

Methyl 2-methylalkanoates from the essential oil of *Humulus lupulus* L.

Milena Z. Živković, Niko S. Radulović, Marija S. Genčić

*Department of Chemistry, Faculty of Science and Mathematics, University of Niš, Višegradaska 33, RS-18000
Niš, Serbia*

Corresponding author: nikoradulovic@yahoo.com

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For hundreds of years strobiles from *Humulus lupulus* L. (Cannabaceae) have been used to flavor beer and in the ethnopharmacology of many nations. The essential oil is produced by the female inflorescences (strobuli lupuli) which contain the oil bearing glands. Up to now, more than 200 essential-oil constituents have been identified; however, a large number still remains unknown, either due to their low relative abundance in the essential oil or due to a natural variation of the composition. These minor components are known to significantly contribute to the overall sensory impression, and should not be neglected. Prompted by this, we subjected a sample of hydrodistilled essential oil of fresh hop cones (yield 0.6%, w/w), collected from a wild-growing population of *H. lupulus* near the city of Niš (SE Serbia), to gradient “dry flash” SiO₂ chromatography. A fraction that eluded with 2% (v/v) diethyl ether in pentane had an odor that was reminiscent of the original essential oil. Initial GC and GC-MS analyses revealed that this fraction consisted of a myriad of methyl esters of normal and branched aliphatic carboxylic acids. A series of 2-methylalkanoates (C₈-C₁₁) was tentatively identified based on their mass spectra and retention data. Since, according to a literature survey, methyl 2-methylnonanoate and methyl 2-methyldecanoate were never previously reported for *H. lupulus*, we decided to prepare the two compounds by synthesis and confirm their presence in *H. lupulus* by GC co-injection experiments. The corresponding lithium enolates, obtained in the reaction of methyl nonanoate and methyl decanoate with lithium bis(trimethylsilyl)amide at -78 °C, were alkylated with methyl iodide, and, in this way, following a chromatographic purification, we acquired pure samples of the two esters. The subsequent co-injection experiments corroborated the initial tentative identifications, i.e. this is the first report on the occurrence of methyl 2-methylnonanoate and methyl 2-methyldecanoate in *H. lupulus* essential oil.

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