

Synthesis of Pheromones: Highlights from 2002-2004

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Abstract: This review summarizes the synthesis of pheromones published in the triennium 2002-2004. The syntheses of a total of 66 pheromone compounds (65 from insects, 1 from a crustacean species), belonging to 9 different structural categories, are presented in schemes. New methodologies, but also well-known reactions have been employed to achieve the (in many cases stereoselective) synthesis of the compounds.

1. INTRODUCTION

Since its very beginnings in the mid 19th century, organic chemistry has made advances unimaginable to the early pioneers of the field. Among the experimental key techniques contributing to these advances are chromatography, which made possible the separation of complex mixtures, and spectroscopic (UV, IR, NMR) and mass spectrometric methods, giving organic chemists powerful tools for the structure determination of organic compounds. This, in turn, stimulated research in organic synthesis, as products and by-products of reactions could be easily isolated and characterized. As once stated by Meinwald, "Organic chemistry blossomed into a self-contained, inward-looking science, bringing order and understanding to the synthesis and reactions of millions of compounds" [1]. This order and understanding allowed the development of countless reactions of carbon-carbon bond formation or modification of functional groups, applicable to all classes of organic molecules, which would later eventually be modified or improved, e.g. in terms of scope, yields, reaction conditions, or stereochemical selectivities. Research in chemical communication has been profiting from these decade-lasting and ongoing efforts, as the synthesis of pheromones is of great importance in the process of identifying these chemical messengers. Moreover, a sort of mutualism has been evolving, as many new synthetic methods have been developed with the explicit aim to improve the synthetic route towards a pheromone.

Pheromones are compounds which are produced and liberated by an individual, provoking a behavioural or physiological response in another individual of the same species. As pheromones are usually produced in minute amounts, thus preventing crystallographic or extensive NMR experiments, their independent synthesis is required to confirm the identification and to establish the absolute configuration in case of chiral compounds. Furthermore, chemical synthesis of pheromones provides the amounts necessary for the evaluation of their biological activity in the laboratory or in the field.

The chemical structures of pheromones identified so far are diverse and their complexity ranges from simple *n*-alkanes to highly complex molecules bearing (multiple) cyclic substructures, double or triple bonds, heteroatoms, and/or (multiple) stereogenic centers. In many cases, only one stereoisomer or a defined mixture of stereoisomers is biologically active, while the unnatural isomers or a different ratio of isomers may be inactive or even inhibit the response to the natural compounds. Against this background, methods are required which lead in high yields and with high stereoselectivity to the desired compounds. Pheromone syntheses published over the last few decades have been reviewed repeatedly. The most comprehensive reviews are probably those written by Mori in 1981 and 1992 [2, 3]. Other accounts, relating pheromone synthesis to specific topics [4-6] and a partial, nevertheless impressive update [7] were published by the same author. Most recently, and reflecting a growing branch in organic synthesis, the application of biocatalysis to the synthesis of pheromones has been reviewed [8].

In this article, we review the syntheses of pheromones published in the triennium 2002-2004. The aim is to provide a comprehensive overview of the syntheses, and we sincerely apologize to the authors of those articles which may have escaped our attention. The presentation of the syntheses is done according to the compound class of the respective target compound, adopting the style established by Mori [3].

2. SYNTHESIS OF ALKANES AS PHEROMONES

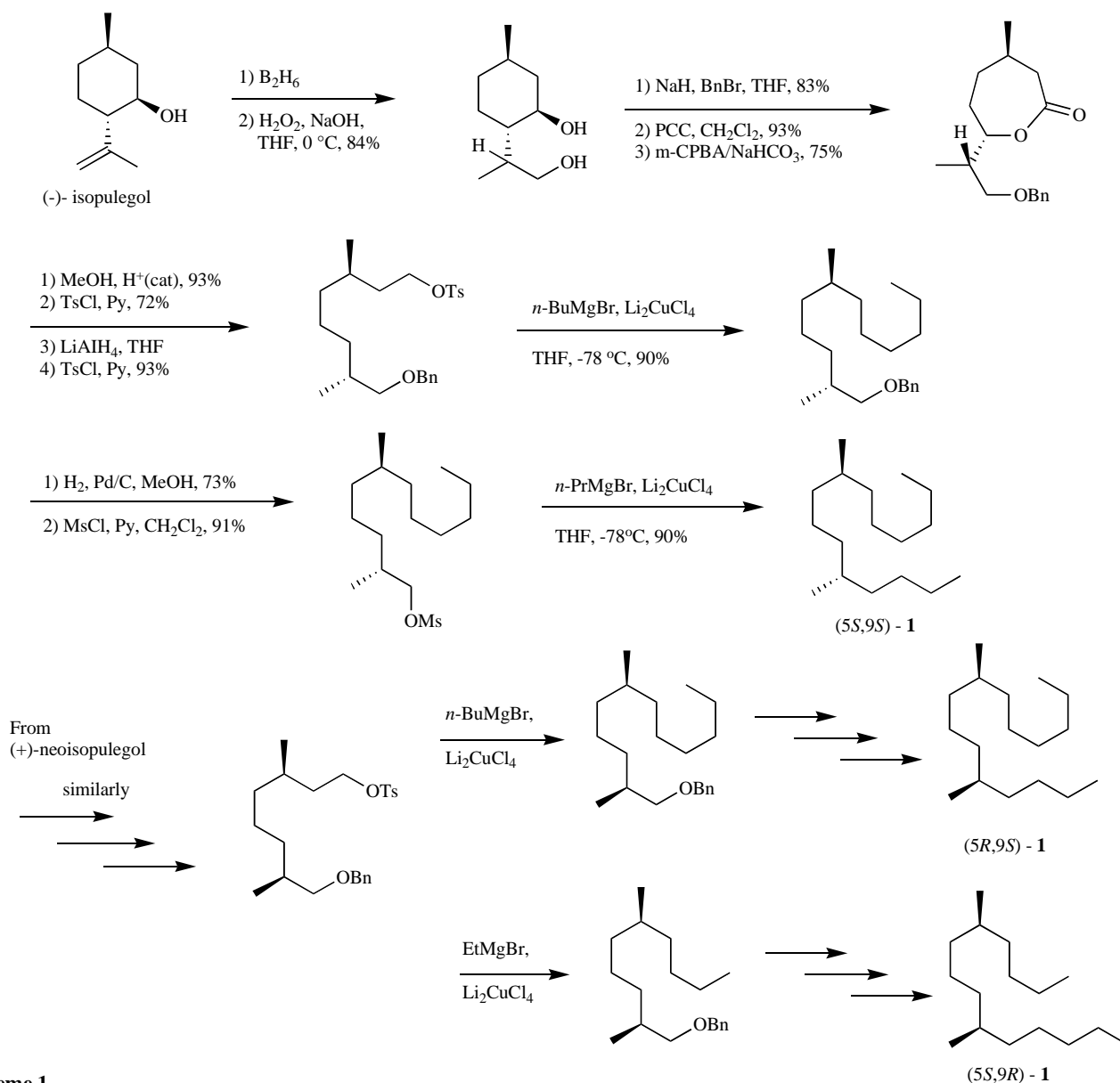
2.1. 5,9-Dimethylpentadecane (1)

The coffee leaf miner, *Leucoptera coffeella*, is an economically important pest of coffee trees in Brazil. It has been demonstrated by Francke and co-workers [9] that the main component of the female-produced sex pheromone of this species is 5,9-dimethylpentadecane (**1**), however, the stereochemistry of the natural pheromone remains unknown.

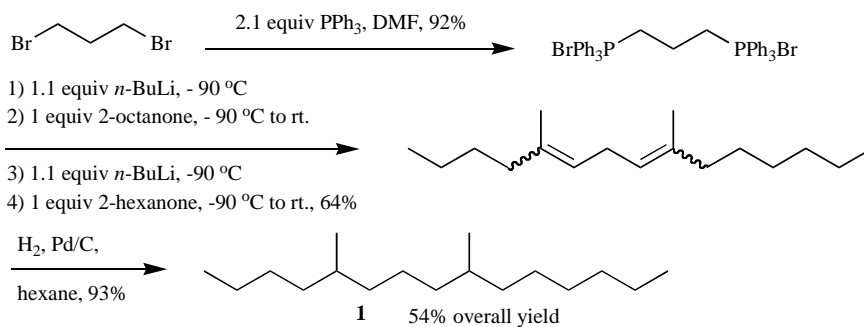
Moreira and Corrêa [10] described an enantioselective synthesis of three stereoisomers of **1**, from commercial isopulegol and synthetic *neo*-isopulegol [11, 12] (Scheme 1).

Zarbin *et al.* [13] described a straightforward synthesis of racemic **1** employing an unsymmetrical double Wittig olefination as the key reaction to build the carbon skeleton of the

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Scheme 1.

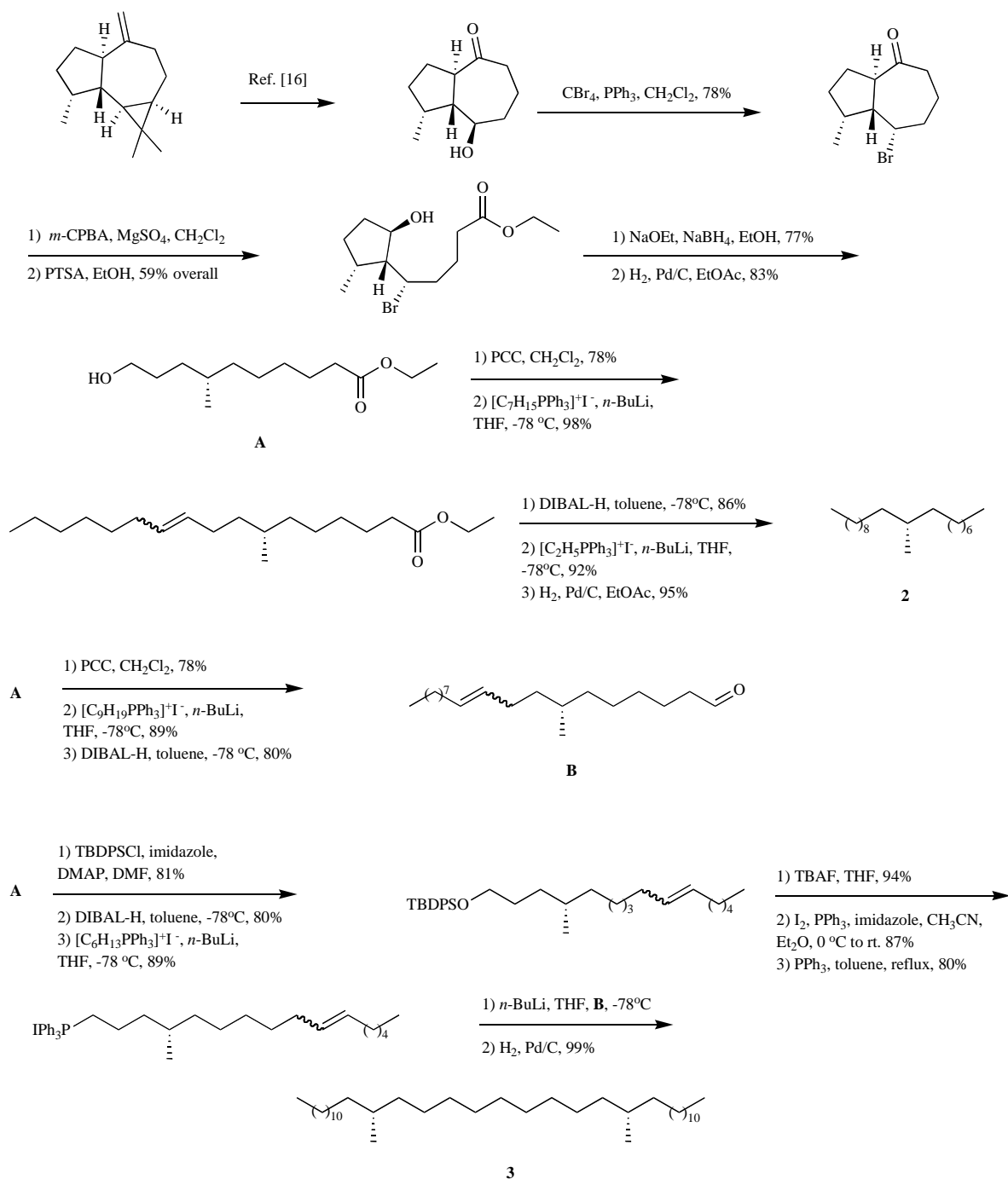


Scheme 2.

molecule. The bis-phosphonium salt obtained from 1,3-dibromopropane and triphenylphosphine, was reacted consecutively with the ketones 2-octanone and 2-hexanone, affording the asymmetric diene, which was readily hydrogenated over Pd/C, furnishing **1** in 54% overall yield (Scheme 2). Synthetic **1** showed high biological activity when tested in field experiments.

2.2. (*S*)-9-Methylnonadecane (**2**) and *meso*-13,23-dimethylpentatriacontane (**3**)

(*S*)-9-Methylnonadecane (**2**) is a sex pheromone component of the cotton leafworm *Alabama argillacea* [14], and *meso*-13,23-dimethylpentatriacontane (**3**), is the sex pheromone of the tse tse fly *Glossina pallidipes* [14].



Scheme 3.

Lamers *et al.* [15] reported the synthesis of these two pheromones starting from the readily available (+)-aromadendrene *via* the chiral intermediate **A** [16] (Scheme 3).

2.3. 7,11-Dimethylheptadecane (4)

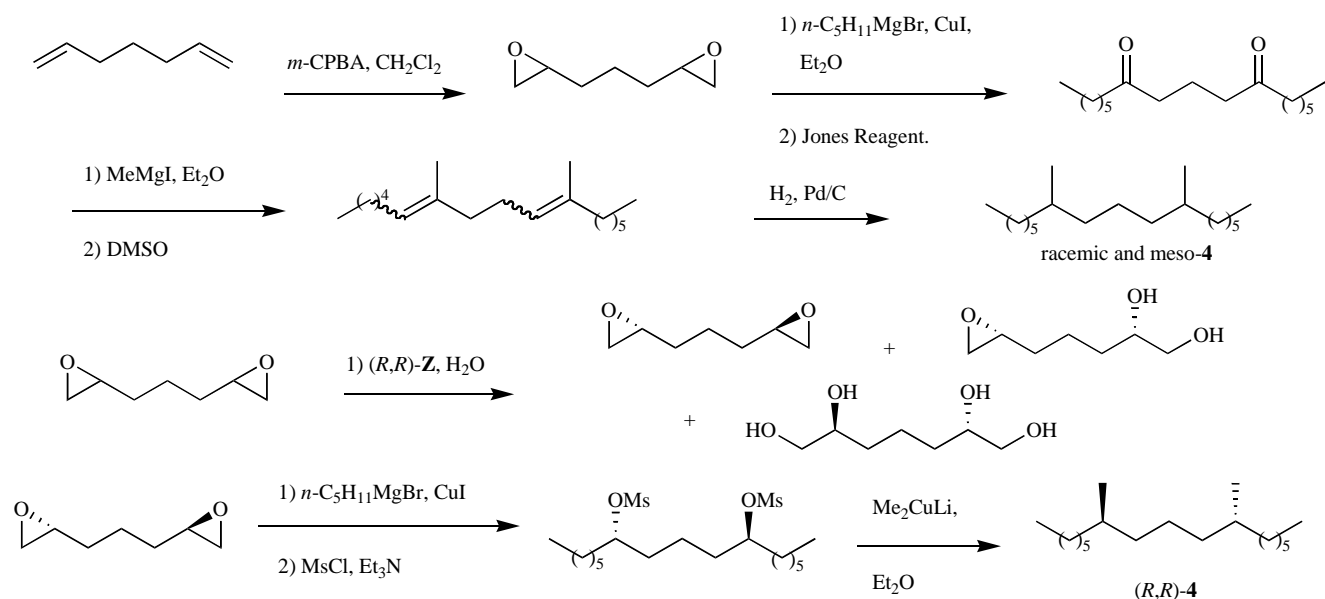
The hydrocarbons 7-methylheptadecane and 7,11-dimethylheptadecane (**4**) have been identified as constituents of the female-produced sex pheromone of the spring hemlock looper (*Lambdina athasaria*) and the pitch pine looper (*L. pellucidaria*) [17, 18]. Subsequently, bioassays confirmed that (*S*)-7-methylheptadecane and *meso*-**4**, that is (*7S,11R*), are the bioactive stereoisomers [19]. Chow *et al.*

[20] described the synthesis of a mixture of all isomers of **4** in 6 steps, starting from hepta-1,6-diene. Pure (*R,R*)-**4** was synthesized by hydrolytic kinetic resolution of the bisepoxide obtained from hepta-1,6-diene using 1.4 % equiv. of [(*R,R*)-(salen)Co(III)(OAc)]-**Z** complex (Fig. 1), followed by a Grignard reaction and methylation (Scheme 4).

3. SYNTHESIS OF ALKENES AS PHEROMONES

3.1. (6*Z*,9*Z*)-Heneicosa-6,9-diene (5), (3*Z*,6*Z*,9*Z*)-heneicosa-3,6,9-triene (6), and heneicosane (7)

(6*Z*,9*Z*)-Heneicosa-6,9-diene (**5**), (3*Z*,6*Z*,9*Z*)-heneicosa-3,6,9-triene (**6**), and heneicosane (**7**), have been identified as



Scheme 4.

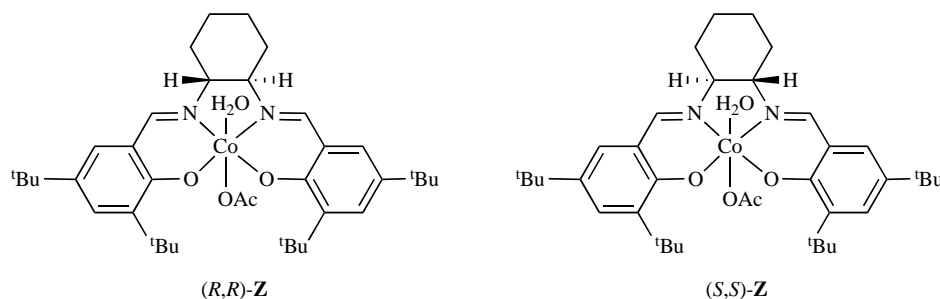
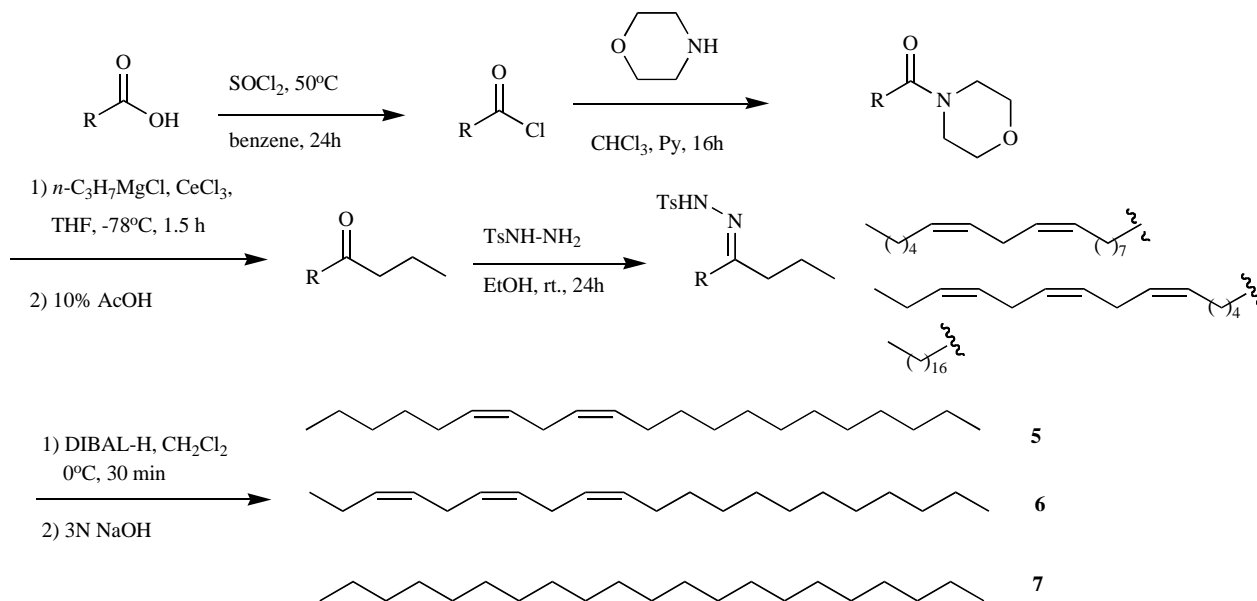


Fig. (1).



Scheme 5.

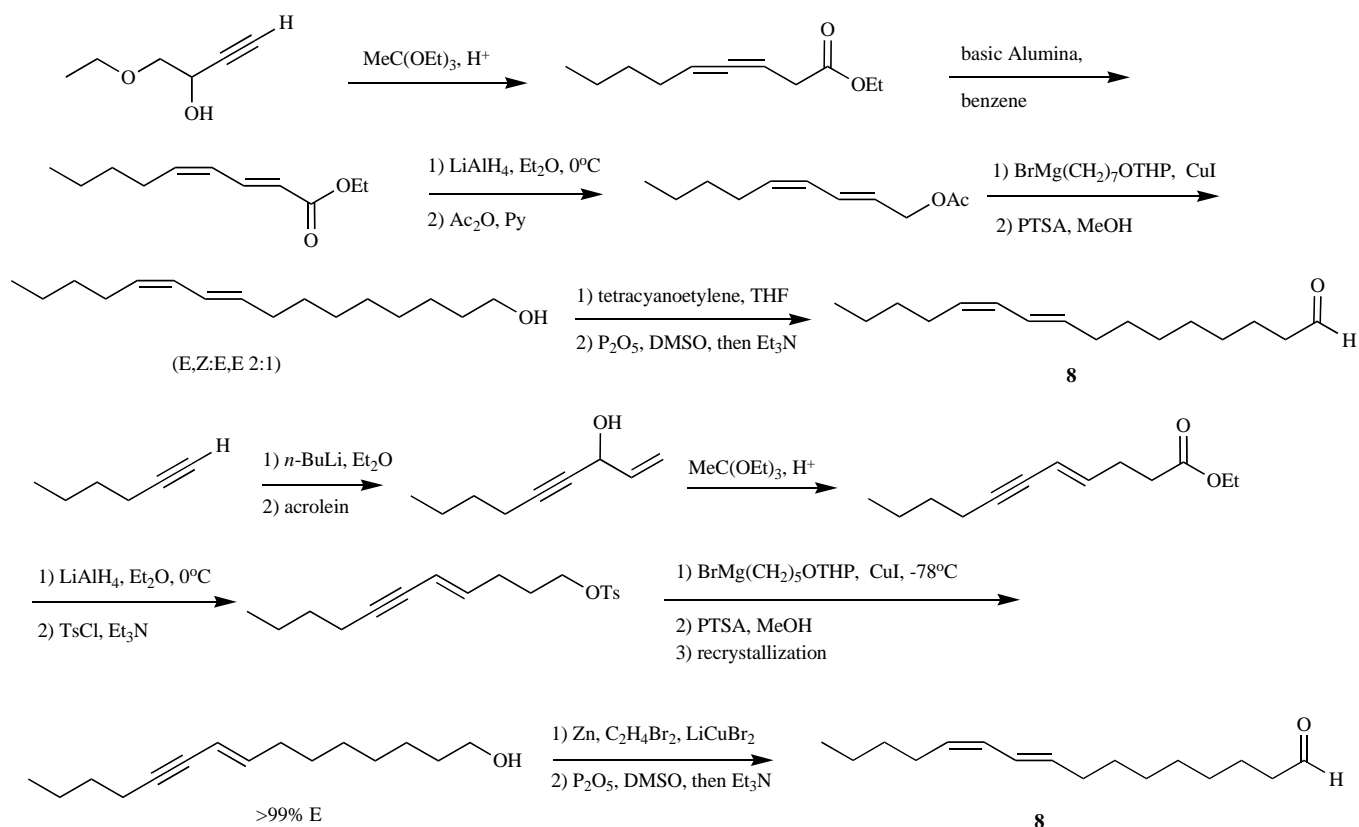
pheromone components of *Achaea janata*, a destructive oligophagous insect for castor crops, especially when young crops are attacked.

