SYNTHETIC APPROACH FOR THE SYNTHESIS OF SULCATOL

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DISSERTATION

DECLARATION

I hereby declare that the matter presented in this dissertation entitled, *''Synthetic Approach for the Synthesis of Sulcatol''* is based on the results of investigation carried out by me in the School of Chemical Sciences, Goa University under the supervision of Dr. Vinod Mandrekar and the same has not been submitted elsewhere for the award of a Degree or Diploma.

Ms. Apeksha Hiru Naik

CERTIFICATE

This is to certify that the dissertation titled *''Synthetic Approach for the Synthesis of Sulcatol''* is bonafide work carried out by Ms. Apeksha Hiru Naik under my supervision in partial fulfillment of the requirement for the award of the degree of Master of Science in chemistry at the School of Chemical Sciences, Goa University.

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ACKNOWLEDGEMENT

I wish to acknowledge many people with great honour for their cooperation and interest. I am extremely grateful to our project guide Dr. Vinod Mandrekar, assistant professor, School of Chemical Sciences, Goa University for his valuable guidance throughout the completion of my report and sharing his valuable knowledge. And also grateful to our Dean of School of Chemical Sciences Prof. Dr. Vidyadatta Verenkar for providing me this opportunity. Lastly I would like to thank the almighty and my parents for their constant support.

ABSTRACT

This report mainly consists of Literature Review on various research papers including research done on synthesis of sulcatol using various starting materials and employing different routes like the use of starting materials such as glutamic acid, deoxyribose, furanone, lactone, etc. The isolation of sulcatol and characterization involving the spectral data is depicted. The ten different synthesis of sulcatol using different routes are included in the project. The information is gathered from research papers from reputed journals. The retrosynthesis for the molecule is mentioned along with the proper formal synthesis of sulcatol.

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INTRODUCTION

Within the family of Scolytidae, Bark and ambrosia bettles are the two main groups which include most of the important forest insect pests. The bark bettles inflicts the majority of the economic impact which attributes to these insects. However, the losses caused by ambrosia bettles are smaller. These mainly attack the felled and/or weakened trees[1].

Sulcatol is the aggregation pheromone firstly isolated from the boring dust of Gnathotrichus sulcatus[2]. It is available as 65:35 ratio of its mixture of R-(-) and S-(+) enantiomers of 6-methyl-5-hepten-2-ol and thus generated interest in the chiral synthesis[3]. The first optically active sulcatol was synthesized from glutamic acid as the starting material. Glutamic acid is preferred as it is relatively inexpensive starting material, also both of its enantiomers are available commercially. Also, glutamic acid has a wide use in chiral pheromone synthesis and it is mostly known in the form of its monosodium salt[3].

The sulcatol was developed from the boring dust of 21000 adult males from which 0.5 mg of the pure pheromone was isolated[4]. The identification of sulcatol that is 6-methyl-5-hepten-2-ol was done from infrared spectroscopy, NMR and mass spectral studies[5]. The alcohol which was synthesized found to be attractive to the natural population. The artificially synthesized sulcatol is used in the pest control programs in various locations[6].

ISOLATION OF SULCATOL

The population aggregation pheromone were produced by the males of Gnathotricus sulcatus, a timber pest, was identified from boring dust as a 65:35 mixture of the (S)-(+) and (R)-(-) enantiomers of sulcatol.

During the experiment of isolation, it was monitored by laboratory bioassay with bettles of both sexes. Around 390 male G. sulcatus bettles were allowed to attack 540.75m long logs (total of about 21000 bettles) of western hemlock which was presoaked in 10% ethanol which was a primary attractant for this species. The boring dust which was falling from logs was stored at -50 ^{c}o in jar container and was later extracted with ethyl ether in Waring blender. The dried ether was concentrated to about 55ml of dark brown solution by distilling the ether through a short column packed with glass beads. The vials were filled with this concentrate was stored at -20 ^{o}C overnight and the precipitate was removed by centrifugation. Now the precipitated material was shaken with fresh ether and the cooling and centrifuging steps were repeated. The combined ether was then concentrated to 15 ml and the volatiles were removed by short path distillation.

Now the distillate was fractionated using the GLC columns. The column effluent was then condensed in 12 in. glass capillary tubes which were held in a thermal gradient collector. The NMR spectra were recorded using 100% deuterochloroform and trimethylsilane as a internal standard. Even the mass spectra was obtained by adding 23 microgram of the pheromone, collected from the gas chromatograph and later sealed in glass capillary tubes and introduced into the micro-inlet system.

The pheromone was synthesized by adding 6-methyl-5-hepten-2-one to sodium borohydride with methanol, water and potassium hydroxide solution. The solution was made acidic after around 0.5 hr using dilute HCl to hydrolyse borate ester. The product was then extracted, dried and distilled[7].

CHARACTERIZATION OF SULCATOL

The sulcatol which was synthesized was subjected to characterization by spectroscopy. The mass spectra showed the molecular ion peak at m/e 128 and a prominent M-18 peak which confirms the presence of OH group[8]. In IR spectra a broad peak around 3300 cm^{-1} was observed confirming the presence of OH group. The nuclear magnetic spectrum gave most of the information about the molecule. It gave the signals as δ5.24-4.97 (br, t, 1H); δ 3.95-3.60 (m,1H); δ 2.22-1.92 (m, 2H); δ 1,71 (br, s, 3H); δ1.64 (br, s, 3H); δ1.60-1.25 (m, 2H); δ1.20 (d, 3H). This information indicated that two methyl groups, a hydrogen atom, and a methylene group were attached to C=C group as mentioned: $(CH_3)_2C=CHCH_2$-. The proton multiplet at δ3.80 represents a methane proton alpha to a hydroxyl group. The doublet at δ1.20 is assigned to methyl group beta to a hydroxyl group. Thus the probable part structure is $–CHOHCH_3$. By connecting this two probable part structures with a methylene group gives the required structure of 6-methyl-5-hept-2-ol. The two hydrogen atoms of this methylene group and hydroxylic hydrogen atom account for δ1.60-1.25 chemical shift[7].

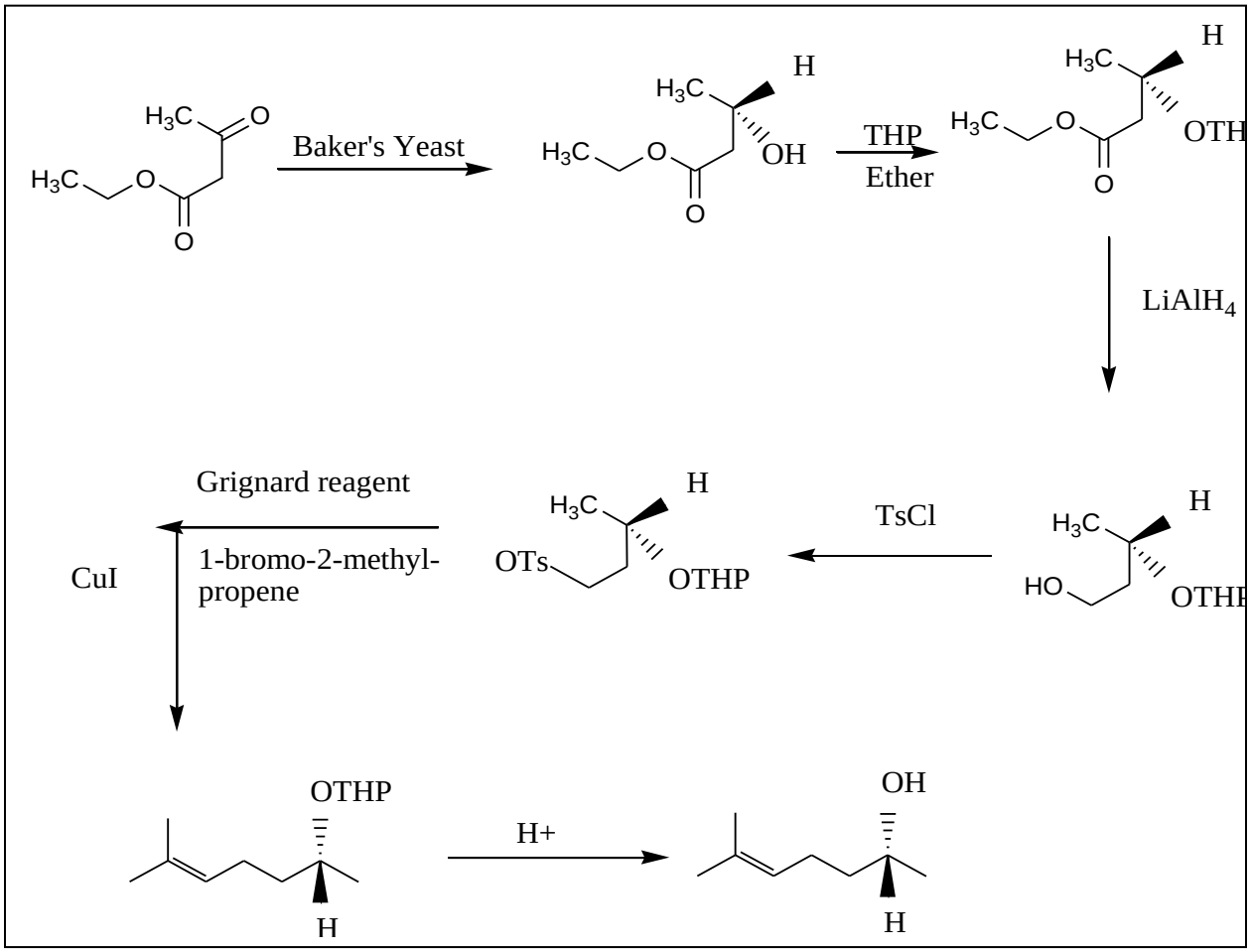
LITERATURE REVIEW

SYNTHESIS OF SULCATOL

[I]Synthesis of s-(+)-sulcatol by employing Baker's Yeast for Asymmetric Reduction

The more simple way to synthesize s-(+)-sulcatol was by asymmetric reduction 6-methyl-5-hepten-2-one. But this process is not favourable due its low optical yield in the case of aliphatic ketones with no unsaturation at the alpha carbon. However, the yield is increased with microbial reduction of ketones catalyzed by the yeast. Thus the process was carried out using Baker's yeast. But in this particular situation the substrate remained unchanged with fermentation. Therefore, the substrate more easily reducible by yeast was chosen[9].

