

Strong influence of the nucleophile on the rate and selectivity of 1,2-epoxyoctane ring-opening catalyzed by tris(pentafluorophenyl)borane

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Introduction

Tris(pentafluorophenyl)borane, B(C₆F₅)₃ (**1**) has been shown to be a strong Lewis acid with high thermal stability, water tolerance and chemical versatility, and has been studied as a catalyst or an initiator in many reactions. Of industrial relevance is the role of **1** in the catalytic, regioselective ring-opening (RO) polymerization of epoxides, as these reactions are essential to the production of polyurethanes, poly(ethylene glycols) and other polymers. Intriguingly, in the presence of **1**, terminal epoxides are activated such that the nucleophile preferentially attacks the more sterically hindered carbon atom [1]. Conversely, other catalysts are either unselective or preferentially attack the unencumbered carbon. Given the role of the above-mentioned polymers for industrial, medical and specialty applications, expanding the current understanding of the unique properties of **1** that facilitate its regioselectivity and reactivity can lead to advances in many fields. In this work, Density Functional Theory (DFT), and microkinetic modelling are used to investigate the mechanisms of 1,2-epoxyoctane RO, catalyzed by **1**, with primary and secondary alcohol nucleophiles, i.e. 1-propanol and *iso*-propanol. This builds upon our initial work [2] where two novel catalytic pathways were proposed in addition to the conventional Lewis acid mechanism, i.e. a water-mediated and an alcohol-mediated pathway, as illustrated in Figure 1. Insights from this study uncover the influence of the nucleophile on terminal epoxide RO catalyzed by **1**.

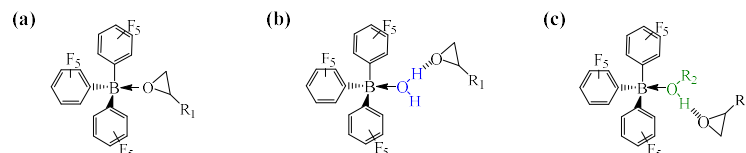


Figure 1. Representations of catalytic species in (a) the Lewis acid, (b) water-mediated and (c) alcohol-mediated pathways.

Materials and Methods

RO experiments were conducted at temperatures from 0°C-70°C and initial water concentrations from 25-3100ppm. Water levels were determined by Karl Fischer titration and are accurate to ±10 ppm, and reactions were analyzed using GC-FID. Regio-selectivity is calculated as the concentration of the primary alcohol products vs. all RO products. DFT calculations were performed using the Gaussian suite of programs. Geometry optimizations and all calculations were performed at the B3LYP-D3BJ/6-31+G(d,p) level of theory. The SMD

universal solvation model was used to capture solvation effects. Microkinetic modeling was performed using in-house developed software.

Results and Discussion

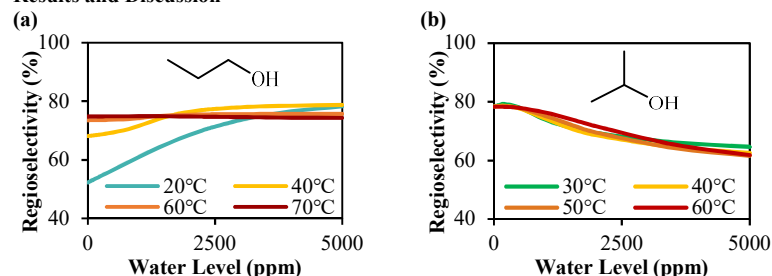


Figure 2. Microkinetic model predictions for regioselectivity vs. water level at temperatures from 20°C-70°C and at 40% epoxide conversion for (a) 1-propanol and (b) *iso*-propanol.

For *iso*-propanol, the Lewis acid RO regime dominates at low water levels, and water-mediated RO dominates as water levels increase, leading to the selectivity pattern in Figure 2,b). The tradeoffs between these two pathways also makes the selectivity trend largely temperature independent. However, for 1-propanol, two regimes operate at low water levels depending on the temperature. The Lewis acid regime, which has fast rates and inherently high selectivity dominates at high temperatures. However, low-water, low-temperature conditions promote the alcohol-mediated pathway which has very low inherent selectivity, as shown in Figure 2,a). Flux analyses indicated that although alcohol-mediated RO had a small contribution to the overall flux for 1-propanol, it significantly suppressed the overall selectivity. At high water levels, water-mediated regimes reduced the overall reaction rate but had variable impacts on selectivity. Binding enthalpies and free energies showed that the unfavourability of *iso*-propanol to bind to the boron center led to the alcohol-mediated pathway having negligible flux for all conditions.

Significance

The triple-pathway (Lewis acid, water-mediated and alcohol-mediated) mechanism proposed for the RO of 1,2-epoxyoctane by 1-propanol and *iso*-propanol, catalyzed by **1**, was studied using both computational and experimental methods. The role of the nucleophile was highlighted by the changes in flux through alcohol-mediated pathways which significantly affected overall rates and selectivities.

References

1. A. Raghuraman, D. Babb, M. Miller, M. Paradkar, B. Smith, and A. Nguyen, "Sequential DMC/FAB-catalyzed alkoxylation toward high primary hydroxyl, high molecular weight polyether polyols," *Macromolecules*, 49, 6790 (2016).
2. Y. Ying et al., "Mechanism of regioselective ring-opening reactions of 1,2-epoxyoctane catalyzed by tris(pentafluorophenyl)borane: a combined experimental, DFT, and microkinetic study," *ACS Catal.*, (Accepted).