**Synthesis of (±)-Estrone**

Significance: (±)-Estrone, a naturally occurring hormone and agonist of estrogen receptors ERα and ERβ, was synthesized in 1979 by Funk and Vollhardt. The presented synthesis allows the stereoselective construction of the B and C steroidal rings in a single step through a thermally induced 4π-electrocyclic ring opening of a benzocyclobutene, followed by an exo-Diels–Alder cycloaddition. Benzocyclobutene G was synthesized by cobalt-catalyzed cyclotrimerization of E with F gave benzocyclobutene G along with small quantities of tetracycle H. Heating G in decane afforded H in 71% combined yield over two steps. Subsequent protodehydroxylation and oxidative desilylation steps culminated in formation of (±)-estrone. Notably the synthesis proceeds in only six steps and 24% overall yield.

Comment: Vinyl cuprate addition to cyclopentene A and subsequent trapping of the resulting enolate gave silyl enol ether C in 89% yield. Formation of the lithium enolate and alkylation with D afforded diyne E. Importantly, the trans-substituted cyclopentanone was formed as the major product. Cobalt-catalyzed cyclotrimerization of E with F gave benzocyclobutene G along with small quantities of tetracycle H. Heating G in decane afforded H in 71% combined yield over two steps. Subsequent protodehydroxylation and oxidative desilylation steps culminated in formation of (±)-estrone. Notably the synthesis proceeds in only six steps and 24% overall yield.