Badioli *et al.* [21] described the synthesis of these three hydrocarbons from linoleic, linolenic, and stearic acid, respectively, by addition of organocerium reagents to the cor-

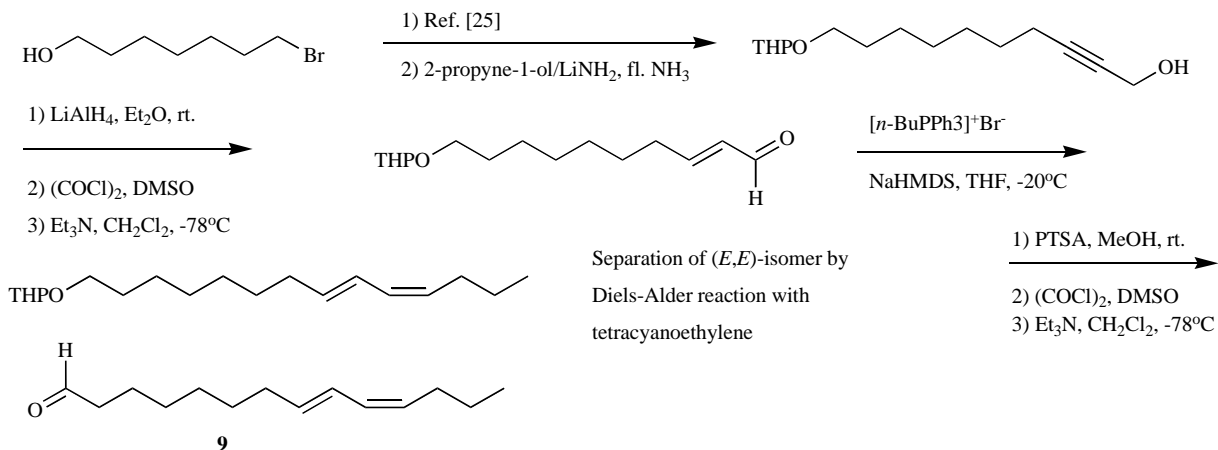
responding morpholine amides. The resulting propyl ketones were reduced via their tosylhydrazones (Scheme 5).

3.2. (9E,11Z)-Hexadeca-9,11-dienal (8)

(9E,11Z)-Hexadeca-9,11-dienal (8) has been identified as a female-produced sex pheromone of the pecan nut casebearer (*Acrobasis nuxvorella*) [22].



Scheme 6.



Scheme 7.

Two alternative syntheses were described by Passaro and Webster [23]. The key steps in both sequences is an orthoester Claisen rearrangement (Scheme 6).

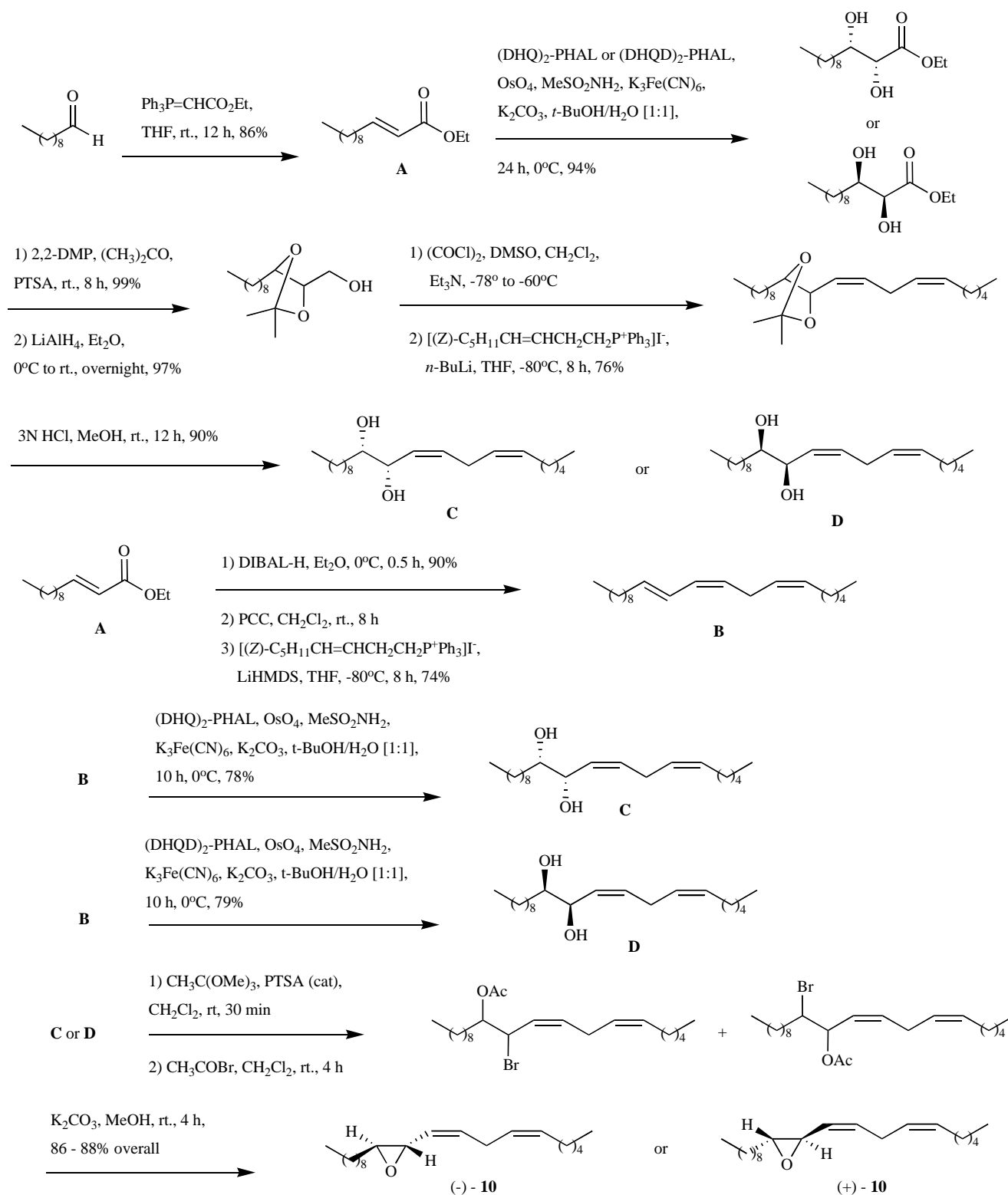
3.3. (8*E*,10*Z*)-8,10-Tetradecadienal (9)

Francke *et al.* described the synthesis of (8*E*,10*Z*)-8,10-tetradecadienal (9), the female produced sex pheromone of the horse-chestnut leafminer (*Cameraria ohridella*) [24]. The synthesis of 9 was carried out in 30% overall yield, starting from 7-bromoheptanol. The (8*E*) configuration was achieved by stereoselective reduction of an acetylene, while the (10*Z*) configuration results from a stereoselective Wittig reaction (Scheme 7).

4. SYNTHESIS OF EPOXY PHEROMONES

4.1. (6*Z*,9*Z*,11*S*,12*S*)-*trans*-11,12-Epoxyheneicosa-6,9-diene (10) (Posticlude)

Wakamura *et al.* [26] identified posticlude [(6*Z*,9*Z*,11*S*,12*S*)-*trans*-11,12-epoxyheneicosa-6,9-diene, 10] as the female-produced pheromone of the tussock moth *Orgyia postica*. Fernandes and Kumar [27] described a highly enantioselective synthesis of (+)- and (-)-posticlude employing the Sharpless asymmetric dihydroxylation of olefin A or the regio- and stereoselective mono-dihydroxylation of the *trans* olefin bond of the (*Z,Z,E*)-triene B to obtain the enantiomerically pure diols C and D, which were transformed into (+)-



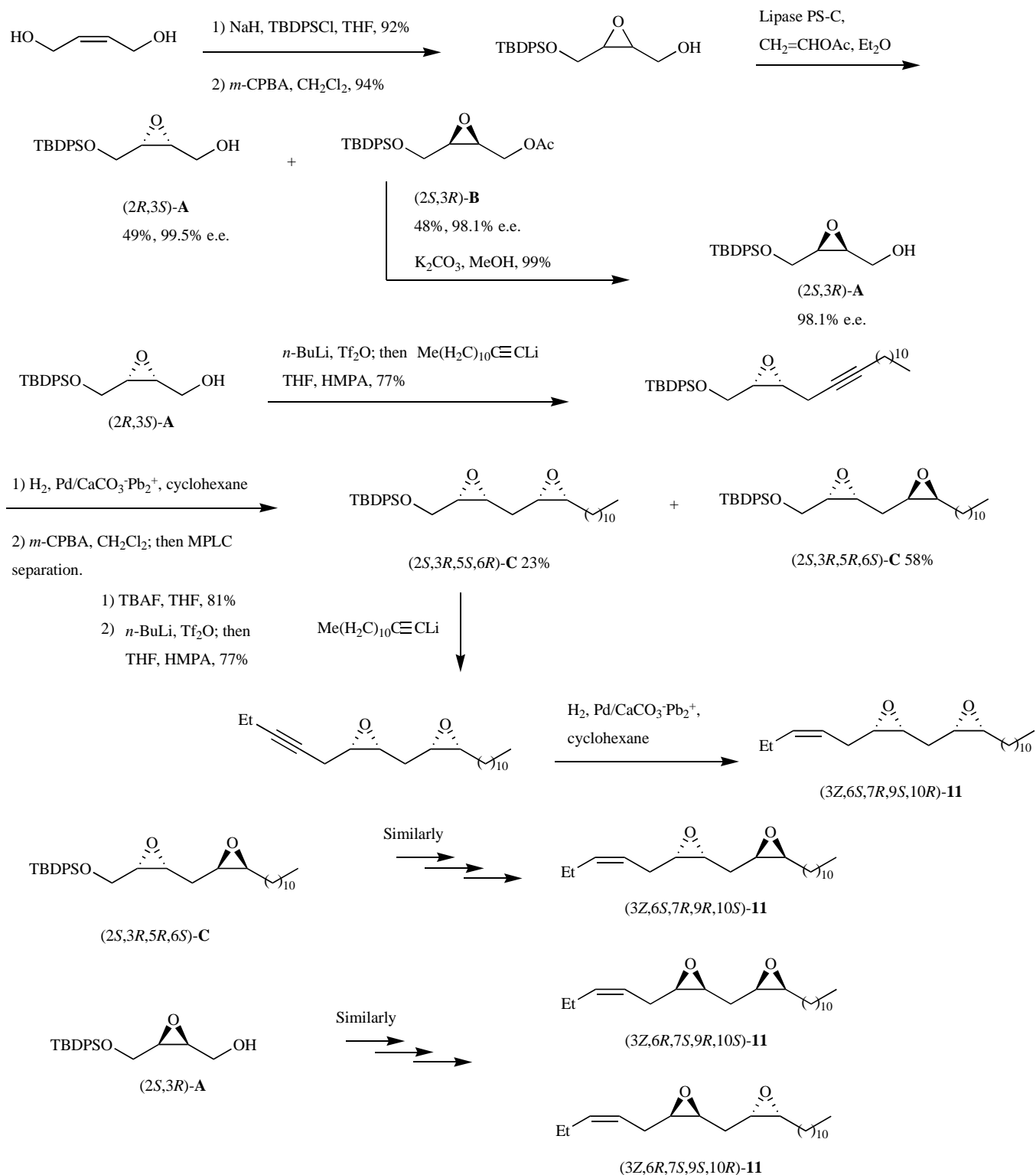
Scheme 8.

and (-)-**10** via the respective acetoxybromides in a one-pot reaction (Scheme 8).

4.2. (3*Z*)-*cis*-6,7-*cis*-9,10-Diepoxyheneicos-3-ene (**11**) (leucomalure)

Gries *et al.* identified leucomalure [(3*Z*)-*cis*-6,7-*cis*-9,10-diepoxyheneicos-3-ene, **11**] as the major component of the

female-produced sex pheromone of the Satin moth, *Leucoma salicis* [28]. Muto and Mori [29] employed the lipase PS-C(Amano)-catalyzed asymmetric acetylation of (\pm)-4-(*tert*-butyldiphenylsilyloxy)-*cis*-2,3-epoxybutan-1-ol, which afforded the (2*R*,3*S*)-epoxy alcohol **A** and the (2*S*,3*R*)-epoxyacetate **B** as optically active building blocks to prepare all isomers of **11** (Scheme 9).

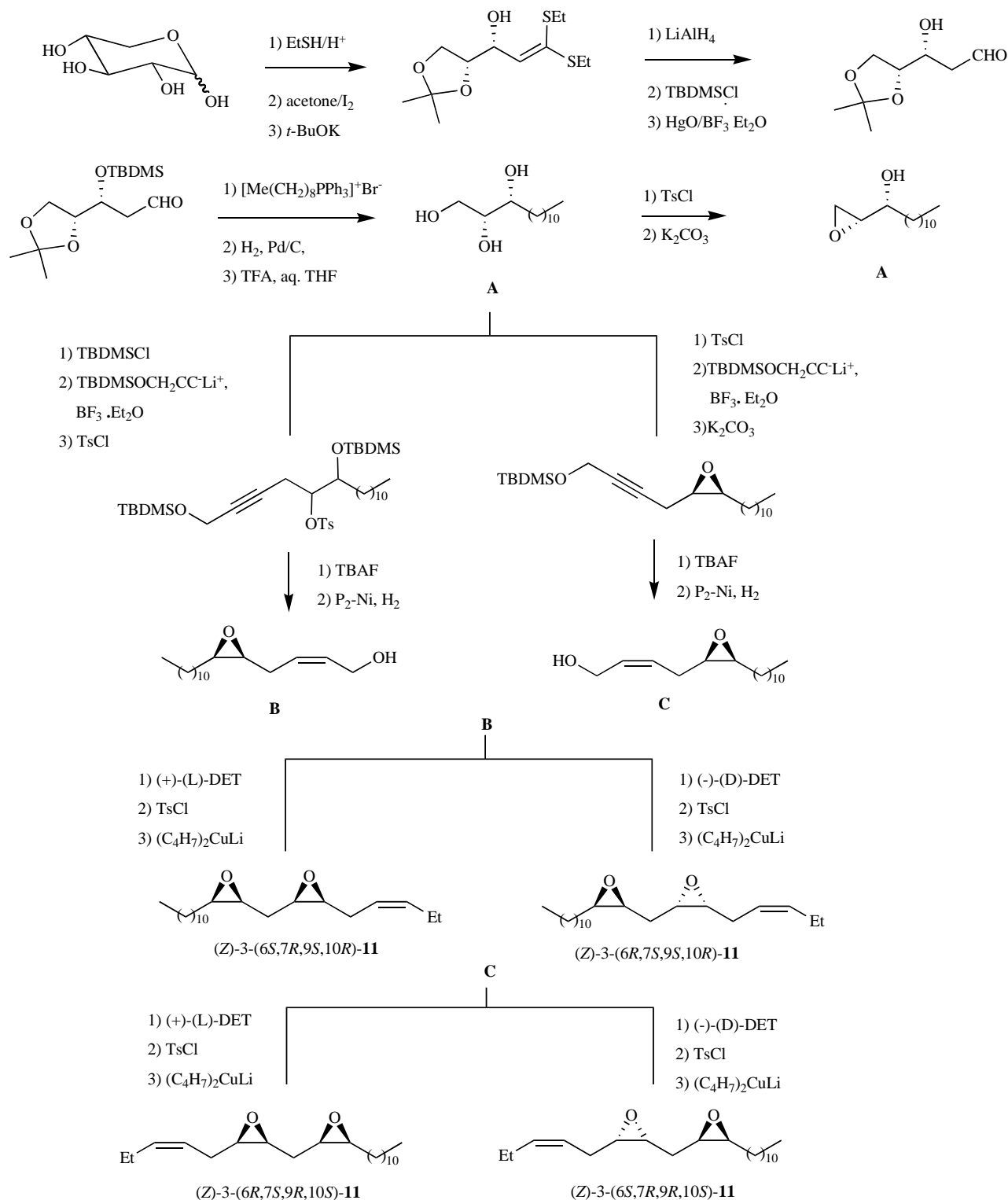


Scheme 9.

All four isomers of **11** have also been synthesized by Wimalaratne and Slessor, using D-xylose as the optically pure starting material [30]. The epoxy alcohol **A** was transformed to chain-elongated epoxy alcohols **B** and **C**, respectively, which were subsequently epoxidized by the method of Sharpless and finally alkenylated to give the pure isomers of **11** (Scheme 10).

4.3. (6*Z*)-*cis*-9,10-Epoxyheneicos-6-ene (**12**) and (6*Z*)-*cis*-9,10-epoxyeicos-6-ene (**13**)

The pure enantiomers of epoxide **A** used in Mori's synthesis of **11** [29] (Scheme 9) were also the key intermediates for the synthesis of the enantiomers of (6*Z*)-*cis*-9,10-epoxyheneicos-6-ene (**12**) and (6*Z*)-*cis*-9,10-epoxyeicos-6-ene (**13**) [31] (Scheme 11).



Scheme 10.

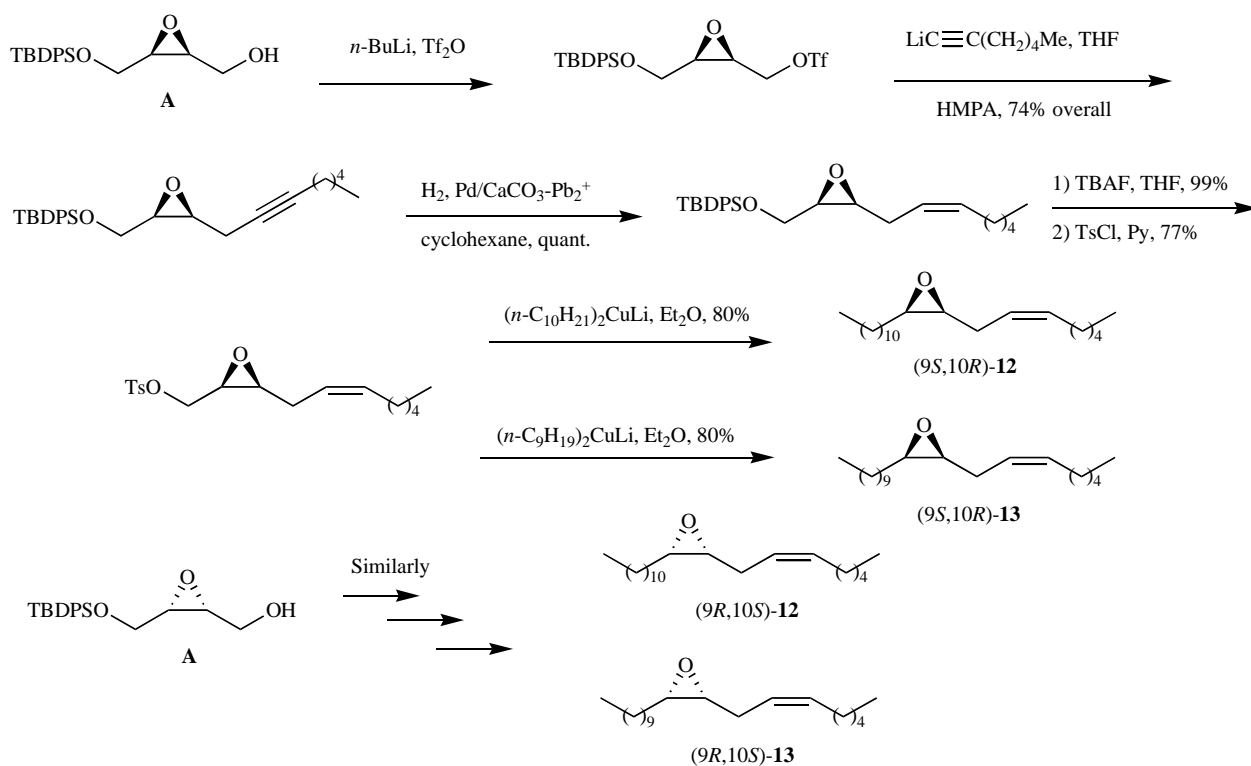
5. SYNTHESIS OF NON-ISOPRENOIDAL PHEROMONE ALCOHOLS AND THEIR ESTERS

5.1. 2-Methyl-4-octanol (14)

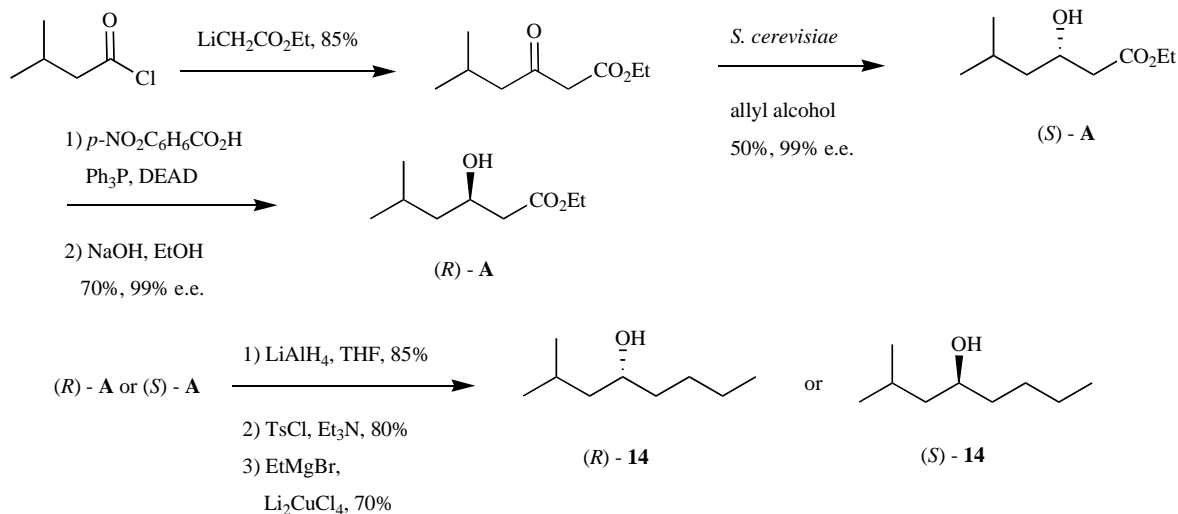
2-Methyl-4-octanol (**14**) has been described as a component of the aggregation pheromones of several weevil spe-

cies [32, 33]. Baraldi *et al.* [34] reported the enantioselective synthesis of (*R*)- and (*S*)-**14** starting from isovaleryl chloride.

The key step of this synthetic route is the asymmetric reduction of ethyl 5-methyl-3-oxohexanoate with *Saccharomyces cerevisiae* to the corresponding hydroxyester (*S*)-**A** in high enantiomeric excess (Scheme 12). The (*S*) isomer was



Scheme 11.



Scheme 12.

prepared in five steps and 20% overall yield, while the (*R*) enantiomer was obtained in six steps and 14% overall yield.

The key step of the synthesis of (*R*)-**14** described by Dhotare *et al.* [35] is the K-selectride reduction of the intermediate ketone **A** obtained from D-mannitol. The reduction proceeded with absolute *syn* selectivity (Scheme 13).

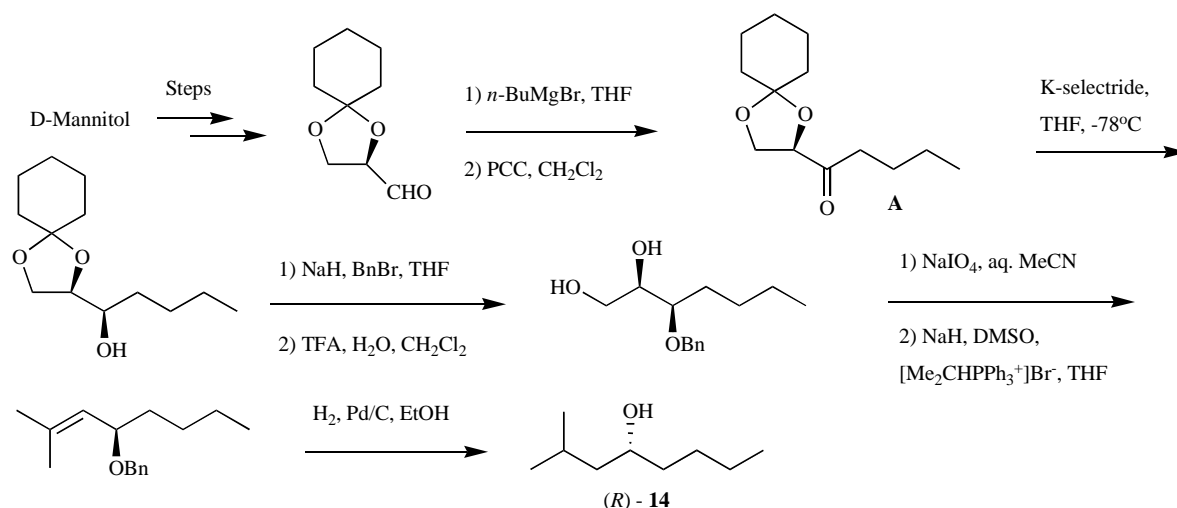
D-mannitol was also used by Zarbin *et al.* [36] to obtain (*S*)-**14** by a new and highly enantioselective approach, involving the known (*R*)-glyceraldehyde acetonide **A** as key intermediate (8.8% overall yield) (Scheme 14).

