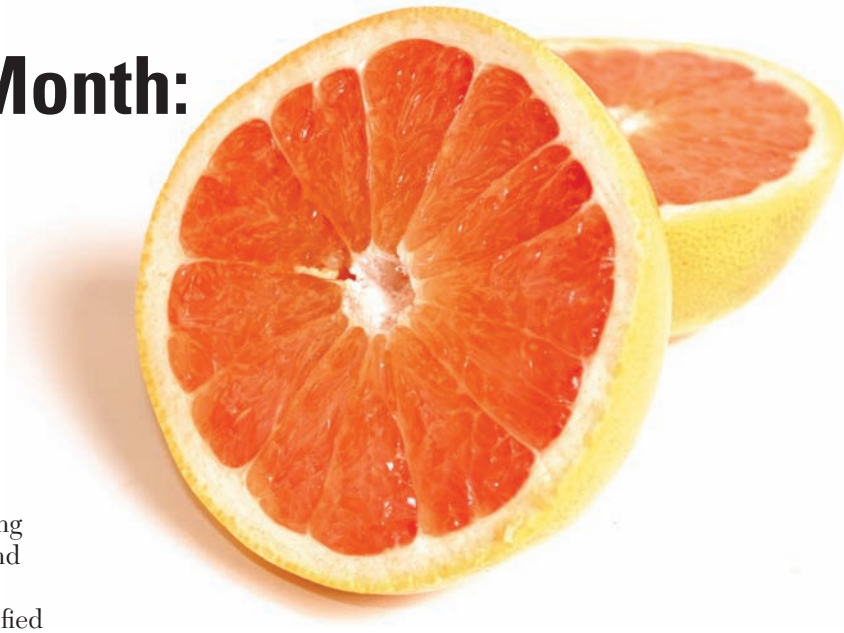
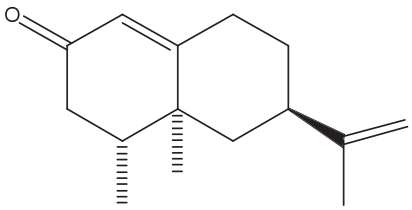
Molecule of the Month: Nootkatone

Michael Zviely, CIC



Nootkatone is a crystalline material possessing an extremely powerful grapefruit aroma and a woody topnote (**see F-1**.) It is found in citrus oils (for example, grapefruit) and can be purified from both citrus cold pressed oils as well as essential oils.* Pure nootkatone products are white to yellowish crystals, whereas nootkatone products of lesser purity are transparent yellowish to yellow colored liquids.

Nootkatone **F-1**



Due to its powerful citrusy, woody, sweet juicy notes, peely and grapefruitlike aroma profile, nootkatone is used in formulation of grapefruit and other citrus-flavored beverages. In fragrances, it is used in creation of dry and citrusy compounds for men's perfumes; however, for such applications, the material needs to be 98% pure and with a melting point of at least 32°C, as lower purity grades are not suitable to be used as a fragrance ingredients.[1]

(+)-Nootkatone has a φ value of $2.7x10^{11}$, whereas (-)-nootkatone has a φ value of 3.6×10^{8}; the latter is an optical isomer of nootkatone, with a dusty-woody, spicy, slightly fresh, green, sour and herbal organoleptic profile.[2]

Nootkatone is available from different market sources in different concentrations. The primary content of a 85% pure nootkatone crystal from valencene is (+)-nootkatone with other sesquiterpenes and related materials, which gives this product an effective grapefruit odor and flavor. Nootkatone can be used in grapefruit beverages at a level of 2–6 ppm; in fragrance compositions, it can be used in combination with other citrus oils (such as bitter orange oil, bergamot oil etc.,) to add an interesting citrus note.

Except for the physical methods, *i.e.* high-vacuum distillations, molecular distillations and crystallizations, nootkatone can be prepared synthetically in several ways. The most important method uses valencene—a natural sesquiterpene hydrocarbon product found in citrus oils (for example, orange cold pressed oil at 0.1% concentration)—as a starting material (**see F-2**.) In this process, valencene is oxidized using chromium as bichromate, or in catalytic amount as oxide, in the presence of *tert*-butyl-hydroperoxide (TBHP).

