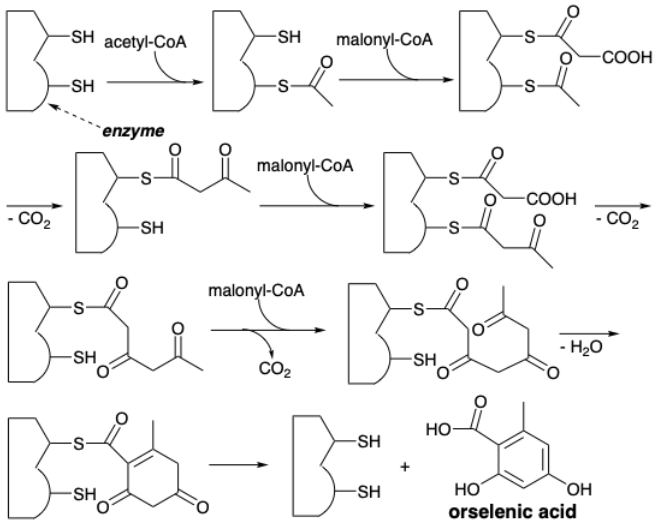
5.1: Orselenic Acid

Formation of the intermediate polyacetyl or propionyl chains in the biosynthesis of polyketides is closely related to fatty acid biosynthesis. Thus, for example, acetyl CoA acylates an enzyme-bound malonylthioester to yield an enzyme bound acetoacetylthioester. In fatty acid biosynthesis, this would then be reductively deoxygenated prior to undergoing Claisen condensation with a second molecule of malonyl-S-ACP (see section 3.1). In polyketide biosynthesis, repeated aldol condensations yield an enzyme bound polyacetyl chain in which many acetyl carbonyls are retained or only partially reduced to hydroxyls. The name **acetogenin**, a synonym for polyketides, arises from their poly- acetyl biogenesis. Cyclization of the polyacetyl chain occurs completely, or at least partially, prior to its release from the polyacetyl synthetase enzyme surface. For example, orselenic acid is constructed biosynthetically from acetyl CoA and three molecules of enzyme-bound malonyl-thioester.



A total synthesis of orselenic acid was achieved by a **biomimetic strategy**, that is, by a strategy that mimics the biosynthesis of this acetogenin.[1] Thus, the trianion of 2,4,6-heptanetrione was carboxylated to yield 3,5,7-triketo octanoic acid (**1**) that readily underwent intramolecular aldol condensation and dehydration to give orselenic acid (**2**).