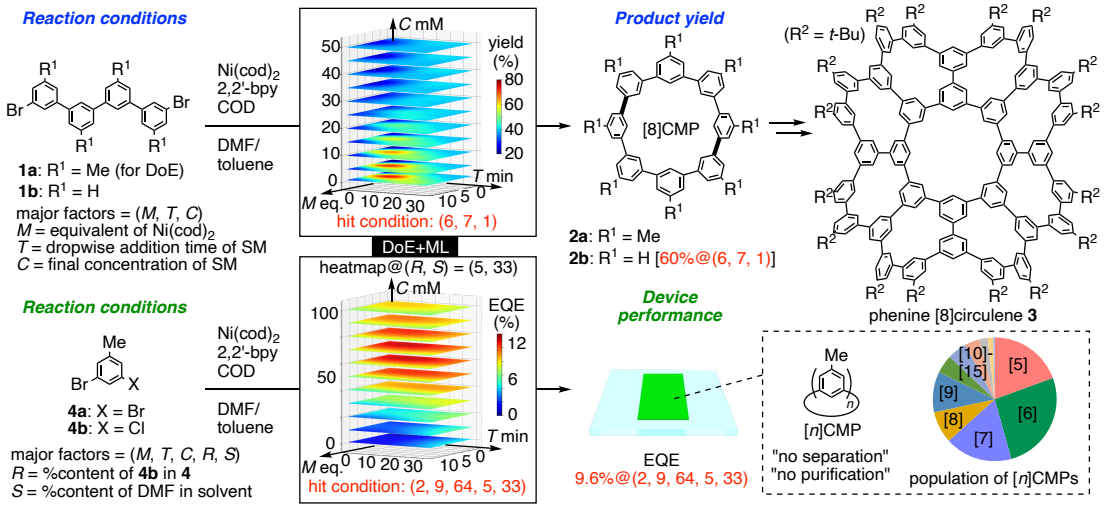
Combination of Design-of-Experiments and Machine Learning for Optimization of Reaction Conditions

([1]*Department of Chemistry, The University of Tokyo*, [2]*Konica Minolta*) ○Misato Akiyoshi,[1] Koki Ikemoto,[1] Ayano Kobayashi,[1] Hiroshi Kita,[2] Hideo Taka,[2] Hiroyuki Isobe[1]

Keywords: Design-of-Experiments; Machine Learning; Nanocarbon Molecules; Coupling; Devices

Setting the conditions for a chemical reaction is the very first, fundamental step in exploring chemistry. In this study, we show that the strategy and approach to optimizing reaction conditions can be dramatically altered by introducing machine learning (ML). We first demonstrate that combining ML with Design-of-Experiments (DoE) optimization allows us to find an optimal condition for a reaction that proceeds through complicated reaction pathways.[1,2] Thus, high-yield conditions for the synthesis of [8]cyclo-*meta*-phenylene ([8]CMPs, **2**) via a dimerization reaction of **1** were found by adopting DoE-guided conditions of three factors, *M* = equivalent of $Ni(cod)_2$, *T* = addition time of the starting material (SM) and *C* = final concentration of SM, with ML-supplemented yield predictions. As the result, a large nanocarbon molecule, phenine [8]circulene (**3**), was successfully synthesized. We next find that the DoE+ML approach to optimization can be used not only to increase the yields of chemical reactions, but also to maximize the performance of organic light-emitting devices (OLEDs).[3] Thus, the reaction conditions were directly correlated to the external quantum efficiency (EQE) of printed phosphorescent OLEDs using a crude [*n*]CMP mixture as a host material to achieve a high EQE value of 9.6%.



1) Ikemoto, K.; Akiyoshi, M.; Mio, T.; Nishioka, K.; Sato, S.; Isobe, H. *Angew. Chem. Int. Ed.* **2022**, *61*, e202204035. 2) Akiyoshi, M.; Ikemoto, K.; Isobe, H. *Chem. Asian J.* **2023**, *18*, e202201141. 3) Ikemoto, K.; Akiyoshi, M.; Kobayashi, A.; Taka, H.; Kita, H.; Isobe H. *Chem. Sci*. **2025**, published online. doi: 10.1039/D4SC07039A.