Use of the natural product (–)-sparteine as a ligand on palladium enables the enantioselective aerobic oxidation of activated secondary alcohols to ketones. From quantum mechanical (QM) calculations (DFT with a polarizable continuum solvent model) we found that the enantioselectivities observed in these reactions follow directly from calculated energies of diastereomeric beta-hydride elimination transition states incorporating (R) and (S) substrates. Attempts to design chiral bispidines to mimic the reactivity of (–)-sparteine using the predictive calculations resulted in ligands with high predicted selectivity but poor stability on palladium. We subsequently used QM to study the mechanism of alcohol oxidation by (N-heterocyclic carbene)Pd(II) complexes. We found that a mechanism for the C-H activation step which does NOT involve beta hydride elimination is consistent with the experimental measurements (activation parameters, kinetics, kinetic isotope effect).