Design and Synthesis of Imidazo[1,2-*a*]pyridines as ER-Subtype Selective Ligands.

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Selective estrogen receptor modulators (SERMs) are currently sought for use in a variety of endocrine therapies such as anticancer drugs and hormone replacement therapies. Previous work by our labs has led to the advancement of a general pharmacophore for ERβ-selective ligands. This model consists of a heterocyclic core bearing at least one hydroxyl group, a phenolic sidechain, and an internal substituent (halogen, alkyl, or phenyl). In order to further probe the efficacy of this model and gain a greater understanding for ER pharmacology, we have synthesized a number of ligands based on the imidazo[1,2-*a*]pyridine core structure. The general core is synthesized via the condensation of 2-aminopyridine and 2-bromo-4'-methoxyacetophenone, and further functionalized to incorporate a diverse set of substituents probing SARs critical to binding affinity and selectivity. Preliminary data has led to the identification of a ligand with a nanomolar IC_{50} and 41-fold selectivity for ERβ.