Reaction Optimization of Electrochemical Synthesis of Ketimines by Machine-Learning-Assisted Multiparameter Screening

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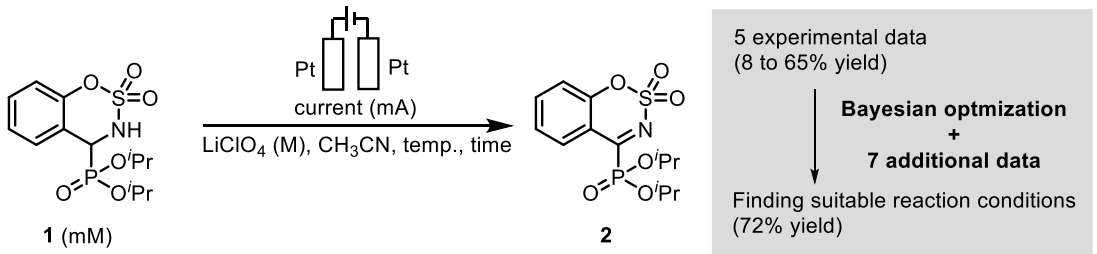
Reaction optimization is an inevitable step for developing a novel reaction. A traditional exhaustive screening by a chemist is often time-consuming and costly. Machine-learning-assisted screening and optimization have been increasingly utilized in organic synthesis to reach optimal reaction conditions, rapidly. Among them, multi-parameter screening using Bayesian optimization (BO) is an attractive and robust tool since this algorithm efficiently finds a global maximum with a small number of experimental data.[1] Here, we report BO-assisted multiparameter screening for electrochemical synthesis of cyclic ketimines.

To optimize five kinds of reaction parameters for the electrochemical oxidation of **1** such as concentration of **1** (5–20 mM) and $LiClO_4$ (0.05–0.2 M) in CH_3CN, current (1–5 mA), temperature (25–60 °C), and reaction period (60–180 min), we collected five experimental data to obtain **2** (8–65% yield). Using BO and these dataset, next parameters to examine were suggested. When we evaluate these variables by an experiment, the cyclic ketimine **2** was obtained in 60%. Repeating further six times of BO-assisted screening to improve the yield of **2**, we found suitable reaction conditions affording the desired product **2** in 72% yield ([**1**]: 10.4 mM, [$LiClO_4$]: 0.19 M, current: 3 mA, temperature: 45 °C, reaction period: 120 min).[2]



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