5.2. 4-Methylheptan-3-ol (**15**)

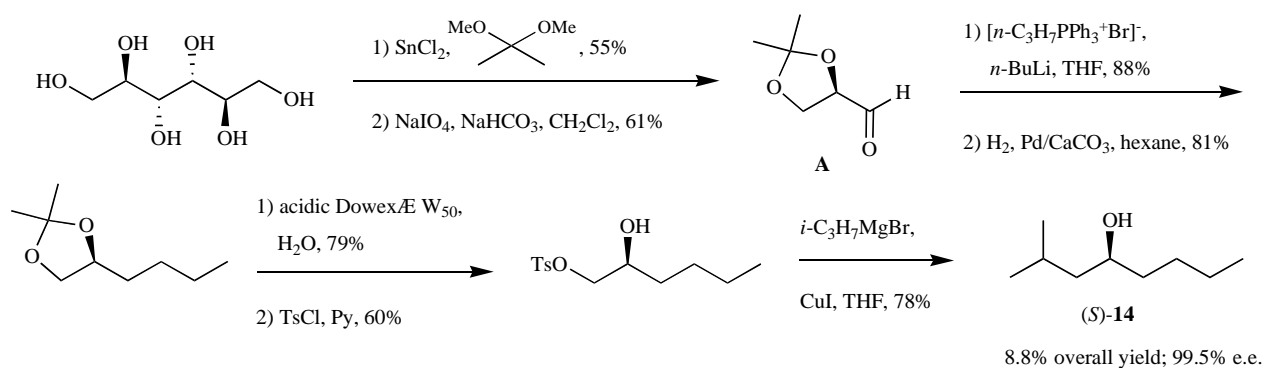
(3*S*,4*S*)-4-Methylheptan-3-ol [(3*S*,4*S*)-**15**] is the major component of the aggregation pheromone of the bark beetles

Scolytus scolytus and *S. multistriatus* [37-40]. Recently, (3*S*,4*S*)-**15** was tentatively identified as the main component of the aggregation pheromone of the almond bark beetle, *Scolytus amygdali*, along with (3*S*,4*S*)-4-methyl-3-hexanol, which functions as a synergist. Substitution of the pure (3*S*,4*S*) isomer with racemic 4-methyl-3-heptanol in field tests resulted in a lower trap catch of beetles in the field, indicating the possibility that one or more of the unnatural stereoisomers has an inhibitory effect [41].

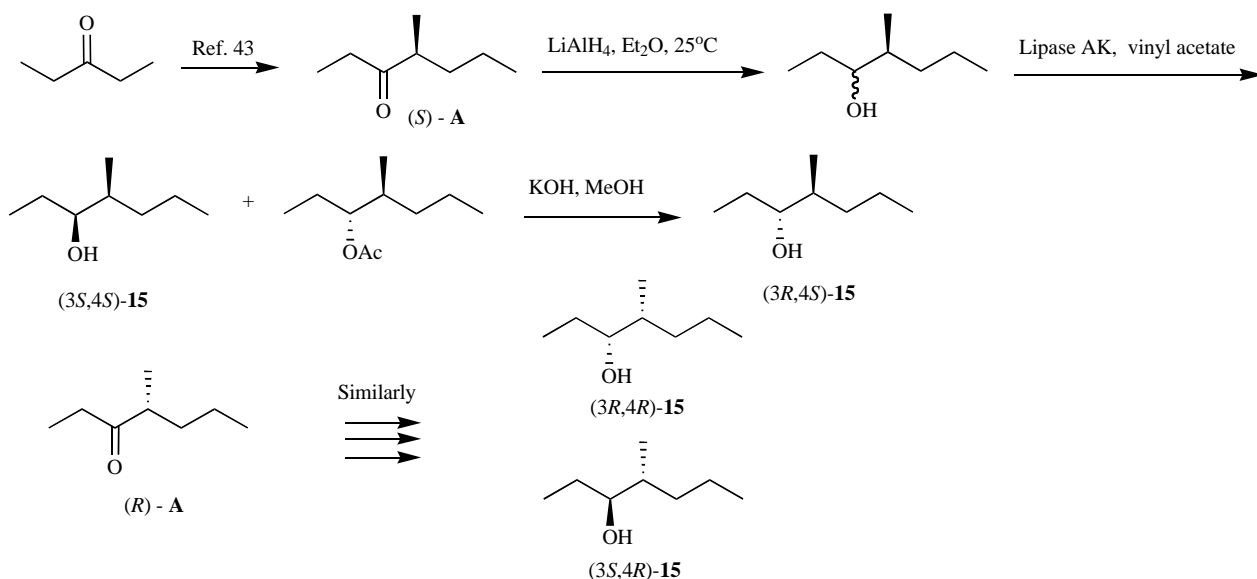
Zada *et al.* [42] described the synthesis of all four stereoisomers of **15**. Key steps included preparation of enantiomerically pure (*R*)- and (*S*)-4-methyl-3-heptanone (**A**) by the SAMP/RAMP method, reduction to the corresponding alcohols, and stereospecific transesterification with vinyl acetate by lipase AK catalysis (Scheme 15). In field tests,



Scheme 13.



Scheme 14.



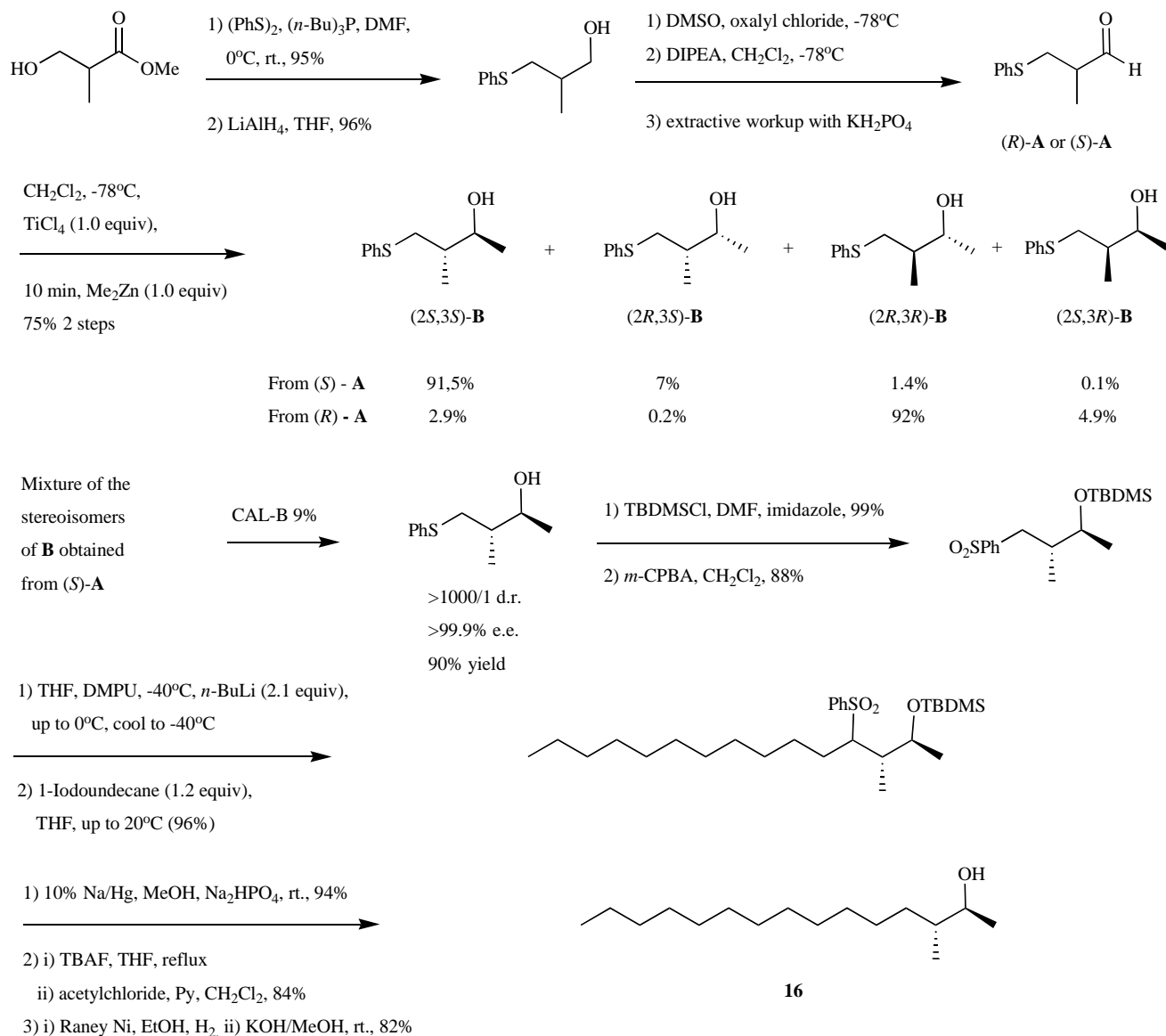
Scheme 15.

only (3S,4S)-**15** attracted beetles in combination with the synergist (3S,4S)-4-methyl-3-hexanol, whereas the (3R,4S) and (3R,4R) isomers were inhibitory.

5.3. (2S,3R)-3-Methylpentadecan-2-ol (**16**)

Larsson *et al.* [44] described the synthesis of (2S,3R)-3-methylpentadecan-2-ol [(2S,3R)-**16**], a putative pheromone

precursor isolated from some pine sawflies of the genus *Gilpinia*. The enantiomers of 2-methyl-3-(phenylsulfonyl)propanal [(S)-**A** or (R)-**A**] were prepared from readily available (S)- and (R)-3-hydroxy-2-methylpropanoic acid methyl ester and were reacted with dimethylzinc to give the isomers (2S,3S)-**B** or (2R,3R)-**B**, respectively, both of high d.e. and e.e. These products were further purified by lipase catalysed



Scheme 16.

acylation to give the enantiomerically and diastereomerically highly pure enantiomers (>99% d.e., >99.9% e.e.). Pure (2*S*,3*S*)-**B** was transformed to (2*S*,3*R*)-**16** in 54% yield over eight steps (Scheme 16).

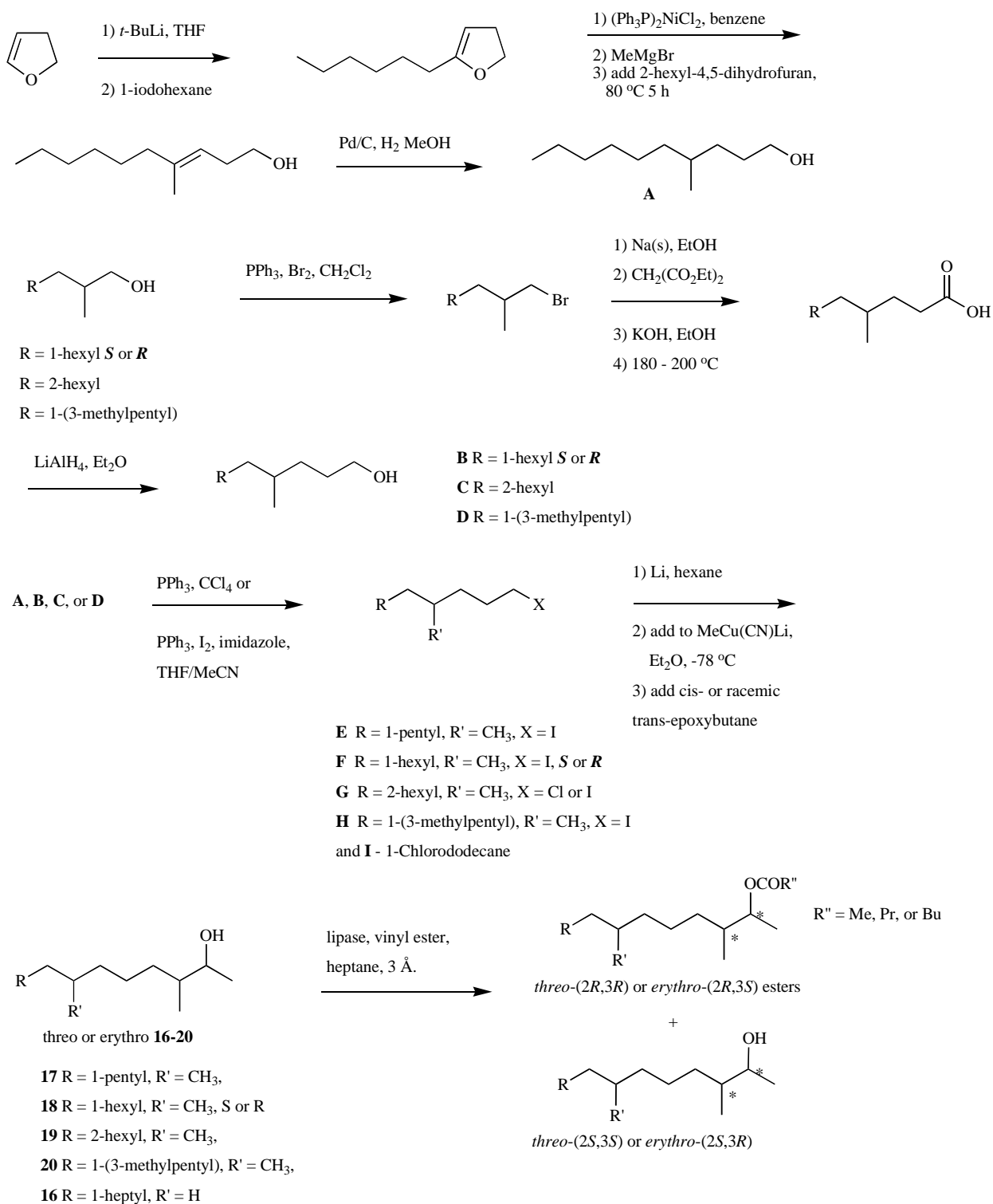
5.4. 3-Methylpentadecan-2-ol (16), 3,7-dimethyltridecan-2-ol (17), 3,7,11-trimethyltridecan-2-ol (18), 3,7,9-trimethyltridecan-2-ol (19), and 3,7-dimethyltetradecan-2-ol (20)

Hedenström *et al.* [45] reported the synthesis of precursors of the sex pheromones of females of pine sawfly species [46–49]. The key reaction sequence in the syntheses was the ring opening of either *cis*- or racemic *trans*-2,3-epoxybutane using a higher order cyanocuprate as nucleophile, obtained from iodides or chlorides **E** – **I**, followed by a highly efficient lipase catalysed stereoselective acylation of the resulting 3-methylalkan-2-ols (Scheme 17).

5.5. (2*S*,3*R*,7*RS*)-3,7-Dimethyltridecan-2-yl acetate (21) and propanoate (22)

3,7-Dimethyltridecan-2-yl acetate (**21**) and propanoate (**22**) are sex attractants of the sawfly *Diprion pini* [48].

Bekish *et al.* [50] described a synthesis of a mixture of the diastereomers (2*S*,3*R*,7*S*)- and (2*S*,3*R*,7*R*)-**21**, as well as (2*S*,3*R*,7*S*)- and (2*S*,3*R*,7*R*)-**22** by cyclopropanation of the ethoxycarbonyl group in *O*-THP protected ethyl (*S*)-lactate with ethylmagnesium bromide in the presence of titanium(IV) isopropoxide, and subsequent C2–C3 ring opening of the resulting cyclopropanol (Scheme 18). The resulting (*S*) configured bromoalkenol **A** (stereoisomeric purity 98%) was chain-elongated and hydrogenated. The (3*R*) configuration was established by esterification with phthalic anhydride followed by salt formation with pure (*S*)-1-phenylethylamine and several recrystallisations of this salt to give the alcohol with 92% e.e. at C-3.

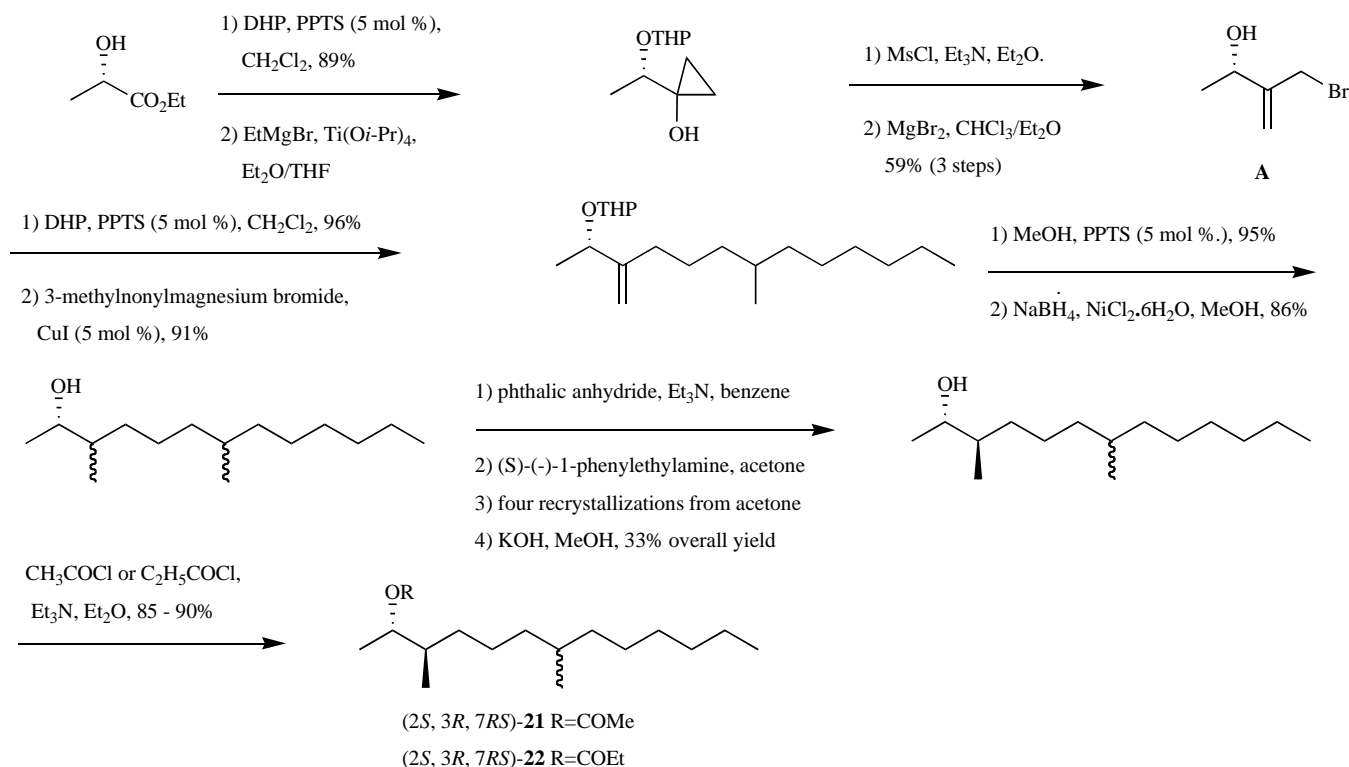


Scheme 17.

5.6. 3,7-Dimethyltridec-2-yl propanoate (23)

Dandapani *et al.* described a synthesis of all 16 stereoisomers of 3,7-dimethyltridec-2-yl propanoate (**23**), the sex pheromone of the pine sawfly *Microdiprion pallipes*, by a fluorine mixture-synthesis approach [51]. Each of the four stereoisomers of 2-methyl-1,3-butanediol was marked separately with a different fluorine-containing group, then the

quasi isomers were mixed and subjected to reactions, and finally demixed by fluorine silica chromatography, making use of the different fluorine tag of each isomer. In the first step of the reaction sequence, each of the quasi isomer in the mixture **M-1** was reduced, partially oxidized, then the mixture was split and each part chain-elongated using the chiral building block (*S*)-**E** or (*R*)-**E**. Each mixture obtained [**M-2** (*R*) and **M-2** (*S*)] was split again and chain-elongated sepa-



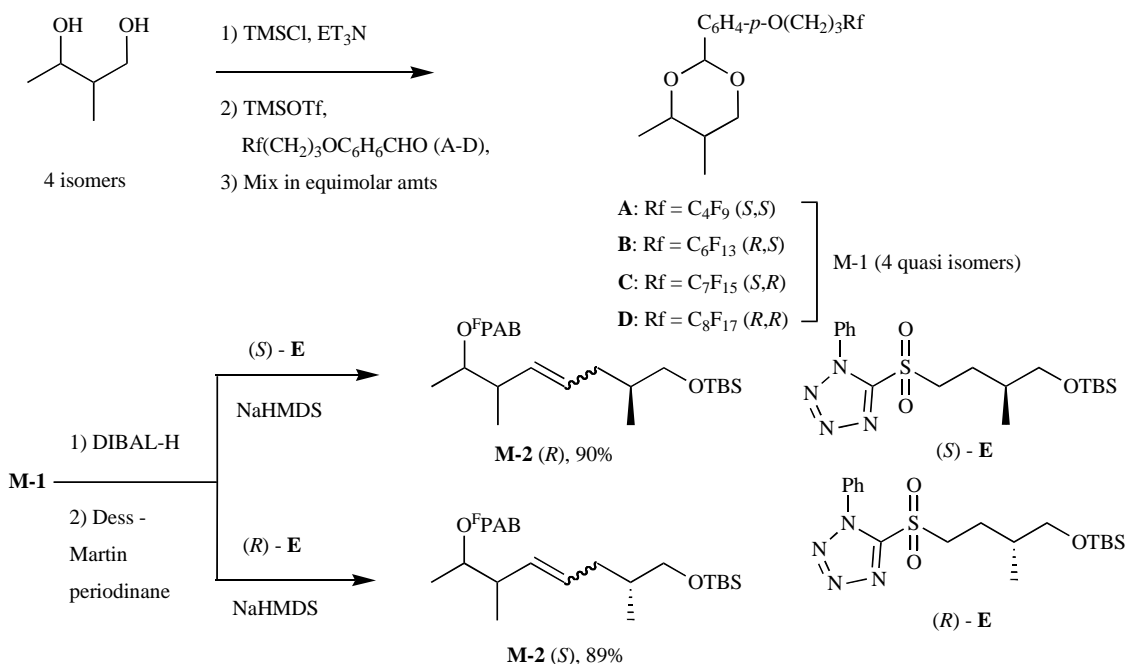
Scheme 18.

rately with the same reagent (*S*)-**E** or (*R*)-**E**, giving rise to four mixtures **M-3**. After hydrogenation, each mixture was separated by HPLC and the fluorine-containing group was removed to give the target compounds (Scheme 19).

