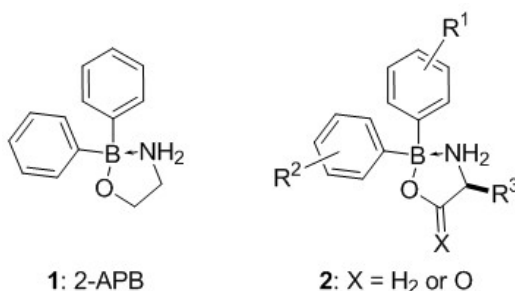


Diaryl Borinic Acids Modulate Store-operated Calcium Entry (SOCE)A. Schild¹, R. Bhardwaj², M. A. Hediger², M. Lochner^{1,2*}¹Department of Chemistry and Biochemistry, ²Institute of Biochemistry and Molecular Medicine

The intracellular Ca^{2+} concentration is carefully controlled, as changes in $[\text{Ca}^{2+}]_i$ mediates a plethora of cellular and ultimately physiological processes, such as cell differentiation, muscle contraction, neurotransmission, proliferation and immune cell mobility, among many others.

Intracellular Ca^{2+} is stored in the endoplasmic reticulum (ER) and released upon activation of ER-receptors (e.g. IP_3). Refilling of the ER Ca^{2+} stores requires an intricate interplay and assembly between Ca^{2+} sensing proteins (STIM1 and STIM2) located in the ER membrane and proteins (Orai1, 2 and 3) in the plasma membrane. The resulting STIM/Orai complexes form a Ca^{2+} channel that causes a measurable calcium-release activated calcium current (I_{CRAC}). Mutations in STIM or Orai that either cause enhanced or reduced store-operated calcium entry (SOCE) have been associated with muscular and immunodeficiency diseases, respectively.

Diphenyl borinate 2-APB (**1**) exhibits a dual function on SOCE, as it blocks at high concentration (e.g. $50 \mu\text{M}$) but potentiates SOCE at lower concentrations (e.g. $5 \mu\text{M}$). In this work, we present the synthesis of novel 2-APB analogues (**2**), some of their crystal structures and their concentration-dependent influence on SOCE. Specifically, we have investigated Orai-subtype selectivity (Orai1 vs. Orai3) and have also generated some fluorescent 2-APB congeners.



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