Spivey Group Problem Session May 2010

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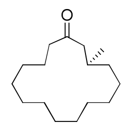
Flavours and Fragrances

The origin of using odorous substances simply for enjoyment or medicinal reasons is as old as mankind. We have come to rely heavily on the use of synthetic compounds in all aspects of life such as in aftershave and perfumes, flavoured drinks, exotic foods, savoury snacks, beauty products and household products.

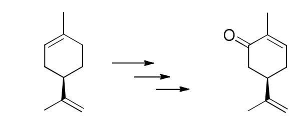
The synthesis and application of chiral molecules in fragrance research as very important as similar to other natural proteins, then odour receptors are chiral entity composed of *(S)*-configured amino acids and thus the binding pocket formed by a receptor protein is chiral and can discriminate between the two enantiomers of a chiral molecule.[1]

1) Musk is the dried secretion from an internal pouch found between the hind legs of the Himalayan musk deer. 30-50 animals had to be killed to produce 1kg of musk grains. The odour or dry musk is mainly down to (R)-(-) muscone. Its S enantiomer has the same odour but less pronounced. **Propose an enantioselective synthesis of (R)-(-) Muscone.**



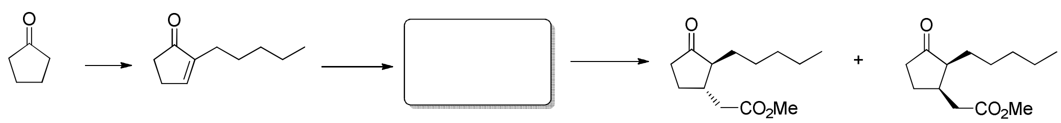
(R)-(-)-muscone

2) (R)-(-) Carvone has a spearmint odour and is widely utilised in dental products. Its enantiomer (S)-(+) Carvone smells of caraway and serves as flavourants for foods and beverages. Industrially (R)-(-) Carvone from (R)-(+) Limonene, a component of citrus peel. **Propose a synthesis of (R)-(-) Carvone from (R)-(+) Limonene.**



(R)-(+)-limonene (R)-(-)-carvone

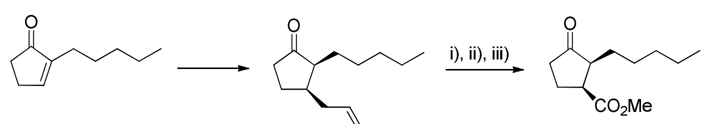
3) Hedione was developed in 1966 and has a floral jasmine smell which has been used in perfumes such as 'Diorella' by Dior and 'First' by Van Cleef and Arpels. The *u* isomer of Hedione is 70x more powerful than the *l* isomer
Fill in the reagents and intermediate compound in the synthesis of Hedione



(±)-*(l)*-Hedione (±)-*(u)*-Hedione

9:1

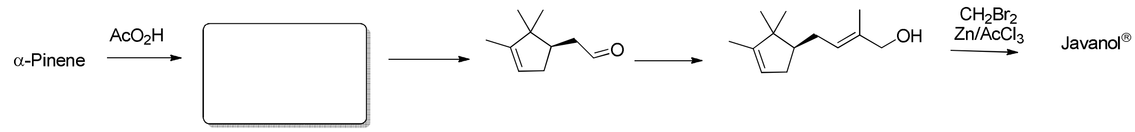
Another approach to the synthesis of the more powerful (±)-(*u*)-Hedione is outlined below
Fill in the reagents and intermediate compound in the synthesis of (±)-(*u*)-Hedione, give mechanisms and account for selectivity.