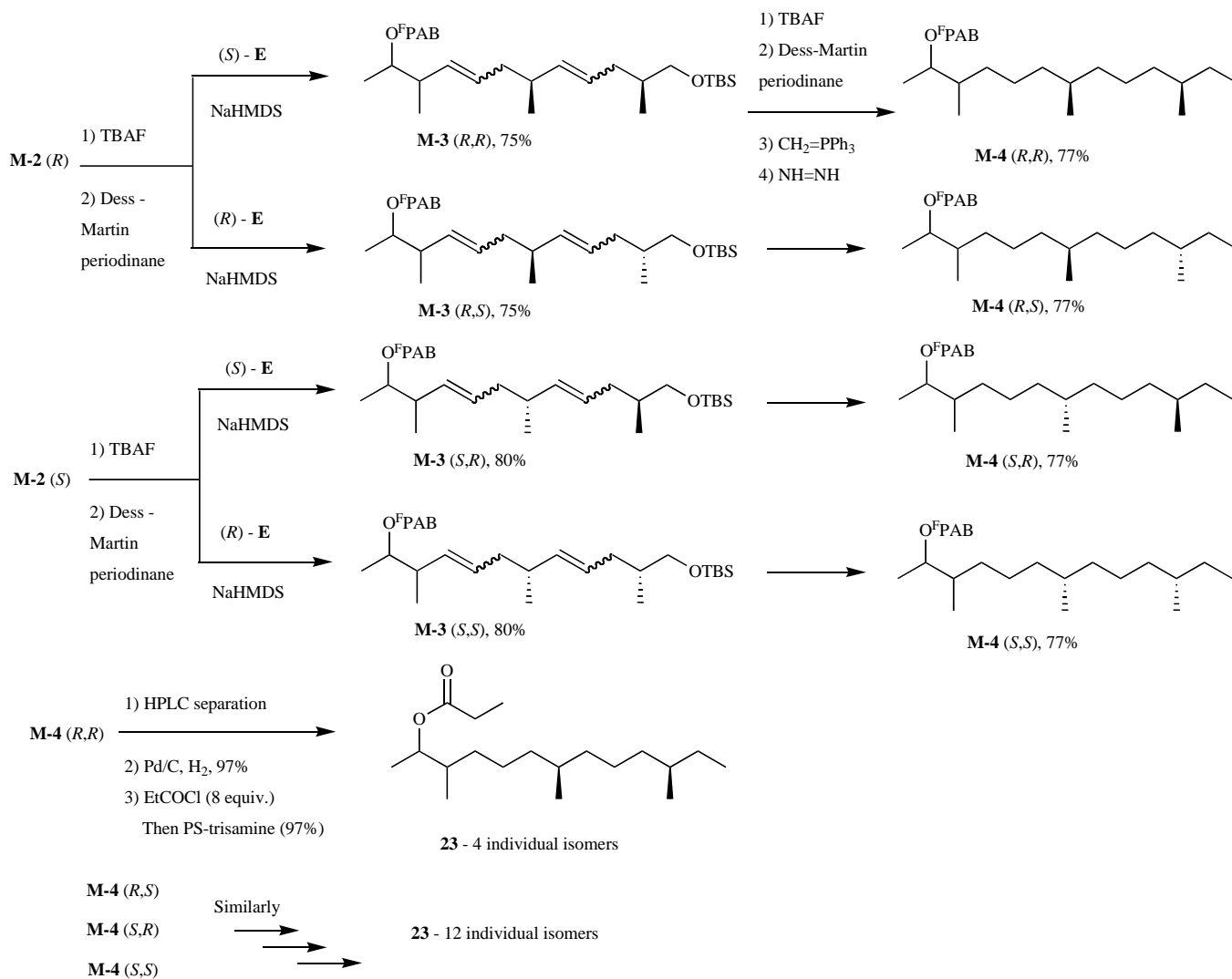
5.7. (*R*)-2-Methyl-4-octanol (**14**), (*R*)- and (*S*)-3-octanol (**24**), (*R*)-2-dodecanol (**25**), and (*R*)-2-methyl-4-heptanol (**26**)

(*R*)-3-Octanol [(*R*)-**24**] is the sex attractant pheromone of the ant *Myrmica scabrinodis* [52] while (*S*)-**24** is an alarm

pheromone found in the ants *Crematogaster castanea* and *C. liengmei* [53, 54]. (*R*)-2-Dodecanol (**25**) is a component of the hind leg tibial gland secretion of worker ants of *C. auberti* [55]. (*R*)-2-Methyl-4-heptanol (**26**) and (*R*)-2-methyl-4-octanol (**14**) were identified as the male-produced aggregation pheromones of the West Indian sugarcane weevils *Metamasius hemipterus* [32, 56]. Scheme 20 shows the synthesis of the optically active insect pheromones **14** and **24-26** described by Cho and Kim, starting from enantiomerically pure β -hydroxy sulfides [57]. The β -hydroxy sulfides were



Scheme 19. Contd....



Scheme 19.

prepared by enantioselective reduction of the corresponding β -keto sulfides, catalyzed by oxazaborolidine (*R*)- or (*S*)-**X** with 74 – 81% e.e. Recrystallization of the acylated β -hydroxy sulfides in appropriate solvents increased the enantiomeric purity to 96 – 99% e.e. The sulfides were deacylated, oxidized to the sulfoxides, alkylated if necessary, and reduced with Raney-Ni to furnish the target compounds.

5.8. (-)-(2*R*,6*Z*)-Undec-6-en-2-ol (**27**) (nostrenol)

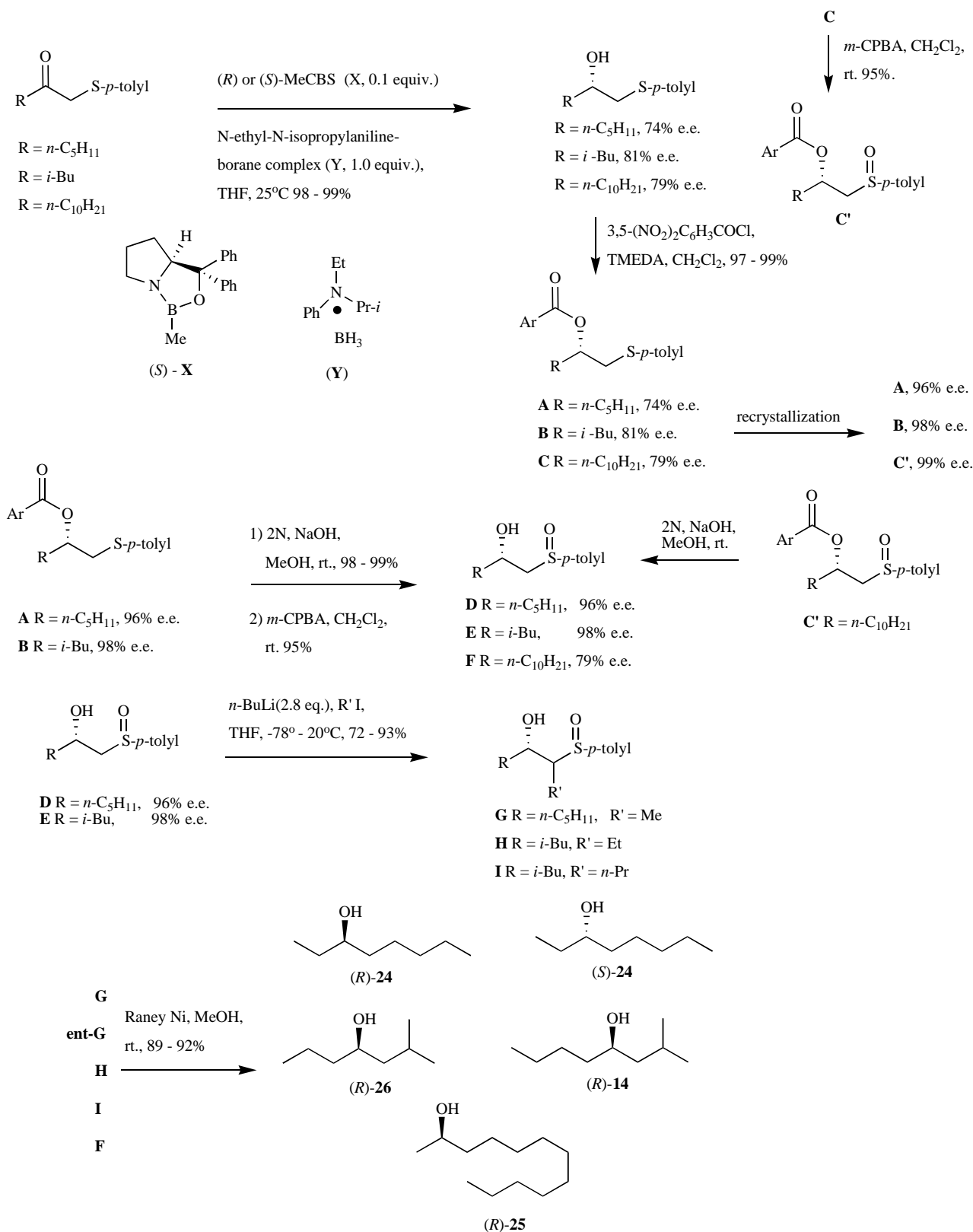
Nostrenol [(2*R*,6*Z*)-undec-6-en-2-ol, **27**] was identified from thoracic glands of the ant-lion species *Euroleon nostras* and *Grobus bore* [58]. Chow and Kitching [59] described the synthesis of this and other insect pheromones (sections 5.9., 5.11., 5.12., and 6.4.) by hydrolytic kinetic resolution (HKR) of functionalised epoxides, using (salen)Co(OAc) complexes (*R,R*)-**Z** and (*S,S*)-**Z** (Fig. 1), providing enantiomerically enriched epoxides and diols. The synthesis of **27** started from undec-1-en-6-yne (**A**), which was epoxidised with *m*-chloroperbenzoic acid in dichloromethane [59]. HKR of the resulting epoxide furnished the (*S*)-epoxide **B** and diol **C**. (*S*)-**B** was further transformed to **27** (Scheme 21)

5.9. (-)-(*R*)- and (+)-(*S*)-10-Methyldodecyl acetate (**28**)

(*R*)- and (*S*)-10-Methyldodecyl acetate (**28**) are components of the pheromone of the lesser tea tortrix moth, *Adoxophes* spp. [60, 61]. Chow and Kitching [59] described the synthesis of both enantiomers. Benzyl ether **A** was epoxidized with *m*-CPBA and the enantiomers of the resulting epoxide **B** were kinetically resolved by stirring with 0.5 mol% of (*R,R*)-**Z** and 0.55 mol equiv. of H₂O at room temperature (22°C) for ca. 24 h, giving (*R*)-epoxide **B** and (*S*)-diol **C**, which were straightforwardly converted to (*R*)-**28** and (*S*)-**28**, respectively (Scheme 22).

5.10. 6-Acetoxy-19-methylnonacosane (**29**) and 7-acetoxy-15-methylnonacosane (**30**)

In 1993, Pomonis *et al.* reported the identification of six-teen compounds in a pheromonally active HPLC fraction extracted from the females of the screw-worm fly *Cochliomyia hominivorax* [62]. In 2002, Furukawa *et al.* synthesized five possible pheromone candidates [63], and a bioassay of these five compounds showed activity for 6-acetoxy-19-



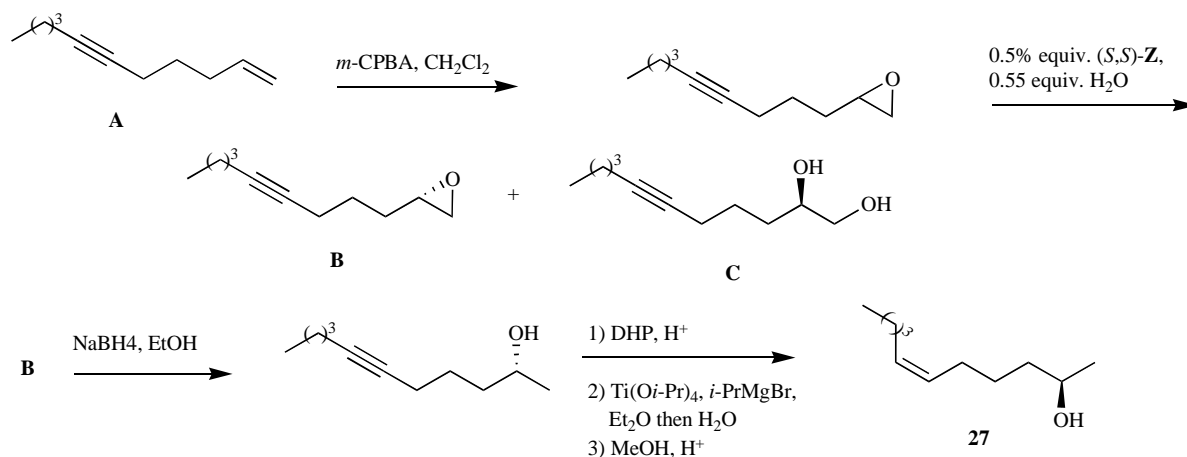
Scheme 20.

methylnonacosane (**29**) and 7-acetoxy-15-methylnonacosane (**30**).

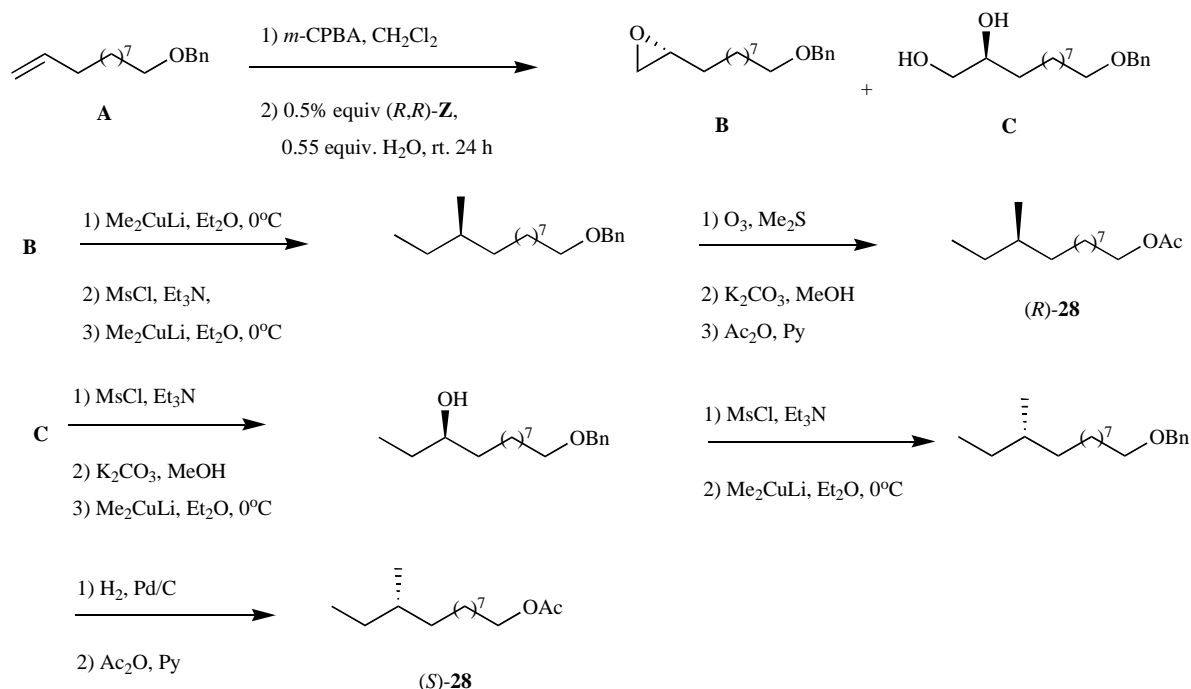
Mori *et al.* described a synthesis of all possible stereoisomers of **29** [64] and **30** [65]. Starting from the enantiomers of citronellal and oct-1-yn-3-ol, all four stereoisomers of **29**

(Scheme 23) were synthesized with high stereochemical purities (more than 90% e.e. at C-6; about 97% e.e. at C-19).

The stereoisomers of **30** (Scheme 24) were obtained starting with the pure enantiomers of citronellal. The (*R*) and (*S*) configuration, respectively, was carried through to C-15,



Scheme 21.



Scheme 22.

while a lipase-catalyzed asymmetric acetylation defined the absolute configuration at C-7.

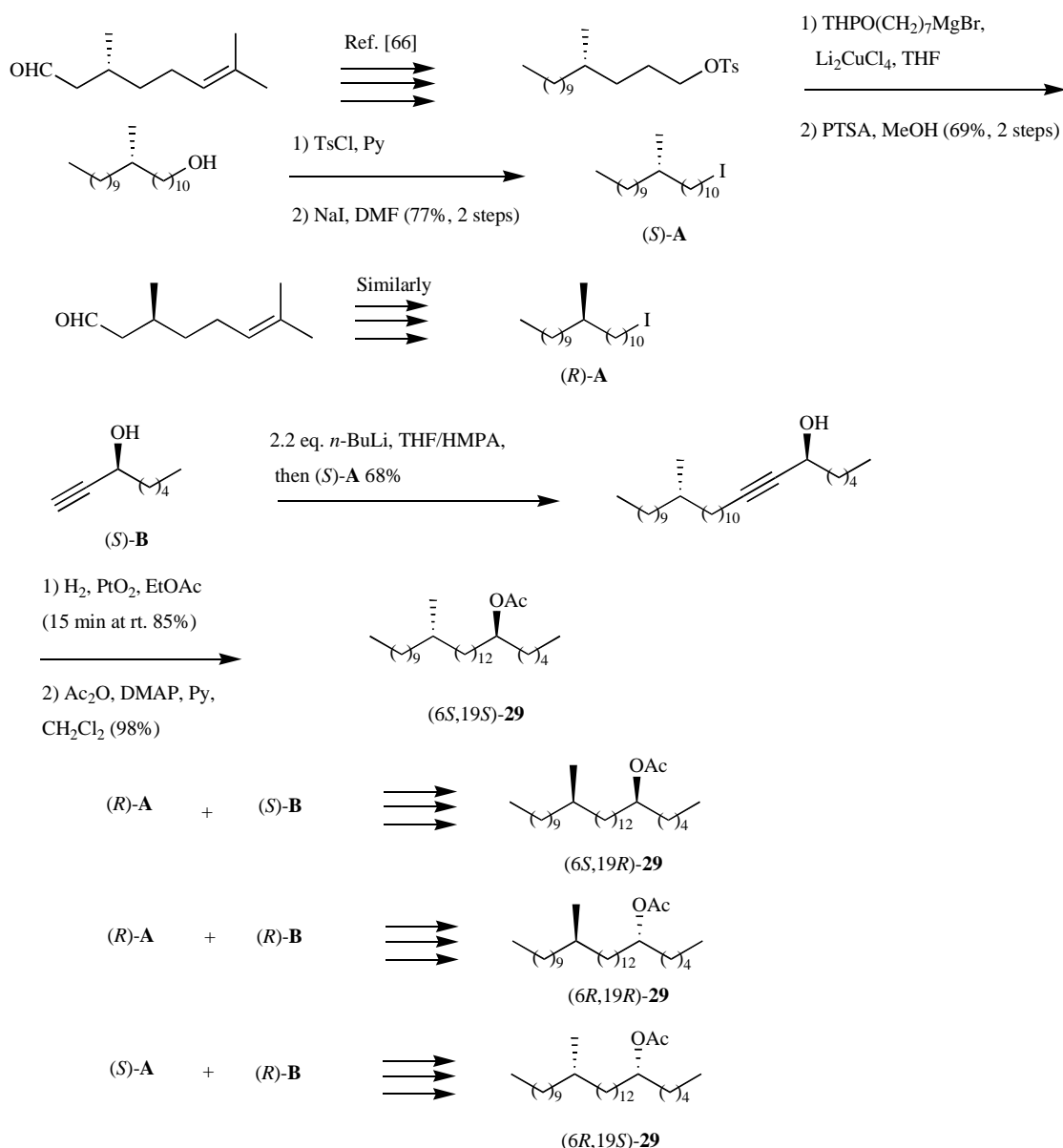
5.11. (2*S*,11*S*)-2,11-Diacetoxytridecane (**31**) and (2*S*,12*S*)-2,12-diacetoxytridecane (**32**)

(2*S*,11*S*)-2,11-Diacetoxytridecane (**31**) and (2*S*,12*S*)-2,12-diacetoxytridecane (**32**) are two of the three active components identified by coupled gas chromatography–electroantennography of extracts from the pheromone glands of female pea midges (*Contarinia pisi*) which are serious pests of commercial peas [67]. The key step in the synthesis of diester **31** was the HKR of a stereoisomeric mixture of the diepoxide **A** affording the epoxydiol (2*R*,11*S*)-**B**, which was transformed to (2*S*,11*S*)-**31** [59] (Scheme 25).

Similarly, HKR of a stereoisomeric mixture of diepoxide **C** afforded pure (2*R*,12*R*)-**C**, which was transformed to (2*S*,12*S*)-**32** [59] (Scheme 26).

5.12. (1*R*,7*R*)-1,7-Dimethylnonyl propanoate (**33**)

Various isomers of 1,7-dimethylnonyl propanoate (**33**) exhibit attractancy for males of corn rootworms, with the western corn rootworm (*Diabrotica virgifera virgifera*) and the northern corn rootworm (*D. barberi*) responding strongly to the (1*R*,7*R*)-isomer [68]. The synthesis of this isomer is shown in Scheme 27. The racemic bisepoxide **A** obtained by *m*-CPBA epoxidation of 1,8-nonadiene was treated with 1.0% equiv. of (2*R*,2*R*)-**Z** and 0.8 equiv. of H₂O, providing a mixture of the (2*S*,2*S*)-bisepoxide, the (2*S*,2*S*)-epoxydiol **B** and the (2*S*,2*S*)-tetraol. After column chromatography, epoxydiol **B**



Scheme 23.

was transformed to (1*R*,7*R*)-**33** in nine steps [59] (Scheme 27).

6. SYNTHESIS OF NON-ISOPRENOIDAL ALDEHYDES, KETONES, ACIDS, AND ESTERS AS PHEROMONES

6.1. (*R*)-4-Methylnonan-1-ol (**34**) and (4*R*,8*RS*)-4,8-dimethyldecanal (**35**)

(*R*)-4-Methylnonan-1-ol (**34**) was identified as a sex attractant of the yellow mealworm *Tenebrio molitor* by Tanaka [69, 70] *et al.* In 1980, Suzuki identified 4,8-dimethyldecanal (**35**) as the aggregation pheromone of the red flour beetle (*Tribolium castaneum*) and of the confused beetle (*Tribolium confusum*), notorious pests of various stored products [71, 72] Mori and co-workers [73, 74] established the absolute configuration of natural **35** as (4*R*,8*R*). Suzuki *et al.* [75] later found that a 8:2 mixture of the isomers (4*R*,8*R*)- and

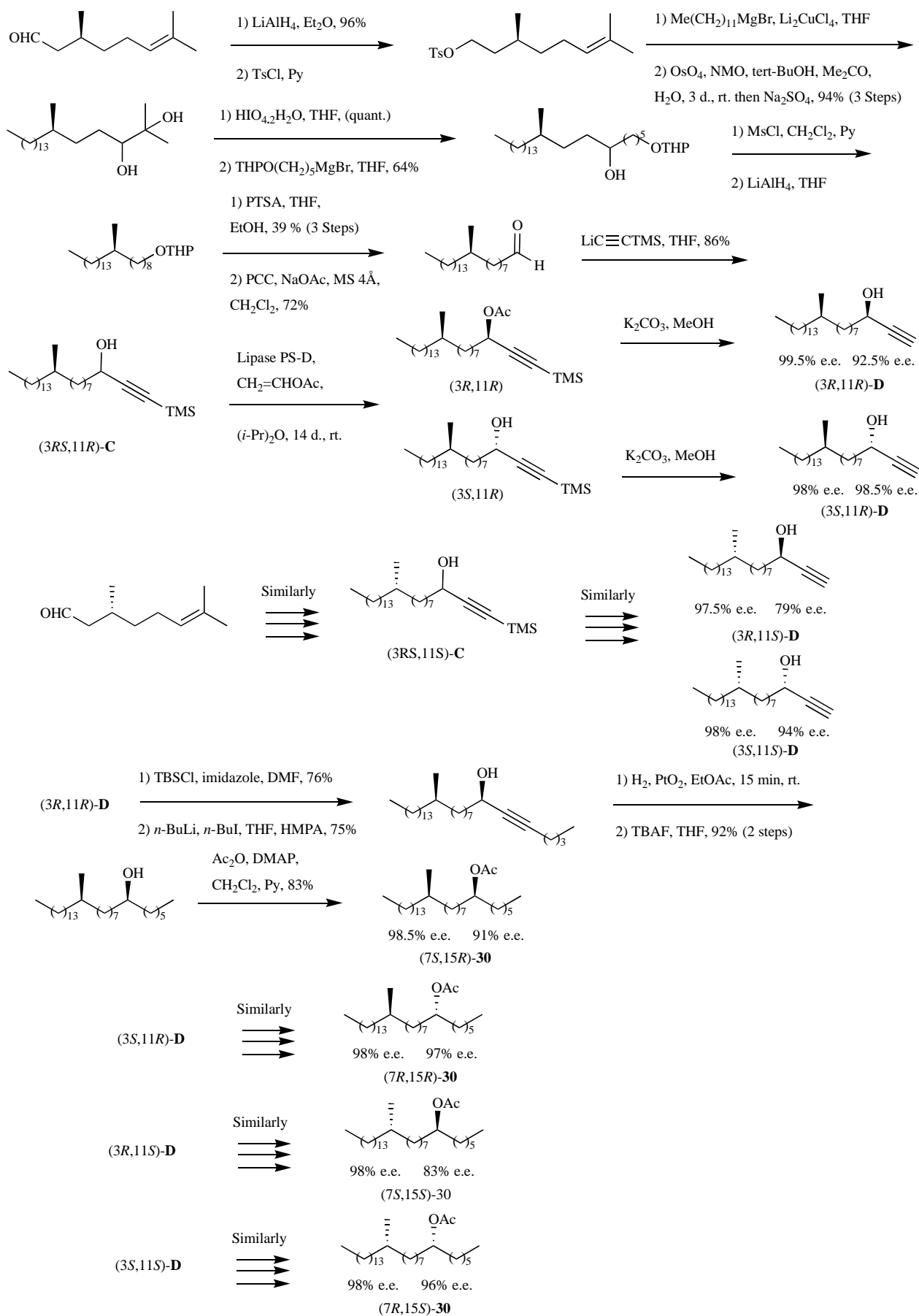
(4*R*,8*S*) was about 10 times more active than (4*R*,8*R*)-**35** alone.

