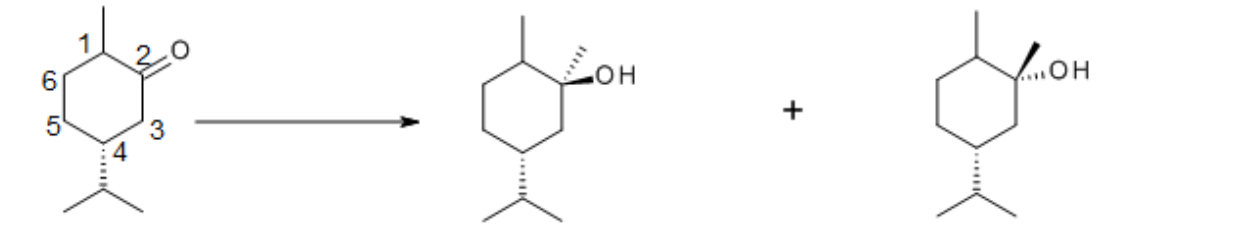
Chemistry 342 Laboratory Research Project 2016

Methylation of carvomenthone

Overview of the 2016 project

Carvomenthone (**1**), also called tetrahydrocarvone, is an isomer of menthone (the ketone related to menthol). It has a minty smell and is a natural constituent of several essential oils. The purpose of this project is to investigate the product of methylation of carvomenthone at the carbonyl carbon; this produces a new tertiary alcohol containing a new chiral center. The most usual reagent would be methylmagnesium bromide (CH_3MgBr) or some related Grignard reagent, but methyllithium (CH_3Li) might also be used. Also possible could be a Barbier coupling using samarium(II) iodide and iodomethane, which form *in situ* an organosamarium compound that reacts like the above reagents. Some procedures may also include added cerium(III) chloride to promote the reaction.

Two different types of alcohol products are possible: (*2S,4R*)-2-methylcarvomenthol (**2**) and (*2R,4R*-2-methylcarvomenthol (**3**), of which **2** is more predicted to be the major product. Note that since **1** is a mixture of diastereomers, **2** and **3** will be also.



Carvomenthone (**1**)
Carbon-1 is mixed
R/S stereochemistry

(*2S,4R*)-2-methylcarvomenthol (**2**)

(*2R,4R*)-2-methylcarvomenthol (**3**)

Again, the stereochemistry of C-1 will be mixed

We would like to have one pure product if possible – either **2** or **3** would be acceptable, but this is unlikely to be possible given the fact that the carvomenthone itself is a mixture. A product like this could be used either for the preparation of either chiral terpene derivatives (for example, as possible medicinal products) or of chiral catalysts.

The goal of this project is to find a suitable method for making **2** or **3**, or a mixture of the two, starting from carvomenthone (**1**). "Suitable" in this case means appropriate for undergraduates working with standard lab equipment and affordable chemicals, preferably within a normal laboratory period (3 hours).

Search strategy

It is very unlikely that you will find a perfect match for this reaction, unless you are (a) lucky or (b) using a high-powered search tool such as STN Easy/SciFinder. You will therefore need to find ways to broaden the search terms enough to get useful hits, but not so much that you get too much, or things that are only tangentially useful.

Consider a geographical search; some maps cover the whole world, whereas some are just for the US, and some may be just for New York State. If you are looking for SUNY Potsdam on a map – if you don't find it, you may decide to look for Potsdam. If you can't find Potsdam, you may look for St. Lawrence County. If you can't find the county, you may have to settle for New York State as the closest "hit". The same will apply to your chemical search – and you will have to judge what searches are a good match.

Here are some suggested search methods:

Using chemical reactant words

Level 1: Exact – chemical reactants or products

These are some suitable search terms for this project. Note that chemists often use formulae or abbreviations in place of chemical names, even in the titles of papers.

Carvomenthone AND methylmagnesium (chloride or bromide or iodide)

Carvomenthone AND CH3Mg (this should find CH3MgCl, CH3MgBr or CH3MgI)

Carvomenthone AND MeMg (this should find MeMgCl, MeMgBr or MeMgI)

Carvomenthone AND methyllithium (or search on CH3Li or MeLi)

Carvomenthone AND samarium(II) iodide (or search on samarium diiodide or SmI2)

Products: Unlikely to be found, but you may try searching for methylcarvomenthol

Level 2: Broader – chemical terms to use – may use a level 1 together with a level 2 (e.g, use "cyclohexanone" with CH3Mg)

Cyclohexanone, "Cyclic ketone", cycloalkanone

Grignard reagent, alkylmagnesium, RMgX, alkyllithium, organolithium

Products: Not so useful in this particular search, since these are not common substances.

Using chemical identifiers *(InChIKeys and CAS Nos.)*

Level 1: Exact

Most useful with Google Web, ChemSpider, or similar. CAS numbers are commonly used, but may not be known for your product, so they may not be found. InChIKeys are only used rarely, but will give exact "hits" where they occur. Use combinations of InChIKeys if you have many hits.

Level 2: Broader – using InChIs

Strip away the end part of the InChI after the later slashes, and you will be able to search for InChIs that contain the same skeleton, but perhaps different stereochemistry. This may be useful if the exact search gives no hits.

Reactant

- Common name: Carvomenthone
- IUPAC name: (5R)-5-isopropyl-2-methyl-cyclohexanone
- CAS No: [59471-80-6]
- InChI: InChI=1S/C10H18O/c1-7(2)9-5-4-8(3)10(11)6-9/h7-9H,4-6H2,1-3H3/t8?,9-/m1/s1
- InChIKey: GCRTVIUGJCJVDD-YGPZHTELSA-N

Product

- Common name: 2-methylcarvomenthol
- IUPAC name: ((1S,5R)-5-isopropyl-1,2-dimethylcyclohexanol or (1R,5R)-5-isopropyl-1,2-dimethylcyclohexanol
- CAS Nos: Not knowns
- InChI: InChI=1S/C11H22O/c1-8(2)10-6-5-9(3)11(4,12)7-10/h8-10,12H,5-7H2,1-4H3/t9?,10-,11+/m1/s1 or InChI=1S/C11H22O/c1-8(2)10-6-5-9(3)11(4,12)7-10/h8-10,12H,5-7H2,1-4H3/t9?,10-,11-/m1/s1
- InChIKey:BKAOOCFAQUVPLH-ZOCYIJKUSA-N or BKAOOCFAQUVPLH-FHZGLPGMSA-N

Other broader searches

Reaction type – often used along with search terms like "carvomenthone"

Grignard reaction with ketone, methylation, alkylation

Searching using chemical identifiers