

## Development of High-throughput Screen for PAR-regulating Enzyme by Chemical Synthesis of Alternative Substrate

Bryon S. Drown and Paul J. Hergenrother

Poly(ADP-ribosylation) is an important post-translational modification responsible for regulating DNA damage repair, transcription, chromatin structure, and telomere maintenance. Despite PAR being recognized as a valid target for anticancer therapy, modulation and measurement of PAR metabolism remains challenging. Here we report the design and synthesis of a substrate analogue for an enzyme responsible for regulating PAR metabolism. This substrate enabled the development and execution of a high-throughput screen for inhibitors of this enzyme.

## Catalytic, Stereospecific *Syn*-Dichlorination of Alkenes

Alexander J. Cresswell,<sup>†</sup> Stanley T.-C. Eey<sup>†</sup> and Scott E. Denmark

As some of the oldest organic chemical reactions known, the ionic additions of elemental halogens such as bromine and chlorine to alkenes are prototypical examples of stereospecific reactions, typically delivering vicinal dihalides with exceptional *anti*-diastereoselectivity. Whilst the invention of enantioselective variants is an ongoing challenge, the ability to overturn the innate diastereoselectivity of these transformations is also a largely unsolved problem. In this work, we describe the first catalytic, *syn*-stereospecific dichlorination of alkenes, employing a group transfer catalyst based on a redox-active main group element (i.e., selenium). Thus, with diphenyl diselenide (PhSeSePh) (5 mol %) as the pre-catalyst, benzyltriethylammonium chloride (BnEt<sub>3</sub>NCl) as the chloride source, and an *N*-fluoropyridinium salt as the oxidant, a wide variety of functionalized cyclic and acyclic 1,2-disubstituted alkenes, including simple allylic alcohols, deliver *syn*-dichlorides with exquisite stereocontrol. This methodology is expected to find applications in streamlining the synthesis of polychlorinated natural products such as the chlorosulfolipids.

<sup>†</sup>These authors contributed equally.

