Hybrid Computational Strategy for Predicting Ligand-to-Metal Coordination Modes in Organometallic Structures

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Abstract:

As deep generative models for molecular design transition from purely organic space into the organometallic domain, a critical bottleneck has emerged: the reliable prediction of ligand-to-metal coordination. While current generative pipelines can suggest sophisticated ligand architectures, they often lack a structural validation layer to ensure that the resulting transition metal complex is chemically realistic. This is particularly problematic for polydentate or hemilabile ligands where multiple coordination modalities exist, potentially leading to unrealistic organometallic structures and invalid downstream property predictions. We present a hybrid computational framework (figure 1) designed to resolve this coordination ambiguity. Our model integrates machine-extracted reaction rules mined from the Cambridge Structural Database (CSD) to generate a comprehensive set of possible coordination structures. These candidates are then scored using a Directed-Message Passing Neural Network (D-MPNN). Rigorous statistical analysis highlights the model's robust extrapolative performance, achieving 90% accuracy for top-1 predictions and maintaining nearly 80% accuracy on out-of-distribution (OOD) datasets. This predictive model enables (1) the automated validation of generative model outputs, (2) high-throughput virtual screening of ligands for metal-ion sensors, and (3) the assembly of transition metal complexes. This work is available to the community via the RDMetallics Python wrapper for RDKit (https://github.com/moldagulovg/RDMetallics_coordinate) and an interactive web portal (https://coordinate.rdmetallics.net/).

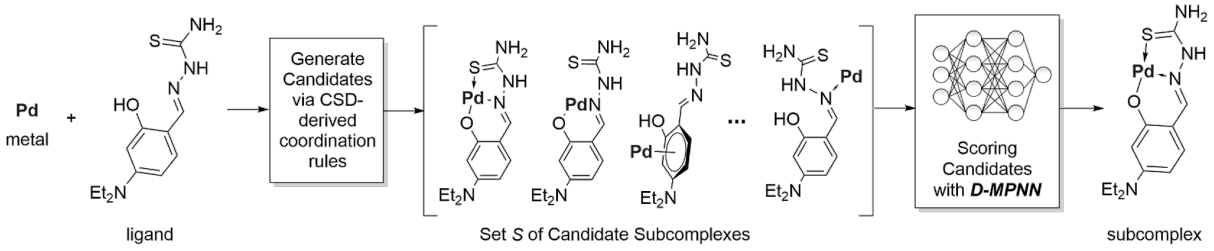

Figure 1. Metal-to-ligand coordination mode prediction via cheminformatics coordination templates and D-MPNN scoring.

Bibliography:

[1] G. Moldagulov, K. Lee, S. Nurgaliyev, A. Salem, A. Kuznietsov, B.A. Grzybowski*. Hybrid Computational Strategy for Predicting Complex Ligand-Metal Architectures. *Angew. Chem. Int. Ed.* **2026**, e24655. https://doi.org/10.1002/anie.202524655