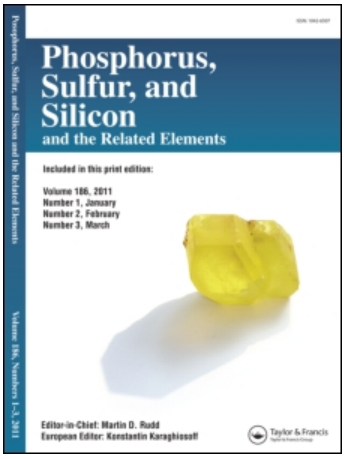

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SILICON-CONTAINING HETEROCYCLES IN STEREOCONTROLLED RADICAL ADDITIONS TO CHIRAL HYDRAZONES

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Chiral amino alcohols[1] are components of commonly used chiral building blocks, auxiliaries, and ligands in asymmetric synthesis, and are also key functional elements within a wide range of biologically active compounds.[2] We have developed several methods[3] for asymmetric synthesis of 1,2-amino alcohols via radical cyclizations of chiral α-hydroxyhydrazones.[4]

A silicon tether approach provides stereocontrol in radical addition to chiral hydrazones (Figure 1). Silicon-tethered bromomethyl, vinyl, or ethynyl groups can be employed as radical precursors on which the action of stannyl or thiyl radicals generates carbon-centered radicals. Silatetrahydrofurans and silatetrahydropyrans are formed upon radical cyclization.

First, the silicon tether is established by formation of a silyl ether from an α-hydroxyhydrazone. From the bromomethylsilyl ethers, cyclization is followed by oxidative cleavage of the C–Si bond by Tamao oxidation[5] to generate hydroxymethyl adducts. From the vinyl- or ethynylsilyl ethers, cyclization is followed by fluoride-induced elimination or protodesilylation affords access to allylic amino alcohols.

Diastereomer ratios in the cyclization range from 4:1 up to >50:1 favoring the *anti* diastereomer. A preferred chair like transition state is consistent with the mode of stereocontrol; this working model is also

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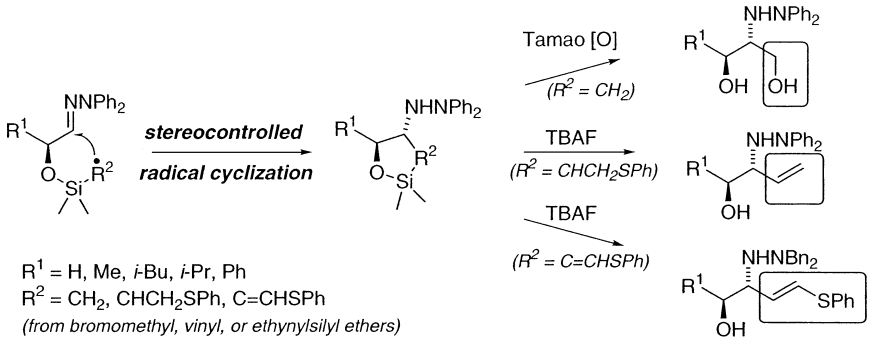

FIGURE 1 Stereocontrol in radical additions to chiral hydrazones.

fully consistent with the Beckwith–Houk models[6] for stereoselectivity in radical cyclizations.

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