Biomimetic access to yellow pigment found in red sandalwood

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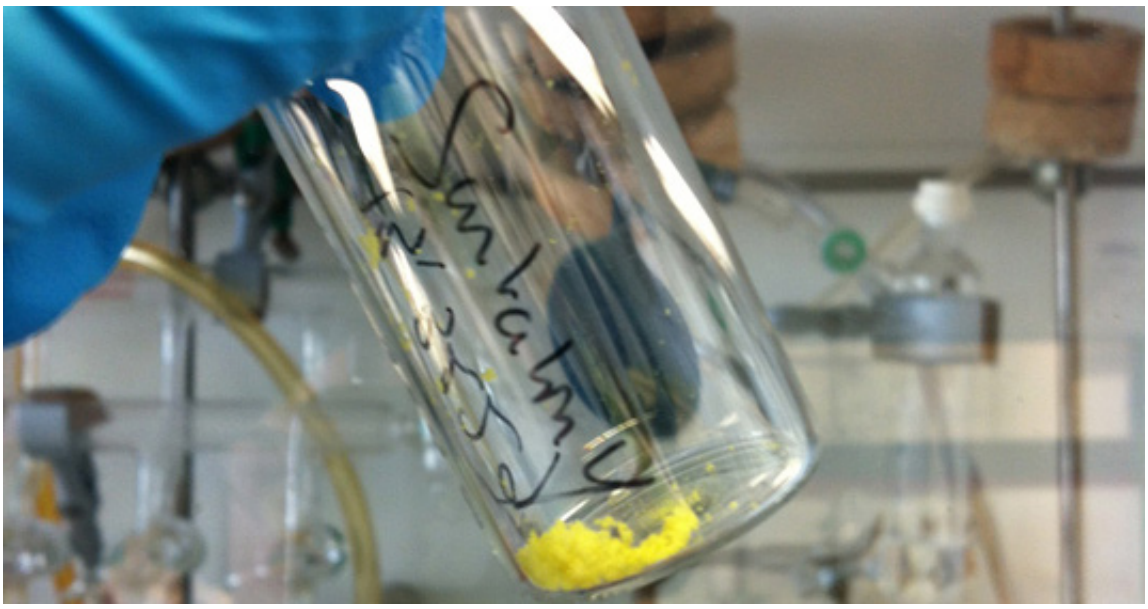

Santalin Y crystals. Credit: Dr. Guillaume Journot, LMU

The sandalwood tree (Pterocarpus santalinus) provides a durable timber that is used in Asia both as a source of incense and as the basis for devotional figurines, chess-pieces, and prayer beads. The characteristic red color of this precious hardwood is due to the presence of several complex secondary metabolites, such as the santalins and santarubins.

However, not all natural santalins are red: "Sandalwood also contains santalin Y, which is yellow in color. It is present only in small amounts,

but it is very interesting for us because its structure is much more complicated than that of the red pigments," says Dirk Trauner, Professor of Chemical Biology and Genetics at the Department of Chemistry at LMU. Trauner and his team have now developed a biomimetic method (modelled after the most probable biosynthetic route) for the total chemical synthesis of santalin Y, and shown that the resulting product is indistinguishable from the substance isolated from the sandalwood tree. "And along the way, we discovered that the biosynthesis of santalin Y includes an unprecedented type of reaction," Trauner adds.

Santalin Y contains a highly unusual so-called "fenestrane" structure, which is not found in any other known natural product in this form. "The term fenestrane is derived from the Latin word for window, because the structure it refers to is characterized by a set of four linked rings, arranged like the panes of a lattice window," as Trauner explains. "Sitting at the point where mullion and transom meet is a central carbon atom that is shared by all four rings." In the plant, the molecule occurs as a "racemic" mixture of two structural forms, which are mirror images of one another. This feature is also quite unusual for a natural product.

"How this complex molecule is assembled in the sandalwood tree was previously unknown," Trauner says. "But we have now shown that the final steps in santalin Y formation occur spontaneously. When the right precursors are brought together under the right conditions, no other enzymes are required." The key step involves the addition of a benzylstyrene to a 'vinylogous oxidopyrylium' – a novel reaction, which initiates a cascade of intramolecular events that gives rise to the unique window-like structure of santalin Y.

The synthetic scheme will make it possible to produce santalin Y in much larger quantities than could be harvested directly from sandalwood trees. The new findings also provide new insights into the compound's properties and function, and allow its biomedical activity to be explored.

"Santalins are used in traditional Ayurvedic medicine. Whether the yellow santalin Y plays a role may become clear in a follow-up study, in which we hope to define its biological activity," says Trauner.

More information: "Total Synthesis of Santalin Y." *Angew. Chem. Int. Ed.*, 54: 5079–5083. doi: 10.1002/anie.201411350

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