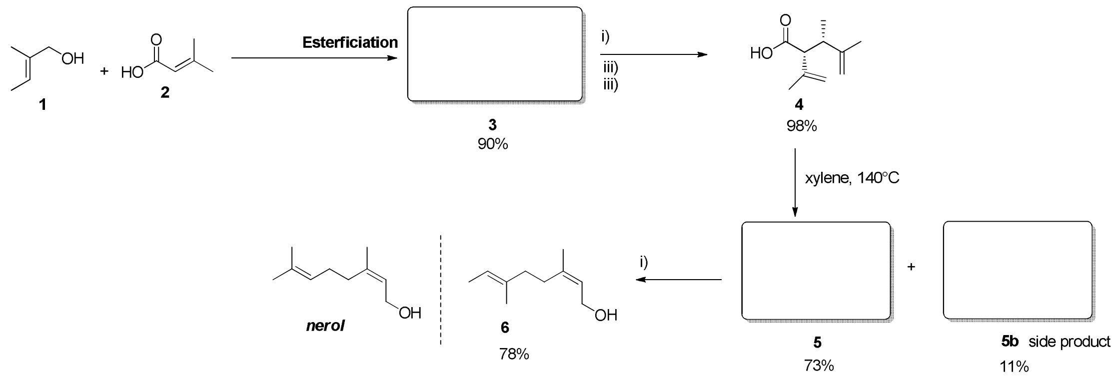
70%
94:6
u:l

(±)-*(u)*-Hedione

4) *β*-Santalol, the key olfactory component of sandalwood oil is difficult to synthesise in an industrially viable manner. **Fill in the reagents and intermediate compounds in the synthesis of Javanol, a sandalwood oil substitute**

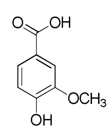


5) SAR studies – The influence of the shift of one methyl group in Nerol to constitutional isomer **6** was investigated to give unexpected results, not predicted by any existing olfactophore models[2]. The olfactory properties changed from Rosy to Muguet (lily of the valley)[2].
Fill in the blank reagents, products, give named reactions and account for selectivity using TS where necessary



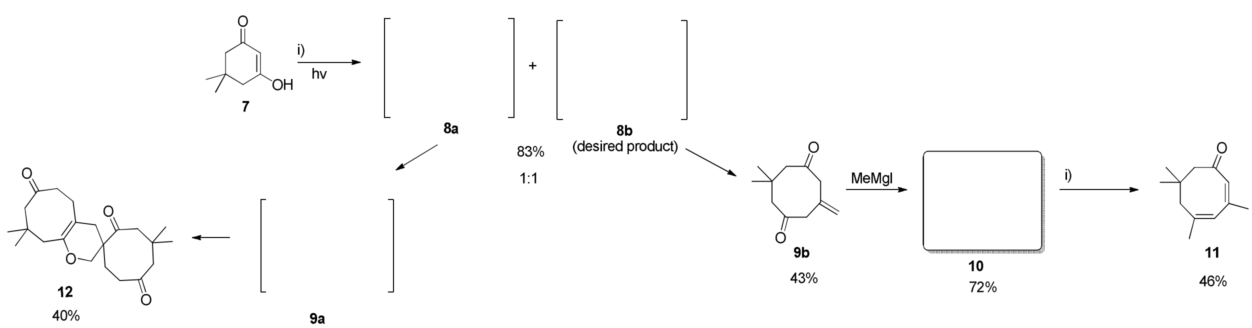
6) The demand for vanilla flavour has long surpassed its natural availability from vanilla pods. Synthetic vanillin is thus used extensively in the flavours industry. **Propose disconnections and forward syntheses of vanillin**

6b) Vanillin is synthesised industrially from a petrochemical raw material (structure to be given). **Propose a forward synthesis.**



Vanilin

7) Compound **11**, was found to be the major contributor to the rich ambery scent of odorant Kephalis even though only present in trace amounts. The synthetic route developed to **11** is outlined below. **Fill in the reagents and products and give mechanisms.**



(1) Kraft, P. *J. Chem. Educ.* **2010**, *87*, 598.
(2) Kraft, P.; Eichenberger, W.; Fráter, G. *Eur. J. Org. Chem* **1999**, *1999*, 2781.