Scheme 1: Synthesis of s-(+)-sulcatol by employing Baker's Yeast for Asymmetric Reduction



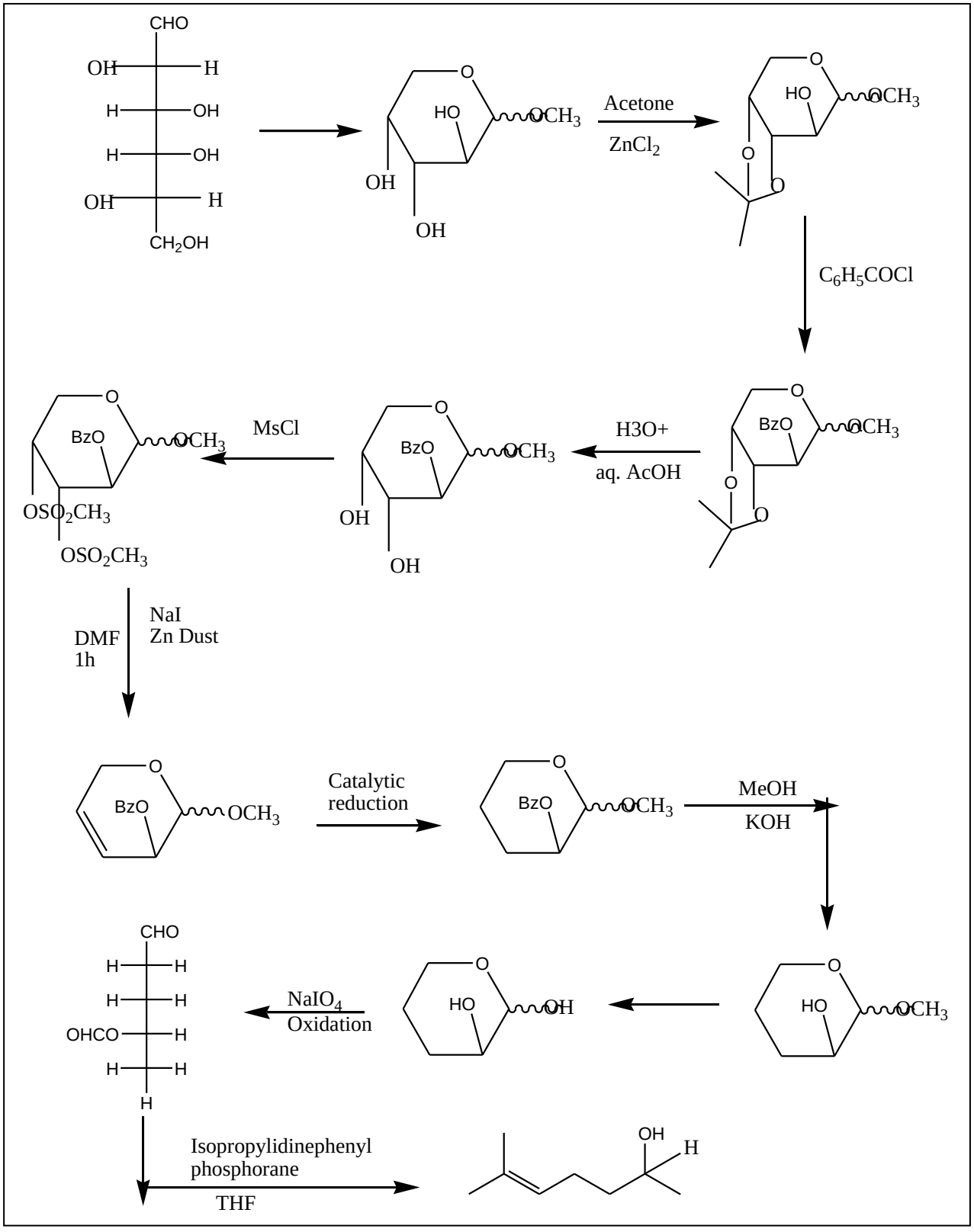
The keto group of starting material, Ethylacetoacetate is reduced to an alcohol. To obtain chemical selectivity the OH group is protected as THP ether. Now the ester part is reduced to primary alcohol using strong reducing agent such as $LiAlH_4$. This is then reacted with TsCl to give tosylate group. The corresponding tosylate was treated with Grignard reagent prepared from 1-Bromo-2-methylpropene in presence of CuI to give the corresponding coupling product. Later the THP protecting group was removed by acid hydrolysis thus yielding the desired product in 73% yield as mentioned in Scheme 1. The optical purity determined by the gas chromatography was 96% pure sulcatol[10].

[II] Synthesis of Enantiomers of Sulcatol

The synthesis of enantiomers of sulcatol that is R-(-) and S-(-) 6-methylhept-5-en-2-ol (sulcatol) was reported from commercially available carbohydrate precursors. The four hydroxyl function of 2-Deoxy-D-ribose was utilized for the synthesis of R-(-) enantiomer as a precursor of the chiral secondary alcohol centre. For the synthesis of S-(+) enantiomer the five hydroxyl group of L-fucose was used. To test the aggregation response of Gnathotricus Sulcatus, these isomers were used[11].

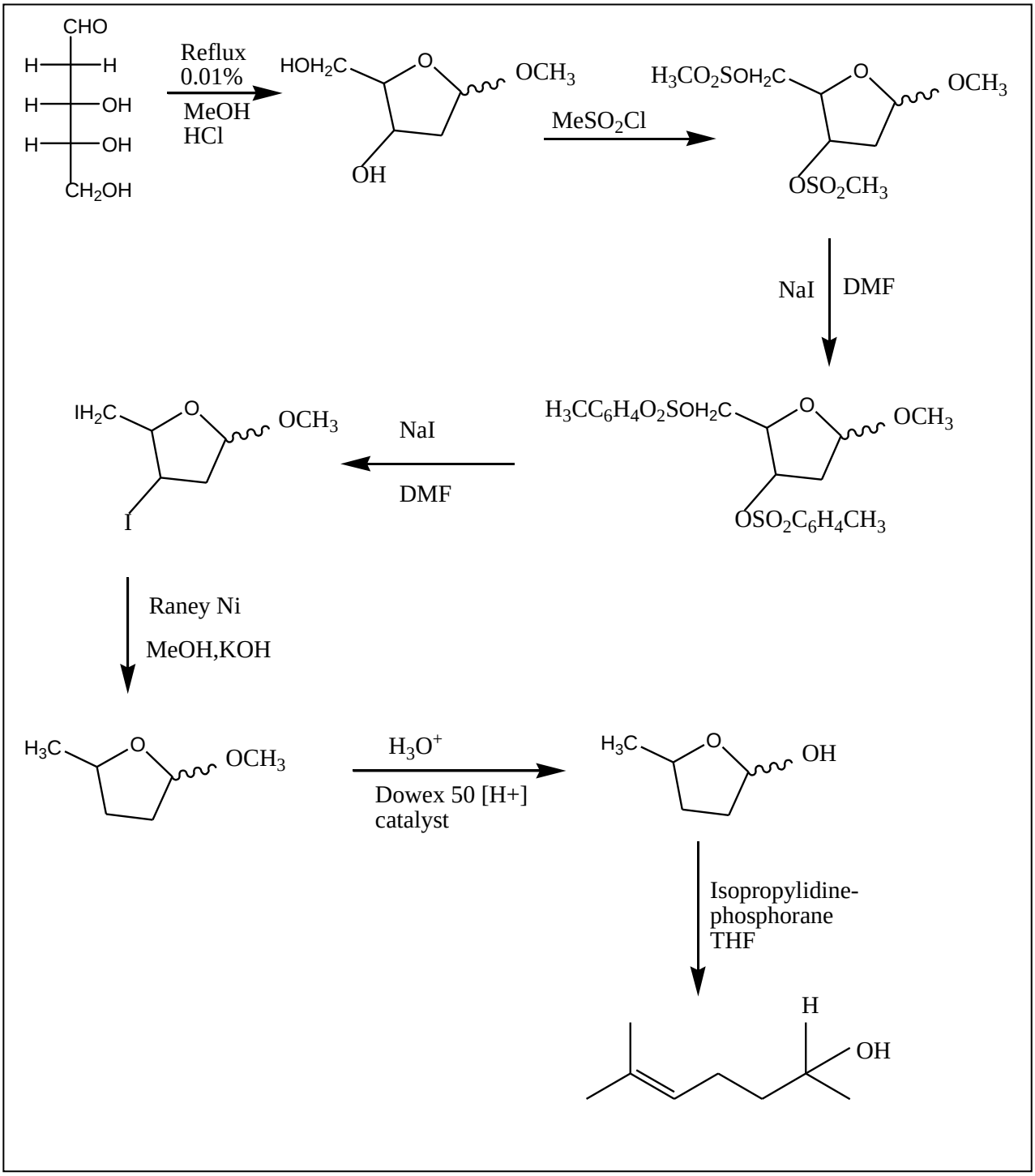
The synthesis of two pure enantiomer of sulcatol was carried out by two different routes starting from commercially available sugar precursors such as L-fucose and 2-Deoxy-D-ribose. The basic or slightly acidic reaction conditions were maintained[12].

Scheme 2: Synthesis of s- (-)-sulcatol using carbohydrate precursor



The synthesis of (R)- sulcatol can be carried out using similar sequence of reactions starting with D-fucose. However, due to the unavailability of its L-enantiomer made to search for another starting material followed by alternative synthetic route. Thus deoxy-D-ribose was selected based upon its availability and synthetic potential. The configuration at the carbon which was supposed to become the chiral centre in (R)- sulcatol was to be retained, as done in the case of (S)- sulcatol as mentioned in scheme 2. The formation and maintainance of a glycoside ring throughout the synthesis helped in retaining the configuration. The 2-deocy-D-ribose was refluxed with 0.01% methanolic hydrogen chloride to obtain the methyl- α,β-furanoside. There was no necessity to separate the anomeric mixture obtained. Thus further reaction was carried out with an excess of methylsulfonyl chloride to yield syrupy dimesylate. This was further treated with sodium iodide in dimethylformamide at 70^{o}C resulting in the effective displacement of primary methylsulfonyloxy group at C-5 within 5 Hr. The substitution of the secondary sulfonyloxy function at C-3 was very slow and the reaction was unable to get completed even after five days at that particular temperature. It was necessary to isolate the diiodide from the reaction mixture due to many side reactions being taking place and the unreacted 5-deoxy-5-iodo-3- mesylate was further reacted with NaI. The diiodide was obtained in 51% yield. The hydrogenolysis of diiodide was carried out using Raney nickel (W-7) catalyst in methanolic potassium hydroxide to obtain the volatile methyl 2,3,5-trideoxy- α,β -D-glycero-pentofuranoside. With the hydrolysis in the presence of a cation exchange resin catalyst, Dowex 50[H+], the reaction was carried further. It was found to be very difficult to isolate the hydrolysis product as this hemiacetal was found to be soluble in various organic solvents as well as in water and found to be unstable. The crude hemiacetal which was isolated in 52% yield, was used for the further step without carrying out any purification. Reaction with isopropylidenephosphorane in THF as a solvent produced the (R)-sulcatol as mentioned in scheme 3which was underwent purification by column chromatography and distillation. The yield of laevorotatory (R)-sulcatol was 30% in this Wittig reaction and 5% overall from 2-deoxy-D-ribose. The purity of sulcatol products was determined and found to be greater than 99% for both the (R)- and the (S)-isomers.

