Fishing for Furans with a Diels–Alder Covalent Probe

Significance: The discovery of natural products is an essential lead source for drug development; however, compound isolation and elucidation represent time-intensive bottlenecks. This is particularly challenging for highly potent compounds produced at low levels (e.g., signaling hormones). Here, Parkinson and co-workers developed a covalent probe that can undergo a [4+2] Diels–Alder cycloaddition to identify furan-containing natural products from complex cell supernatants.

Comment: The probe follows a conventional three-component design, comprising a target-reactive warhead, a UV-active chemical unit, and a halogen with a readily identifiable isotopic signal. As proof-of-concept, the authors converted a series of synthesized furans in vitro, including hormones MMF1-5 and metabolite flufuran, and successfully identified MMF5 from the crude cell supernatant of Streptomyces bacterial culture.