Physical Data

CAS# 4674-50-4
FEMA# 3166
CE 2179
Synonyms: (+)-Nootkatone;
5,6-dimethyl-8-isopropenyl-bicyclo[4.4.0]dec-1-en-3-one

Physical Data for Nootkatone Crystals

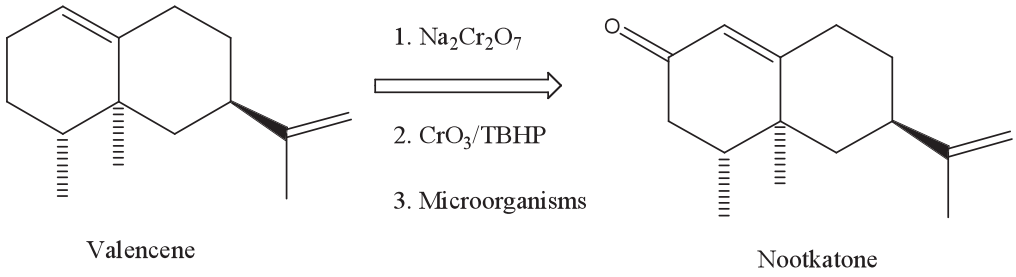
Appearance	White to yellowish crystals
Molecular Weight	218.3
Molecular Formula	$C_{15}H_{22}O$
Assay (GC)	98% (min.)
Melting Point	33°C (min.)
Optical Rotation	+184° to 196°

Physical Data for Nootkatone 85%

Appearance	Transparent straw-yellow colored liquid
Molecular Weight	218.3
Molecular Formula	$C_{15}H_{22}O$
Refractive Index (20°C)	1.515–1.526
Specific Gravity (25°C)	0.997–1.012
Optical Rotation	+145° to 155°

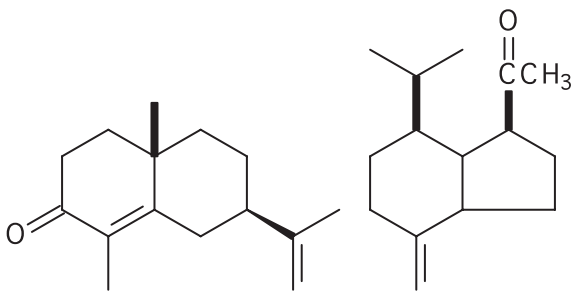
*Most of the information on organoleptic properties and uses are taken from FRM 2001 and PMP 96 *Databases of Perfumery Materials & Performance*, Boelens Aroma Chemicals Information Services, Netherlands and from several producers' specification sheets, *e.g.* Frutarom, Aromor, Givaudan, Bedoukian.

Preparation of nootkatone using valencene as the starting material **F-2**



To obtain a high yield of nootkatone, valencene can also be bio-transformed by the green algae species like *chlorella* and fungi species such as *Mucor* species, *Botryosphaeria dothidea*, and *Botryodiplodia theobromae*.[3] In addition, some other molecules, like α-cyperone and β-opiapenone, may accompany nootkatone products obtained from valencene (**see F-3**).

α-Cyperone and β-opiapenone **F-3**



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References:

1. Research Institute for Fragrance Materials, Repeated insult patch test with nootkatone. Unpublished report from Bedoukian Research, May 11, Report number 46155 (2005)
2. HG Haring, F Rijkens and H Boelens, Olfactory Studies on Enantiomeric Eremophilane Sesquiterpenoids *J Agric Food Chem*, 20, 1018 (1972); MH Boelens, H Boelens and LJ van Gemert, Sensory Properties of Optical Isomers, *Perfum Flavor*, 18(6), 1–15 (1993)
3. M Furusawa, T Hashimoto, Y Noma and Y Asakawa, Highly Efficient Production of Nootkatone, the Grapefruit Aroma from Valencene, by Biotransformation. *Chem Pharm Bull*, 53 (11), 1513 (2005); MA Fraatz, RG Berger and H Zorn, Nootkatone: a biotechnological challenge. *Appl Microbiol Biotechnol*, 83(1), 35–41 (2009)