

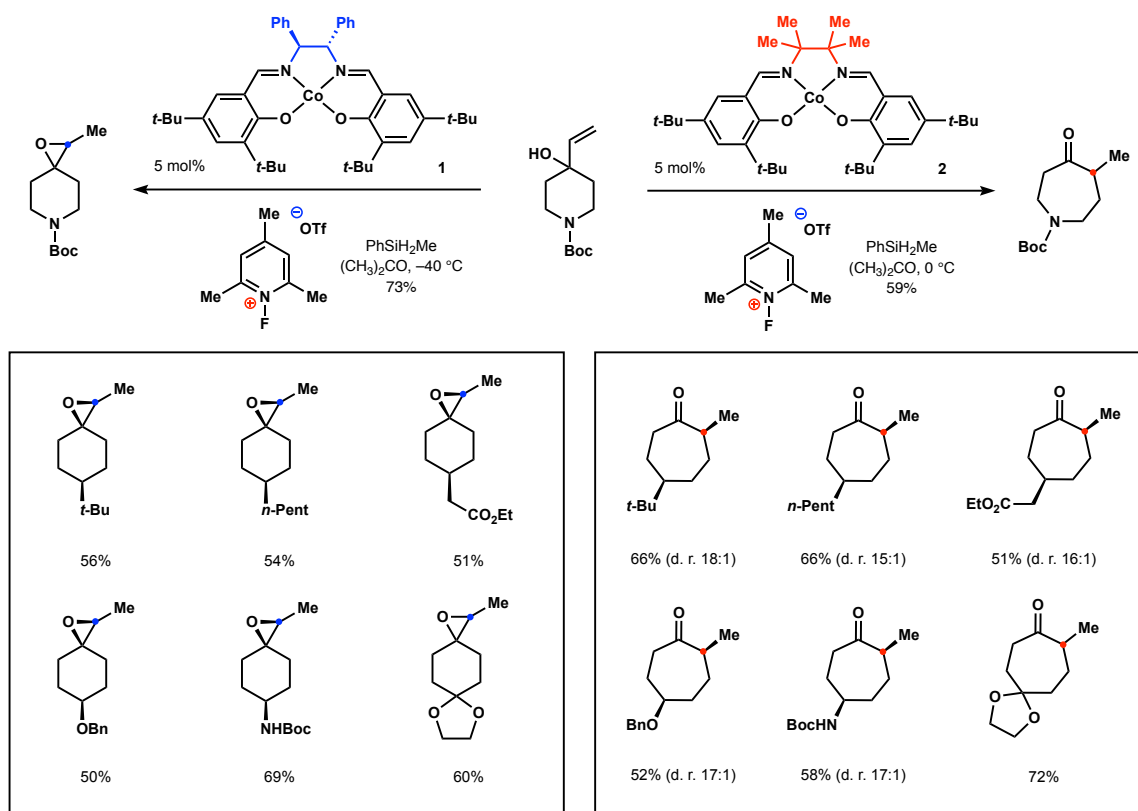
Development of Cobalt(I)-Catalyzed Radical-Polar Crossover Reactions

