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Chemoselective additions of thiophenol to carvone and perillaldehyde

Olof Smitt and Hans-Erik Högberg*

Chemistry, Department of Natural and Environmental Sciences,
Mid Sweden University, SE-851 70 Sundsvall, Sweden

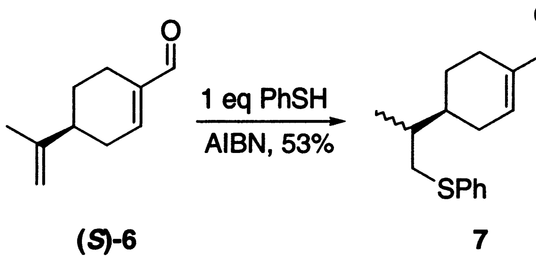
Depending on the reaction conditions addition of thiophenol can be directed to either of the two C=C-double bonds of the monoterpenes carvone and perillaldehyde.

Keywords: chemoselectivity, terpene, thioethers, radical reactions

We are interested in the preparation of heavier analogues of the monoterpene carvone (**1**). One way of achieving this is to transform the exocyclic double bond of carvone into a functional group that can then be used for further C–C bond formation. It is known that thiophenol readily adds to α,β-unsaturated carbonyl compounds via an ionic 1,4-addition mechanism. Thus, carvone at 0°C gives the kinetically controlled product **2**,[1] and at higher temperature, the thermodynamically more stable product **3**.[2] When reacting via a radical mechanism, thiophenol undergoes anti-Markovnikov addition to non-conjugated double bonds.[3–6] In compounds containing two types of double bonds, selectivity could be expected. To our knowledge, the sole example of such selectivity is provided by the reaction of diallyl fumarate with thiophenol, which, when reacting via a radical mechanism, adds predominantly to the double bond of one of the allyl groups.[7] We wanted to find out if this type of selectivity could also be obtained with compounds like carvone and perillaldehyde.

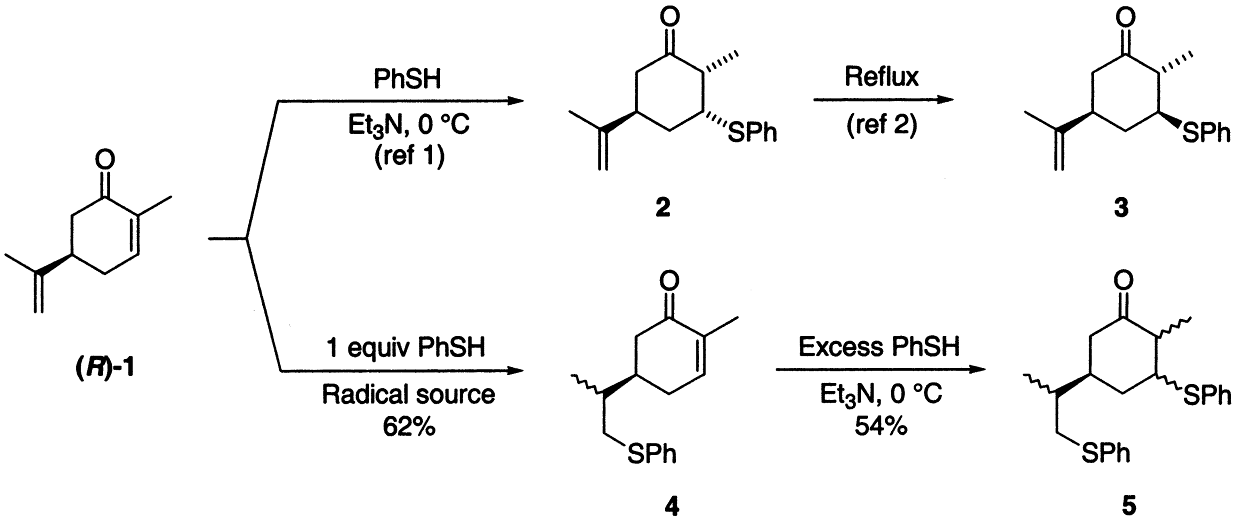
Thus, when heating a mixture of carvone and an equimolar amount of thiophenol together with a radical source, we obtained a 62% isolated yield of the thioether **4** as a 1:1 mixture of diastereoisomers (Scheme 1). When an excess of thiophenol was used, the product was the diadduct, disulfide **5**, as a complex mixture of isomeric diadducts. A less complex mixture of isomers of **5** was obtained when subjecting the radical monoadduct **4** (1:1 mixture of diastereomers) to the procedure described by others for the preparation of the kinetically controlled 1,4-adduct of carvone (**2**, cat. Et_3N, thiophenol, hexane, 0°C,[1] Scheme 1). Thus, the disulfide **5** was obtained as a 1:1 mixture of diastereoisomers, epimeric with respect to the side-chain -CH_2-SPh group (corroborated by the ^1H NMR spectrum of the diadduct **5**).

This type of chemoselective radical addition was not limited to an α,β-unsaturated ketone. Thus, when thiophenol was subjected to radical addition conditions, it also reacted with perillaldehyde (**6**), affording the thioether **7** as a diastereoisomeric mixture confirming the general chemoselectivity in this type of radical addition. The 1,4-adduct (cat. Et_3N, thiophenol, CH_2Cl_2, 0°C),[1] has previously been used for the preparation of an imine derivative.[8]



Scheme 2

To summarise, we have shown that it is possible to direct the addition of thiophenol chemoselectively to carvone and perillaldehyde. Due to the variety of functional groups present, the phenylthioethers prepared (**4** and **7**) offer great potentials as starting points for further multistep syntheses. If the exocyclic part can be desulfurised, this will give access to 8,9-dihydrocarvone.



Scheme 1

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* To receive any correspondence. E-mail: Hans-Erik.Hogberg@mh.se

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