Quantitative structure–reactivity relationship-guided mechanistic study of nitroxyl radical-catalyzed alcohol oxidation

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Alcohol oxidation is a fundamental reaction in organic synthesis, producing valuable intermediates and functional compounds. In this study, we investigated the reaction mechanism of alcohol oxidation with a nitroxyl radical catalyst and a hypervalent iodine reagent using data-driven quantitative structure–reactivity relationship (QSRR) analyses. The purpose of the study was to clarify the rate-determining step and guide reaction optimization. The QSRR analyses revealed that the percent buried volume (%Vbur) with a radius of 2.5 Å centered on the α-carbon of alcohol substrates was highly correlated with initial reaction rates for diverse substrates, supporting that the addition of the alcohol to the catalyst is involved in the rate-determining step. Based on this hypothesis, the oxidation reaction was optimized by water addition, leading to the design of more efficient nitroxyl radical-catalyzed alcohol oxidation.