Natural crystalline fibers of (*E*)-(*R*)-*4*-thujanol: green kilogram production from a selected wild thyme. *X*-ray and NMR characterization of a spiral structure.

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BREAKTHROUGH

The LAHN (Laboratory for the Analysis of Natural Oils, ANASCAN sarl, FR) has developed for 3 years with Anne-Julie Dixon (farmer), an abundant production (per kg) of the thyme aroma: (*E*)-(*R*)-*4*-thujanol (figure 1). It is also named *trans*-*4*-thujanol or *trans*-*4*-sabinene hydrate. (*E*)-(*R*)-*4*-thujanol is a bioactive mono-terpene molecule.

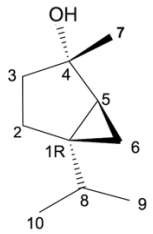

Fig. 1. Molecular structure of (*E*)-(*R*)-*4*-thujanol.

The innovations outlined below focus on three areas:

1-The isolation and cultivation of a wild thyme ecotype (figure 2) that produces (*E*)-(*R*)-*4*-thujanol in abundance.

Fig. 2. Thyme production (selected ecotype). Julien Bourjac's farm.

2-The development of an extraction process which makes it possible to obtain (*E*)-(*R*)-*4*-thujanol in solid form.

3-A method of purifying the compact solid form (or raw crystal) into crystalline fibers (or crystal of pure (*E*)-(*R*)-*4*-thujanol).

To meet environmental requirements, these extraction and purification processes are solvent free and are environmentally friendly. Part of the crystal production is already labeled by Ecocert (EU).

To date, (*E*)-(*R*)-*4*-thujanol produced through chemical synthesis was very expensive (≈ 40,000 $ Fujifilm Wako Chemicals USA). In fact, although (*E*)-(*R*)-*4*-thujanol is an active compound, its agronomical and therapeutic applications are non-existent outside of research laboratories.

Due to the innovative production of the crystal of (*E*)-(*R*)-*4*-thujanol, the molecule will be able to be produced at a more competitive cost, which will open up new opportunities for research and application.

NATURAL AROMA

(*E*)-(*R*)-*4*-thujanol is a flavoring substance with a delightful taste of thyme. The food industry uses some essential oils such as marjoram and thyme containing *4*-thujanol (mix of *cis*- and *trans*-isomer) as a flavoring agent. However, due to its absence in the catalogs as aromatic molecules, less than 100 kg of pure of *4*-thujanol equivalent are traded worldwide every year. Which is very small in comparison with other aromatic substance (several tons per year).

Organoleptic analysis of the thyme crude crystal (figure 3) takes place in three phases. i) A very refreshing heady scent reminiscent of peppermint. ii) A warm crescendo of floral and herbaceous thyme spices that rises in the mouth a few seconds. iii) A return to a lightly fresh flavor.

Fig. 3. Raw crystal of (*E*)-(*R*)-*4*-thujanol.

A head of raw crystal pin (≈ 3 mg) laid on the tongue is enough to invade the mouth with its aromas. It is therefore an exceptionally powerful strength of taste.

The nutrition value of the crystal is zero. See table below.

Nutritional value	Crystal
Water	0
Proteins	0
Carbohydrates	0
Dietary fibers	0
Lipids	0
Sodium	0

Claude-Emmanuel Robin (Evolugout SARL), *Michelin*-starred chef passionate about molecular cuisine, very enthusiastic about discovering this crystal, is already working on developing new products with new flavors.

CRYSTALLIN EDIFICE

The pure crystalline form of (*E*)-(*R*)-*4*-thujanol looks fibrous and appears to naked eye like cotton (figure 4).

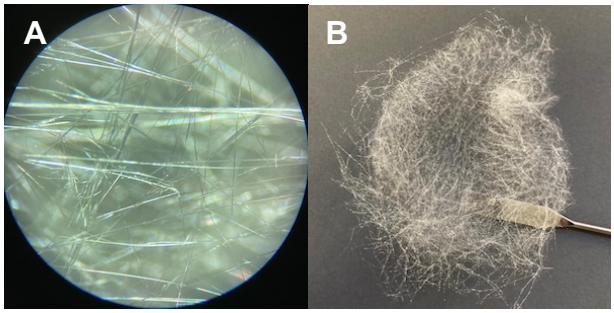

Fig. 4. Crystalline fibers of (*E*)-(*R*)-*4*-thujanol. Observation with a microscope (A) or naked eyes (B).

The crystal structure is outstanding. Indeed, it was unexpected that a molecule with structure as simple as this, could construct crystalline fibers (fig. 4). Specifically, (*E*)-(*R*)-*4*-thujanol forms a trimmer (fig. 5A) that overlays itself indefinitely at a slight angle, constituting a *P*-type helix (fig. 5B). At the heart of the structure, the alcohol functions are interconnected through hydrogen bonds.

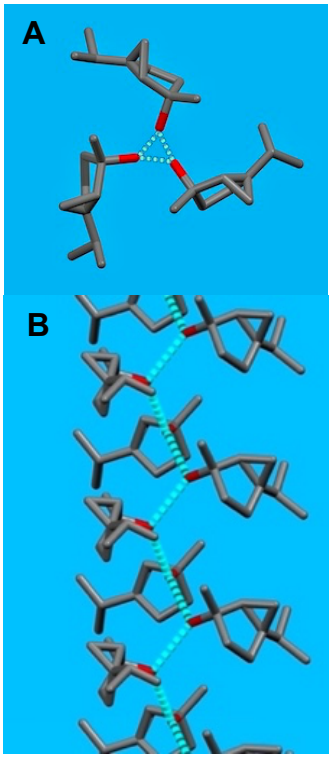

Fig. 5. Molecular model of (*E*)-(*R*)-*4*-thujanol crystal. A. Trimmer of (*E*)-(*R*)-*4*-thujanol. **B.** Superposition of trimers in helix structure. Red: alcohol. Cyan: hydrogen bond. Grey: carbon skeleton.

The fibrous structure of the crystal opens new research possibilities such as the manufacture of bioactive fibrous assemblies that may have antiseptic properties. The crystal may also have some organic semi-conductors' properties.

BIOACTIVES PROPERTIES

(*E*)-(*R*)-*4*-thujanol is a molecule with various already known physiological properties: pollen attractor (activator of bee antennae) and insect repellent (female bark beetles). The production of pure and natural (*E*)-(*R*)-*4*-thujanol in abundance is likely to stimulate research on its physiological functions and to support uses in the wild or in culture.

The (*E*)-(*R*)-*4*-thujanol is also now studied in a drug biophysics laboratory for its menthol-like properties.

STABILITE

(*E*)-(*R*)-*4*-thujanol is quite an inert structure (except in extreme alkaline pH >12). (*E*)-(*R*)-*4*-Thujanol does not carry unsaturation that may be responsible for the formation of hydro-peroxyde. Therefore, it cannot be altered by the presence of molecular oxygen. The alcohol function, carried by a tertiary carbon, cannot be oxidized. All this is a precious asset for its use, the maintenance of its active properties over time, and for its storage. The pure (*E*)-(*R*)-*4*-thujanol has a melting point of 60 °C.

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