

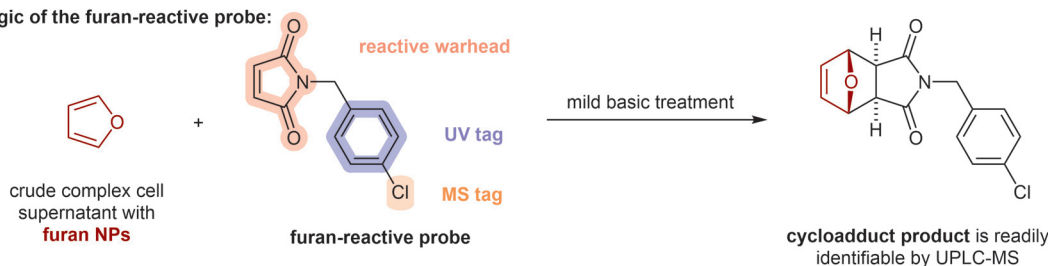
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A Diels–Alder Probe for Discovery of Natural Products Containing Furan Moieties

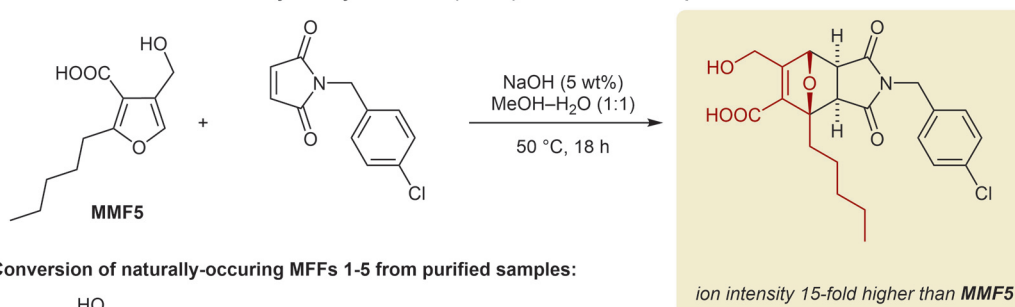
Beilstein J. Org. Chem. **2024**, *20*, 1001–1010, DOI: 10.3762/bjoc.20.88.

Fishing for Furans with a Diels–Alder Covalent Probe

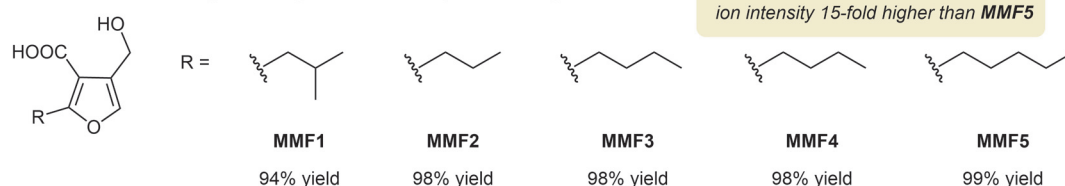
Logic of the furan-reactive probe:



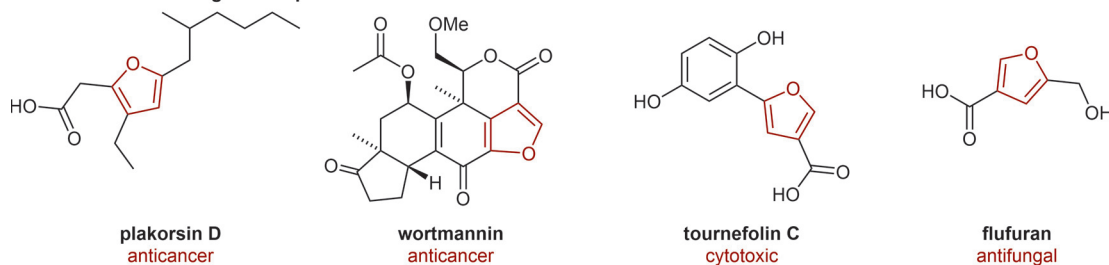
Identification of metabolite methylenomycin furan 5 (MMF5) from crude cell supernatant:



Conversion of naturally-occurring MFFs 1-5 from purified samples:



Other furan-containing natural products:



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.

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Key words

Diels–Alder
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covalent probe
methylenomycin
furans (MMFs)

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