Ismuratov and co-workers [76] described a synthesis of **34** and **35** starting from (*S*)-3,7-dimethyl-1,6-octadiene. The hydroxyketone **B**, obtained by ozonolysis of the unsaturated ketone **A** followed by reductive workup, was either transformed to (*R*)-**34** or (4*R*,8*RS*)-**35** (Scheme 28).

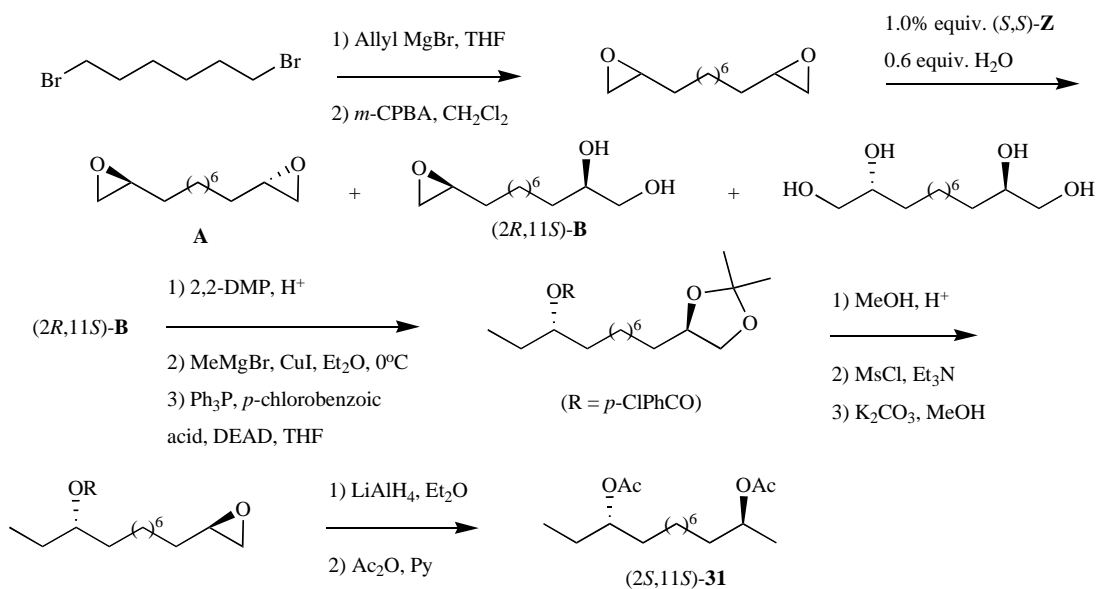
6.2. (*E*)-2-(4-Methyl-3-pentenylidene)butanedial (**36**) (β-acaridial)

β-Acaridial [(*E*)-2-(4-methyl-3-pentenylidene)butanedial, **36**] is known as the sex pheromone [78] and aggregation pheromone [79] of *Caloglyphus polyphyllae* and as the alarm pheromone [80] of *Tyrophagus longior*.

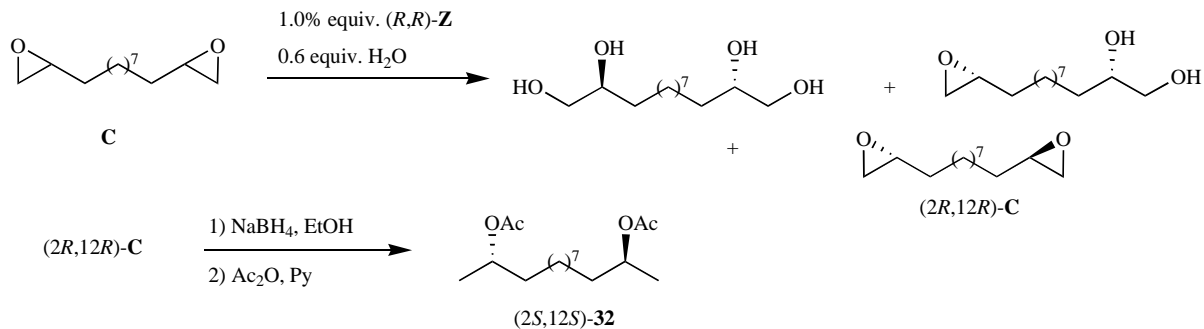
Shimizu *et al.* [81] described the synthesis of **36** in five steps from 1,2,4-butanetriol with 19 % overall yield (Scheme 29). *Z*-selective Wittig reaction allowed the preparation of



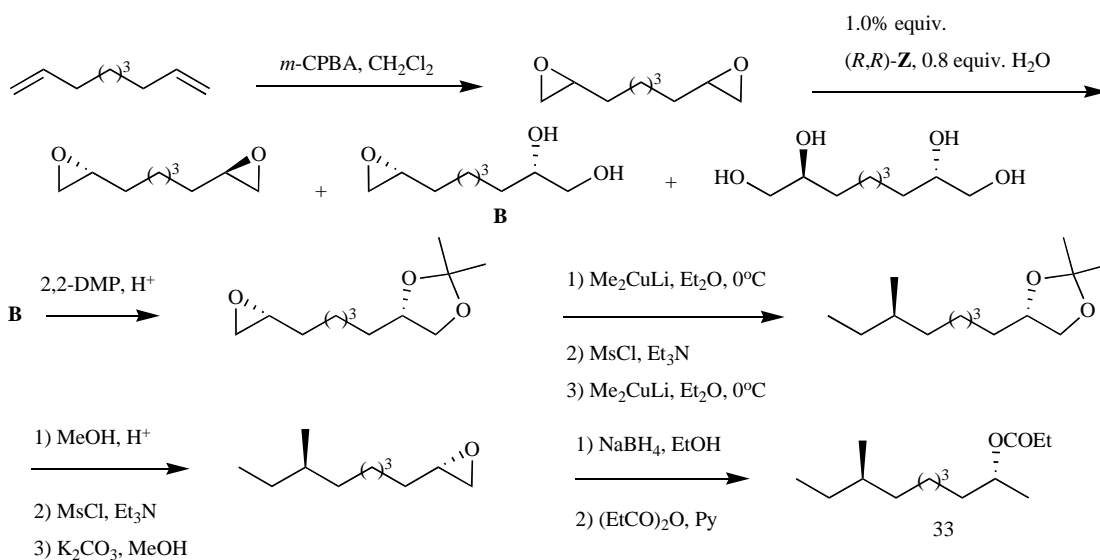
Scheme 24.



Scheme 25.



Scheme 26.

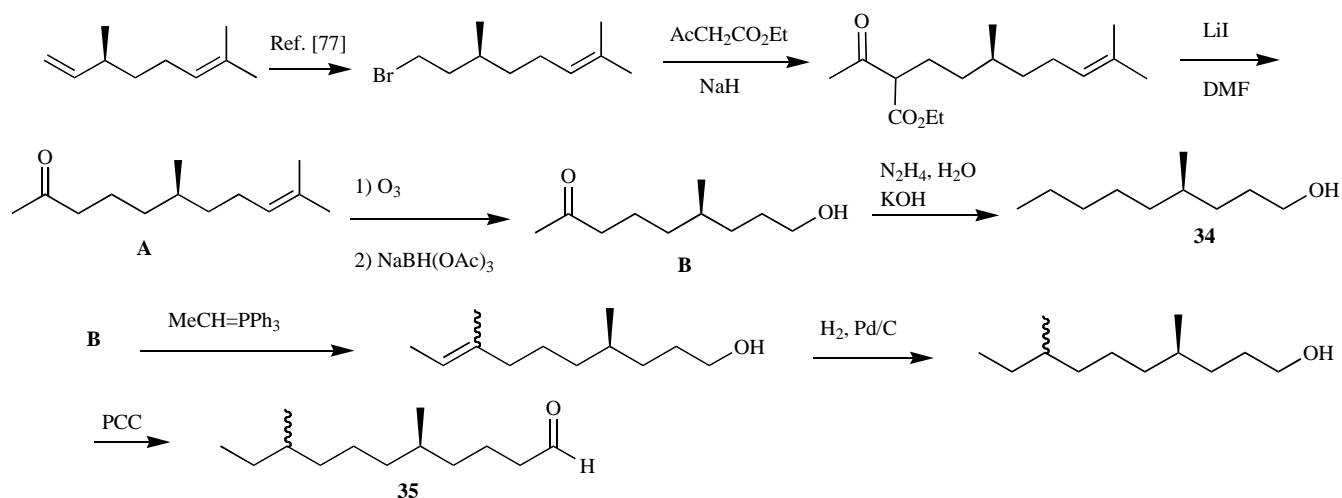


Scheme 27.

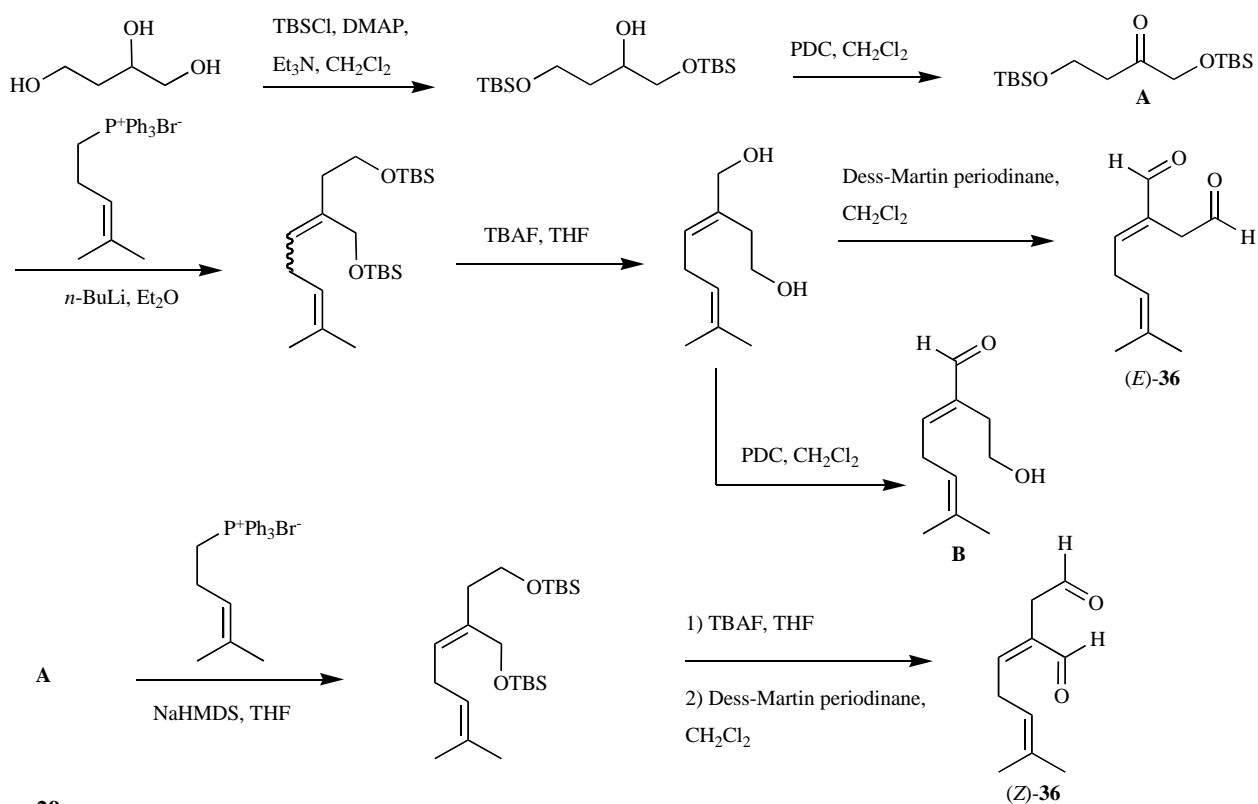
the geometric isomer, (*Z*)-**36** (β -(*Z*)-acardial), which was detected as a trace component in the secretion of *C. polyphyllae*, together with the (*E*)-configured hydroxy aldehyde **B**.

6.3. (*R*)-10-Methyl-2-tridecanone (**37**)

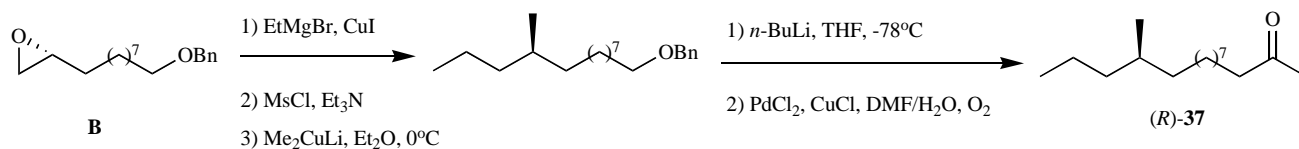
10-Methyl-2-tridecanone (**37**) is the sex pheromone of the southern corn rootworm (*Diabrotica undecimpunctata howardi*), and biological evaluation of the enantiomers indi-



Scheme 28.



Scheme 29.



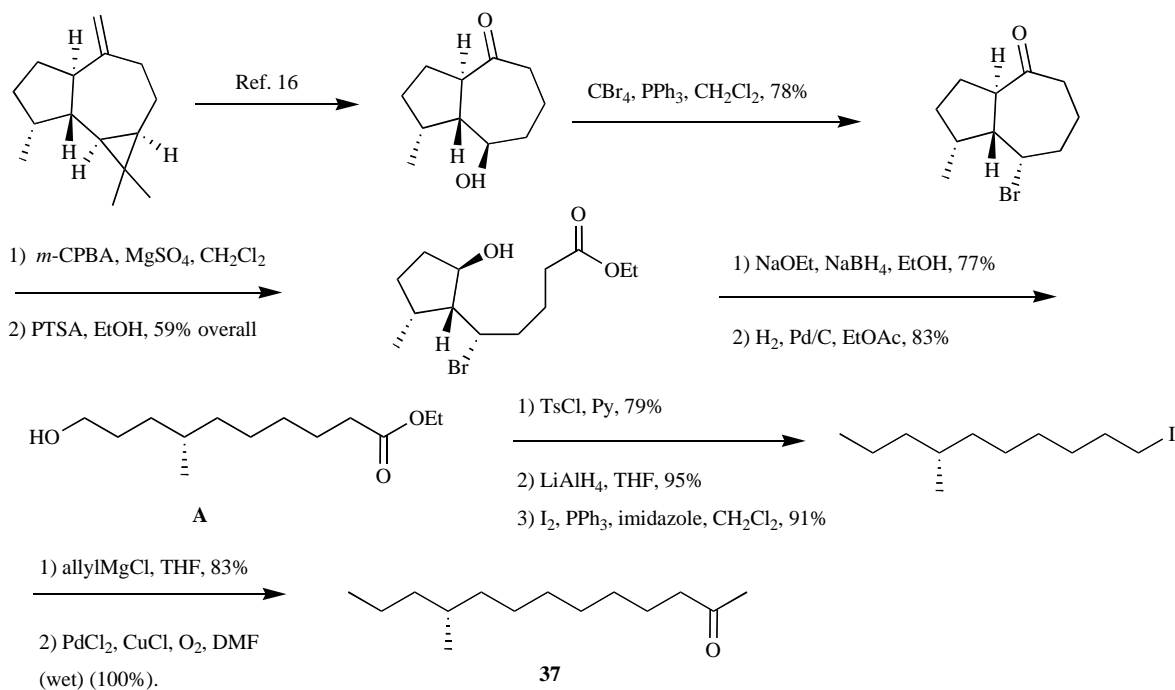
Scheme 30.

cated that the (*R*) enantiomer was preferred by males [82]. The epoxide (*R*)-**B** from scheme 22 was converted to (*R*)-**37** in five steps (Scheme 30).

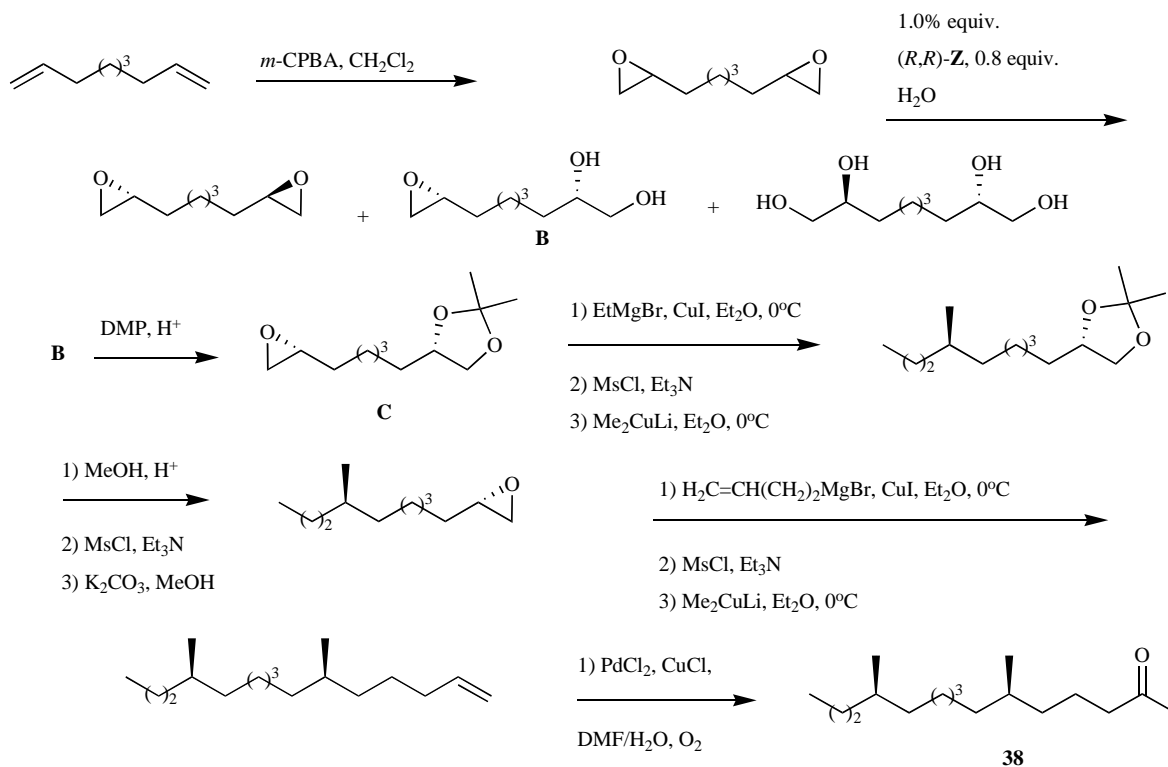
Another synthesis took a similar approach as shown in scheme 3, starting from (+)-aromadendrene [16] (Scheme 31).

6.4. (6*R*,12*R*)-6,12-Dimethylpentadecan-2-one (38)

(6*R*,12*R*)-6,12-Dimethylpentadecan-2-one (**38**) is the female produced sex pheromone of the banded cucumber beetle (*Diabrotica balteata*), the larvae of which are serious pests of crops such as cucurbits and sweet potatoes [83].



Scheme 31.



Scheme 32.

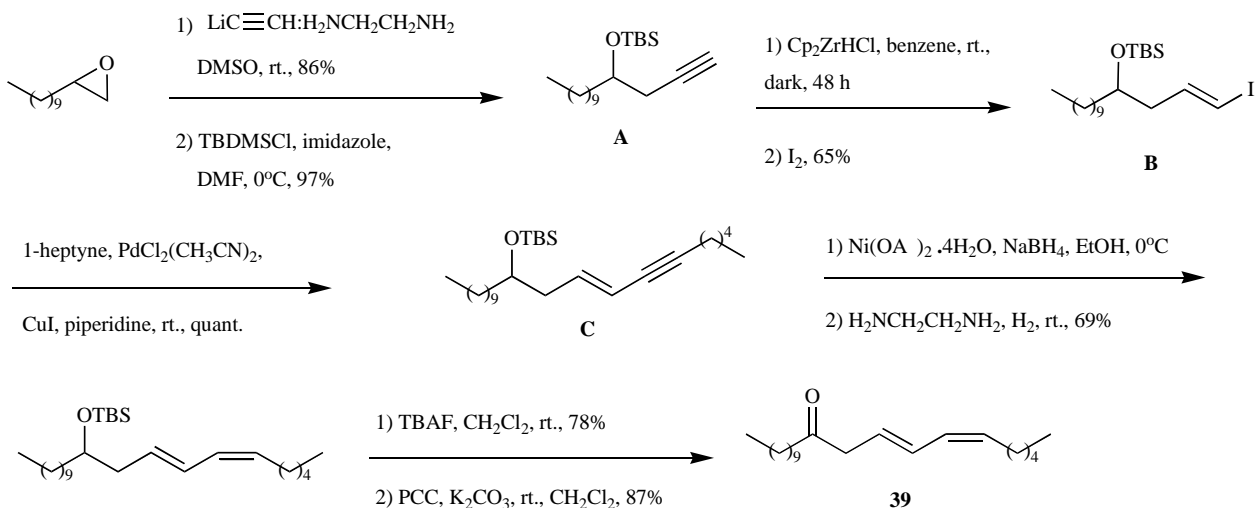
Chow and Kitching [59] described the synthesis of (6*R*,12*R*)-**38** from epoxy-acetonide **C** (Scheme 32).

6.5. (6*Z*,8*E*)-Heneicosa-6,8-dien-11-one (**39**) and (*Z*)-6-heneicosen-11-one (**40**)

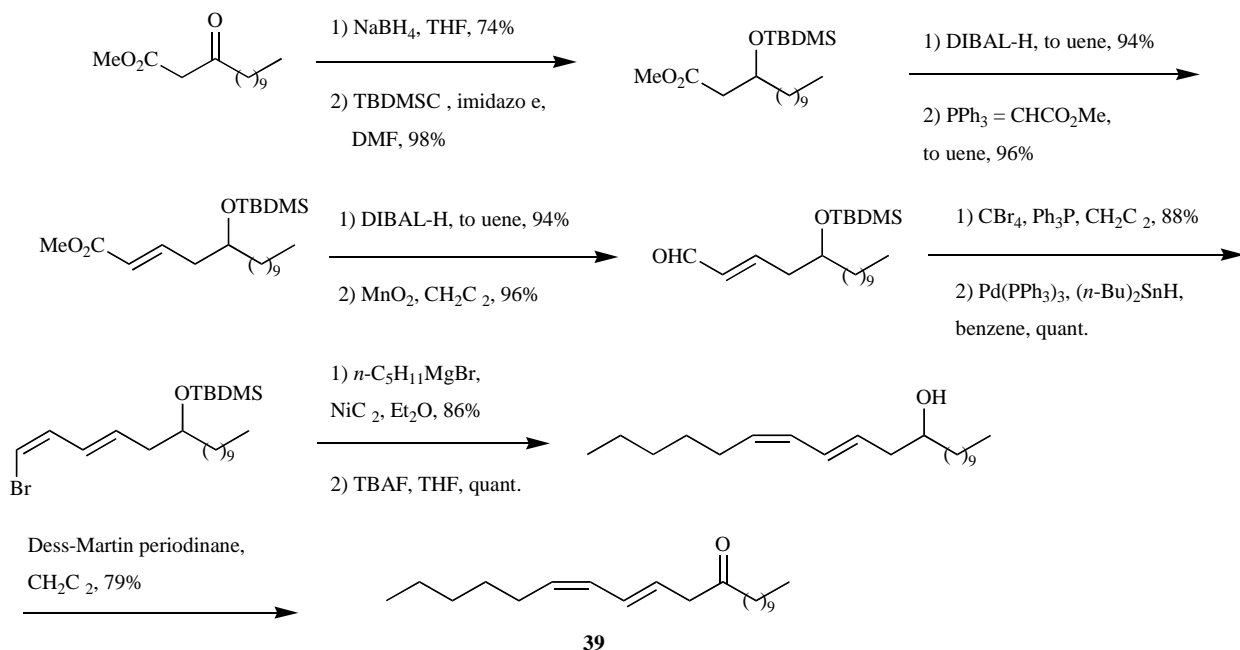
(6*Z*,8*E*)-Heneicosa-6,8-dien-11-one (**39**) and (6*Z*)-heneicos-6-en-11-one (**40**) are sex pheromone components of the Douglas-fir tussock moth (*Orgyia pseudotsugata*)

[84]. Additionally, **39** has been identified as a major sex pheromone component of *O. vetusta* [85] and was also found in the painted apple moth (*Teia anartoides*) [86].

Jury *et al.* [87] reported the synthesis of **39** in seven steps from 1,2-epoxydodecane in an overall yield of 25% (Scheme 33). (*E*)-Vinyl iodide **B** was obtained as a single stereoisomer in good yield by the hydrozirconation-iodination of acetylene **A** with Schwartz's reagent and freshly sublimed



Scheme 33.



Scheme 34.

iodine. The (*E,Z*)-diene system was obtained in good yield by the partial reduction of **C** in the presence of catalytic P2-Ni under a hydrogen atmosphere.