Scheme 3: Synthesis of R- (+)-sulcatol using carbohydrate precursor



[III] Synthesis of sulcatol using Glutamic acid as the starting material.

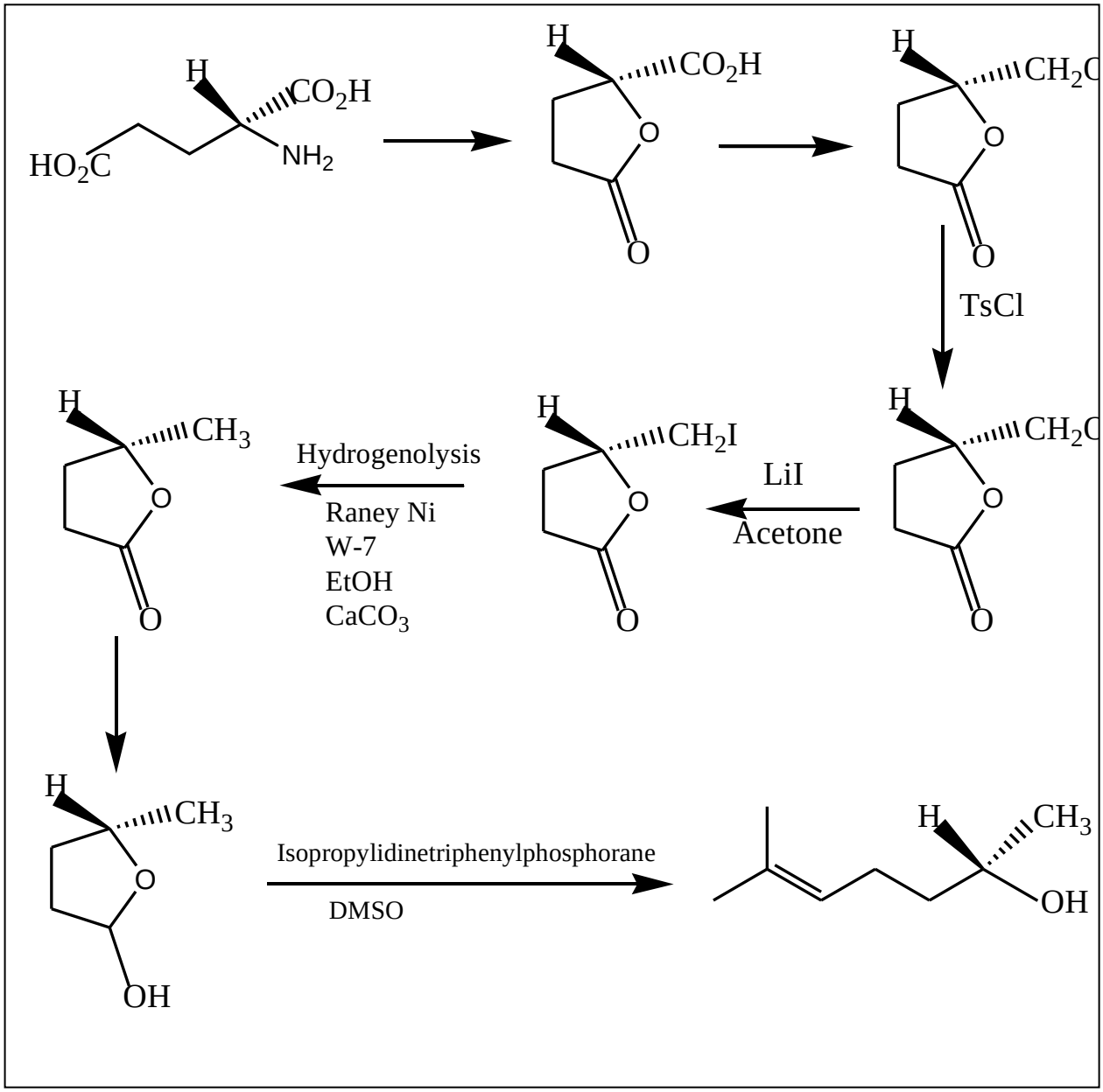
In this the synthesis of both (R)- and (S)-forms of optically pure sulcatol is carried out. This enabled us to know the sign of the optical rotation of each enantiomer and to do comparative study of the biological activity of enantiomers.

The synthesis of optically active sulcatol can be carried out in two ways. Firstly by the conventional resolution of (+/-)-sulcatol. The second way is to use an optically active compound of absolute configuration as the starting material. The latter method preferable to synthesize sulcatol with known absolute stereochemistry. Optically active propylene oxide was chosen as a good starting material in combination with an isoprenyl synthon. However, completely optically pure propylene oxide was not easily accessible due to oily nature of propylene oxide and its intermediated it was difficult to purify. Therefore, readily available (R)-(-)- and (S)-(+)-glutamic acid as starting materials were employed and converted them to (S)- (+)- and (R)-(-)-sulcatol[13].

(R)-(-)-γ-Hydroxymethyl-γ-butyrolactone was synthesized from (R)-(-)-glutamic acid as mentioned the with the formation of crystalline lactonic acid as a intermediate. Tosylation of the hydroxy lactone yielded a crystalline tosylate. This was repeatedly recrystallized to ensure the highest optical purity. The pure crystalline tosylate was heated with LiI in presence of acetone to give an iodide. The reaction of hydrogenolysis of iodide with Raney nickel W-7 in EtOH in the presence of $CaCO_3$, and after chromatographic purification and distillation, yielded (S)- (-)-γ-methylbutyrolactone. Both (R)- and (S)-enantiomers of this lactone was recorded in literature. The lactone synthesized is optically pure, as optically pure sulcatol were further prepared from this lactone. The lactone was reduced with i-Bu_2AlH to give a lactol. This was treated with isopropylidene triphenyl phosphorane in DMSO to give (S)-(+)-sulcatol mentioned in scheme 4, which was dextrorotatory[14].

The same sequence of reaction were carried out starting with (S)-(+)-glutamic acid to prepare (R)-(-)-sulcatol.

Scheme 4: synthesis of (S)-(+)- sulcatol using Glutamic acid

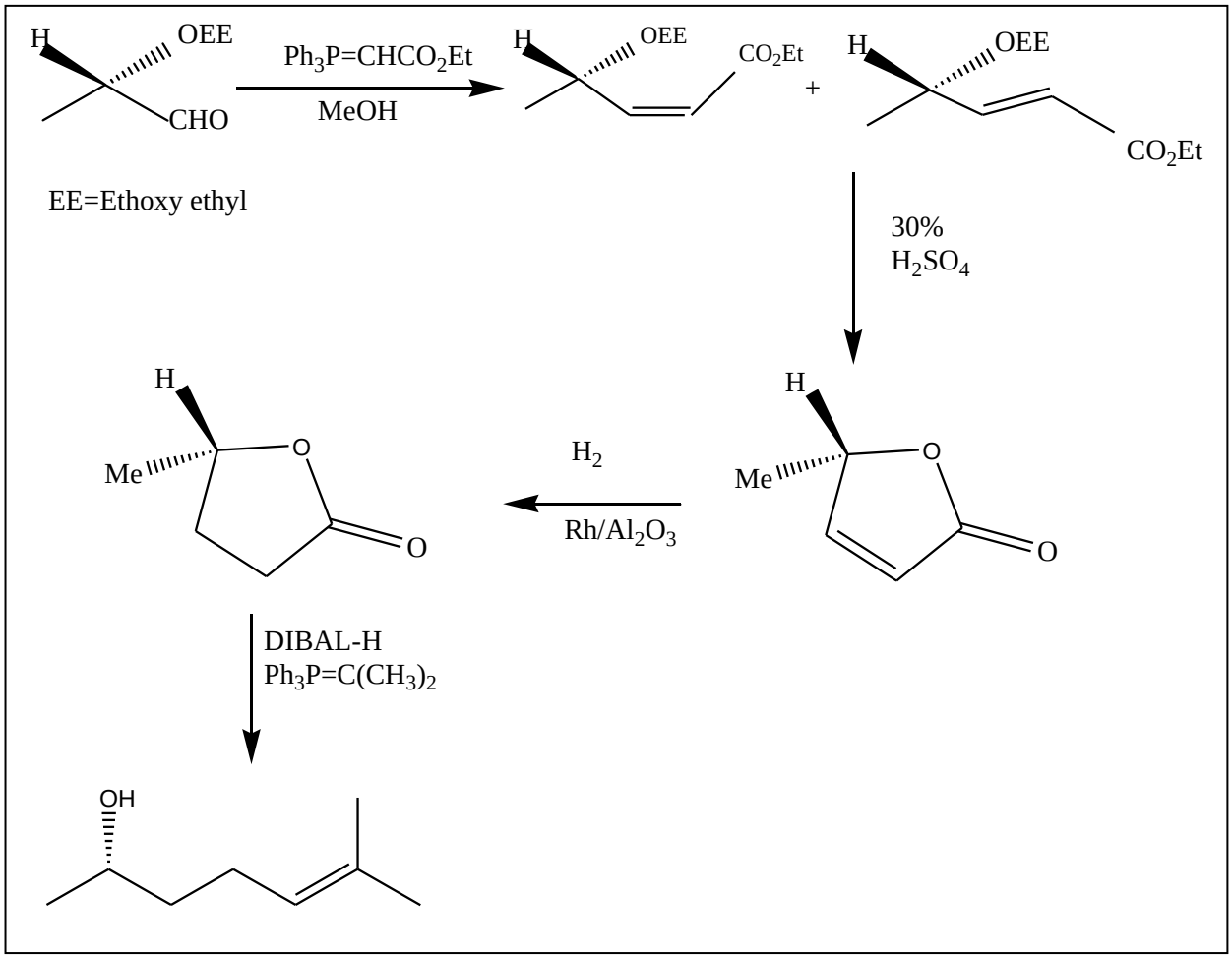


[IV] Synthesis of (S)-(+)- sulcatol through convenient synthesis of (+)-5(S)-Methyl-2(5H)-Furanone

(+)-5-Methyl-2(5H)-furanone is known to be an important synthon for the synthesis of substituted γ-valerolactonic natural products by regio- and stereocontrolled functionalization at the C_2, and C_3 carbon atoms of the γ-lactone moiety. Using diethyl L(+)-tartarate, Lactone(+) was prepared in nine steps and from unnatural (R)-(-)-glutamic acid in nine steps.

