M. L. MADDESS,* J. P. SCOTT* ET AL. (MERCK & CO., INC., RAHWAY, USA AND MERCK SHARP & DOHME RESEARCH LABORATORIES, HODDESDON, UK)
Enantioselective Synthesis of a Highly Substituted Tetrahydrofluorene Derivative as a Potent and Selective Estrogen Receptor Beta Agonist

Synthesis of an Estrogen Receptor Beta Agonist

**Significance:** The target tetrahydrofluorene is an estrogen receptor β agonist that is of interest for the treatment of symptoms associated with reduced estrogen levels in post-menopausal women. The large-scale synthesis depicted features a chiral auxiliary mediated dialkylation to construct the quaternary center in G with excellent stereoselectivity. Note the intramolecular enolate alkylation F → G in which phenoxide ion is the leaving group.