

# Co(III)-Porphyrin-Mediated Highly Regioselective Ring-Opening of Terminal Epoxides with Alcohols and Phenols

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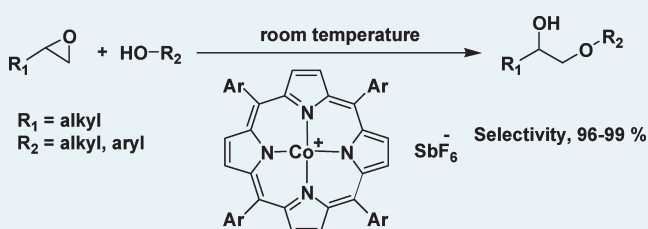
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**S** Supporting Information

**ABSTRACT:** Co-T(*p*-OMe)PP-SbF<sub>6</sub> (**1-SbF<sub>6</sub>**, T(*p*-OMe)PP = 5,10,15,20-tetrakis(4-methoxyphenyl)porphyrinato) is demonstrated to be a highly active and regioselective catalyst in the ring-opening of various epoxides with alcohols and phenols. **1-SbF<sub>6</sub>** is demonstrated to be twice as active as the established Co-salen-SbF<sub>6</sub> (**2-SbF<sub>6</sub>**, salen = *trans*-N,N-bis(3,5-ditertbutylsalicylidene)-1,2-cyclohexanediamine) catalyst, exhibiting >99% regioselectivity in many cases. The catalyst is suggested to promote the ring-opening via a cooperative bimolecular mechanism because the Co-porphyrin dimer, **1d-OTs**, is significantly more active compared with the monomeric catalyst, **1-OTs**.

**KEYWORDS:** epoxides, co-porphyrin, ring-opening,  $\alpha$ -alkoxy alcohols,  $\alpha$ -aryloxy alcohols



## INTRODUCTION

Epoxides are highly valuable intermediates in organic synthesis,<sup>1</sup> and their synthetic potential to undergo regioselective ring-opening with different species, such as OH<sup>-</sup>,<sup>2-4</sup> Cl<sup>-</sup>,<sup>5</sup> CN<sup>-</sup>,<sup>6-8</sup> amines,<sup>9</sup> or other nucleophiles,<sup>10-15</sup> makes them especially interesting candidates for organic synthesis in the chemical, polymer, and agrochemical industries. The nucleophilic attack on a 1,2-epoxide can occur at either the C1 or C2 position, depending on the nature of the substituent groups, catalyst, and reaction temperature. The ring-opening of epoxides with oxygen-based nucleophiles, such as alcohols and phenols, is documented as a challenging reaction and often requires elevated temperatures, high catalyst loadings, or both.<sup>16</sup> In many instances, the regioselectivity was found to be poor; for instance, use of aluminum triflate or potassium hydroxide as catalyst gave nearly a 50:50 ratio of the products 2-methoxy-1-butanol and 1-methoxy-2-butanol when methanol and 1,2-epoxybutane were used as reagents.<sup>17-19</sup>

Metalloporphyrins have been used to catalyze a wide variety of important chemical transformations,<sup>20</sup> including epoxidations,<sup>21</sup> aminations,<sup>20</sup> epoxide ring-opening,<sup>22</sup> and cyclopropanations,<sup>23</sup> among others. Epoxide carbonylation by Coates,<sup>24</sup> olefination of aldehydes and ketones by Zhang,<sup>25</sup> and epoxidation of olefins by Nguyen and Hupp<sup>21</sup> are other notable examples. More recently, Monnereau et al.<sup>26</sup> used a manganese macrocyclic porphyrin as an efficient epoxidation catalyst. In a continuation of our ongoing research on epoxide ring-opening reactions,<sup>27-33</sup> we report herein a new catalytic methodology for regioselective 1,2-epoxide ring-opening with alcohols and phenols using a Lewis acidic Co(III)-porphyrin catalyst. In contrast to past work that has

focused on enantioselectivity using Co(III)-salen catalysts, this work focuses on regioselective ring-opening using porphyrin catalysts. To the best of our knowledge, this is the first example of the use of a cobalt-porphyrin for 1,2-epoxide ring-opening using alcohols and phenols as nucleophiles.

