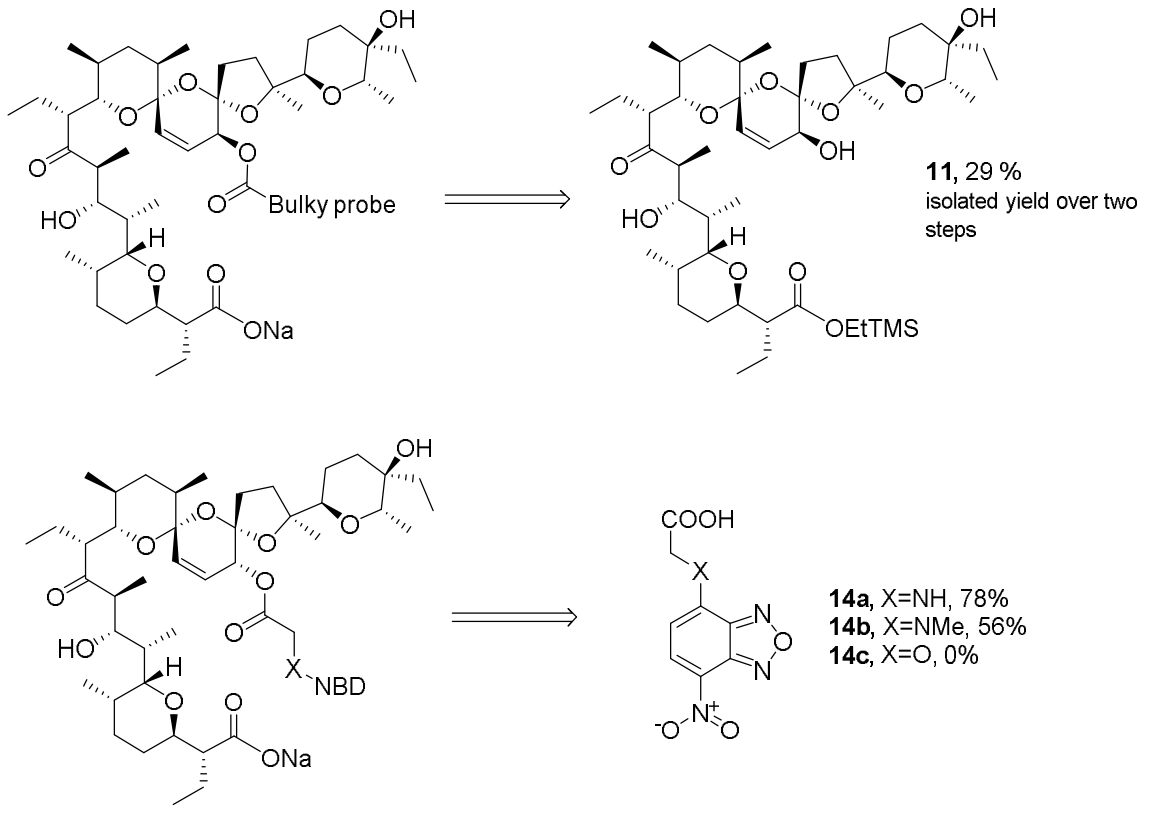
Abstract

Cancer is one of the leading causes of death worldwide. Recurrence, drug resistance and metastasis are common clinical problems that affect patients suffering from cancer. These effects may be caused by so-called cancer stem cells (CSCs), a small population of cells within a tumor, able to induce carcinogenesis. Current anticancer therapies are based on their ability to shrink tumors, leaving highly resistant CSCs nearly untouched. Salinomycin was shown to reduce the population of CSCs but the mechanism remains unknown. We aimed towards the attachment of a suitable fluorescent probe to the salinomycin core structure which could reveal the localization of SA in cells. Such a SA probe analog with at least retained activity of SA would greatly assist in explaining the molecular mode of action of SA in cells. Computational models have shown that attaching a large fluorescent core to 20-epi salinomycin results in less steric interaction than if the probe was connected to unmodified salinomycin. In order to access the C20 epimer of salinomycin, the Mitsunobu reaction was performed. The method was however shown not to be practical for making a SA probe. We then envision the core of a simplified fluorescent probe whose attachment did not require inversion. Synthetic routes of novel probes and attempts to attach them to SA are also presented.



Scheme 1 Proposed structures of fluorescent derivatives of SA (**1**)