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REGIOSPECIFIC SYNTHESIS OF ENONES *VIA* α-(PHENYLTHIO)-KETONES: 2,5-DIMETHYL-4-HEXEN-3-ONE, *E*-6-METHYL-2-HEPTEN-4-ONE, *E*-7-METHYL-4-OCTEN-3-ONE, AND AR-TURMERONE

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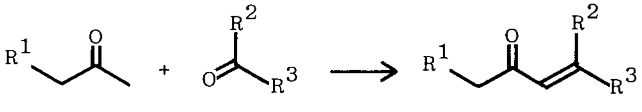
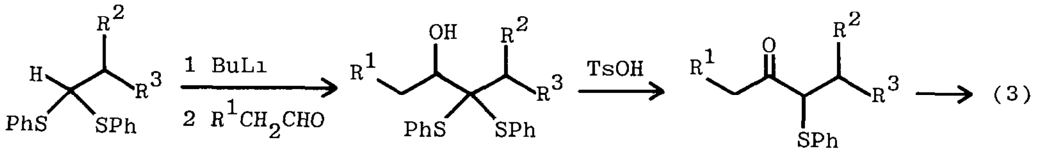
Summary: Enones not available from aldol condensations may be synthesised regiospecifically *via* α-(phenylthio)ketones: the title compounds have been made by this route.

Enones are simply synthesised if the aldol condensation between two carbonyl compounds is regiospecific. An entire volume of Organic Reactions[1] is devoted to this reaction and yet it contains few examples where an unsymmetrical ketone (1) enolises regiospecifically and attacks the carbonyl group of an aldehyde or another ketone (2) to give an enone (3). For this type of condensation a specific enol equivalent is needed such as O-silylated[2] or kinetic[3] enolates. We report a general method for the synthesis of enones of this type (3) by a different strategy: the acylation of a vinyl anion equivalent. Rearrangement of adducts (5) from bis[phenylthio(PhS)]acetals (4) and aldehydes provides α-(PhS)ketones[4] (6) which give enones by oxidation to the sulphoxide and thermolysis (refluxing in toluene if the double bond has two substituents, distillation in a kugelrohr apparatus if it has three) Four examples follow.



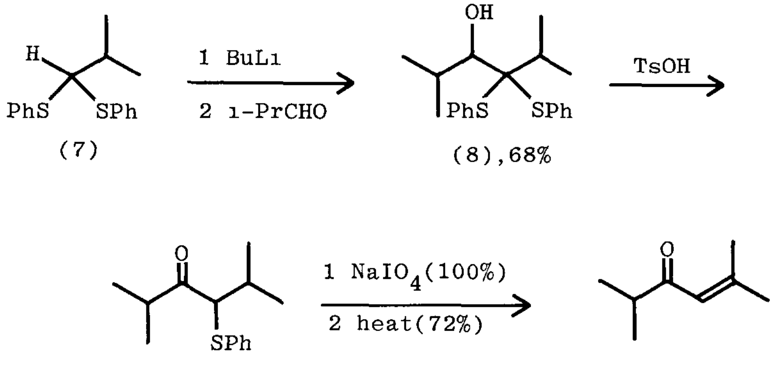
(1) (2) (3)



(4) (5) (6)

2,5-Dimethyl-4-hexen-3-one (10) has been made by a variety of methods[5] and used in chrysanthemic acid synthesis.[6] In our route (scheme 1) the same aldehyde (i-PrCHO) provides both halves of the adduct (8) which rearranges in acid[4] to give the α-PhS-ketone (9). Oxidation with $NaIO_4$ is slow but reliable and the sulphoxides (mixture of diastereoisomers) give enone (10) on distillation (kugelrohr).

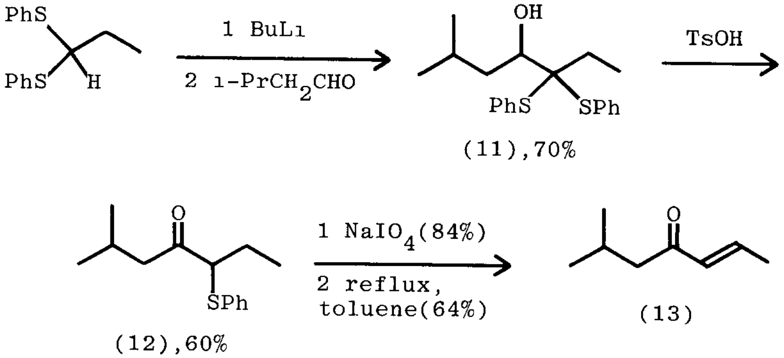
Scheme 1



(7) (8),68% (9),63% (10)