## RESULTS AND DISCUSSION

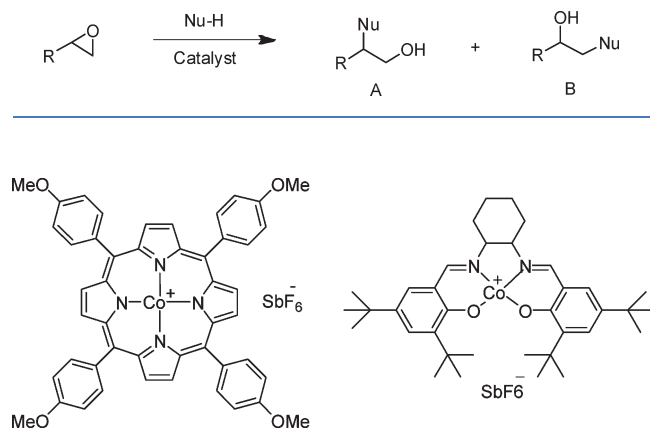
Co-T(*p*-OMe)PP-SbF<sub>6</sub> (**1-SbF<sub>6</sub>**, T(*p*-OMe)PP = 5,10,15,20-tetrakis(4-methoxyphenyl)porphyrinato) was synthesized by oxidation of Co-T(*p*-OMe)PP using AgSbF<sub>6</sub> as an oxidizing agent in 79% yield. The formation of **1-SbF<sub>6</sub>** (Figure 1) was confirmed using <sup>1</sup>H NMR as well as single crystal X-ray crystallography (Figure 2). In the asymmetric unit, there are two independent porphyrin molecules: one has a relatively planar porphyrin core conformation, and the second has a ruffled or puckered conformation. It is noteworthy that the solvent molecule (DMSO) coordinates through an oxygen atom in one molecule and via the sulfur atom in the second molecule. Although DMSO coordination through the sulfur atom is preceded in complexes of other metals, it has not been previously reported with cobalt. The metric parameters are given in the Supporting Information.

The ring-opening of 1,2-epoxyhexane with methanol was chosen as the model reaction to elucidate the activity of the catalyst **1-SbF<sub>6</sub>**. At room temperature with 2 mol % catalyst loading, **1-SbF<sub>6</sub>** showed superior activity and selectivity over the related salen catalyst **2-SbF<sub>6</sub>** (Figure 1). With **1-SbF<sub>6</sub>**, the

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Chart 1



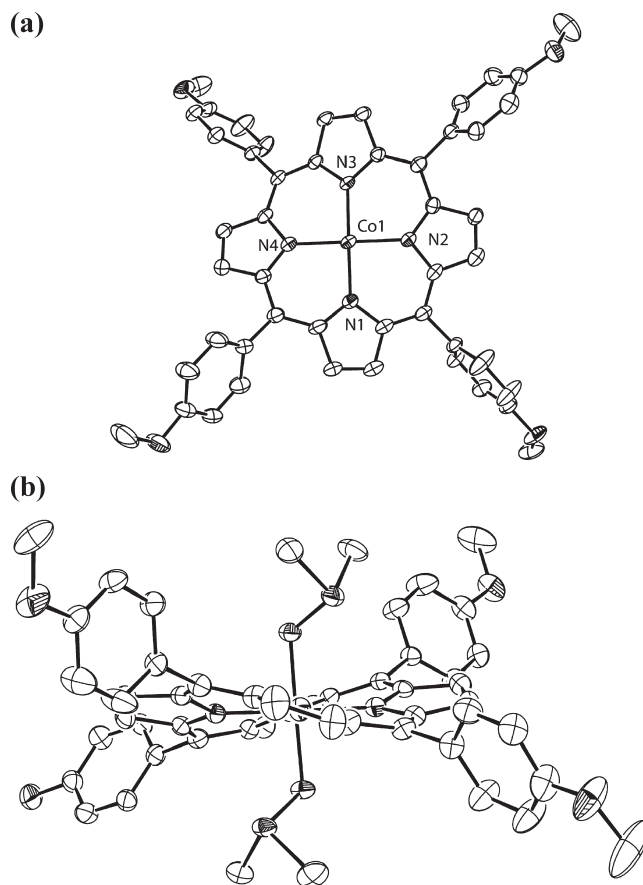
**Figure 1.** Co-T(*p*-OMe)PP-SbF<sub>6</sub> (**1-SbF<sub>6</sub>**) and Co-salen-SbF<sub>6</sub> (**2-SbF<sub>6</sub>**).

reaction was complete in 1 h with 99% regioselectivity, whereas **2-SbF<sub>6</sub>** required 6 h for full conversion with lower selectivity (94%) (Figure 3). The porphyrin-based catalyst was twice as active as the salen catalyst, with an initial turnover frequency of (3.3 min<sup>-1</sup>).