Muto and Mori [31] described the synthesis of **39**, employing a Wittig reaction for the formation of the (*8E*) double bond, while the conjugated (*6Z*) double bond was established by Uenishi's procedure (CBr_4 , PPh_3) [88] (Scheme 34).

Comeskey *et al.* [89] described the stereospecific synthesis of all four isomers of **39**, using the Suzuki coupling of vinylic boronic acids **A** and **C** and vinylic iodide intermediates **B** and **D** (Scheme 35).

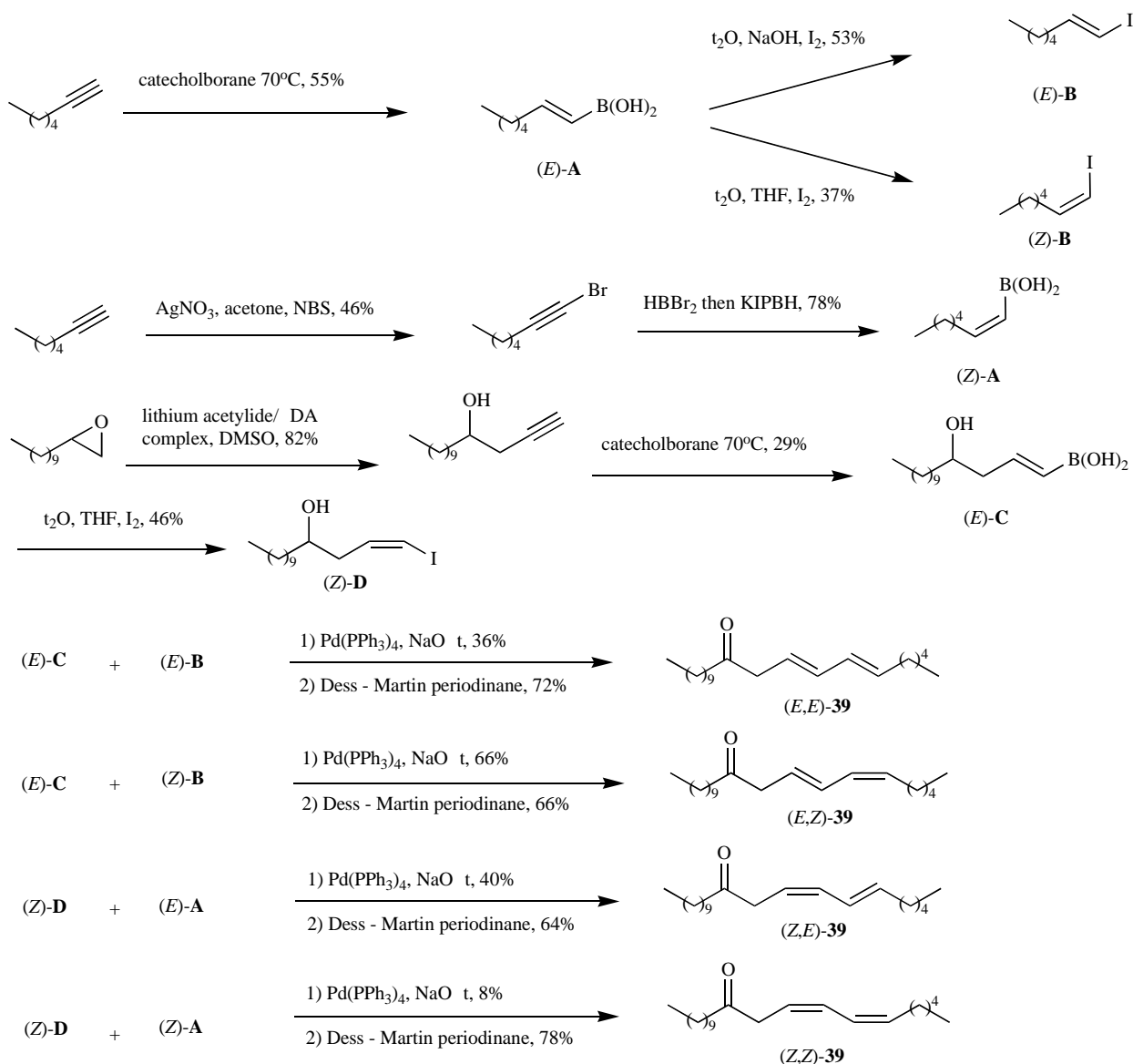
Muto and Mori [31] described the synthesis of (*Z*)-6-heneicosen-11-one (**40**), starting from 2-dodecanone in three steps and 65% overall yield (Scheme 36).

6.6. (4*S*,6*S*,7*S*)-7-Hydroxy-4,6-dimethyl-3-nonanone (**41**) (Serricornin)

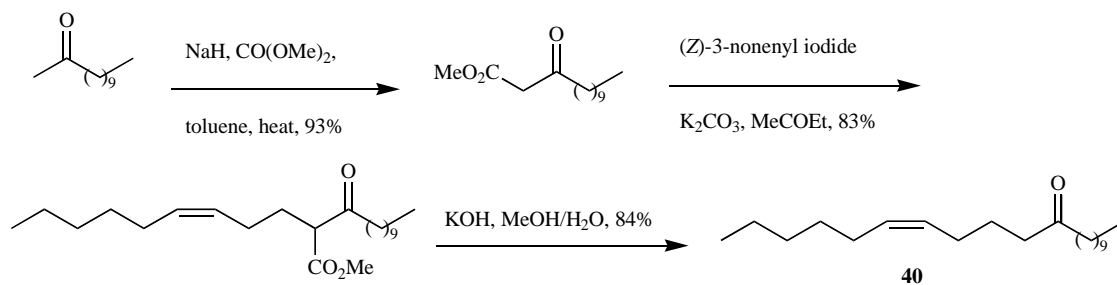
Serricornin [(4*S*,6*S*,7*S*)-7-hydroxy-4,6-dimethyl-3-nonanone], (*4S,6S,7S*)-**41** is the sex pheromone produced by female cigarette beetle, *Lasioderma serricorne*. [90-95]. Zlo-kazov and Veselovsky [96] developed a synthesis of **41** starting from (*4S,5E*)-4-methylhept-5-enenitrile [97] (Scheme 37).

6.7. (4*R*,6*S*,7*R*)-7-Hydroxy-4,6-dimethyl-3-nonanone (**41**) and (3*R*,5*S*,6*R*)-6-hydroxy-3,5-dimethyl-2-octanone (**42**)

In 1999, Francke *et al.* found a stereoisomer of serricornin as a pheromone component of the beetle *Dinoderus bifoveolatus* [98]. The synthesis of (*4R,6S,7R*)-**41** and (*3R,5S,6R*)-6-hydroxy-3,5-dimethyl-2-nonanone (**42**) and



Scheme 35.

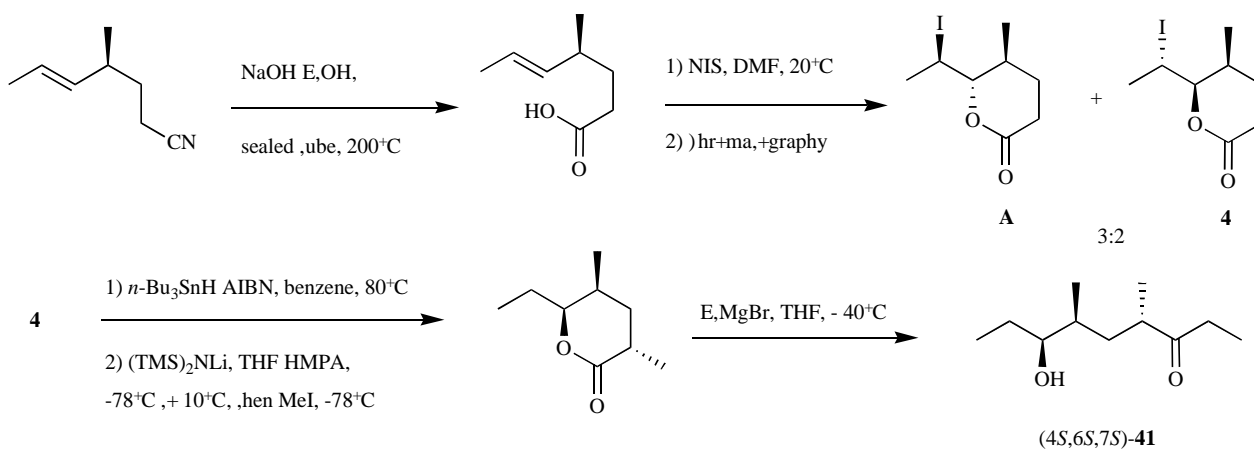


Scheme 36.

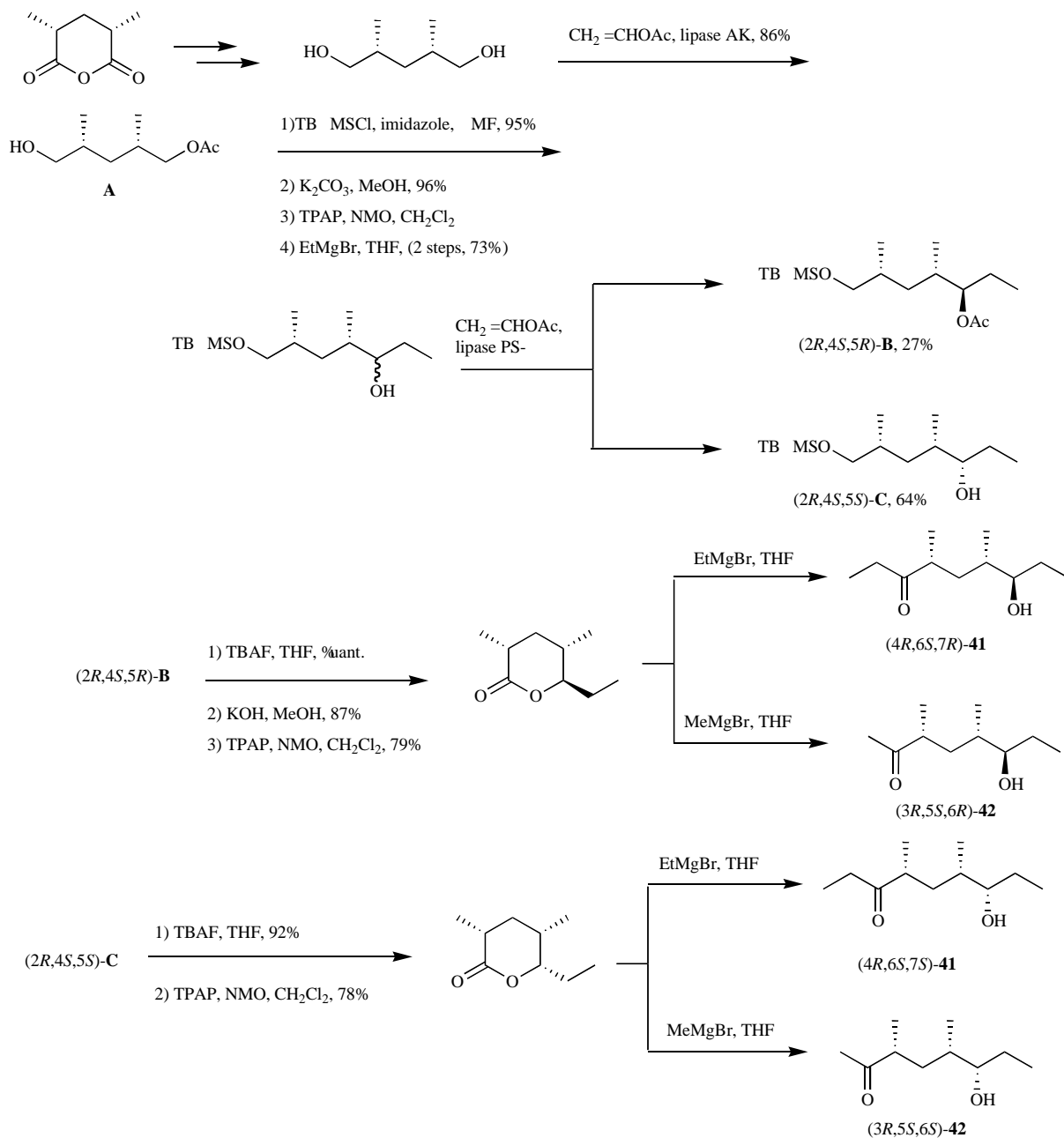
their stereoisomers was performed by Masuda *et al.* [99]. The starting chiral building block **A** was obtained by lipase AK-catalyzed asymmetric acetylation of *meso*-2,4-dimethyl-1,5-pentanediol. Asymmetric acetylation with vinyl acetate and lipase PS-D (Amano) furnished the acetate (2*R*,4*S*,5*R*)-**B** and the alcohol (2*R*,4*S*,5*S*)-**C**, which were further transformed to the target compounds (Scheme 38).

6.8. (*E*)-2,4-Dimethyl-2-hexenoic acid (**43**)

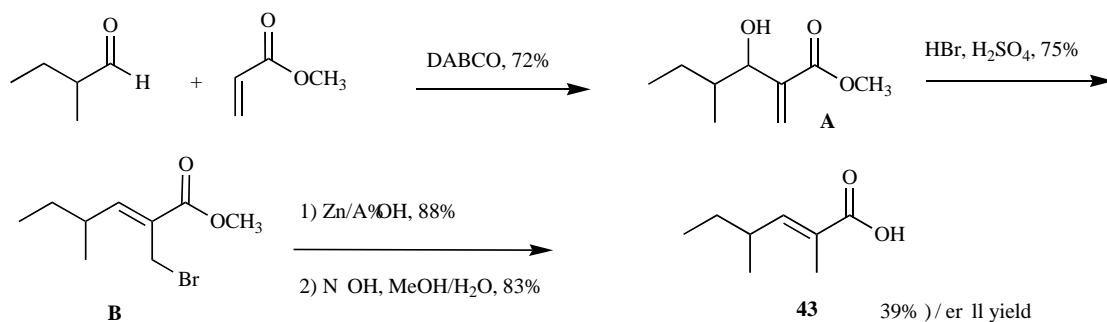
(*E*)-2,4-Dimethyl-2-hexenoic acid (**43**) is a caste-specific substance present in the mandibular glands of male ants in the genus *Camponotus* [100]. Fernandes *et al.* [101] described a synthesis of **43** with high stereoselectivity and 39% overall yield, by zinc-promoted reduction of the 2-(bromo-



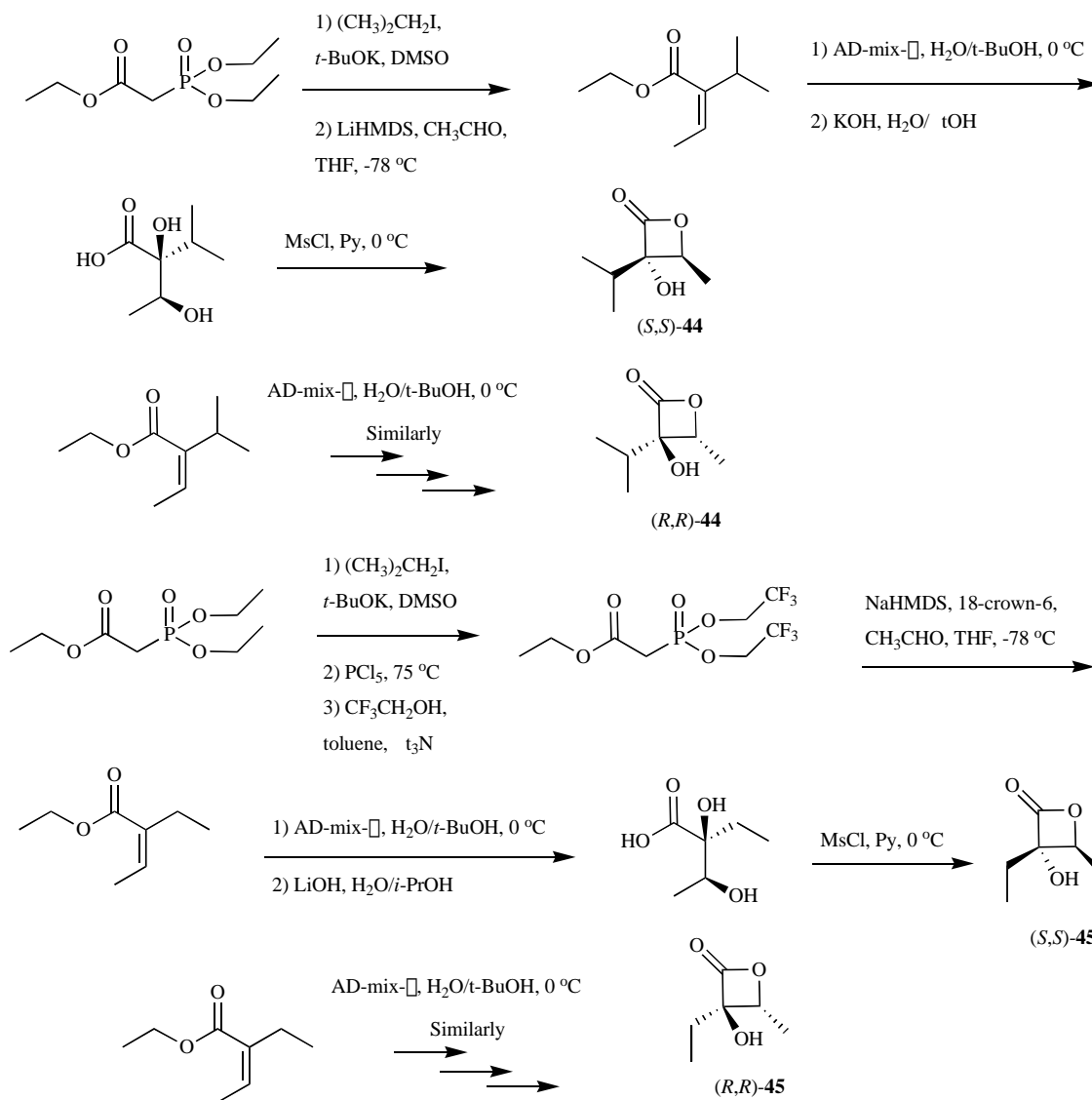
Scheme 37.



Scheme 38.



Scheme 39.



Scheme 40.

methyl) alkenoate **B** derived from the corresponding Baylis–Hillman adduct **A** (Scheme 39).

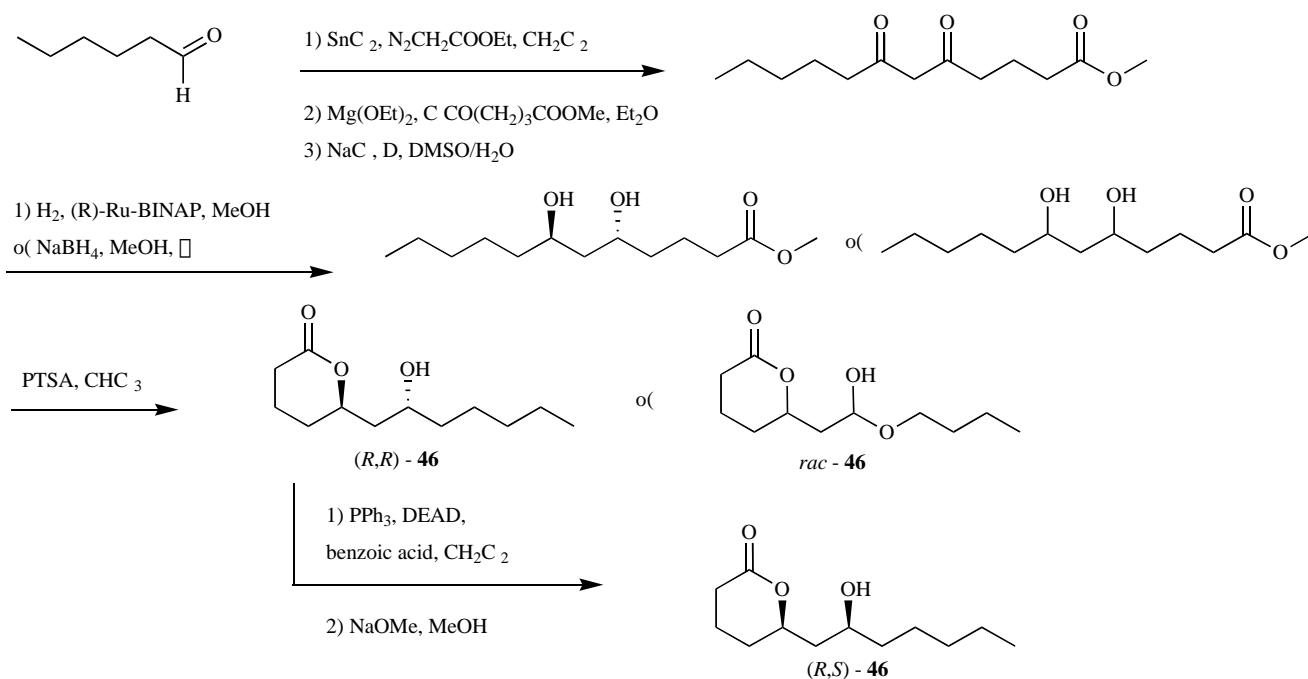
7. SYNTHESIS OF LACTONES AS PHEROMONES

7.1. 2-Hydroxy-2-(1-methylethyl)-3-butanolide (**44**), 2-ethyl-2-hydroxy-3-butanolide (**45**), 7-hydroxy-5-dodecanolide (**46**)

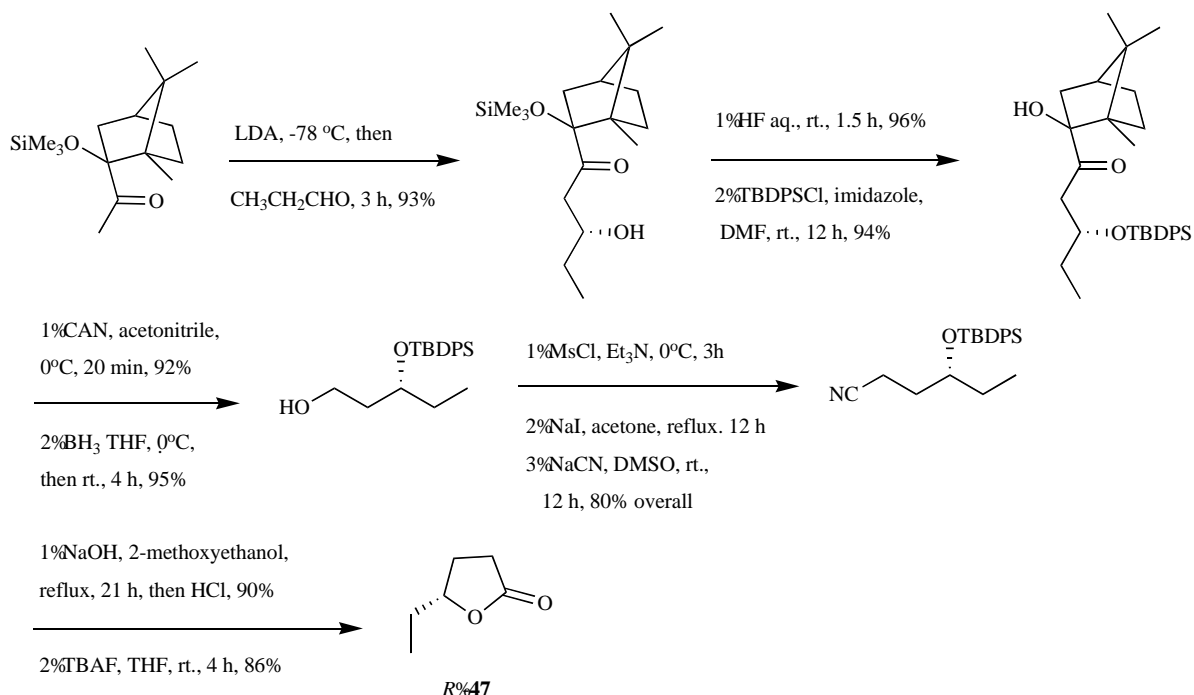
Schulz and Nishida [102, 103] reported that males of the giant white butterfly *Idea leuconoe* release a complex mix-

ture of compounds containing alkaloids, aromatics, terpenoids, hydrocarbons, and lactones, during courtship.

The pure (*S,S*) and (*R,R*) enantiomers of the β -lactones 2-hydroxy-2-(1-methylethyl)-3-butanolide (**44**) and 2-ethyl-2-hydroxy-3-butanolide (**45**) were synthesized based on a controlled C–C coupling by a Horner–Wadsworth–Emmons approach, followed by asymmetric dihydroxylation (Scheme 40). The absolute configuration of the natural lactones was determined to be (*S,S*) by enantioselective gas chromatography [104].



Scheme 41.



Scheme 42.

