Carboxylic Acid-Cooperative Ru(bpga)-Catalyzed Highly Site-Selective C–H Oxygenation

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C–H oxygenation is a useful and powerful tool for the short-step and atom-economic organic synthesis.[1] Recently, highly practical and site-selective C–H oxygenation has been revealed by using Ru(bpga) [bpga: *N*,*N*-bis(2-pyridylmethyl)glycinamide] **1a** as the catalyst, albeit with requiring atom-economically unfavored hypervalent iodine regent as the terminal oxidant.[2,3] Fortunately, during these studies, we found that the C–H oxidation dramatically accelerated through hydrogen bonding between an oxo ligand and a carboxylic acid. On the other hand, in non-heme-enzymatic catalysis, carboxylate ligands have been known to activate H_2O_2 to give the putative metal(oxo) species. Thus, ruthenium-catalyzed oxidation combined with these acid-cooperative effects was thought to be able to use hydrogen peroxide, an environmentally friendly and atom-economic reagent, as the terminal oxidant.

Based on this consideration, we investigated the acid-cooperative C–H oxidations using Ru(bpga) catalysts and hydrogen peroxide, and achieved a highly practical and useful catalytic site-selective C–H oxygenation by introducing Ru(bpga)(H-maleate)$_2$ complex **1b** as the catalyst (Figure 1).[4] Intramolecular acid-cooperative complex **1b** with hydrogen peroxide presented excellent site-selectivity on even late-stage C–H oxygenation, and high turnover frequency (up to 600 rph). The C–H oxygenation allowed wide functional group tolerance; the substrates bearing nitro, cyanide, alcohol, sulfonamide, carbamate, pyridine, and amine groups can also produce oxygenated compounds with excellent site-selectivity.

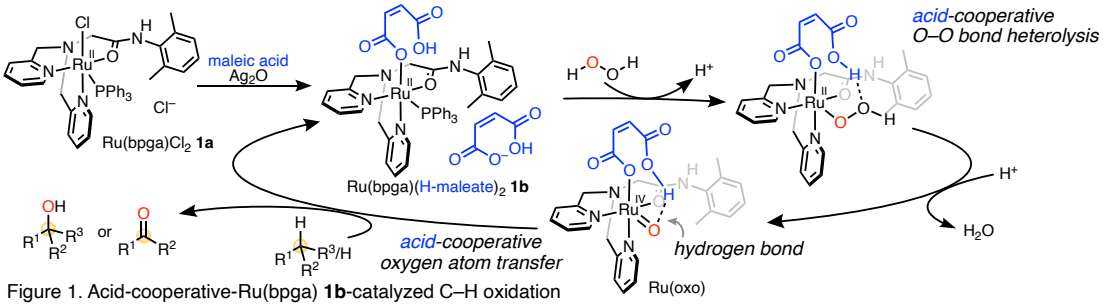

Figure 1. Acid-cooperative-Ru(bpga) **1b**-catalyzed C–H oxidation

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