Due to the chiral synthesis of natural products, amount of (+)-1 was required in large amounts, therefore a short and convenient route was selected to synthesize (+)-1 of very high optical purity and thus started with the readily available ethyl-(S)-(-)-Lactate in only five steps[15].

Scheme 5: Synthesis of (S)-(+)- sulcatol through synthesis of (+)-5(S)-Methyl-2(5H)-Furanone



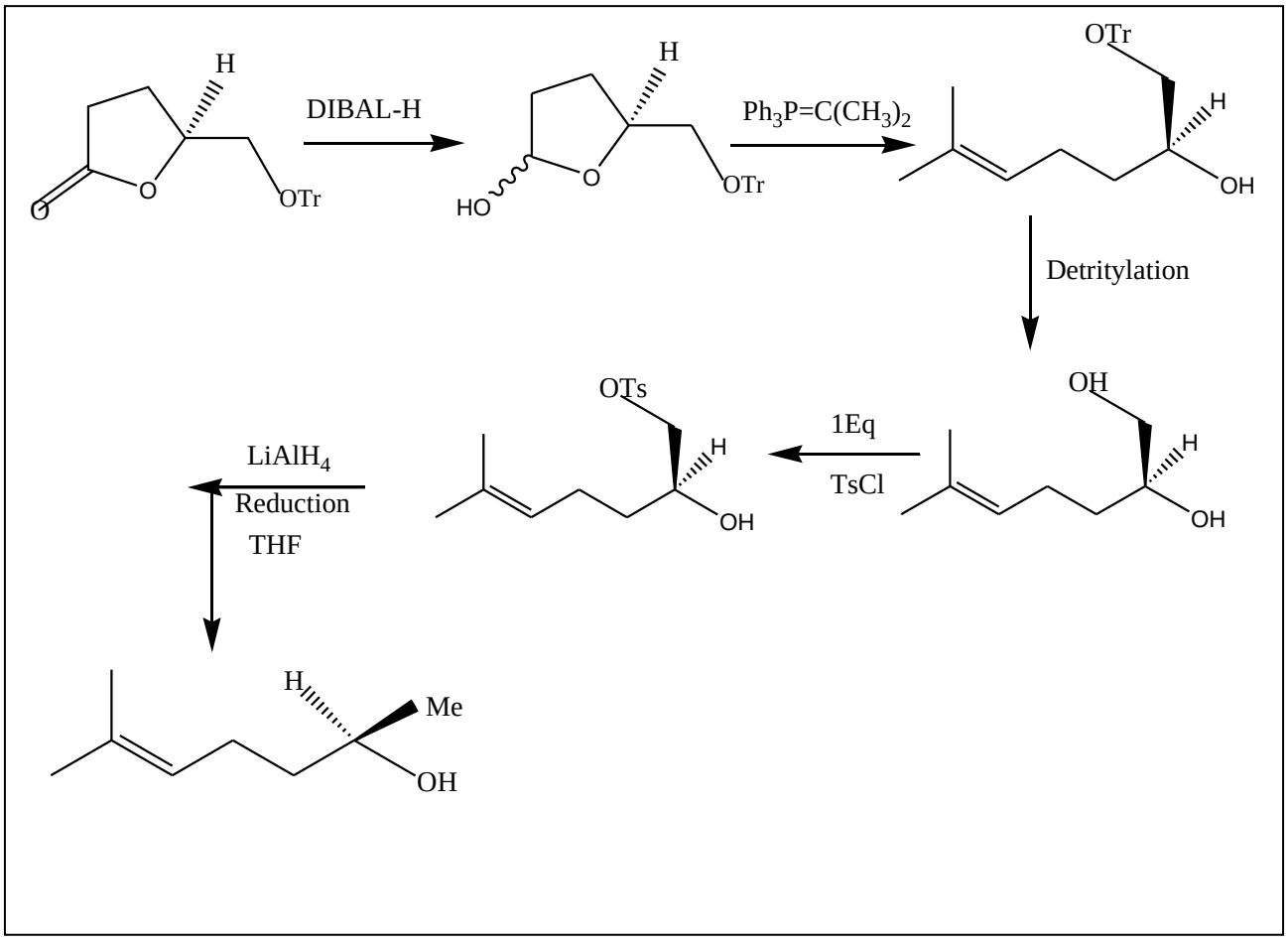
Aldehyde formed was prepared in three steps usig ethyl (S)-(-)-lactate with the overall yield of 69%. The stereoselective Wittig olefination of the respective aldehyde with (ethoxy-carbonylmethelene)triphenylphosphorane in methanol resulted in a mixture of the (E)- and (Z)-pentenoates with a ratio of about 82:18 after column chromatography. The reaction of (Z)-pentenoate with a catalytic amount of sulfuric acid (30%) in methanol at a room temperature for a duration of 0.5 hour to yield (+)-5(S)-methyl-2(5H)-furanone. The overall yield of (+)-1 from ethyl-(S)-Lactate was 47%.

Using the lactone (+)-1 as a chiral synthon, enantio-specific synthesis of (S)-(+)-6-methyl-5-hepten-l-o1 [(S)-(+)-sulcatol] was carried out, which is the aggregation pheromone of Gnathotrichus retus and is sensitive to the S enantiomer of sulcatol, and its response seems to be inhibited by the R enantiomer. The catalytic hydrogenation of the unsaturated lactone (+)-1 with rhodium on alumina furnished (S)-(-)-γ-butyrolactone in 98% yield. On the other hand catalytic hydrogenation of (+)-1 with Pd/C or PtO_2 did not give high optical purity of (S)-(-)-γ-butyrolactone. The reduction of the lactone (+)-4 with i-Bu_2AlH, which was later followed by Wittig reaction with isopropylidenetriphenylphosphorane in THF to provide (S)-(+)-sulcatol as the target molecule.

[V] A simple enantioselective synthesis of both enantiomers of sulcatol using a single chiral precursors

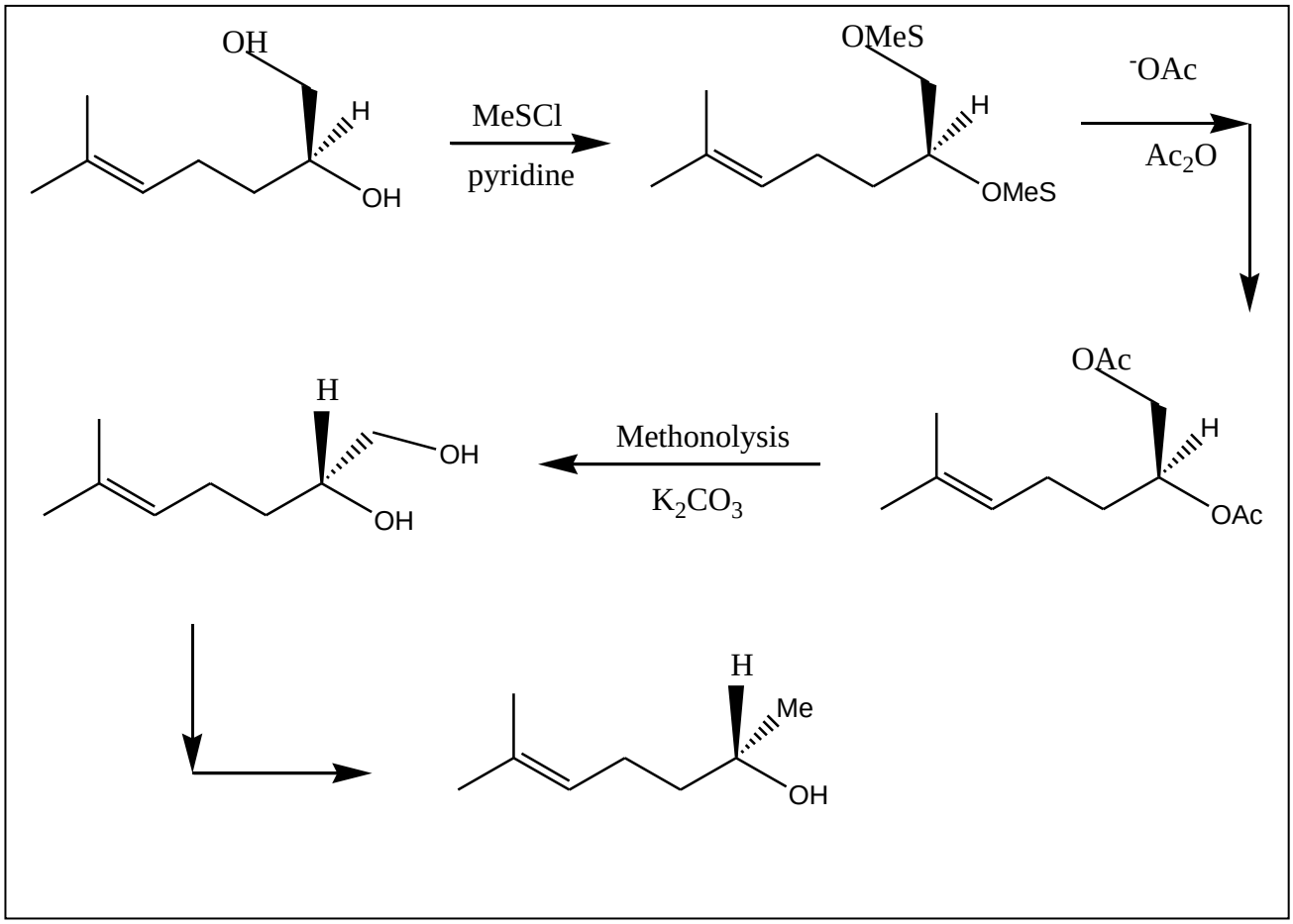
The reduction of chiral lactone easily available from L-Glutamic acid or D-mannitol using DIBAL resulted to give the lactol, which was later converted to olefin by Wittig reaction. For this resultant molecule Detritylation reaction was carried out which afforded the (S)-1,2-glycol, with the overall yield of 58%. The (S)-1,2-glycol was treated with one equivalent of p-toluenesulfonyl chloride in the presence of pyridine to give the mono-tosylate which on further reduction with LAH in THF gave (R)-(-)-Sulcatol mentioned in scheme 6 with the overall yield of 49%[16].