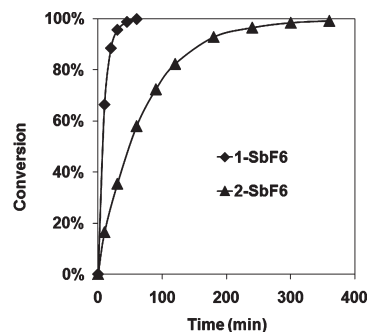
The scope of the reaction was studied with different alcohols and epoxides. Reaction of 1,2-epoxyhexane with alcohols such as methanol, ethanol, and hexanol proceeded smoothly to afford the ring-opened products with high regioselectivity. The less nucleophilic alcohols, ethanol and hexanol, required longer reaction times of 10 and 15 h, respectively, whereas the methanol reaction was complete in 1 h. The ring-opening was also evaluated with different epoxides using methanol as the nucleophile. Under the same experimental conditions, epichlorohydrin and allylglycidyl ether were converted with excellent regioselectivity with extended reaction times (Table 1).

The ring-opening of phenols is a related reaction that has proven to be challenging to perform at lower catalyst loadings, and in some instances, 10 mol % of catalyst was required to achieve good yields.<sup>3,34</sup> The high regioselectivity in the synthesis of  $\alpha$ -aryloxy alcohols reported above prompted the evaluation of the activity of **1-SbF<sub>6</sub>** in 1,2-epoxide ring-opening with phenols. The results are presented in Table 2. Although the reaction of epoxides with phenols under neat conditions gave good conversions and selectivities at 1 mol % catalyst loading, to avoid solubility issues, the reactions were performed in TBME at 2–4 mol % catalyst loading. Both electron-donating and electron-withdrawing groups on the phenolic species allowed for the synthesis of  $\alpha$ -aryloxy alcohols with excellent regioselectivity and with good conversions. It is noteworthy that 1,2-epoxyhexane afforded the corresponding  $\alpha$ -aryloxy alcohols at 2 mol % catalyst loading but epichlorohydrin needed a slightly higher catalyst loading (4 mol %) due to the electronic suppression of the reactivity of this epoxide.

It is known that Co-salen catalysts achieve epoxide ring-opening through a cooperative, bimetallic transition state in many cases.<sup>35–37</sup> On the basis of this precedent along with the tendency for M-porphyrins to aggregate in solution,<sup>38,39</sup> and the crystal packing of the **1-SbF<sub>6</sub>** catalyst, we considered that this catalyst may also operate via a cooperative mechanism.<sup>40</sup> Measuring the order of the ring-opening reaction with respect to **1-SbF<sub>6</sub>** demonstrated the reaction may, indeed, proceed in a cooperative manner because



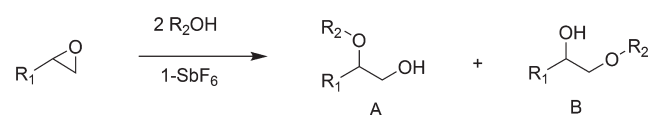
**Figure 2.** ORTEP representation of **1-SbF<sub>6</sub>**. One of the two independent cations is shown with thermal ellipsoids at 50% probability. The anions, hydrogen atoms, and solvent molecules are omitted for clarity. (a) Top view (coordinated DMSO omitted for clarity) and (b) side view. Selected interatomic distances (Å): Co1–N1, 1.949(3); Co1–N2, 1.946(3); Co1–N3, 1.947(4); Co1–N4, 1.946(3); Co1–O5, 1.929(3); Co1–O6, 1.923(3); Co1A–N1A, 1.976(4); Co1A–N2A, 1.971(4); and Co1A–S1A, 2.481(15).



