

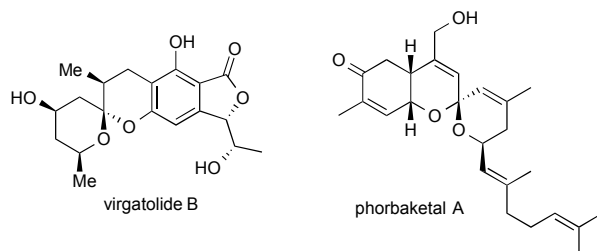
## SYNTHESIS OF NATURAL PRODUCTS CONTAINING SPIROKETALS

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Natural products have long been regarded as “Nature’s medicine chest” providing invaluable platforms for developing front-line drugs. The chemical structures of natural products have evolved over several millennia for a specific biochemical purpose and their molecular frameworks can be considered “privileged scaffolds.” This lecture will showcase how natural products that contain intricate spiroketal scaffolds can be synthesized thus providing a platform to develop novel anticancer and anti-obesity agents.

The virgatolides are a family of natural products containing a rare benzannulated 6,6-spiroketal moiety isolated in 2011 from *Pestalotiopsis virgatula*.<sup>1</sup> Virgatolides A-C exhibit cytotoxicity against HeLa cells ( $IC_{50} \sim 20 \mu M$ ). The first synthesis<sup>2</sup> of virgatolide B is described. Phorbaketal A and alotaketal A are two pseudoenantiomeric natural products, containing a unique spiro-sesterterpenoid core structure.<sup>3,4</sup> Phorbaketal A possesses moderate cytotoxicity against a range of cancer cell lines, as well as exhibiting osteoblast and mast cell differentiation activity and inhibition of fatty acid synthesis in the liver. Additionally, alotaketal A activates the cAMP signalling pathway at nanomolar concentrations. Our efforts directed towards the enantioselective syntheses of phorbaketal A and alotaketal A will be described.<sup>5</sup>



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