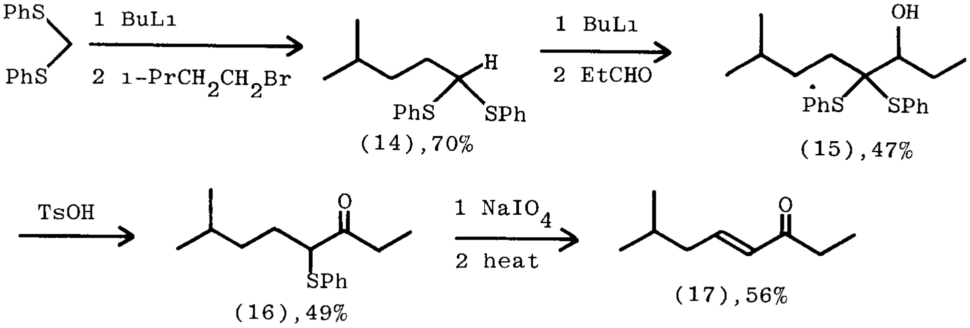
A direct aldol route has been reported for 6-methyl-2-hepten-4-one (13) but the yield is poor.[7,8] It has been used in a synthesis of juvabione[7] and synthesised by other strategies.[9] Our route (scheme 2) gives only E-(13) as expected from the stereoselective elimination of PhSOH from α-phenylsulphinyl-esters.[10]

Scheme 2



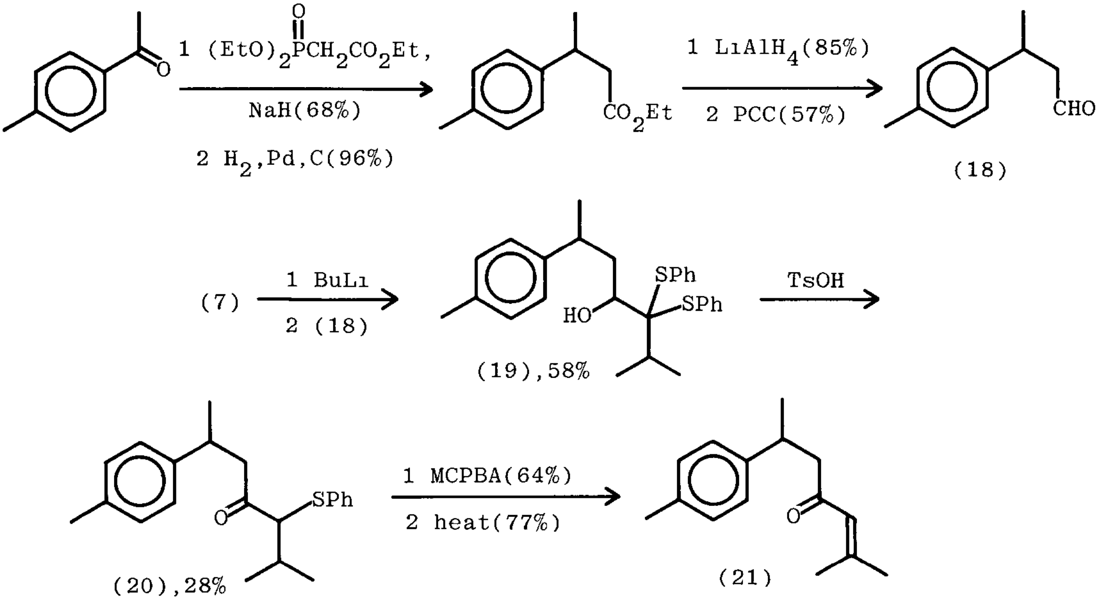
The isolation of the perfume E-7-methyl-4-octen-3-one (17) from a sponge was followed by a synthesis using interesting chemistry but giving a poor yield.[11] We alkylated bis(PhS)methane to give bis(PhS)acetal (14) and eventually α-PhS-ketone (16). Elimination again gave the E-isomer of enone (17) (scheme 3).

Scheme 3



The best known[12] of the enones we have synthesised is ar-turmerone (21). The rearrangement of (19) to (20) gave a poor yield, probably because the aromatic ring intercepts one of the cationic intermediates in the rearrangement,[4] and this synthesis (scheme 4) cannot compete with other published methods.[13] For the more demanding aliphatic enones, the route is short, convergent, and regiospecific.

Scheme 4



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