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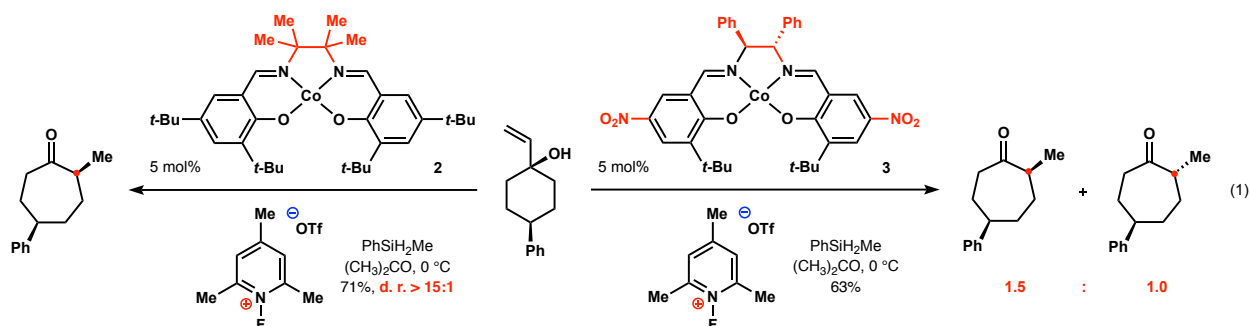
The long-term goal of our research is to develop new chemical methods and approaches that allow for direct and selective access to useful structural motifs and valuable synthetic intermediates. We proposed the development of new methods for catalytic radical alkylation reactions. Specifically, we sought to generate alkyl radicals from the corresponding alkylcobalt(III) complexes, which would be obtained via the intermediacy of nucleophilic cobalt(I) species. To investigate the utility of the proposed catalytic transformations, we planned to exploit this reactivity in the alkylation of heteroaromatic compounds in Minisci-type processes.

During the course of our studies we came across a different, but related reactivity of cobalt complexes that allowed for catalyst control in the hydrogen atom transfer (HAT)-initiated transformations. We discovered that cobalt-catalyzed intramolecular hydrofunctionalizations of tertiary allylic alcohols produced corresponding epoxides or semipinacol rearrangement products, and the outcome of the reaction was dependent of the structure of the cobalt salen catalyst (Table 1). These radical-polar crossover processes utilized a *N*-fluoropyridinium salt as an oxidant and

Table 1. Catalyst controlled synthesis of epoxides and semipinacol rearrangement products.



methylphenylsilane as a reductant. Application of complex **1** as a catalyst allowed for efficient conversion of various dialkyl(vinyl)carbinols to the corresponding trisubstituted epoxides (see Table 1 for selected examples). Switching the catalyst to complex **2** allowed for efficient production of corresponding semipinacol rearrangement products instead. Notably, the rearrangement of 4-substituted cyclohexanol derivatives in the presence of catalyst **2** proceeded with high diastereoselectivity, yielding the corresponding cycloheptanones with the *cis* configuration of substituents. We found that the stereochemical outcome of the ring expansion events was also dependent of the structure of the catalyst. Thus, application of complex **3**, which contains nitro-substituted arene fragments in the salen motif, resulted in the conversion of a 4-phenylcyclohexanol derivative to a nearly equimolar mixture of the corresponding diastereomeric cycloheptanones (equation 1). This result stood in stark contrast to the highly diastereoselective production of the *cis* diastereomer in the presence of complex **2**. Notably, small amounts of the semipinacol rearrangement products observed during the conversion of the same 4-phenylcyclohexanol derivative to the corresponding epoxide



in the presence of catalyst **1** were also formed with low diastereoselectivity (ca. 3:1 at $-40\text{ }^\circ\text{C}$, not shown).

The strong catalyst control observed during the epoxide synthesis and semipinacol rearrangements indicates that cobalt complexes are involved in the key bond forming events. We propose, among other considerations, that the reactions catalyzed by complexes **1** and **3** proceed via the intermediacy of the corresponding alkylcobalt(IV) complexes that serve as electrophiles. Nucleophilic displacements of related alkylcobalt species were previously studied, for example, in the pioneering work of Halpern and Johnson, but their participation in the catalytic processes has yet to be explored. We expect our studies to provide a starting point for the development of enantioselective HAT-initiated hydrofunctionalizations – a challenging feat in the realm of transformations that typically rely on atom and group transfer reactivity of free alkyl radical intermediates. Our preliminary inquiries into the possibility of absolute stereocontrol in these reactions are encouraging and we continue our explorations in the area.

The transformative effect of the funding from the ACS PRF on the research in our laboratory is evident from the new directions we have undertaken in the catalytic organic synthesis. While the intended catalytic transformations have yet to be realized, the newly discovered catalytic processes lay foundation for a plethora of new projects and for the training of new synthetic chemists.