The δ -lactone 7-hydroxy-5-dodecanolide (**46**) was synthesized as a mixture of stereoisomers and as the pure (*R,R*) isomer, the latter by enantioselective reduction of the methyl dioxoalkanoate precursor employing Ru-BINAP catalyst. The (*R,S*) isomer was obtained by Mitsunobu inversion of the (*R,R*) isomer (Scheme 41). The natural product was shown to be a mixture of all stereoisomers [104].

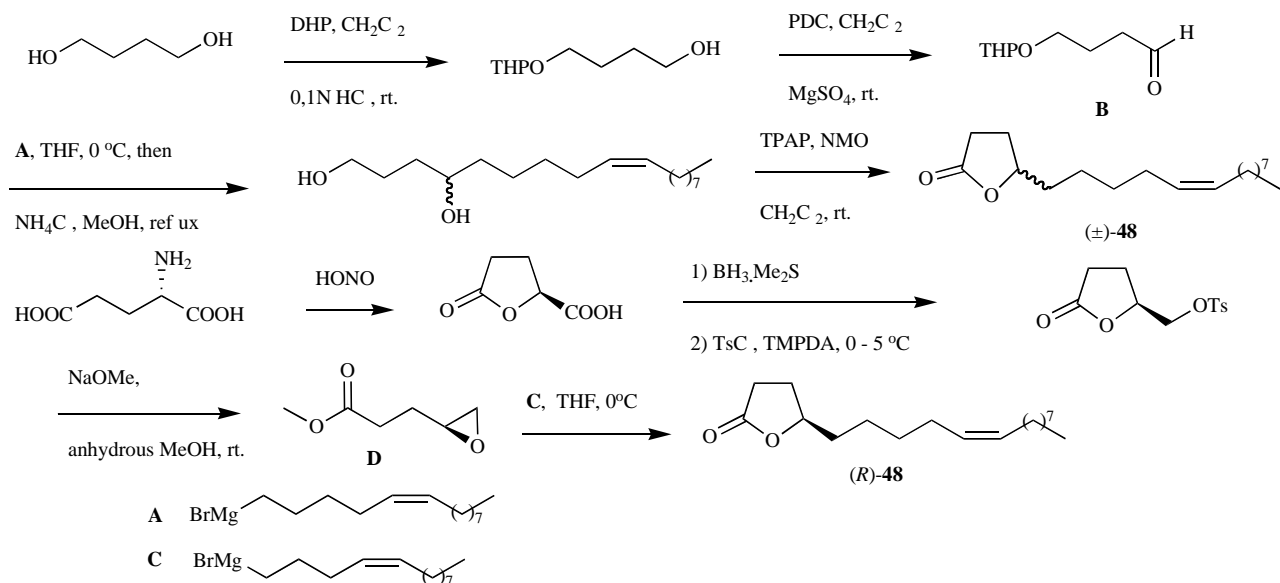
7.2. (*R*)-4-Hexanolide (**47**)

(*R*)-4-Hexanolide (**47**) was identified as a component of the sex pheromone of females of the dermestid beetle *Trogoderma glabrum* [105, 106].

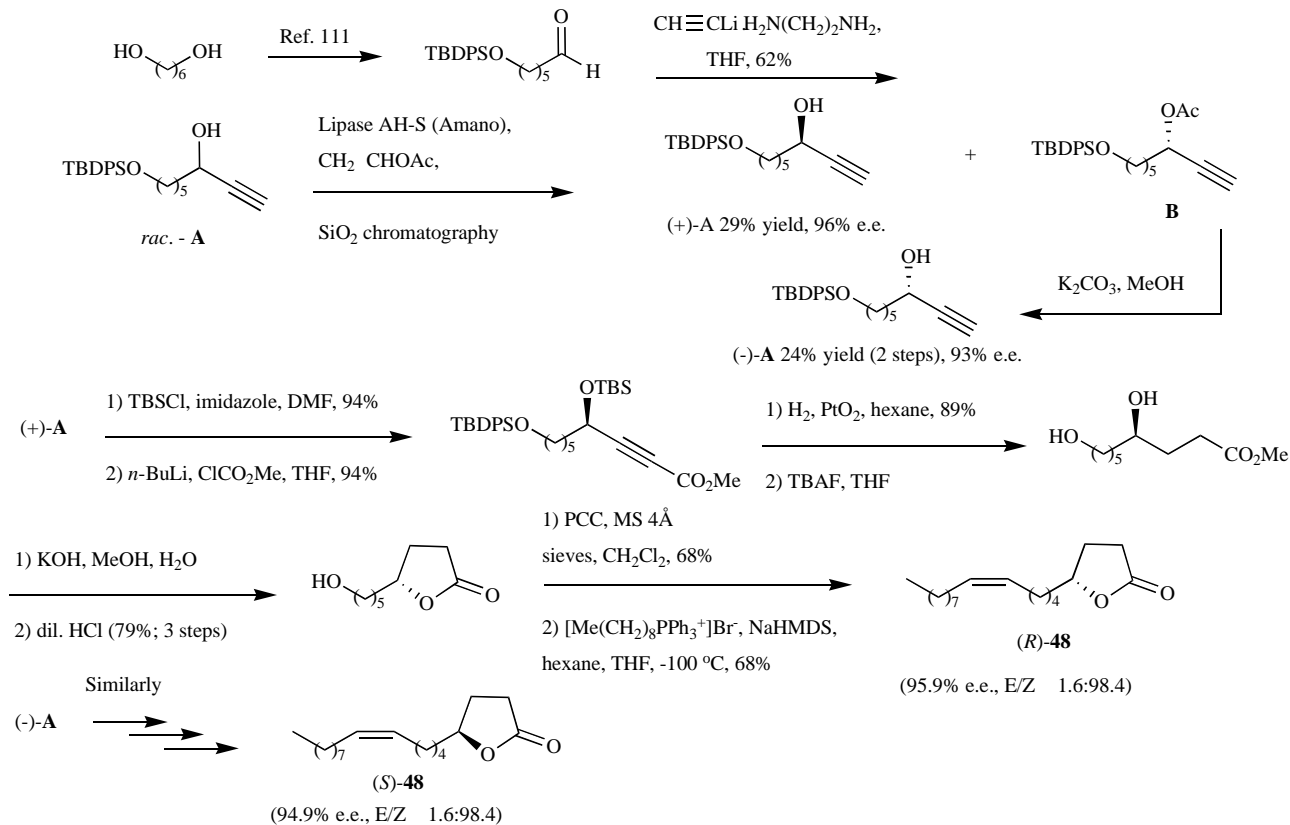
Arceo *et al.* [107] described the synthesis of **47** with 45% overall yield in high enantiomeric purity using a chiral auxiliary derived from (*S*)-camphor (Scheme 42).

7.3. (4*R*,9*Z*)-Octadec-9-en-4-olide (**48**)

Cossé *et al.* [108] reported the occurrence of a female-specific compound from the currant stem girdler (*Janus integer*), which they identified as the chiral lactone (*Z*)-octadec-9-en-4-olide (**48**). The structure was proven by synthesis of the racemic compound. Upon chiral GC analysis, only one enantiomer was detected to be produced by the insects, but the absolute configuration was not determined.



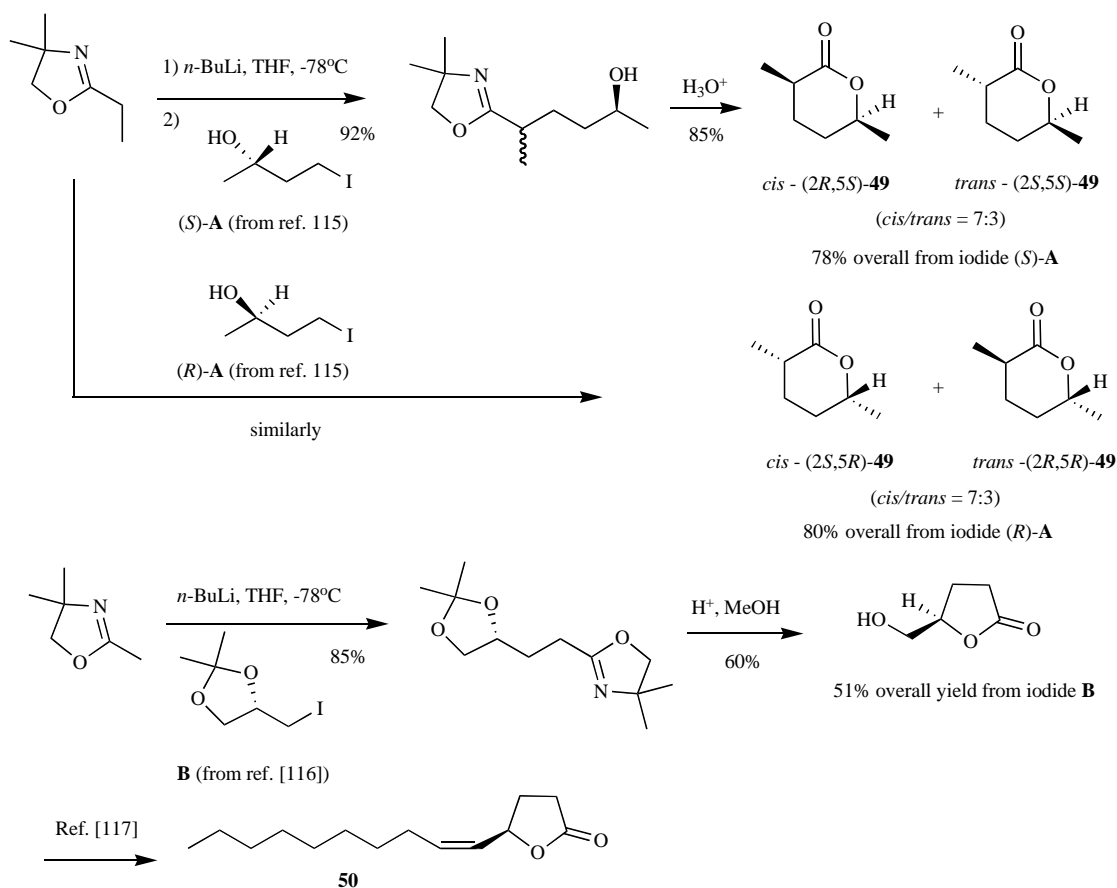
Scheme 43.



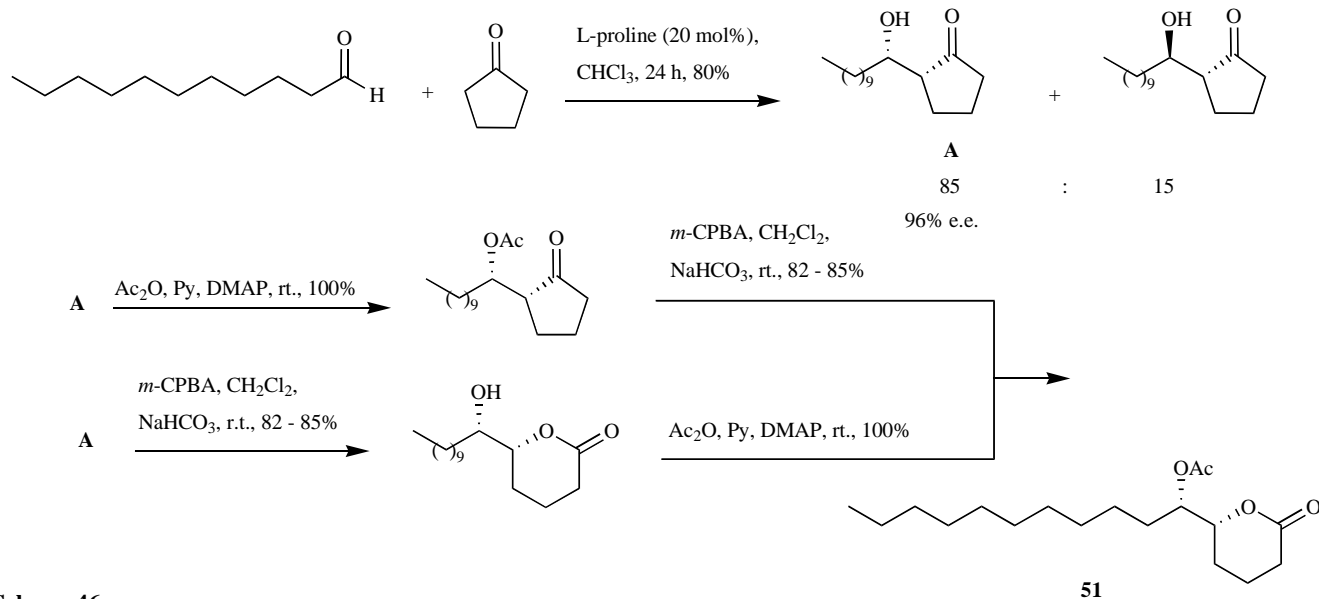
Scheme 44.

James *et al.* [109] described the synthesis of racemic and the pure enantiomers of **48** and determined the absolute configuration of the natural compound to be (*R*). In the racemic route, Grignard reagent **A** was added to aldehyde **B**, followed by deprotection and selective oxidation of the primary hydroxyl group with tetrapropylammonium perruthenate (TPAP). (*R*)-**48** was synthesized by addition of Grignard reagent **C** to the chiral epoxide **D** prepared from (*S*)-(+)-glutamic acid (Scheme 43).

Shibata and Mori [110] synthesized both enantiomers of **48**. The key step was the lipase-catalyzed asymmetric acetylation of a racemic mixture of the acetylenic alcohol **A** with vinyl acetate and lipase AH-S, which furnished (+)-**A** (96% e.e.) and the acetylated product **B**, which was hydrolyzed to give (-)-**A** (93% e.e.). (+)-**A** and (-)-**A** were transformed to (*R*)-**48** and (*S*)-**48**, respectively (Scheme 44).



Scheme 45.



Scheme 46.

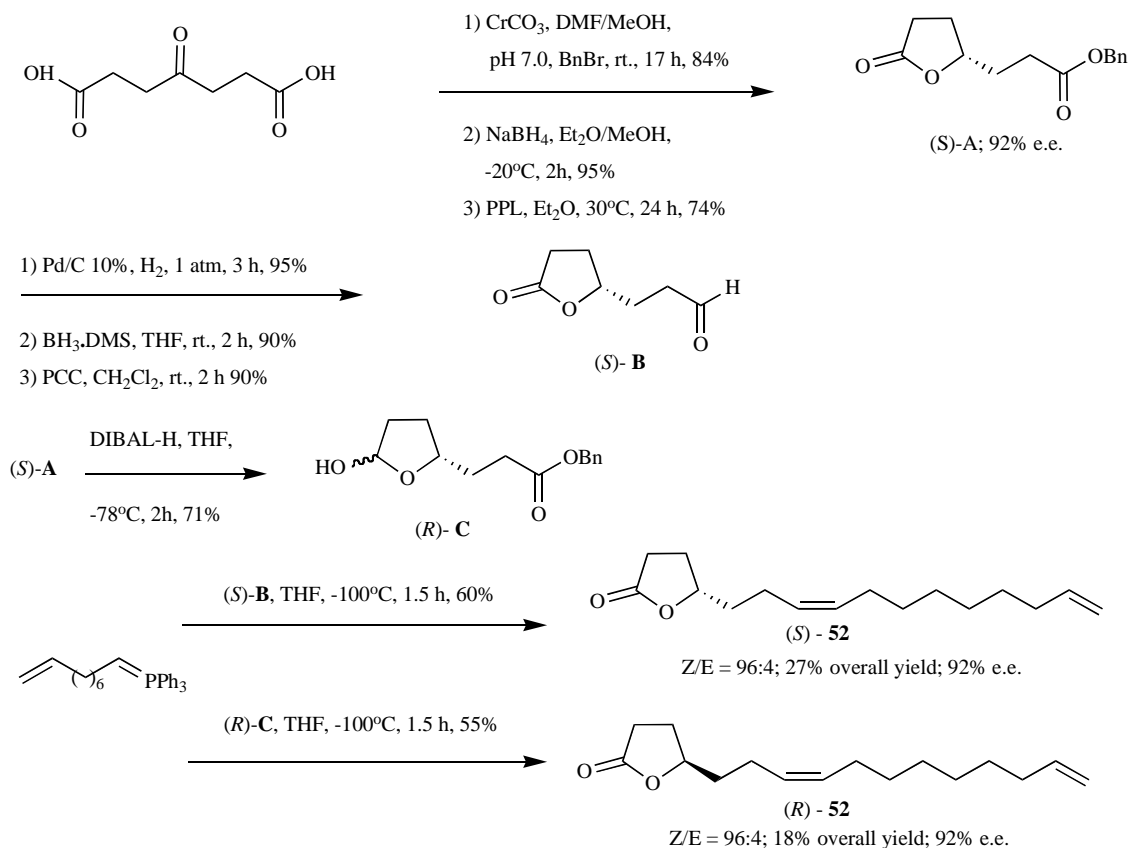
7.4. *cis*- and *trans*-2-Methyl-5-hexanolide (49) and (4*R*,5*Z*)-tetradec-5-en-4-olide (50)

cis-2-Methyl-5-hexanolide (49) is a component of the pheromone blend of the carpenter bee *Xylocopa hirtissima* [112], while (4*R*,5*Z*)-tetradec-5-en-4-olide (50) is the sex pheromone of the Japanese beetle, *Popillia japonica* [113]. Zarbin *et al.* [114] proposed a general approach to the synthesis of chiral pheromone lactones using readily available

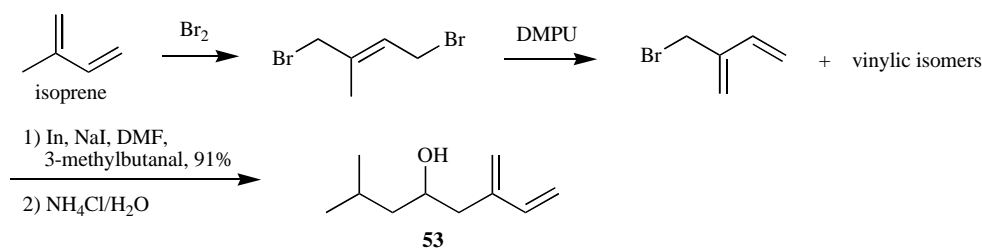
starting materials derived from 2-oxazolines. To show the usefulness of this approach, the diastereoselective synthesis of *cis*- and *trans*-49 and a formal synthesis of (4*R*,5*Z*)-50 were performed (Scheme 45).

7.5. (5*R*,6*S*)-6-Acetoxyhexadecane-5-olide (51)

Laurence and Pickett described for the first time a natural mosquito oviposition attractant pheromone in 1982 [118]. A synthesis of the compound, (5*R*,6*S*)-6-acetoxyhexadecane-5-



Scheme 47.



Scheme 48.

olide (**51**) was carried out by Sun *et al.* [119], employing a L-proline-catalyzed asymmetric aldol condensation between cyclopentanone and undecanal, followed by oxidation and acetylation (Scheme 46).

7.6. (Z)-Hexadeca-7,15-dien-4-olide (**52**)

(Z)-Hexadeca-7,15-dien-4-olide (**52**) was described by Leal *et al.* [120] as the female sex pheromone of the yellowish elongate chafer (*Heptophylla picea*). Clososki *et al.* [121] described an enzymatic synthesis of (R)- and (S)-**52**. A known lipase-catalysed enantioselective lactonization in the key step afforded the common precursor (S)-**A** for both enantiomers of the pheromone, in 92% e.e. (overall yield: 27% for (S) and 18% for (R)-isomer) (Scheme 47).

8. SYNTHESIS OF ISOPRENOIDS AS PHEROMONES

8.1. Synthesis of Isoprenoidal Alcohols As Pheromones

8.1.1. 2-Methyl-6-methyleneoct-7-en-4-ol (**53**) (ipsenol)

Ipsenol (2-methyl-6-methyleneoct-7-en-4-ol, **53**) was identified as the aggregation pheromone of the California bark beetle (*Ips paraconfusus*) [122]. Ceschi *et al.* [123] de-

scribed a short synthesis of racemic **53** employing a selective indium insertion on a mixture of 2-bromomethylbuta-1,3-diene and its vinylic isomers, in good yields (Scheme 48).

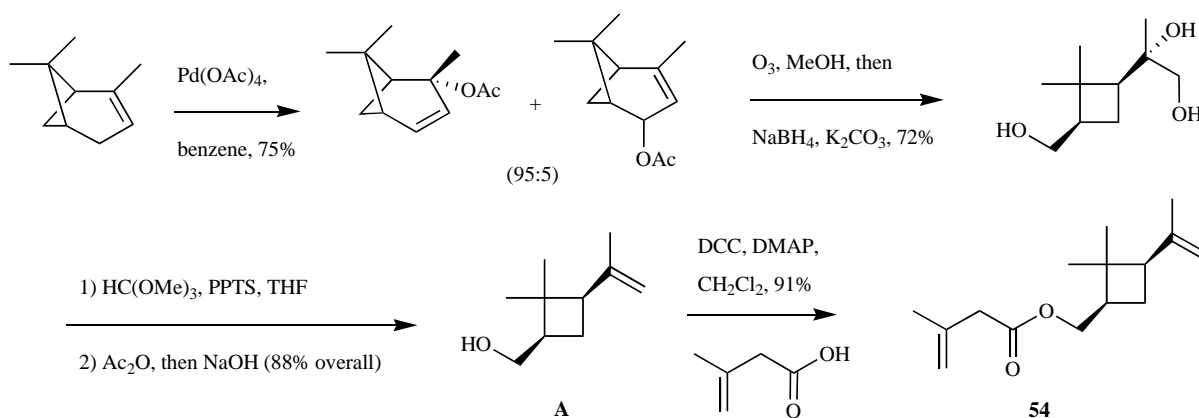
8.1.2. (1R,3R)-(3-Isopropenyl-2,2-dimethylcyclobutyl)methyl 3-methyl-3-butenolate (**54**)

(1R,3R)-(3-Isopropenyl-2,2-dimethylcyclobutyl)methyl 3-methyl-3-butenolate (**54**) has been identified as the sex pheromone produced by virgin females of the mealybug *Pseudococcus cryptus* [124].

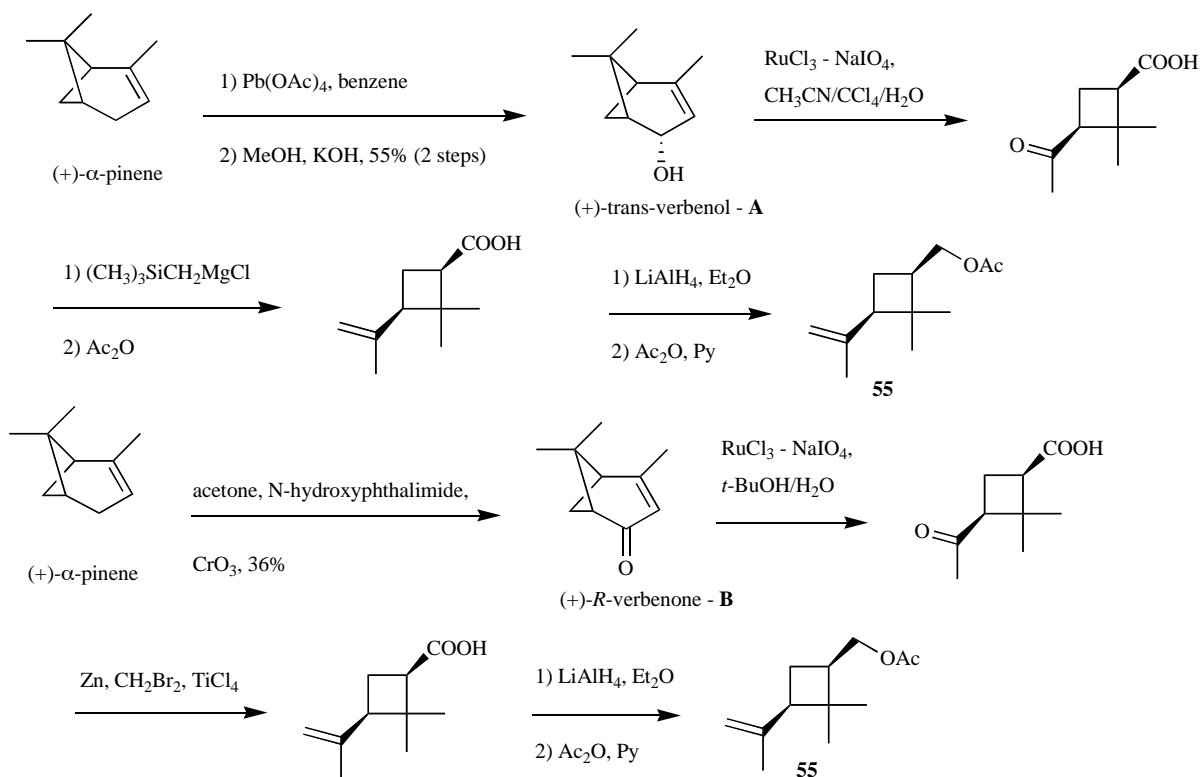
Nakahata *et al.* [125] acetylated (+)- α -pinene with lead acetate and cleaved the resulting acetate by ozonolysis. The triol obtained by reductive workup was reacted with trimethyl orthoformate, and subsequent treatment with acetic acid yielded the alcohol **A**, which was esterified to give **54** in 43% overall yield (Scheme 49).

