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SEPARATION OF A MIXTURE OF *R*-MENTH-4-EN-3-ONE AND (-)-MENTHONE

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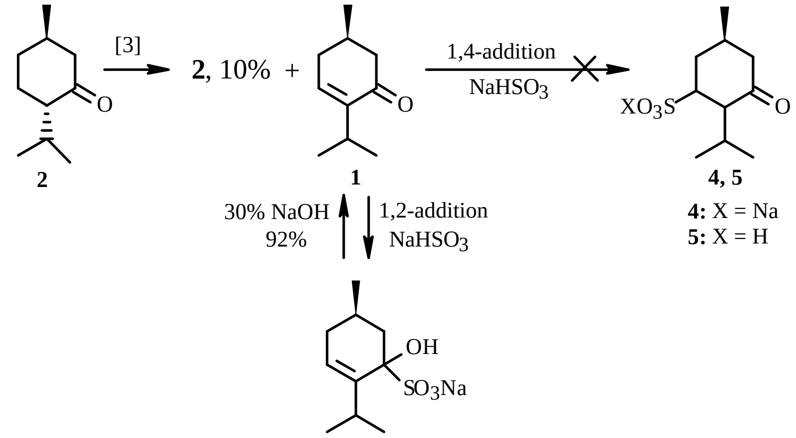
A promising chiral synthon is *R*-menth-4-en-3-one (**1**) [1-4], which is produced from the natural monoterpenoid *l*-menthol through the intermediate (-)-menthone (**2**) [5, 6] and is often contaminated (up to 10%) with the latter. The usual purification methods, including chromatographic ones, do not produce **1** of the desired purity.

It is known [7] that **2** does not form bisulfites. Therefore, we supposed that it might be possible to isolate **1** from a mixture with **2** by forming the bisulfite derivative (**3**) of the carbonyl. According to our previous research [1], nucleophilic addition to **1** should occur via 1,2-addition to the carbonyl. Furthermore, the reaction was performed under the literature conditions [8, 9] in order to prevent 1,4-addition of $NaHSO_3$.



In fact, treatment of a mixture (9:1) of **1** and **2** with a four-fold excess of $NaHSO_3$ followed by standard workup gave chemically pure (>99%) **1** in 92% yield. The 1,4-addition product (**5**) was not observed in the reaction mixture.

Thus, pure **1** could be isolated from its mixture with **2** by using the unusual behavior of **1** in nucleophilic addition reactions.

Separation of *R*-Menth-4-en-3-one from (-)-menthone. A mixture (9.20 g, 9:1) of **1** and **2** was treated with a solution of Na_2SO_3 (27.34 g, 217 mmol) in H_2O (50 mL) and several drops of phenolphthalein. The reaction mixture was stirred at 95-97°C for 1 h adding dropwise AcOH (25 mL, 50%) until the color faded and was extracted with petroleum ether (3 × 30 mL). The extract was dried over Na_2SO_4 and filtered. The solvent was evaporated in vacuo. Compound **5** was not observed in the solid. The aqueous layer was treated with NaOH solution (30%) and extracted with methyl-*t*-butylether (3 × 30 mL). The extract was dried over Na_2SO_4 and filtered. The solvent was evaporated in vacuo to afford **2** (7.64 g, 92%) that was pure according to GC, PMR, and ^{13}C NMR [10].

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Chromatographic analysis was performed on a Chrom-5 instrument [column 2.4 m, stationary phase PEG-6000 (5%) on Inerton AW-DMSC (0.125-0.160 mm), working temperature 50-200°C] using He carrier gas. NMR spectra (δ, ppm, J/Hz) were obtained on a Bruker AM-300 spectrometer (working frequency 300.13 MHz for PMR and 75.47 MHz for ^{13}C) in $CDCl_3$ relative to TMS.

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