Controlled Cyclization of Arylalkynes through Folding inside a Molecular Cage

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Intramolecular cyclization involving ene and yne moieties is versatile for construction of polycyclic hydrocarbons from a linear precursor. However, the flexibility of the linear precursor hampers the control of the conformation, which causes low reactivity and selectivity in the cyclization. Here, we achieved controlled cyclization reactions of linear arylalkyne precursors by folding inside a molecular cage. The confined cavity of cage 1 forces the precursors to adopt a fixed fold conformation which is advantageous to the selective electrophilic or thermal cyclization reactions (Fig. a).

When bis(biphenyl)acetylene 2 (1.4 equiv) was suspended in an aqueous solution of cage 1 (10 mM) and heated at 80 °C for 1 h, 80% of the cage formed inclusion complex 1·2 (Fig. b). The folded conformation of 2 in cage 1 was revealed by X-ray crystallographic analysis. The fixed conformation resulted in an unusual ipso-cyclization with an electrophile. Cage 1 also induced folded conformation of oligoalkyne 3 to accelerate thermal tetradehydro-Diels-Alder (TDDA) type cyclization (Fig. c). We also achieved site-selective TDDA reactions with non-symmetric arylalkynes, which produced sterically hindered biaryl compounds.