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Highly Convenient Syntheses of Manoalide Analogues and Udoteafuran via an Alkylstannane Route

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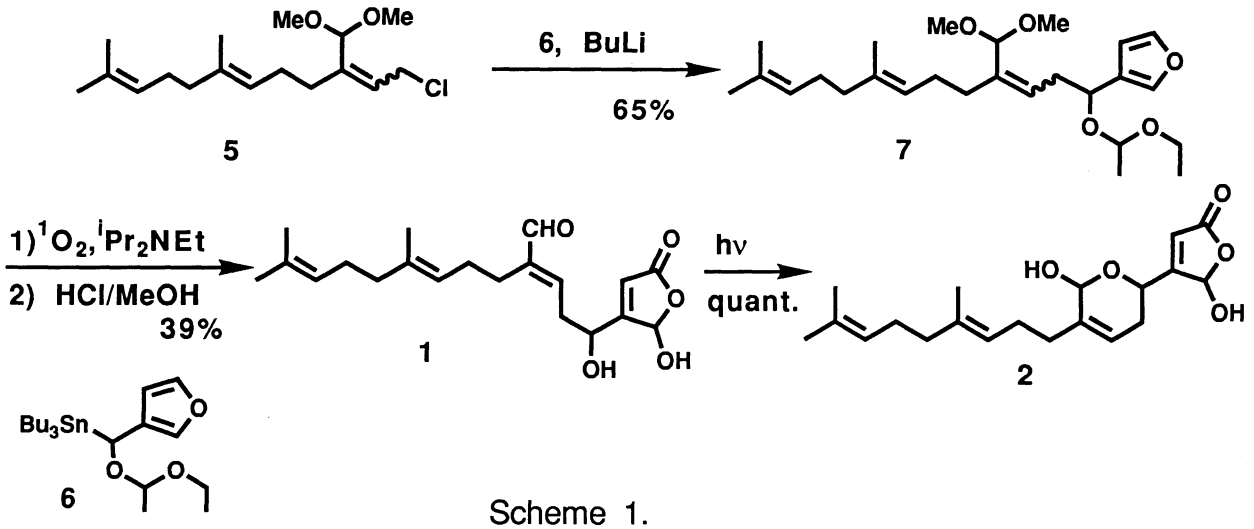
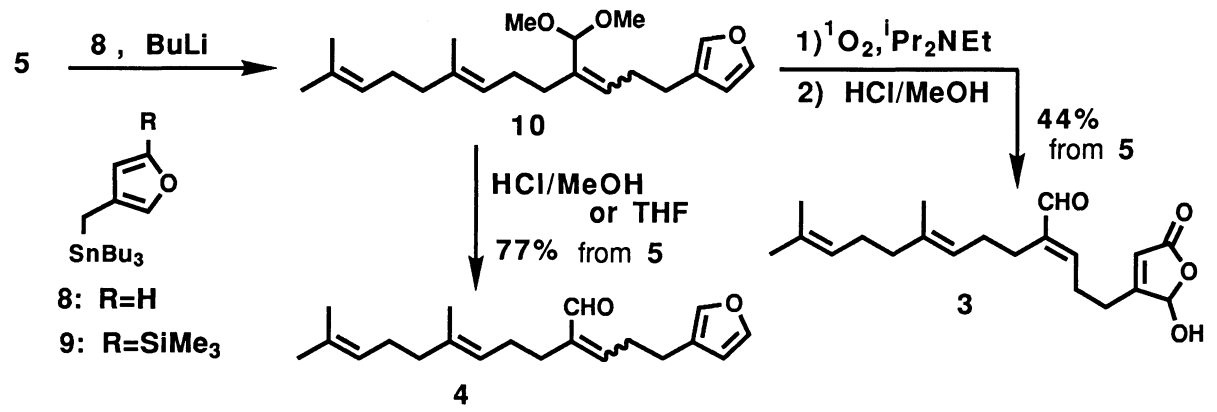
Manoalide analogues, which inhibit bovine pancreatic phospholipase A_2 to the same extent as manoalides, a deshydroxymanoalide analogue, and udoteafuran were synthesized in short steps.

Previously, we reported that manoalide analogues **1** and **2** were as effective as (±)-manoalide in the inhibition of bovine pancreatic phospholipase A2 (PLA2) and selectively modified the only two out of eleven lysine residues of the native bovine pancreatic PLA2.[1] Although highly selective synthesis of analogue **1** has already been established,[1, 2] considering the instability of both the starting stannylfuran and intermediates of the previous synthesis, the route may not be satisfactorily practical to obtain sufficient quantity of **1**. Now, we describe the easy and convenient synthesis of manoalide analogue **1** in addition to deshydroxymanoalide analogue **3**[3] and udoteafuran (**4**).

As shown in Scheme 1, anion generated from **6**[4] was reacted with allyl chloride **5** to give **7** in 65% yield. Photosensitized oxygenation of **7** in the presence of ethyldiisopropylamine[5] followed by acid treatment with 2 M HCl in methanol afforded seco-manoalide analogue **1** in 39% overall yield after chromatography. Thus, a highly convenient and easy method for synthesis of manoalide analogues **1** and analogue **2** were established, since **1** has been quantitatively converted



Scheme 1.



Scheme 2.

to **2** by photoirradiation.[2] This method should be applicable to the synthesis of manoalide and seco-manoalide.

As shown in Scheme 2, the alkylation of allyl chloride **5** with anion prepared from **8** [6] gave acid sensitive product **10** in an excellent yield, while alkylation of **5** with **9** was unsuccessful and most of the starting **5** was recovered. Remarkable deactivation of the benzylic anion of furan by trimethylsilyl group at α position of furan ring might be concluded. Compound **10** was oxygenated without purification with singlet oxygen in the same manner as above followed by acid treatment to yield deshydroxymanoalide analogue **3** in 44% overall yield from **5**.[3] E-udoteafuran (**4**), isolated from green algae *Udotea flabellum*,[7] was obtained from **10** by treatment with 1 M HCl in methanol (77% yield from **5**). Treatment of **10** with 1 M HCl in tetrahydrofuran afforded Z-udoteafuran whose isolation has not been reported so far.

As mentioned above, manoalide analogues could be obtained very easily and conveniently.

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