Industry's quest for the ultimate in catalyst cost and efficiency has led to the creation of atomically dispersed metal catalysts (ADECs), which only provide isolated metal active sites with no crosstalk between two neighboring metal atoms but strong chemical bonding interaction to the support. The ultimate atomic efficiency as well as the unique electronic structure within the unsaturated coordination of the atomically dispersed metal species is also distinct from its metallic nanoparticle counterparts and has been shown to confer unprecedented catalytic properties. Using the strong interactions between metals and defect-rich non-reducible supports, I explore various methods to synthesize ADECs. Using them as model systems, I studied (a) the evolution of different active centers in catalytic conditions; (b) the dynamics and reactivity of isolated metal atoms, clusters, and nanoscale particles (NPs); (c) the electromagnetic interactions and catalytic synergy among atoms determined by the spatial positions of isolated atoms; (d) relay catalysis of isolated heteroatoms; and (e) the correlation between catalytic reactivity and non-equilibrium oscillations of isolated atoms. A series of operando spectroscopies, including operando high-temperature and high-pressure Fourier-transform infrared spectroscopy (FT-IR), X-ray absorption spectroscopy (XAS), UV-visible light absorption spectroscopy (UV-vis), and Raman spectroscopy, were employed to reveal the surface dynamics of the working ADECs. Furthermore, I combined these spectroscopic results with ab initio density functional theory (DFT) calculations and molecular dynamics simulations (MDS) to achieve a fundamental understanding of catalytic reaction mechanisms at the atomic level. Building upon these acquired insights, high-throughput screenings based on theoretical calculations were employed to discover new catalytic materials with industrial potential for the selective hydrogenation of CO2 and the selective oxidation of methane. The methodologies established for the operando characterization and theoretical simulation of ADMCs have the potential to alleviate the ambiguity surrounding the atomic-level comprehension of the catalytic mechanisms.