica gel plates. Spots were detected by UV light (254 nm) and by use of a cerium molybdate stain. Melting

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[8] Jacobsen, E. N. Asymmetric Catalysis of Epoxide Ring-Opening Reactions. Accounts of Chemical Research 2000, 33, 421–431.

[9] Hansen, K. B.; Leighton, J. L.; Jacobsen, E. N. On the Mechanism of Asymmetric Nucleophilic Ring-Opening of Epoxides Catalyzed by (Salen)Cr III Complexes. Journal of the American Chemical Society 1996, 118, 10924–10925.

points were determined in open capillary tubes and are uncorrected. Specific rotations were measured on a JASCO P-2000 polarimeter. ^{1}H NMR spectra were recorded on a 500 MHz ECA-400 JEOL spectrometer. Tetramethylsilane was used as internal standard (0.00 ppm). Chemical shifts (δ) values are reported in parts per million (ppm) downfield from TMS and coupling constants *J* are reported in hertz (Hz). The following abbreviations are used: s (singlet) d (doublet) t (triplet), q (quartet), dd (doublet of doublets), m (multiplet), br (broad). FT-IR spectra were recorded using a diamond attenuated total reflectance PerkinElmer UATR. Two spectrometer and absorptions are reported in terms of wavenumbers ($\tilde{\nu}$, cm^{-1}). Chiral GC analysis was performed on a HP 6890 Series system. Separation was accomplished with a Cyclodex-B column under isothermal conditions (100 °C for styrene oxide, 130 °C for 2,2-dimethyl-4-phenyl-1,3-dioxolane).

(*R, R*)-1,2-diaminocyclohexane mono-(+)-tartrate salt (3). To a 15 mL solution of distilled water was added L-(+)-Tartaric acid **1** (4.5 g, 30 mmol) and a racemic mixture of 1,2-diaminocyclohexane (**2**) (6.8 g, 60 mmol). The mixture was stirred for 5 minutes in a beaker. To the mixture was added glacial acetic acid (3 mL). The thick, yellow mixture was cooled to 5 °C for 30 min. Vacuum filtration yielded a yellow solid, which was washed with cold water (1 x 3 mL) and room temperature methanol (4 x 3 mL). Recrystallization of the salt from hot water (30 mL) and vacuum filtration yielded **3** as a white powder (1.89 g, 15%).

(*R*, *R*)-*N,N*'-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine (5). To a 3 mL solution of water in a round bottom flask was added of (*R*,*R*)-1,2-diaminocyclohexane mono-(+)-tartrate salt (**3)** (0.58 g, 21 mmol) and potassium carbonate (0.62 g, 4.4 mmol). The solution was stirred and 11 mL of ethanol was added. A water-cooled reflux condenser was attached and the solution

was heated to reflux. To the refluxing solution was added 3,5 di-*tert*-butylsalicylaldehyde (**4)** (1.0 g, 4.3 mmol) dissolved in 5 mL ethanol. After refluxing for 60 min, 3 mL of water was added and the vessel was cooled to 5 °C. A solid was collected through vacuum filtration and rinsed with ethanol (5 mL). The solid was dissolved in 15 mL dichloromethane, transferred to a separatory funnel, and washed with water (2 x 5 mL) and a saturated aqueous NaCl solution (5 mL). The organic layer was isolated, dried with sodium sulfate and decanted. Solvent was removed by rotary evaporation to give a bright yellow solid **5** (0.624 g, 55%); Mp 208-209 °C; IR(cm^{-1}, ATR): 2950, 2800, 1629, 1437, 1361, 1269, 1173, 878, 828, 772, 711, 644; $[\alpha]^{20}_{D}$ -378.6 (c 1.0, CH_2Cl_2).