Scheme 6: Synthesis of (R)-(-)-Sulcatol using single chiral precursor.



On the other hand, (S)-1,2-glycol was treated with methanesulfonyl chloride in the presence of pyridine to give the dimesylate. On reflux with potassium acetate in acetic anhydride, the dimesylate was converted into the diacetate along with complete inversion at the chiral center apparently via the intermolecular substitution at the primary center by acetate, followed by intramolecular substitution of the secondary center by the introduced neighbouring acetoxy group. The reaction of methonolysis was carried out in presence of potassium carbonate to give the enantiomeric (R)- glycol with the overall yield of 74% from its (S)-counterpart as depicted in scheme 7. The conversion of (R)-Glycol into (S)-(+)-Sulcatol is carried out like for its enantiomer in a comparable yield.

Scheme 7: Synthesis of (S)-(+)-Sulcatol using single chiral precursor

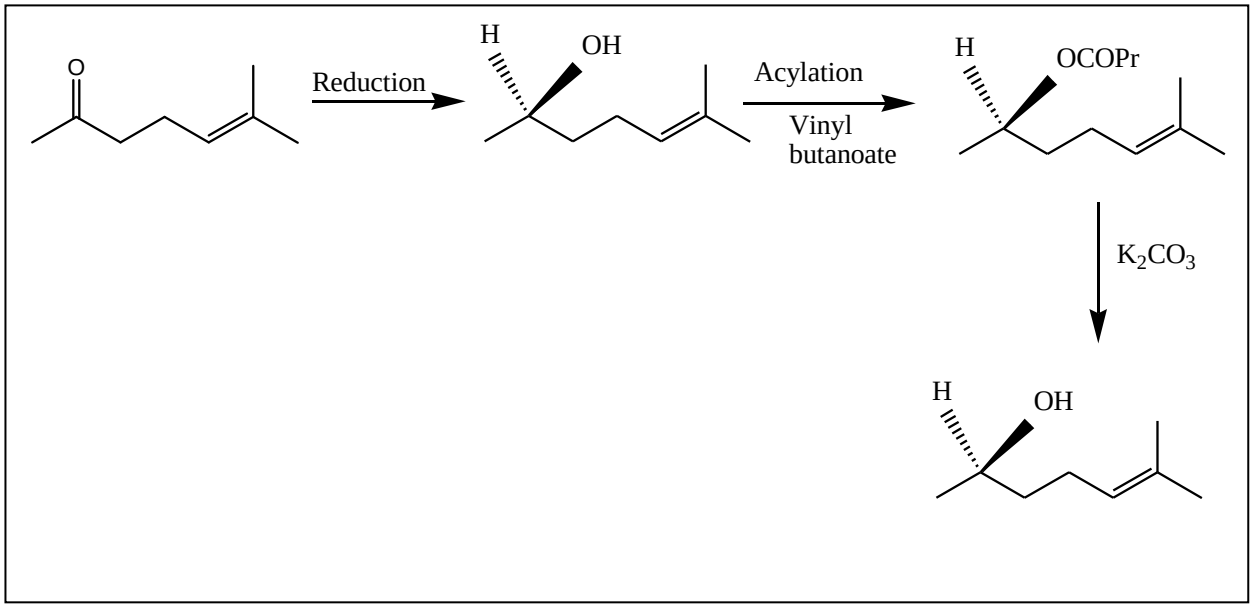


[VI] Biochemical preparation of (R)-Sulcatol

For this process, the particular ketone was added directly to a culture broth, since the reaction was slow, the cells were isolated after cultivation and suspended again in the glucose solution. The substrate was then being added under anaerobic conditions by maintaining the pH at 6.5. The reduction of ketone was very fast due to usage of large amount of microorganisms. When the concentration of substrate was increased to 0.3-0.4%, the reduction process became slower, thus the substarte was occasionally added to the reaction medium to maintain the concentration between 0.1-0.2%. However when the concentration reached 0.3-0.4%, the reduction became slower in spite of further addition of glucose and prolonged reaction time. Thus both the substrate and product seemed to be toxic to the microorganisms.

The mutigram scale preparation of (R)-1a was achieved, and the enantiomeric excess was further increased via enzymatic method. The preferential acylation of (R)-1a already obtained with vinyl butanoate in the presence of pig pancreatic lipase and treatment with potassium carbonate yielded (R)-1a with an optical purity of over 98%. The yield of this acylation of (R)-1a was higher than that of the analogous acylation of the racemate. Thus, (R)-Sulcatol was efficiently obtained in a large scale by the combination of microbial reduction and enzymatic acylation[17] as mentioned in scheme 8.

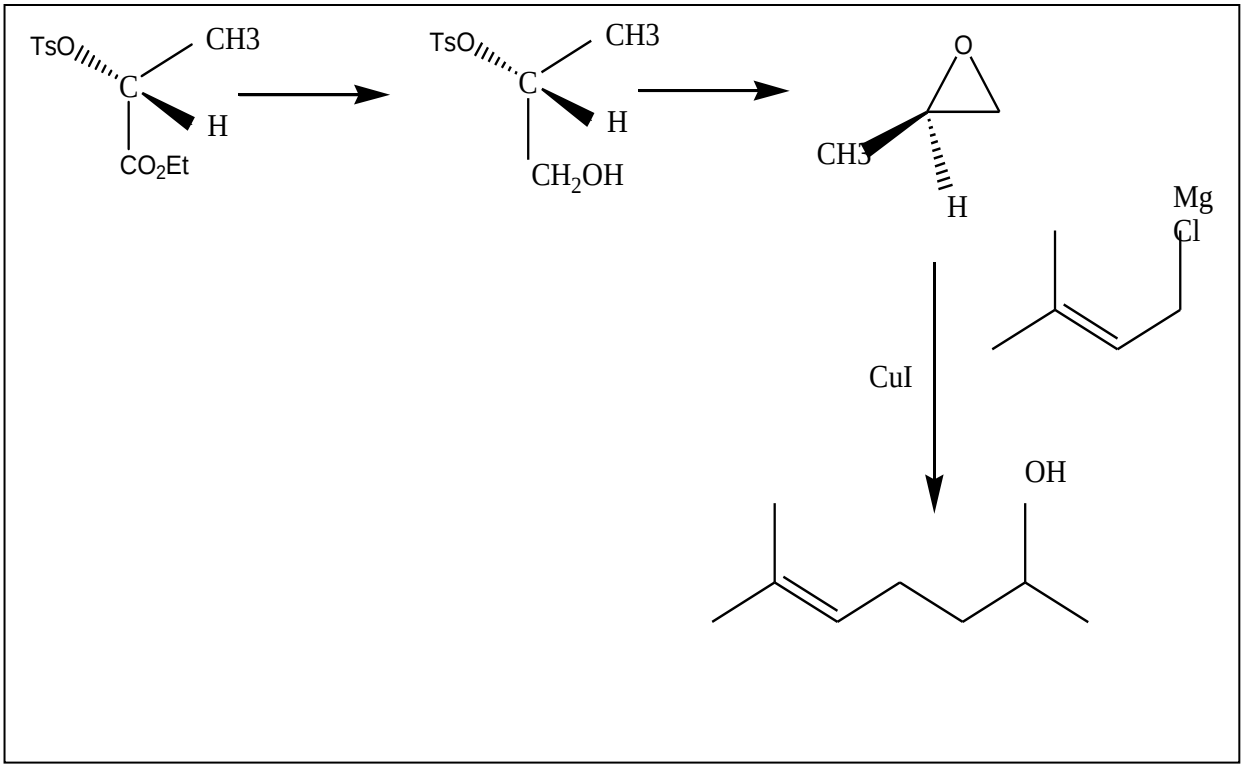
Scheme 8: Biochemical preparation of (R)-Sulcatol



[VII] Facile Synthesis of enantiomers of Sulcatol

The chiral pool strategy was considered as a convenient source of S-(-)-methyloxirane from commercially available ethyl S-(-)-lactate. The chiral purity is enhanced by low melting crystalline intermediated but the crystallization becomes difficult. The fermentation method resulted in the formation of methyloxirane with good results although no crystalline intermediated provided the necessary insurance of optical activity. The diborane reduction of carboxylate ester is very readily occurred. The stereoselective opening of methyloxiranes is established. Thus regioselective alkylation of allylic Grignard reagent has been achieved using copper(I) iodide catalysis. This resulted in the formation of enantiomers of sulcatol[18].