**Figure 3.** Kinetic plot of the ring-opening of 1,2-epoxyhexane with methanol at 25 °C (2 mol % Co loading).

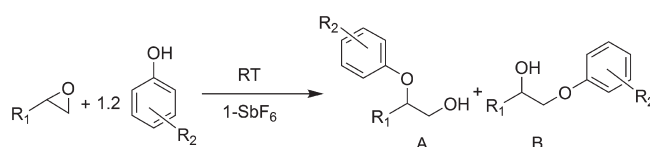
the reaction was 1.6 order in **1-SbF<sub>6</sub>**, akin to catalysts known to operate by a cooperative mechanism in 1,2-epoxide ring-opening with water. It is also possible that multiple pathways operate, including both monometallic and bimetallic pathways.<sup>41</sup>

To further confirm the cooperative nature of the reaction, we designed and synthesized a porphyrin dimer, adopting a procedure

**Table 1. Epoxide Ring-Opening with Alcohols Using 1-SbF<sub>6</sub> at 25 °C**

no.	R1	R2	conv <sup>a</sup> (%)	time (h)	sel. B <sup>a</sup> (%)
1	<i>n</i> Bu <sup>b</sup>	Me	99	1	99
2	<i>n</i> Bu <sup>c</sup>	Et	99	10	98
3	<i>n</i> Bu <sup>c</sup>	hexyl	99	15	96
4	CH <sub>2</sub> OCH <sub>2</sub> CH=CH <sub>2</sub> <sup>c</sup>	Me	98	24	99
5	CH <sub>2</sub> Cl <sup>c</sup>	Me	99	20	99

<sup>a</sup> Determined by GC. <sup>b</sup> 2 mol % catalyst used. <sup>c</sup> 4 mol % catalyst used.

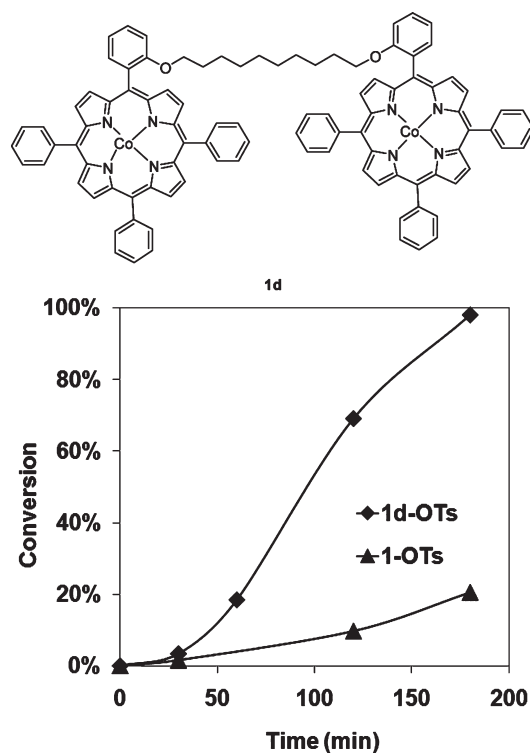
**Table 2. Epoxide ring-opening with phenols using 1-SbF<sub>6</sub> at 25 °C**

no.	R1	R2	conv <sup>a</sup> (%)	time (h)	sel. B <sup>a</sup> (%)
1	<i>n</i> Bu <sup>b</sup>	H	98	5	99
2	<i>n</i> Bu <sup>b</sup>	3-Cl	98	22	99
3	<i>n</i> Bu <sup>b</sup>	3-Me	99	6	99
4	<i>n</i> Bu <sup>b</sup>	4-Me	98	6	99
5	CH <sub>2</sub> Cl <sup>c</sup>	H	96	24	99
6	CH <sub>2</sub> Cl <sup>c</sup>	3-Cl	98	22	99
7	CH <sub>2</sub> Cl <sup>c</sup>	3-Me	93	22	98

<sup>a</sup> Determined by GC. <sup>b</sup> 2 mol % catalyst used. <sup>c</sup> 4 mol % catalyst used.

similar to that reported in the literature.<sup>42</sup> The dimer was characterized using <sup>1</sup>H NMR as well as MALDI mass spectrometry. The MALDI analysis confirms the proposed dimeric structure (Supporting Information). The porphyrin dimer was metalated using cobalt(II) acetate to yield the Co(II) dimer, whose structure was again confirmed by MALDI mass spectrometry.

The dimer **1d** was activated using *p*-toluenesulfonic acid in air and evaluated in the epoxide ring-opening of 1,2-epoxyhexane using methanol as the nucleophile at 0.2 mol %. If the reaction is cooperative, the dimeric catalyst should efficiently proceed at this significantly reduced catalyst loading. Indeed, the reaction was completed in 3 h with more than 99% selectivity, whereas the monomeric catalyst gave only 20% conversion at the same catalyst loading over the same time. The enhanced activity of **1d-OTs** over **1-OTs** is attributed to the cooperativity enforced in **1d-OTs** by design. It should be noted that **1-SbF<sub>6</sub>** and **1-OTs** have approximately equal activity, whereas **1-OAc** was almost inactive under the same experimental conditions. It is further noteworthy that although these catalysts display an induction period, as shown in Figure 4, the other catalysts described here do not have a notable induction period.



