Diels-Alder Reactions of Hexafluoro-2-butyne with 2-Heterosubstituted furans: A Facile and General Synthesis of 1,4-Disubstituted 2,3-di(trifluoromethyl)benzenes

Gui-Dong Zhu*, Michael A. Staeger, and Steven A. Boyd
Abbott Laboratories, Pharmaceutical Products Division, Metabolic Diseases Research, D4MJ, AP10, 100 Abbott
Park Road, Abbott Park, IL 60064-6101, USA

An electron-donating heteroatom substituent at position-2 of a furan promotes regiospecific opening of the 7-oxa bridge of the Diels-Alder cycloadduct with hexafluoro-2-butyne, producing a 4-heterosubstituted 2,3-di(trifluoromethyl)phenol building block in a single step. The phenol and heteroatom substituent are easily transformed to the corresponding iodide or triflate that readily undergoes Heck, Suzuki and Stille reactions to install a variety of substituents in high yields. This methodology provides a facile and general synthesis of 1,4-disubstituted 2,3-di(trifluoromethyl)benzenes.