Scheme 9: Synthesis of sulcatol using ethyl S-(-)-lactate



[VIII] A Useful method for preparing optically active secondary alcohols: A short enantiospecific synthesis of (R) and (S)- Sulcatol

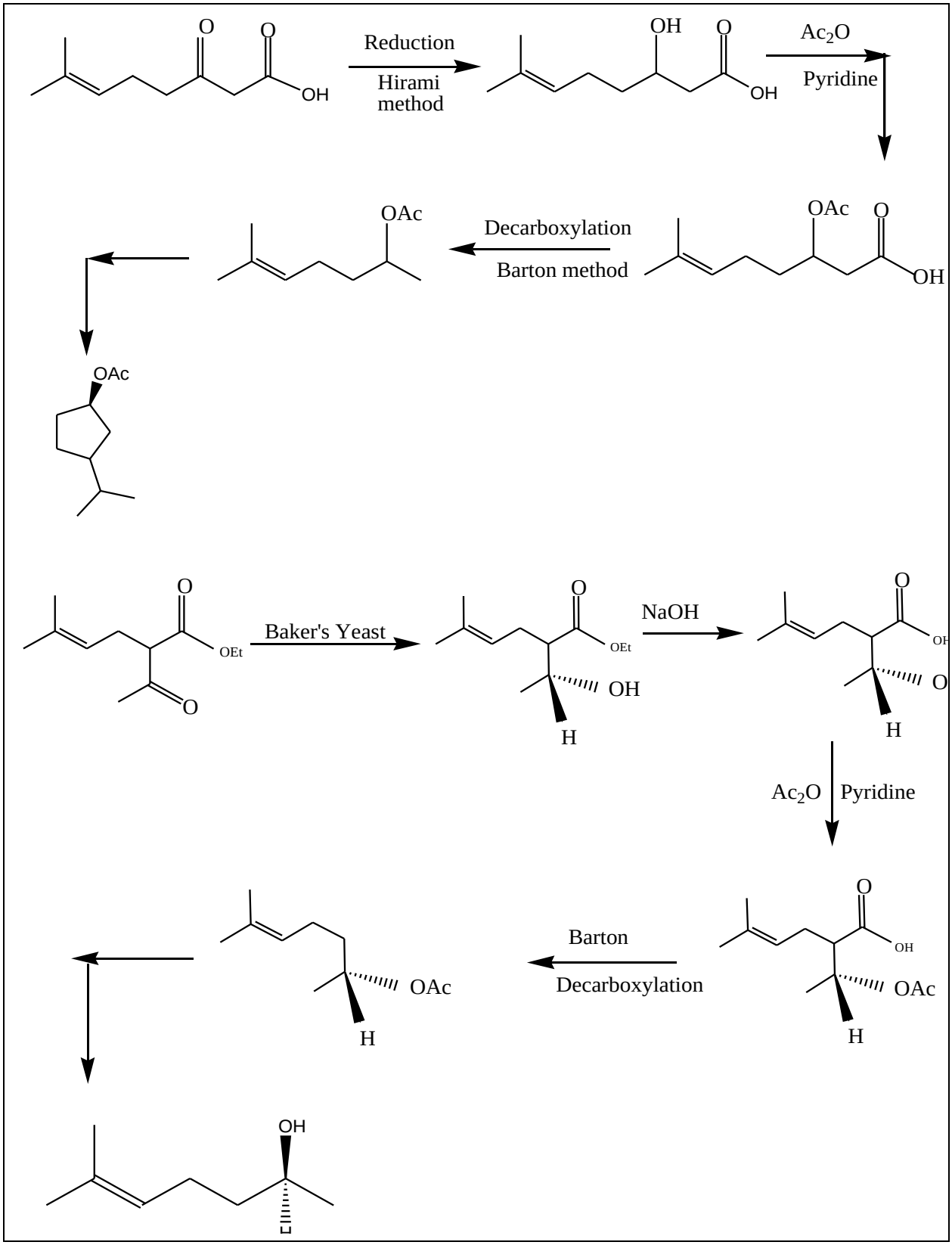
The epimeric 2-(1-Hydroxyethyl)-5-methyl-4-hexenoic acids were prepared from Baker's yeast reduction of the corresponding oxo compound or by alkylation of an optically pure 3-hydroxybutanoate.

Radical chain decarboxylation afforded the antipodes of sulcatol. The method is probably widely applicable to the synthesis of other optically pure alcohols.

For this process, the 3-oxoacids were prepared and reduction was carried out to obtain the hydroxyacids as per the Hirami method. Later the acylation reaction for hydroxyacids in presence of acetic anhydride and sodium bicarbonate yielded the acetate compound with the yield of 84%. The Barton method did not guve the required acetate but led to the formation of a volatile saturated compound which was a cyclic structure.

The Baker's yeast reduction of the 2-acetylhexenoate gave the starting ketone and the respective alcohol with >97% stereochemical integrity at the new carbinol center, as a mixture of diastereomers. On the further hydrolysis of the acid formed with NaOH and followed by acetylation reaction in presence of acetic anhydride and pyridine to give the respective substituted acid. This was again subjected to Barton's decarboxylation conditions. This conditions led to the formation of acetate which can be further hydrolysed with NaOH to produce (S)-Sulcatol with a yield of 90% in an optically pure state[19] as given in scheme 10.

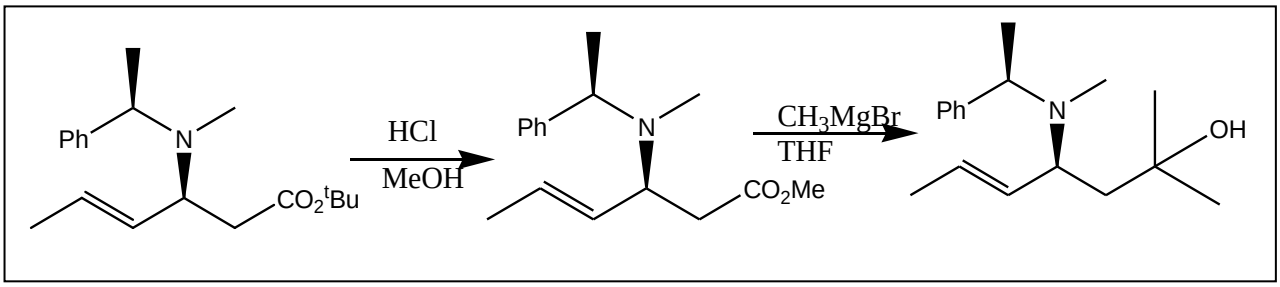
Scheme 10: Synthesis of (S)-Sulcatol using 2-(1-Hydroxyethyl)-5-methyl-4-hexenoic acid



[IX] Asymmetric synthesis of (R)-Sulcatol by employing tandem asymmetric conjugate addition and stereospecific Meisenheimer rearrangement protocol

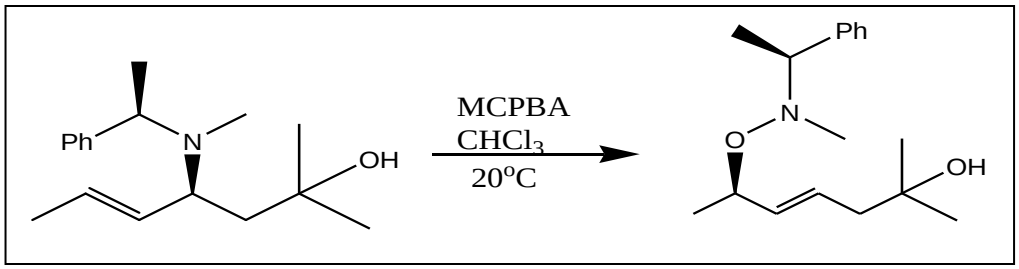
The asymmetric synthesis of insect pheromone sulcatol is based on the protocol of tandem asymmetric synthesis and Meisenheimer rearrangement. On the ester starting material the dimethyl group can be introduced via Grignard reagent as shown in scheme 11. It is then followed with dehydration to get a double bond. Due to the resistance of butyl ester with the methyl magnesium bromide, it was transesterified to the methyl ester, which then later reacted under desired reaction to give tertiary alcohol[20].

Scheme 11: introduction of dimethyl group via Grignard reaction

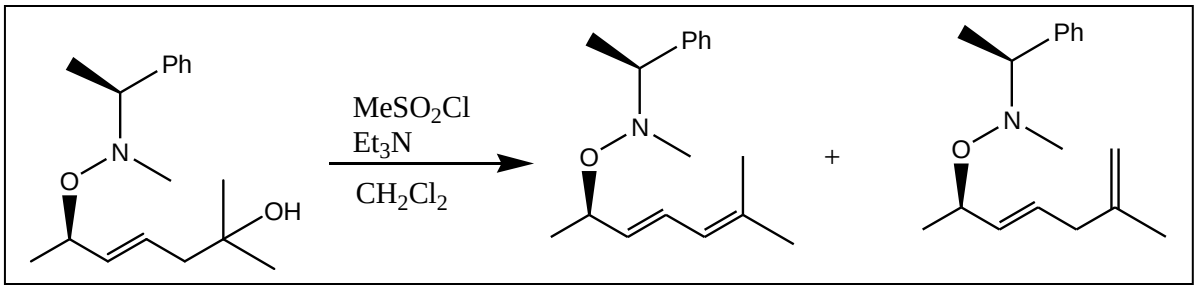


The oxidation of resultant tertiary alcohol with concomitant Meisenheimer rearrangement provided the resultant molecule as shown in scheme 12. To avoid formation of byproducts with the oxidation of the rearranged product, the reaction was carried with slightly with one equivalent of oxidant. The rearranged tertiary alcohol was dehydrated using methanesulfonyl chloride and triethylamine, but it gave low selectivity and resulted in two regioisomers in the ratio of 2:1. The two regiosiomers formed shown in scheme 13 could be separated using chromatography on silica gel doped with silver nitrate.

Scheme 12: oxidation of tertiary alcohol using MCPBA

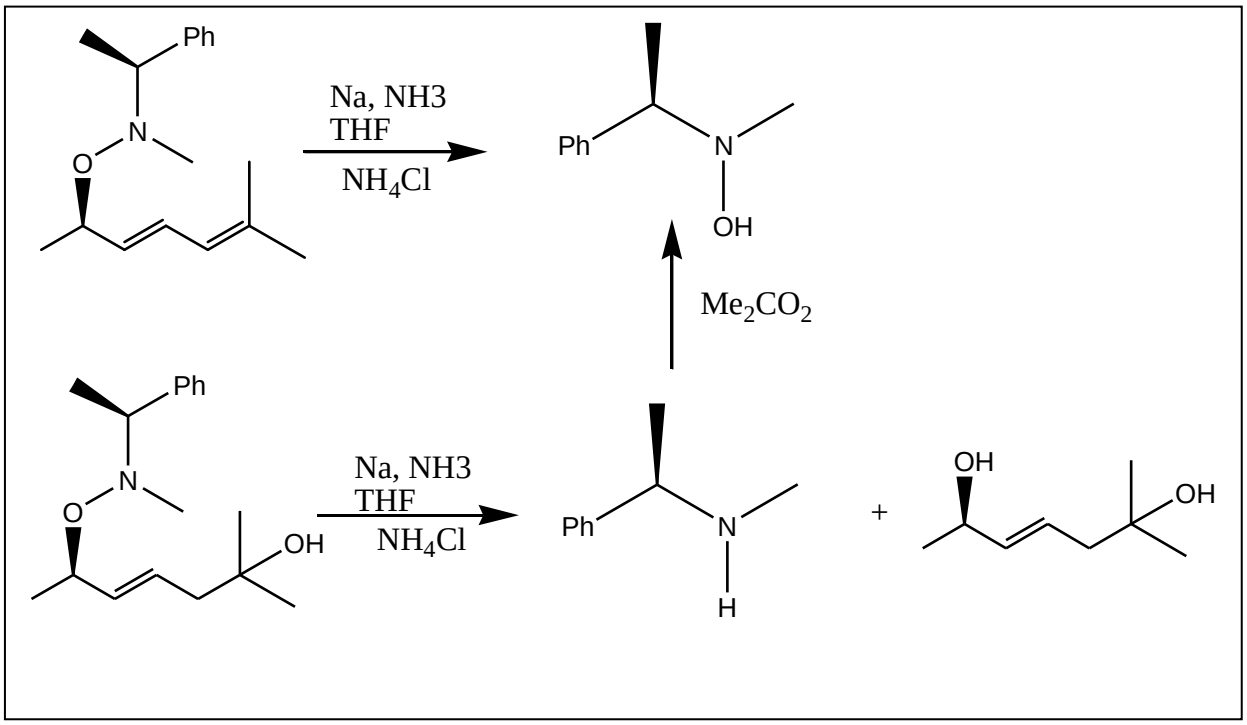


Scheme 13: Formation of two regioisomers



When the higher yield isomer was treated for N-O bond cleavage conditions no required products were formed as mentioned in scheme 14. Instead a hydroxylamine was formed indicating that O-allyl cleavage was taking place.