**Figure 4.** Co(III)-porphyrin dimer, **1d-OTs**, catalyzed ring-opening of 1,2-epoxyhexane with methanol at 25 °C (0.2 mol % Co loading).

## CONCLUSIONS

In summary, we describe here the highly regioselective ring-opening of epoxides with alcohols and phenols as nucleophiles using a Co(III)-porphyrin catalyst. Under mild reaction conditions, the highly active catalyst gives  $\alpha$ -alkoxy and  $\alpha$ -aryloxy alcohols with excellent regioselectivity at high conversion. The porphyrin catalyst is shown to be twice as active as a comparable salen-based epoxide ring-opening catalyst, and the reaction is proposed to proceed via a cooperative bimetallic mechanism. Further studies exploring the mechanism and application of monomeric and dimeric Co(III)-porphyrins for epoxide ring-opening reactions are currently in progress.

## EXPERIMENTAL SECTION

**Synthesis of Co-(T(*p*-OMe)PP)-SbF<sub>6</sub> (1-SbF<sub>6</sub>).** To a solution of Co(T(*p*-OMe)PP) (0.40 g, 0.50 mmol) in dichloromethane (100 mL) was added AgSbF<sub>6</sub> (0.17 g, 0.50 mmol). The solution was stirred for 12 h at room temperature and filtered through a Celite-loaded frit (the filtration process was repeated twice). The solvent was removed using rotovap, and the solid was dried under vacuum for 12 h to get a pink solid. Yield: 0.41 g (79%). <sup>1</sup>H NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO, 25 °C)  $\delta$ : 9.18 (s, 8H, -pyr), 8.09 (d, *J* = 8.4 Hz, 8H, -Ph), 7.41 (d, *J* = 8.4 Hz, 8H, -Ph), 4.04 (s, 16H, -OMe). X-ray quality single crystals were grown by slow evaporation of **1-SbF<sub>6</sub>** in DMSO.

**Synthesis of trans-Salen-Co-SbF<sub>6</sub> (2-SbF<sub>6</sub>).** *trans*-Salen-Co-SbF<sub>6</sub> (**2-SbF<sub>6</sub>**) was synthesized as previously reported.<sup>41</sup> To a suspension of AgSbF<sub>6</sub> (0.28 g, 0.83 mmol) in dichloromethane (10 mL) was added *trans*-salen-Co (**2**) (0.50 g, 0.83 mmol) in dichloromethane (20 mL). The solution was stirred for 4 h and filtered through a frit loaded with Celite. The solvent was

removed using rotovap and was washed with pentane. The green solid obtained was crystallized using dichloromethane and hexanes at low temperature. Yield: 0.62 g (89%).  $^1\text{H}$  NMR (400 MHz,  $(\text{CD}_3)_2\text{SO}$ , 25 °C)  $\delta$ : 7.81 (s, 2H), 7.45 (d,  $J = 2.4$  Hz, 2H), 7.42 (d,  $J = 2.4$  Hz, 2H), 3.59–3.57 (m, 2H), 3.06–3.04 (m, 2H), 2.00–1.98 (m, 2H), 1.90–1.88 (m, 2H), 1.72 (s, 18H), 1.59–1.54 (m, 2H), 1.28 (s, 18H).

**General Procedure for Epoxide Ring-Opening with Alcohols.** The catalyst **1-SbF<sub>6</sub>** (2.0 mol %) was dissolved in racemic 1,2-epoxyhexane (2 mmol) (chlorobenzene was added as an internal reference for the GC analysis). The flask was immersed into a water bath at ambient temperature, and methanol (4 mmol, 2 equiv) was added to the system to start the reaction. Samples were taken from the reaction mixture at each designated time, diluted with anhydrous diethylether and passed through a plug of silica gel in a Pasteur pipet to remove the catalyst. The conversions and selectivity were assessed by GC analysis.

## ■ ASSOCIATED CONTENT

**S Supporting Information.** Experimental procedures as well as characterization of **d**. GC traces and NMR data for  $\alpha$ -alkoxy and  $\alpha$ -aryloxy alcohols are available. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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## ■ ACKNOWLEDGMENT

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