Sometimes It's Better to Be Lucky than Good:
The (Ongoing) Evolution of the Hexadehydro-Diels-Alder Reaction

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Since mid-2011 we have been advancing the generality of a process that we call the hexadehydro-Diels–Alder (HDDA) reaction.1 This net [4+2] cycloisomerization produces an α-benzyne derivative, which is then rapidly captured in a subsequent trapping event. The HDDA reaction is a rare example of a transformation that generates a highly reactive intermediate by way of a highly exergonic (ca. −50 kcal•mol⁻¹) reaction! This two-stage, benzynegeneration-trapping cascade results in the rapid assembly of structurally complex benzenoid products. This chemistry is both preparatively valuable and mechanistically instructive. It also can serve as a platform for i) entirely new modes of reactivity, ii) novel construction of natural products, iii) tri-component reactions, and iv) natural product derivatization reactions.9

The hexadehydro-Diels–Alder (HDDA) cascade

In this lecture I will emphasize a few of the more recent aspects of our studies. These include:

• the domino HDDA reaction,10
• erasable S–I1 and Si-tethers,
• BF₃-promoted carbenic reactivity,12
• metal-catalyzed transformations,13
• access to light-emitting compounds and materials,14
• bi- and tri-directional HDDA reactions,
• a benzyneto-benzyneto-naphthyne strategy,15
• the aza-HDDA reaction.16