Ligand-Controlled Regiodivergent Hydrothiolation: A [Rh]-Catalyzed Pathway to Selectively Form 1,2- and 1,3-Amino Thioethers

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We have developed a [Rh]-catalyzed, atom-economical route to install C–S bonds into electronically unbiased olefins with high degrees of regio-, chemo- and diastereoselectivity. We employ terminal olefins with tethered Lewis-basic functionality (i.e. amines or imines) to (1) increase the relative concentration of olefin to the metal, (2) inhibit catalyst poisoning in the presence of nucleophilic thiols, (3) induce regioselectivity by preferentially forming one metallocycle intermediate, and (4) preclude beta-hydride elimination by prohibiting the necessary syn-periplanar geometry. Excitingly, this [Rh]-catalyzed system is regiodivergent; i.e., from common starting materials, we can access 1,2- or 1,3-amino thioethers by merely varying the phosphine ligand. A variety of aryl and alkyl thiols can be installed. Further, the methodology can be used on electron-rich, electron-poor, and sterically-encumbered N-allyl Lewis bases with isolated yields up to 87% with >20:1 regio- and diastereoselectivity.

Expedient Access to Heterocyclic Natural Products Enabled by Arene Oxides or their Equivalents

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Though arene oxides are common biosynthetic intermediates, they are elusive in synthetic organic chemistry due to their extremely sensitive nature. Many highly biologically active natural products can be traced back to the corresponding arene oxide species. We are developing a strategy for the construction of a series of heterocyclic secondary metabolites by intercepting arene oxides or their chemical equivalents. This method provides a platform for the rapid access to heterocyclic natural products, and its first practical utility is demonstrated in efforts towards the total synthesis of trichodermamide B, a potent anticancer and antibacterial target.