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The terpene mini-path: a new artificial terpene biosynthetic pathway

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PURPOSE OF THE ABSTRACT

Terpenes are the largest class of natural products with more than 100,000 different structures described to date. Due to the diversity of their biological and physicochemical properties, terpenes are the preferred targets of many industries. However, due to their rarity and/or their low concentration in living organisms, access to these molecules is problematic in relation to the protection of living species and the environment. On the other hand, due to their structural complexity, the chemical synthesis of these molecules is hardly possible industrially. Thus, the microbiological production of terpenes using the natural biosynthetic pathways of these compounds (mevalonate and/or methyl erythritol phosphate pathways) starting from glucose, has been developed in recent years. One limitation of this approach is that glucose serves both as a carbon source for terpene production and as a carbon and energy source for the microorganism, making optimization of terpene production difficult. Several groups, including ours, have independently developed what we have called the terpene mini-path, which allows the decoupling of terpene biosynthesis and central metabolism in vivo, but also makes it possible to consider with more simplicity the enzymatic synthesis of terpenes in vitro. We have developed a two-enzymes cascade (2 kinases) to generate from their corresponding alcohols the two universal precursors of terpenes, dimethylallyl diphosphate (DMAPP) and isopentenyl diphosphate (IPP). We were able to apply this enzymatic cascade to the in vivo and in vitro synthesis of a cytotoxic prenyl derivative of brevianamide F, tryprostatin B, to the in vitro synthesis of farnesyl diphosphate (FPP), the precursor of all sesquiterpenes and triterpenes, and to the in vivo synthesis of delta-cadinol, a sesquiterpene of interest. On the other hand, the structure of the terpene mini-path also allows a simplified access to non-natural terpenes. We were thus able to synthesize the cyclobutyl derivatives of both FPP and tryprostatin B. These results, as well as those of other groups, allow to envisage the industrial implementation of a new and very general way of producing terpenes, either in vitro or in vivo.

FIGURES

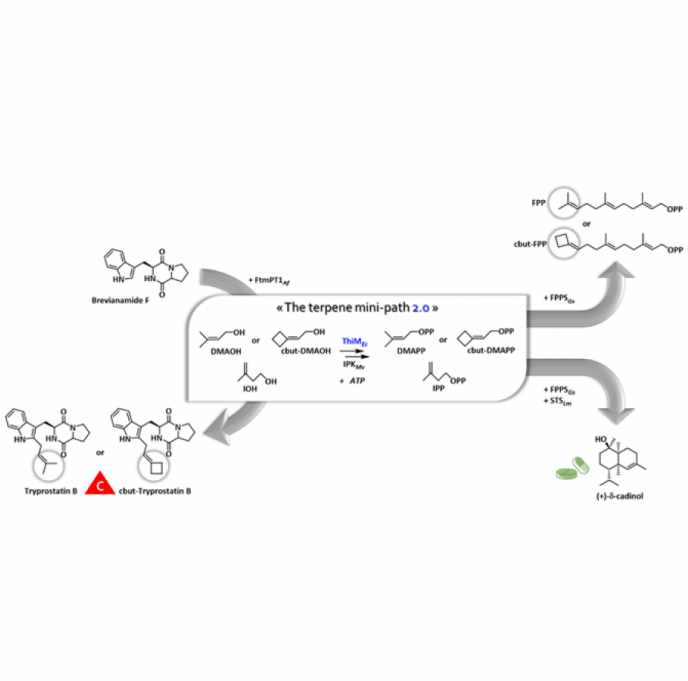

FIGURE 1

The terpene mini-path

The Terpene mini-path, a very short enzymatic cascade to access the universal precursors of all terpenes.

FIGURE 2

KEYWORDS

Terpene mini-path | Terpene production | Enzymatic cascade | Kinases

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