[*(R,R)*-*N,N'*-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanedi-aminato(2-)]cobalt(II) (*(R,R)*-1) (6). A solution of cobalt(II) acetate tetrahydrate (0.27 g, 1.1 mmol) in 4 mL of methanol and a solution of ligand **5** (0.5 g, 0.09 mmol) in 4 mL of dichloromethane were prepared. The two solutions were mixed in an Erlenmeyer flask and stirred for 5 min. A dark red precipitate was observed. The mixture was then covered and cooled to 5 °C for 15 min. A solid was collected by vacuum filtration and washed with cold methanol (2 x 5 mL), yielding a burgundy red solid **6** (0.25 g, 45%): IR(cm^{-1}, ATR): 2950, 1594, 1524, 1317, 1252, 1174, 784, 542.

(*S*)-1-phenyl-1,2-ethanediol (9). To a solution of 1 mL of dichloromethane was added Jacobsen's Salen(Co) complex **6** (0.048 g, 0.08 mmol) and 0.05 mL of acetic acid. The mixture was stirred for 30 min. Solvent was removed by rotary evaporation, yielding the crude catalyst as a dark brown liquid. To the crude catalyst was added THF (0.1 mL) and racemic styrene oxide (**8**) (1.14 mL, 10 mmol). The mixture was cooled to 5 °C for 5 min, then water was added (0.100

mL, 5.5 mmol). The mixture was stirred at room temperature for 90 min then dried exposed to air for a week at room temperature. The crude product (~2 g) was dissolved in dichloromethane (~20 mL) and silica gel (~10 g) was added to form a slurry, which was dried by rotary evaporation to yield a free-flowing powder. The powder was subjected to modified flash chromatography (hexanes:EtOAc 85:15, EtOAc:hexanes 80:20) and rotary evaporation, yielding (*R*)-styrene oxide (**10**) (3.9 mmol) as an opaque liquid: (Cyclodex-B, 100 ºC, isothermal, t_R (minor) = 10.84 min, t_R (major) = 10.41 min); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.24 (m, 5 H), 3.86 (dd, J = 3.3 Hz, 5.0 Hz, 1 H), 3.15 (dd, J = 5.2 Hz, 6.9 Hz, 1 H), 2.80 (dd, J = 3.3, 6.9 Hz, 1 H); R_f = 0.60 (hexanes:EtOAc 85:15, blue in ceric stain); IR(cm^{-1}, ATR, thin film): 3039, 2989, 1685, 1496, 1476, 1389, 1265, 1201, 984, 873, 756, 696; and (*S*)-1-phenyl-1,2-ethanediol (**9**) (0.563 g, 74%) as a brown, crystalline solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.38 (m, 5 H), 4.82 (dd, J = 3.3 Hz, 9.8 Hz, 1 H), 3.85-3.60 (m, 2 H), 3.26 (s, 1 H), 2.85 (s, 1 H); R_f = 0.54 (EtOAc:hexanes 80:20, blue in ceric stain); IR(cm^{-1}, ATR): 3351, 3239, 3030, 2869, 1736, 1447, 1192, 1068, 1047, 1021, 891, 835, 750, 634, 526.

2,2-dimethyl-4-phenyl-1,3-dioxolane (11). To a solution of 2,2-dimethoxypropane (0.5 mL, 4.1 mmol) was added 1-phenyl-1,2-ethanediol (**9**) (0.025 g, 0.18 mmol). The mixture was stirred to dissolve the diol. Amberlyst 15 ion exchange resin (0.04 g) was added and the mixture was stirred for 10 min, yielding dioxolane **11** in 2,2-dimethoxypropane as a clear liquid: (Cyclodex-B, 100 ºC, isothermal, tR (minor) = 10.84 min, tR (major) = 10.41 min).

References

(1) Jacobsen, E. N. Asymmetric Catalysis of Epoxide Ring-Opening Reactions. Accounts of Chemical Research 2000, 33, 421–431.

(2) Scharrer, E. Comments on the Utility of Jacobsen's Catalyst, 2014.

(3) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. Highly Selective Hydrolytic Kinetic Resolution of Terminal Epoxides Catalyzed by Chiral (salen)Co III Complexes. Practical Synthesis of Enantioenriched Terminal Epoxides and 1,2-Diols. Journal of the American Chemical Society 2002, 124, 1307–1315.

