HYDROGENATION OF NATURALLY DERIVED NEPETA LACTONE AS A TOPICAL INSECT REPELLENT

Keith W. Hutchenson, Yamaira I. Gonzalez, Scott C. Jackson, Bo Kou, Leo E. Manzer, Mark A. Scialdone, Mayis Seapan, and Sourav Sengupta

DuPont Company, Chevron, Catalytic Insights

Summary

This presentation describes the development of a selective hydrogenation process to produce a sustainably-sourced insect repellent derived from catmint oil. A Pd/C catalyst and a novel two-step hydrogenation process were identified to maximize the yield of the desired dihydronepetalactone product from treated catmint oil containing mixtures of trans,cis- and cis,trans-nepetalactone isomers and to minimize formation of less desirable by-products such as puleganic acid. DuPont received EPA registration for the active ingredient in April 2009.

Keywords

Sustainability, Chemical Feedstocks from Biomass, Dynamics/Control of Chemically Reacting Systems

Introduction

Dihydronepetalactone (DHN) has been shown to be an effective insect repellent ingredient comparable in efficacy to that obtained with the well-known N,N-diethyl-3-methylbenzamide (DEET) for a broad range of biting insects.\(^1\) DHN can be produced by hydrogenating nepetalactone, which is a component of the essential oil from the renewably-sourced catmint plant, **Nepeta cataria**. This hydrogenated catmint oil (HCO) is a safe topical insect repellent which can be reapplied at higher frequency than market incumbents.

This presentation will describe the development of a novel two-step hydrogenation process to maximize the yield of the desired DHN from treated catmint oil containing mixtures of trans,cis- and cis,trans-nepetalactone (NL) isomers and to minimize formation of less desirable by-products such as puleganic acid. Results will also be shown from the scouting of various catalysts for this transformation which led to the selection of a particular Pd on carbon catalyst for subsequent process optimization and scale-up demonstrations. Finally, results will be presented for replicate experiments with various catmint oil feedstocks to demonstrate the HCO production process for U.S. EPA registration.

Results and Discussion

Crude catmint oil is typically isolated from the plant by steam distillation and contains over 100 compounds, including three of the four NL stereoisomers which typically comprise about 80% of the oil as well as various other components such as \(\beta\)-caryophyllene.\(^5\) Crude catmint oil feedstocks can be treated to remove some of these components that can lead to undesirable impurities in the reaction product as well as catalyst poisoning. One typical mode of refining the crude oil is by adding and then stripping ethanol to remove volatile species, including some sulfur-containing compounds which can poison the hydrogenation catalyst.

Scheme 1 shows the general selective catalytic hydrogenation from the two primary NL isomers present in catmint oil to the three primary active DHN isomers in the product. The trans,cis-NL isomer hydrogenates relatively easily and forms the DHN-1 product isomer stereoselectively. Hydrogenation of cis,tans-NL is more difficult and results in the formation of the DHN-2 and DHN-3 stereoisomers. Over hydrogenation can lead to formation of an undesirable byproduct, puleganic acid, so careful control of the relative reaction rates is critical for high DHN yields and total conversions.

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*To whom all correspondence should be addressed. Experimental Station, Wilmington, DE 19890, USA. E-mail: keith.w.hutchenson@usa.dupont.com, Tel.: 302-695-1389.
Scheme 1. Selective hydrogenation of NL to DHN showing primary stereoisomers.

Development of the hydrogenation process was conducted in batch autoclave reactors and included identification of a suitable catalyst and evaluation of a number of process operating variables such as the reaction temperature and pressure, catalyst loading, influence of solvent, catalyst recyclability, etc. Figure 1 shows a typical reaction profile for the two-step reaction where the trans,cis-NL isomer is hydrogenated at low temperature to minimize puleganic acid formation, and then the temperature is increased to hydrogenate the cis,trans-NL isomer.

The optimized process was subsequently used in replicate hydrogenation runs with various feedstock oils to demonstrate the process for producing HCO. DuPont received registration from the U.S. Environmental Protection Agency (EPA) in April 2009 for this catmint-derived insect repellent ingredient. This is the first new insect repellent biopesticide to be registered by the EPA in eight years.

References


(2) Feaster, J.E.; Scialdone, M.A.; Todd, R.G.; Gonzalez, Y.I.; Foster, J.P.; Hallahan, D.L. Dihydronepetala lactones Deter Feeding Activity by Mosquitoes, Stable Flies, and Deer Ticks. *Journal of Medical Entomology* 2009, 46, 832.