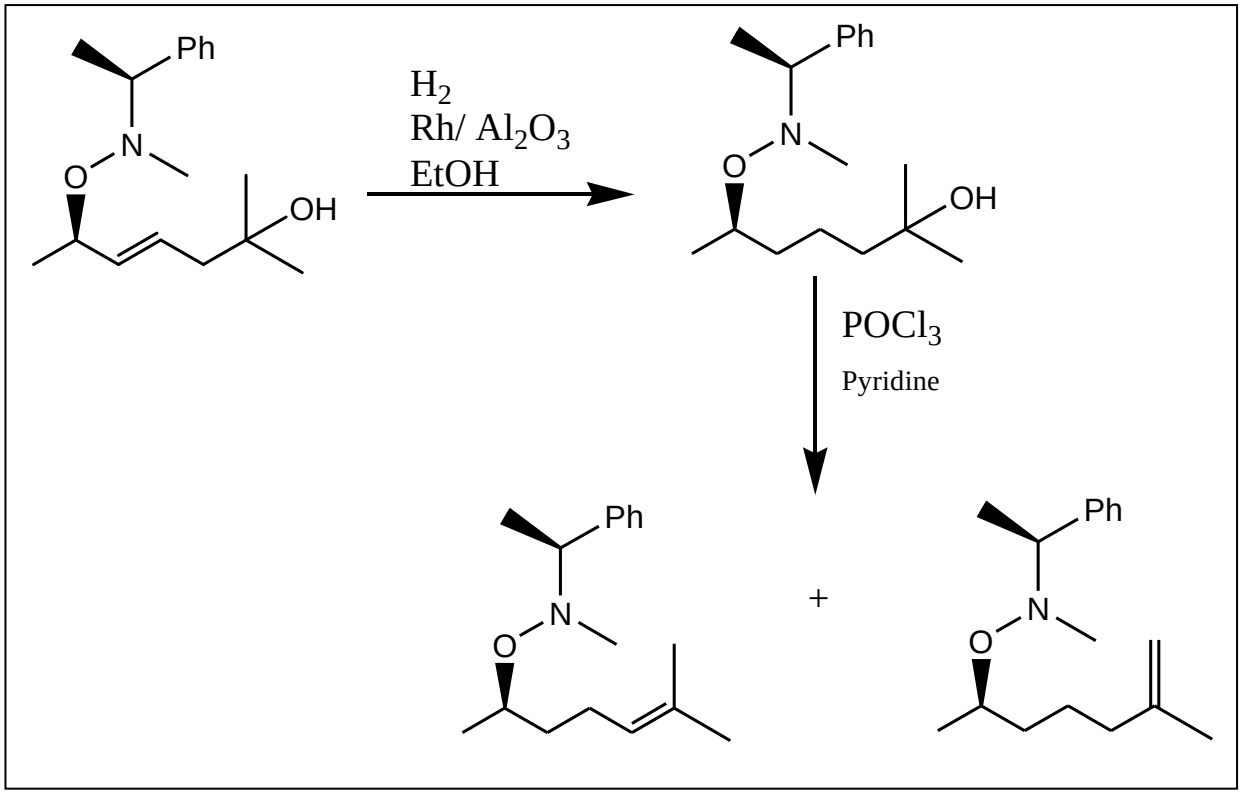
Scheme 14: N-O bond cleavage to form hydroxylamine



Due to the lower selectivity in the dehydration of rearranged alcohol and the drawbacks observed in cleaving the N-O bond, a different route was chosen wherein first the hydrogenation of unwanted double bond took place followed with dehydration step. Therefore it was reacted with catalytic hydrogenation on a rhodium/ alumina catalyst to obtain the reduced product. The

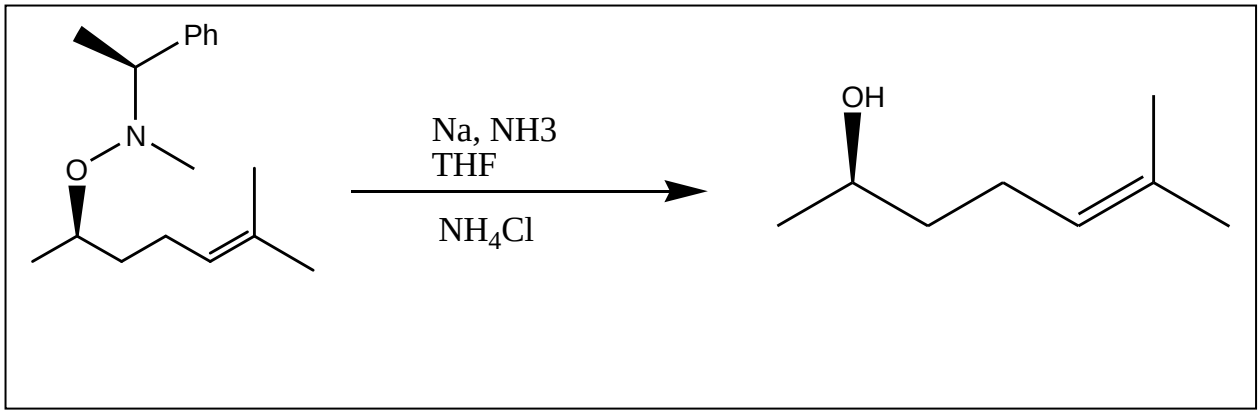
reaction with phosphorus oxychloride in presence of pyridine gave the two regioisomers in the ratio of 2:1 as shown in scheme 15. The isomers were separated using column chromatography

Scheme 15: Reduction followed by reaction with phosphorus oxychloride



The major regioisomer was treated to N-O bond cleavage with sodium in liquid ammonia. This reaction before proceeding to completion yielded the (R)-Sulcatol in comparatively good yield.

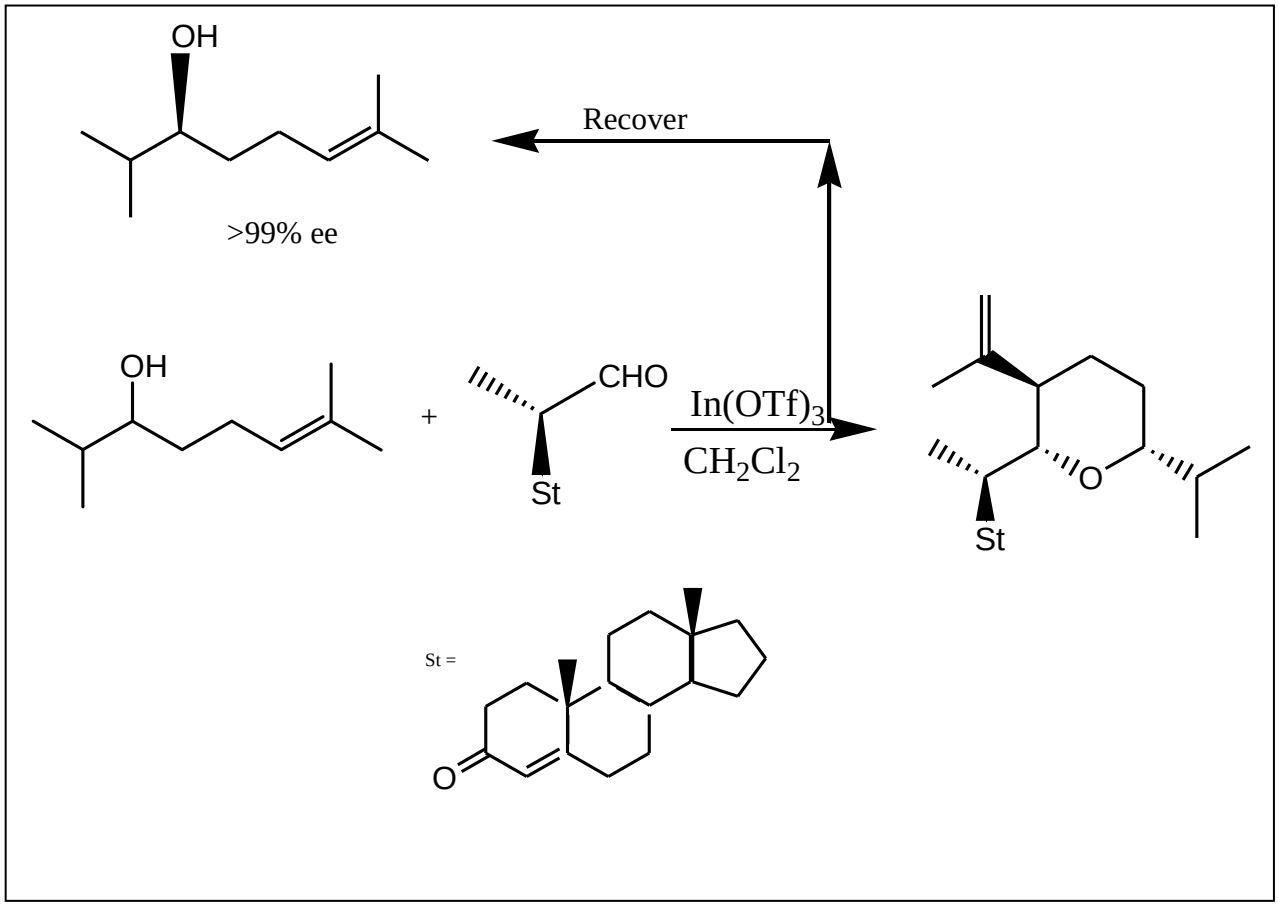
Scheme 16: Synthesis of (R)-Sulcatol



[X] Synthesis of (R) – Sulcatol via highly efficient chemical kinetic resolution of Bishomoallylic alcohols

For the organic synthesis, the optically active allylic, homoallylic and bishomoallylic alcohols are considered to be valuable intermediates. The enantiomerically enriched compounds are obtained through the transformation of their alkenyl functionality. These alcohols are obtained by asymmetric reduction or by carbonyl addition. For bishomoallylic alcohols, enantioselective methods are rare due to not much difference seen between the two substituents of ketone in an asymmetric reduction and much less accessibility of nucleophiles to carbonyl addition. Here, the method of highly efficient chemical kinetic resolution of bishomoallylic alcohols is based upon 1,4-stereocontrolband thus synthesis of (R)-Sulcatol[21] as written in scheme 17.

