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Buchwald-Hartwig coupling of (+)-S-methyl-S-phenyl sulfoximine to 2-bromo-cinnamyl carbonyls and their subsequent intramolecular Michael addition

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The goals of this research are directed at instituting a benzylic methyl group to conjugated electron withdrawing groups in a completely diastereoselective manner using an enantiopure Sulfoximine scaffold as a removable chiral auxiliary. This chiral Sulfoximine will not only allow a diastereoselective addition of the equivalent of a methyl group to the 1,4-business end of a conjugated electron withdrawing group, but will also allow for additional functionality to present itself due to the fact that Sulfoximine can be removed by sodium amalgam and leave that methyl group intact while also leaving the amino group function on the aryl ring. The palladium metal mediated Buchwald-Hartwig coupling reaction between 2-bromo-cinnamyl carbonyls and (+)-Sulfoximine can be readily achieved in excellent yields (based on recovered starting material) using rac-BINAP as a reducing ligand and CsOAc or Cs₂CO₃ as a base in toluene at reflux for 18hrs.-2 days. The poor conversion in most cases is likely attributed to the extremely hygroscopic nature of CsOAc and the failure to reduce the introduction of moisture to the reaction. The coupling products are then treated with 2-2.5eq. of lithium hexamethyldisilazide (LHMDS) at -78degC in tetrahydrofuran (THF), the reaction mixture stirred for 45min.-3hrs., and then quenched with sat. ammonium chloride (sat. NH₄Cl). The Michael addition products were then analyzed by ¹H and ¹³C NMR, high resolution mass spectroscopy, IR, and X-ray crystallography where appropriate to determine the diastereoselectivity (de) of the products. It was found that only one diastereomer was obtained after the Michael addition process (de = 100%).