(4) Hanson, J. Journal of Chemical Education • Vol. 78 No. 9 September 2001. Journal of Chemical Education 2001, 24, 1266–1268.

(5) Hansen, K. B.; Leighton, J. L.; Jacobsen, E. N. On the Mechanism of Asymmetric Nucleophilic Ring-Opening of Epoxides Catalyzed by (Salen)Cr III Complexes. Journal of the American Chemical Society 1996, 118, 10924–10925.

(6) Gadamasetti, K. Process Chemistry in the Pharmaceutical Industry; CRC Press, 1999.

(7) Rui, L.; Cao, L.; Chen, W.; Reardon, K. F.; Wood, T. K. Protein Engineering of Epoxide Hydrolase from Agrobacterium Radiobacter AD1 for Enhanced Activity and Enantioselective Production of (R)-1-Phenylethane-1,2-Diol. Applied and Environmental Microbiology 2005, 71, 3995–4003.

(8) (R,R)-(−)-N,N′-Bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediamine 98% | Sigma-Aldrich http://www.sigmaaldrich.com/catalog/product/aldrich/404411?lang=en&region=US (accessed Dec 4, 2014).

Chem 250 lab reports - Experimental section checklist

Name: Matthew Moreno and Mariah Seller Group: Weds Eve Lab Section

Title of experiment: Jacobsen Catalyst Progress Report

- A "General section" is provided at the beginning of the experimental section. ☐
- Parts of the "General section" that don't apply to the current experiment are not included. ☐
- Numbers never start with a period: there is a zero before the decimal mark if a number is smaller than 1. ☐
  example: it's 0.0013 and *not* .0013
- Correct abbreviations and symbols are used. (Note: Most common abbreviations don't end with a period.) ☐

Quantity	Symbol/abbreviation	Quantity	Symbol/abbreviation
57 grams	57 g	90 Kelvins	90 K (note: *no* ° for Kelvins)
2.3 milliliters	2.3 mL	100 degree Celsius	100 °C
10 liters	10 L	25 seconds	25 s (note: *not* sec)
22 moles	22 mol (note: *not* mols)	12 minutes	12 min
0.0011 moles	11 mmol	24 hours	24 h (note: *not* hrs)
tetrahydrofuran	THF	94 percent	94% (note: *no* space)
dichloromethane	don't abbreviate (DCM *not* accepted)		

- There is always a space between a number and its units, *except* for percentages. ☐
  example: it's 30 °C and *not* 30°C, but it's 78% and *not* 78 %. (Note that for temperatures in degree Celsius, the space is before ° and not between ° and C.)
- Quantities (volume or mass) for reagents are given in parenthesis after the reagent AND the number of moles is also indicated. ☐
  example: 2-butanol (1.20 mL, 0.0131 mol) was added and the solution was stirred
- Quantities for solvents and workup solutions are in parenthesis after the solvent AND the number of moles is NOT indicated. ☐
  example: 2-butanol (1.20 mL, 0.0131 mol) and dicholoromethane (7.3 mL) were added
  example: the organic layer was washed with water (2 x 5 mL) and brine (5 mL)
- Significant figures are respected. ☐
  example: if you weighed 1.2 g, the reported mass is 1.2 g and not 1.20 g
  example: bromobenzene (0.34 mL, 3.2 mmol), magnesium (0.120 g, 4.94 mmol), iodine (5 mg, 0.02 mmol) and THF (11 mL) were added
- When a product has been isolated:
  - the quantity (the mass, or more rarely the volume) is indicated ☐
  - the yield is indicated (with *no* decimals, regardless of significant figures) ☐
  - the physical appearance is indicated ☐
    example: the product, 2-chlorobutane, was obtained as a colorless oil (0.871 g, 72%)
    example: and benzoic acid was isolated as a fluffy white solid (4.02 g, 89%)
    example: the product was obtained as long yellow needles (7.8 mg, 68%)
- NMR and IR spectra are described from left to right. ☐
- When describing IR spectra, all the strong signals are reported, not just the ones you can assign. ☐