Saccharomonospora sp. UR22 and Dietzia sp. UR66, two actinomycetes derived from the Red Sea sponge Callyspongia siphonella, were co-cultured and the induced metabolites were monitored by HPLC-DAD and TLC. Saccharomonosporine A (1), a novel brominated oxo-indole alkaloid, convolutamydine F (2) along with other three known induced metabolites (3-5) were isolated from the EtOAc extract of Saccharomonospora sp. UR22 and Dietzia sp. UR66 co-culture. Additionally, axenic culture of Saccharomonospora sp. UR22 led to isolation of six known microbial metabolites (6-11). A kinase inhibition assay results showed that compounds 1 and 3 were potent Pim-1 kinase inhibitors with an IC50 value of 0.3 ± 0.02 and 0.95 ± 0.01 μM, respectively. Docking studies revealed the binding mode of compounds 1 and 3 in the ATP pocket of Pim-1 kinase. Testing of compounds 1 and 3 displayed significant antiproliferative activity against the human colon adenocarcinoma HT-29, (IC50 3.6 and 3.7μM, respectively) and the human promyelocytic leukemia HL-60, (IC50 2.8 and 4.2μM, respectively). These results suggested that compounds 1 and 3 act as potential Pim-1 kinase inhibitors that mediate the tumor cell growth inhibitory effect. This study highlighted the co-cultivation approach as an effective strategy to increase the chemical diversity of the secondary metabolites hidden in the genomes of the marine actinomycetes