Synthesis of Isopalhinine A and Palhinine D

Significance: Isopalhinine A and palhinine D are Lycopodium alkaloids with highly bridged carbon frameworks that incorporate a 5/6/6 tricycle along with a hemiaminal moiety. Hsieh and co-workers report concise syntheses of both alkaloids, which rely on an oxidative dearomatization/[4+2] cycloaddition strategy to construct the bicyclo[2.2.2]-octane core.

Comment: 9-exo-Tet cyclization of D under basic conditions furnished the azonane ring in E. Subsequent oxidation with hypervalent iodine gave a masked ortho-benzoquinone intermediate that underwent Diels–Alder reaction with acrolein to afford F. Employing Tomioka’s method, acyl radical cyclization of aldehyde furnished the characteristic isotwistane core in K.