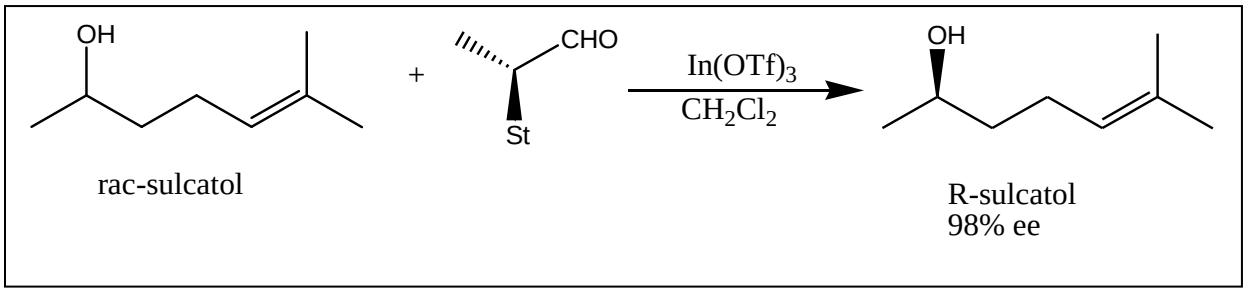
Scheme 17: kinetic resolution of Bishomoallylic alcohol



It was reported that bishomoallylic alcohols and aldehydes undergo facile (3,5)-oxonium ene-type cyclization in presence of catalytic amount of $In(OTf)_3$. In this experiment the solution of bishomoallylic alcohols and steroidal aldehyde was mixed with dichloromethane in presence of catalytic amount of $In(OTf)_3$ at room temperature. After 3-4 hours, TLC analysis indicated that half of the substrates were consumed. There was significant progress with the reaction even with increase in reaction time to 16 hours. The one cyclization product was observed with TLC and H1 NMR, thus indicated that a kinetic resolution of racemate alcohol. This recovered alcohol was found to have an enantiomeric purity of >99% ee which was indentified with chromatography purification.

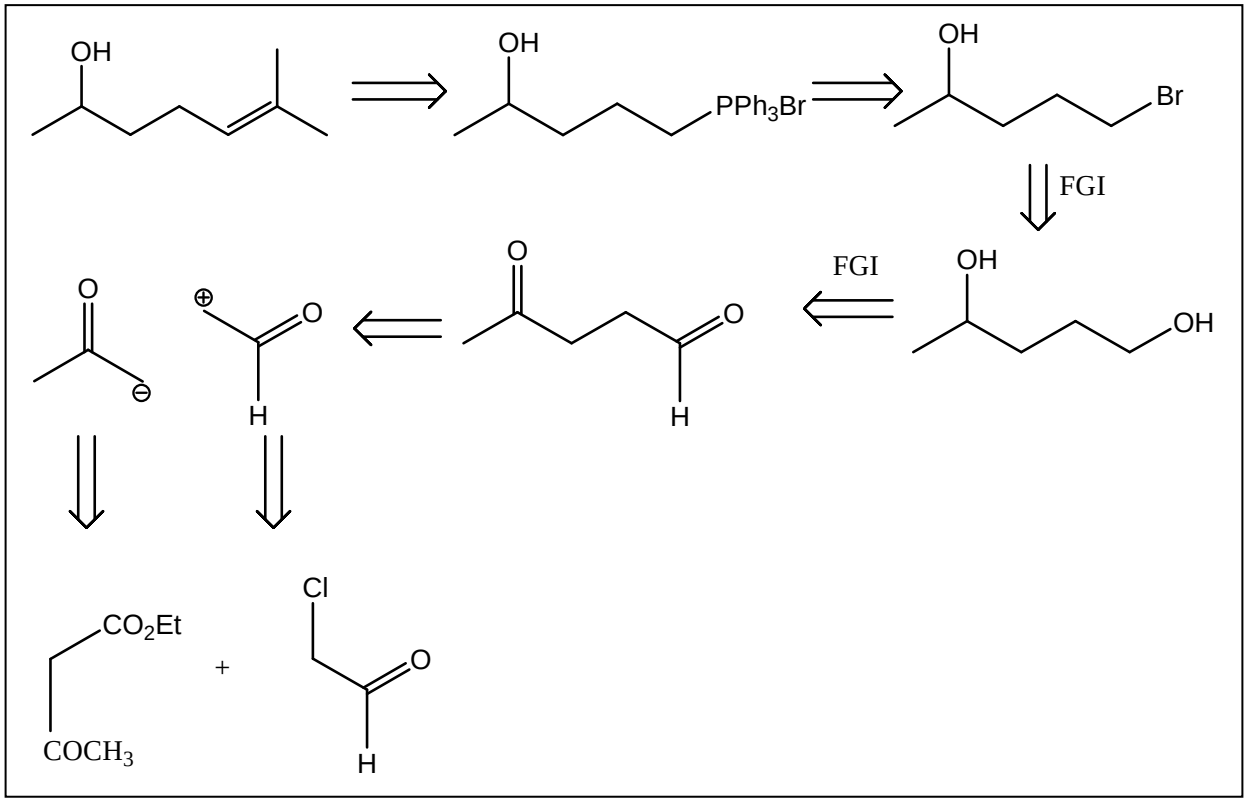
By making use of kinetic resolution method and remote 1,4- stereocontrol mechanism, the natural products were synthesized. Sulcatol the male produced aggregation pheromone, was isolated from Gnathotricus sulcatus. It is important for its biological activity for pest control. By kinetic resolution, the commercially available racemic alcohol was resolved in a single step, thus obtaining (R)- sulcatol in 98% ee as given in scheme 18.

Scheme 18: synthesis of (R)- sulcatol

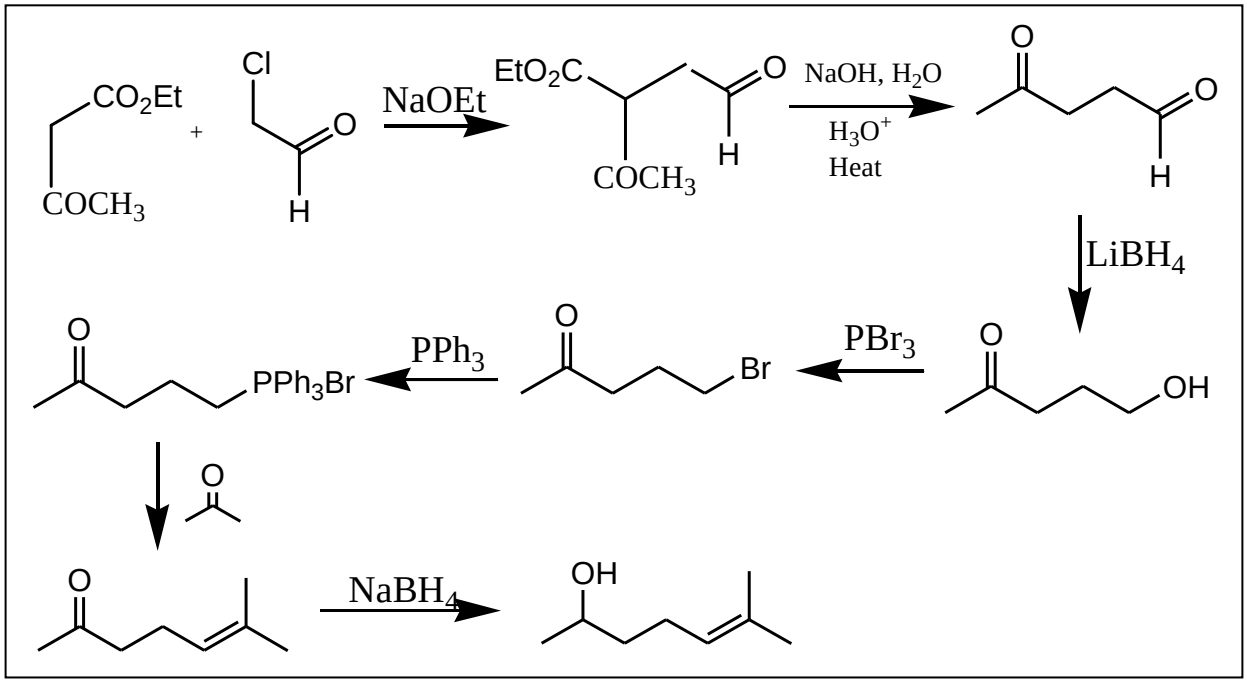


RETRO AND FORWARD SYNTHESIS

Retrosynthesis:



Forward synthesis:



CONCLUSION

The sulcatol was derived from the boring dust of Gnathotricus sulcatus. It is available in its enantiomeric form that is (R) and (S) – 6-methyl-5-hepten-2-ol. The sulcatol can be synthesized by various methods using different starting materials with the variable yield. It can be synthesized from the starting materials like glutamic acid, furanone, lactone, 6-methyl-5-hepten-2-one, etc by maintaining the required conditions for the reaction to be carried feasibly. The artificially synthesized sulcatols can be used as the pest controls. The synthesis of sulcatol by employing Baker's yeast for asymmetric reduction gives a good yield of product. Also, retro and forward synthesis was tried for molecule of sulcatol.

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