# Synthesis of new analogs of forskolin

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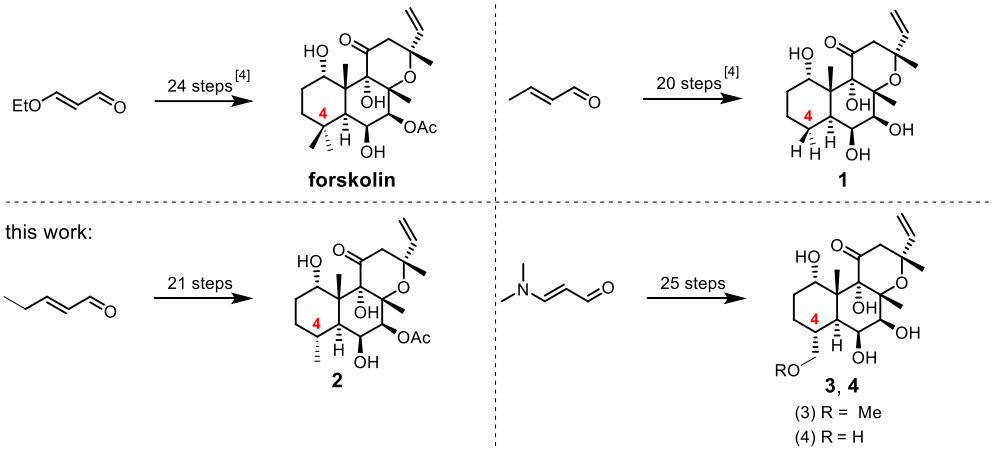
Forskolin, a highly oxygenated labdane diterpene originally isolated from the roots of *Coleus forskohlii*, can activate individual isoforms of adenylyl cyclases (ACs). ACs catalyze the conversion of adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP), which is a key second messenger binding to and regulating numerous downstream effector proteins, thereby modulating various physiological functions.[1] Forskolin represents a valuable tool in biomedical research[2] and considerable effort has been invested in the search of its analogs with improved properties.[3] The approach recently developed at Masaryk University[4] enabled synthesis of the des-dimethylforskolin analog **1**, which showed improved selectivity against the isoforms AC5 and AC7. This observation prompted the synthesis (and profiling) of additional synthetic analogs of forskolin with modified position 4, namely the mono-methyl analog **2** , mono-methoxymethyl analog **3** and mono-hydroxymethyl analog **4** (Scheme 1), described herein.




Scheme 1

1. C. W. Dessauer *Pharmacol. Rev*. **2017**, *69*, 9-139.
2. P. A. Insel, R. S. Ostrom *Cell. Mol. Neurobiol*. **2003**, *23*, 305-314.
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4. O. Hylse, L. Maier, R. Kucera, T. Perecko, A. Svobodova, L. Kubala, K. Paruch, J. Švenda *Angew. Chem. Int. Ed.* **2017**, *56,* 12586-12589.

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