8.1.3. (1R,3R)-(3-Isopropenyl-2,2-dimethylcyclobutyl)methyl acetate (**55**)

(1R,3R)-(3-Isopropenyl-2,2-dimethylcyclobutyl)methyl acetate (**55**) has been identified as the female-produced sex pheromone of the citrus mealybug (*Planococcus citri*) which



Scheme 49.



Scheme 50.

is a major pest of coffee, citrus, and cocoa in both the southern U. S. and the Mediterranean [126].

Pássaro and Webster described two alternative syntheses of **55** [127]. Compound **55** was synthesized starting from (+)-*trans*-verbenol **A** or (+)-*R*-verbenone **B**, obtained from α -pinene. The key step for both syntheses is the oxidative decarboxylation using $\text{RuCl}_3\text{-NaIO}_4$ (Scheme 50).

8.1.4. *cis*-2-(2-Isopropenyl-1-methylcyclobutyl)ethanol (**56**) (*grandisol*)

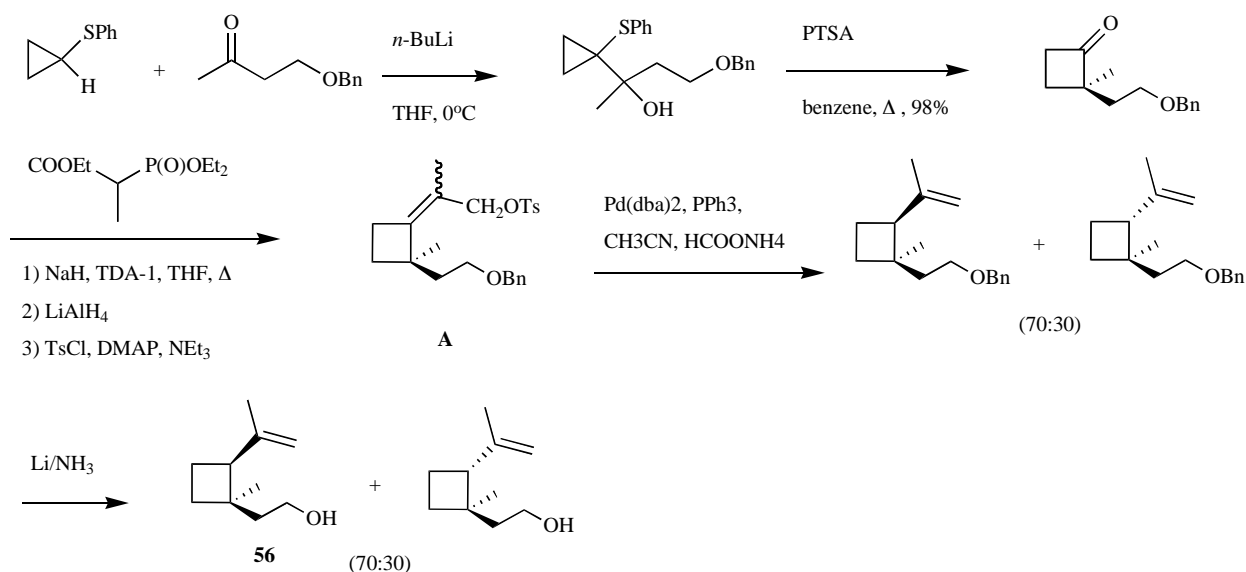
Grandisol [*cis*-2-(2-isopropenyl-1-methylcyclobutyl)ethanol, **56**] is the major component of the male-produced pheromone of the cotton boll weevil (*Anthonomus grandis*) [128] and was also identified from other pests, like bark weevils [129, 130] and bark beetles [131].

The synthesis of a mixture of grandisol and its diastereomer fragranol was described by Bernard *et al.* [132] and is shown in Scheme 51. Key step is the palladium(0)-catalysed reduction of the 2-cyclobutylidenepropyl sulfonic ester **A** (*E:Z* 30:70) by ammonium formate to furnish (\pm)-**56** and (\pm)-fragranol in 70:30 ratio.

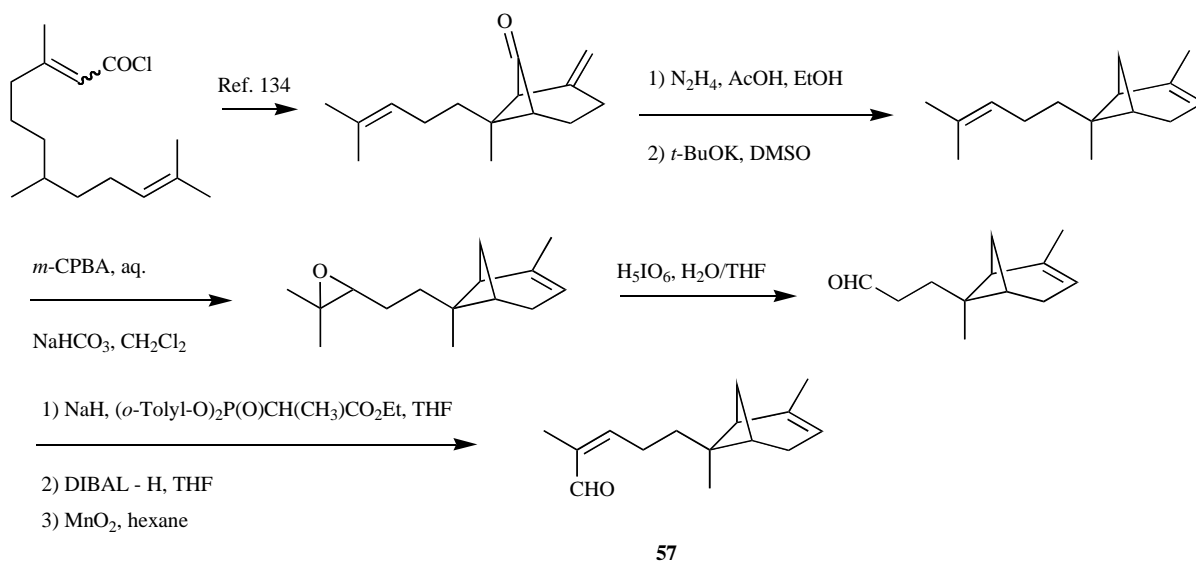
8.2. Synthesis of Isoprenoidal Aldehydes and Ketones as Pheromones

8.2.1. (*Z*)-*exo*- α -Bergamotenal (**57**)

Alizadeh *et al.* [133] described the synthesis of a racemic mixture of (*Z*)-*exo*- α -bergamotenal (**57**), a sex pheromone component of the white-spotted spined bug *Eysarcoris parvus*, from racemic *exo*- α -bergamotene by a five-step se-



Scheme 51.



Scheme 52.

quence involving regioselective epoxidation and (*Z*)-selective Wittig olefination reactions (Scheme 52).

8.2.2. Iridodial (58)

In 2004, Zhang *et al.* [135] identified iridodial [(1*R*,2*S*,5*R*,8*R*)-(2-(1-formylethyl)-3-methylcyclopentanecarboxaldehyde, **58**] as a male-produced male-aggregation pheromone of *Chrysopa oculata*, the first pheromone identified from lacewings.

Chauhan *et al.* [136] described the synthesis of (1*R*,2*S*,5*R*,8*R*)-**58** and of the diastereomers (1*R*,2*S*,5*R*,8*S*)-**58**, (1*S*,2*S*,5*R*,8*R*)-**58**, and (1*S*,2*S*,5*R*,8*S*)-**58** in five steps from (4*aS*,7*S*,7*aR*) and (4*aS*,7*S*,7*aS*)-nepetalactones, which have been isolated by chemical separation from catnip (*Nepeta cataria*) oil [137] (Scheme 53).

8.2.3. 3,7-Dimethyl-2-oxooct-6-ene-1,3-diol (59)

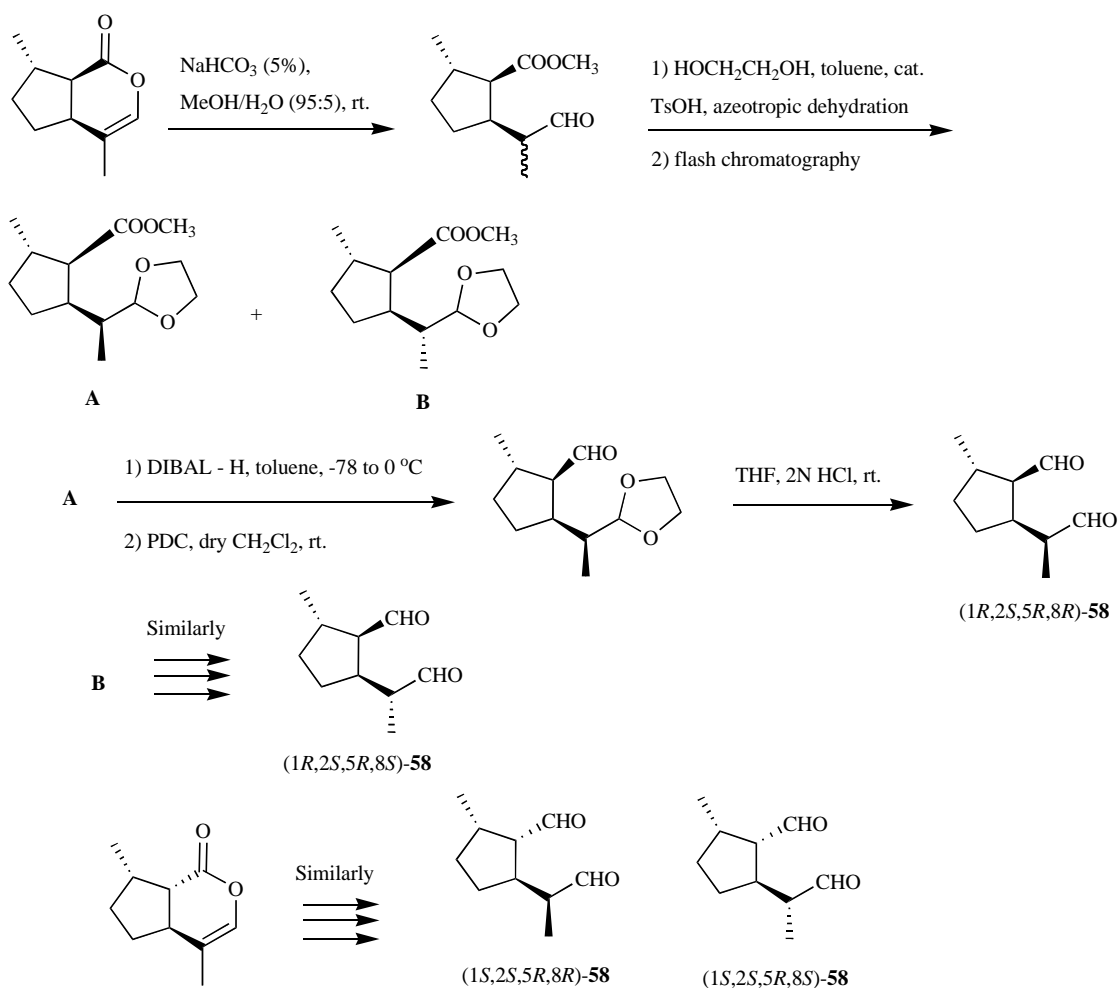
Dickens *et al.* [138] identified 3,7-dimethyl-2-oxooct-6-ene-1,3-diol (**59**) as the male-produced aggregation phero-

mone from the Colorado potato beetle (*Leptinotarsa decemlineata*). The absolute configuration of natural **59** was determined to be (*S*) by syntheses of the racemate and both enantiomers from geraniol and (*R*)- and (*S*)-linalool, respectively, by Oliver *et al.* [139] (Scheme 54).

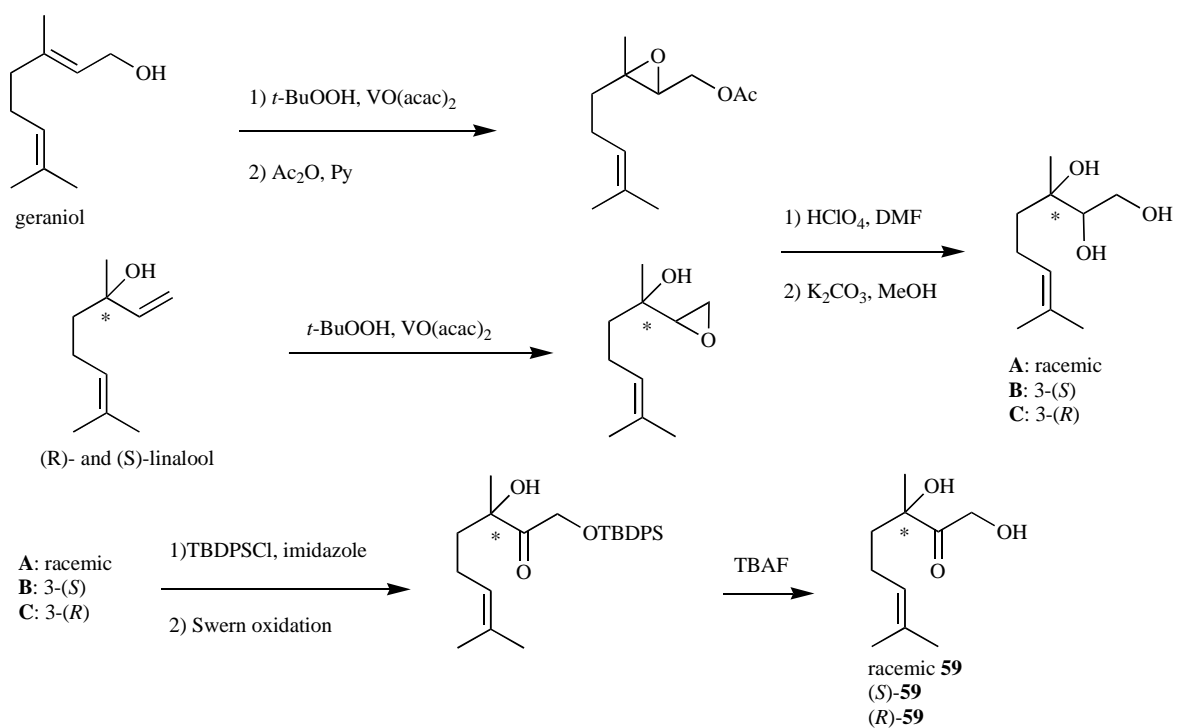
9. SYNTHESIS OF ACETALS AS PHEROMONES

9.1. 4-Hydroxy-1,7-dioxaspiro[5.5]undecane (60)

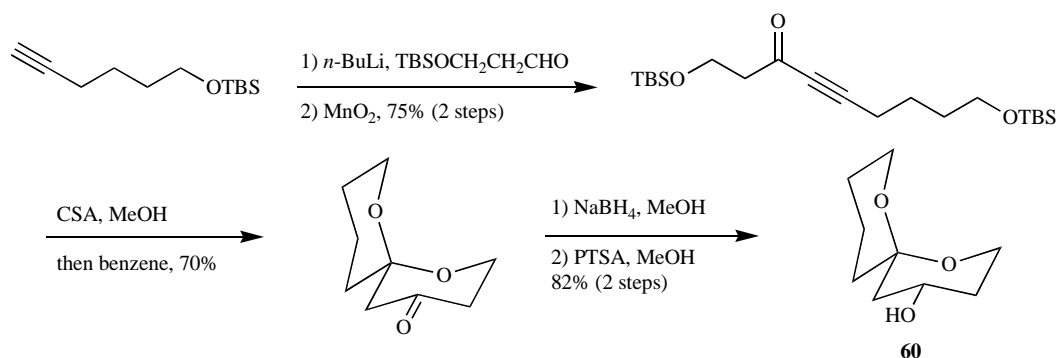
Baker and co-workers described the isolation and identification of 4-hydroxy-1,7-dioxaspiro[5.5]undecane (**60**), a minor component of the female-produced sex pheromone of the olive fruit fly, *Bactrocera oleae*, establishing the most favorable configuration as (4*S*,6*S*) [140, 141]. Hao and Forsyth [142] described a short total synthesis of **60** employing a double intramolecular hetero-Michael addition strategy, applicable to spiroketal synthesis (Scheme 55).



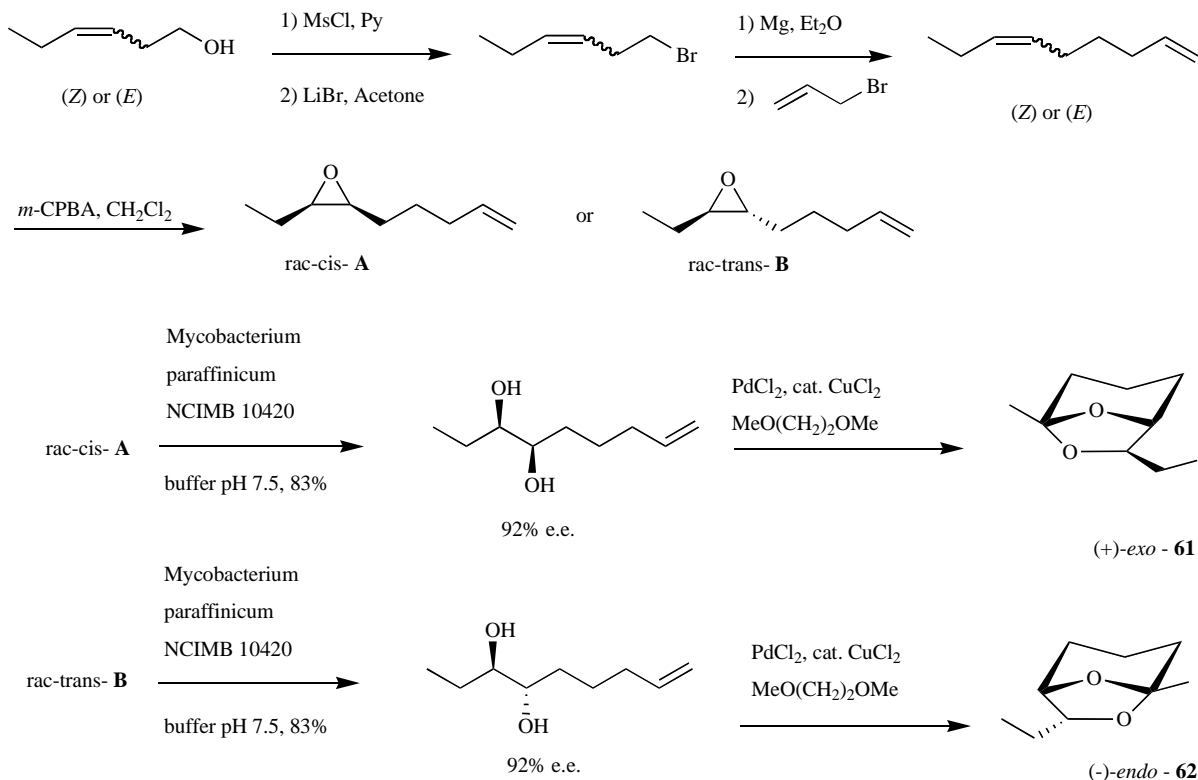
Scheme 53.



Scheme 54.



Scheme 55.



Scheme 56.

9.2. 7-Ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octane (**61**) [*exo*-(**61**) and *endo*-brevicomine (**62**)]

exo-Brevicomine (**61**) and *endo*-brevicomine (**62**) are typical components of the aggregation pheromone system of several bark beetle species of the genera *Dendroctonus* and *Dryocoetes* [143-146]. Mayer *et al.* [147] synthesized (1*R*,5*S*,7*R*)-**61** and (1*S*,5*R*,7*R*)-**62**, employing an enantioconvergent biocatalytic hydrolysis of cis-configured 2,3-disubstituted oxiranes by bacterial epoxide hydrolases (Scheme 56).

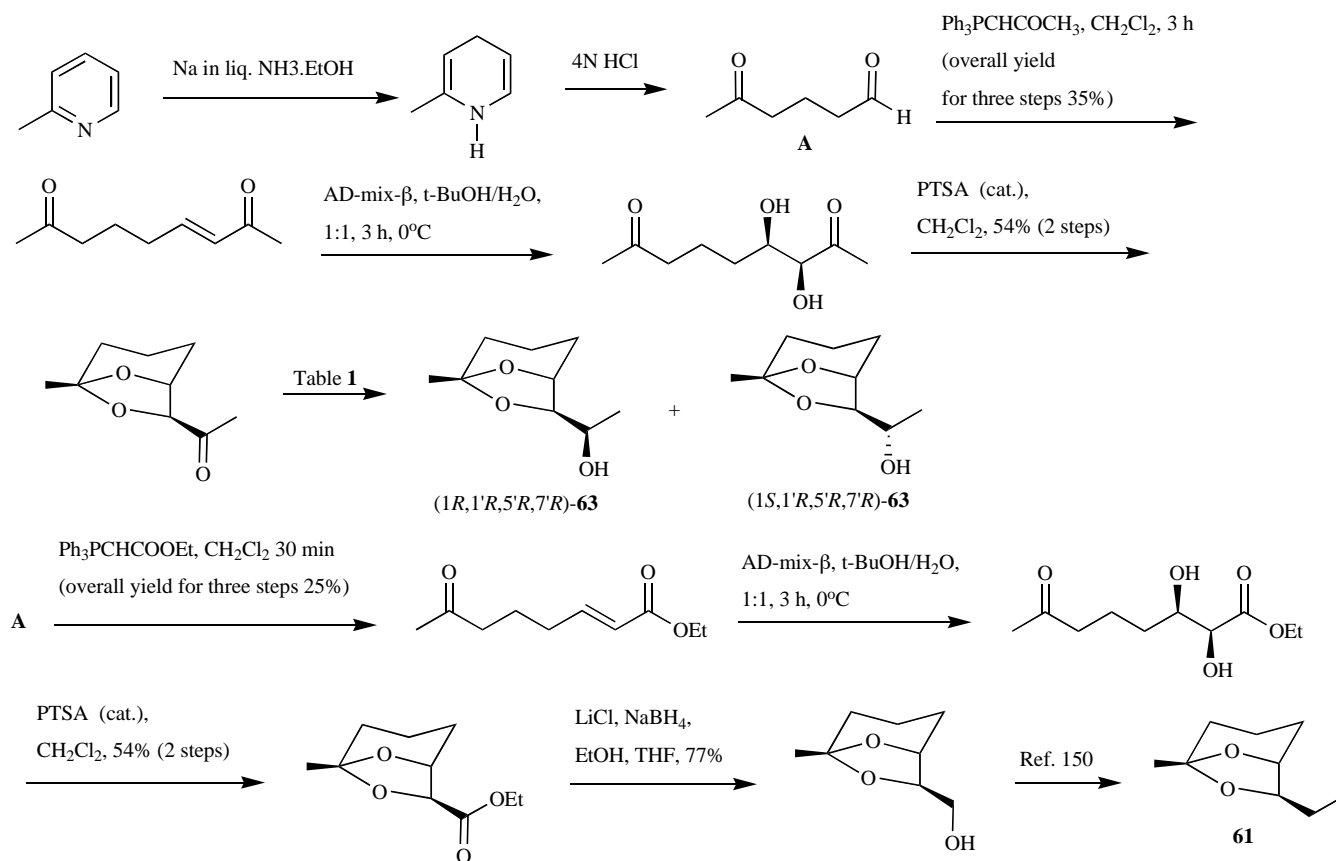
9.3. (1*R*,5*S*,7*R*)-*exo*-Brevicomine (**61**), (1*R*,1'*R*,5'*R*,7'*R*)- and (1*S*,1'*R*,5'*R*,7'*R*)-1-hydroxy-*exo*-brevicomine (**63**)

Francke *et al.* [148] have identified 1-hydroxy-*exo*-brevicomine (**63**) from the pine beetle *Dendroctonus ponderosae*. Kumar and Rao [149] described a synthesis of (1*R*,1'*R*,5'*R*,7'*R*)-**63** and (1*S*,1'*R*,5'*R*,7'*R*)-**63** and of (1*R*,5*S*,7*R*)-**61**, starting from α -picoline ((Scheme 57) (Table 1)).

9.4. 1,5-Dimethyl-6,8-dioxabicyclo[3.2.1]octane (**64**) (frontalin)

Frontalin (1,5-dimethyl-6,8-dioxabicyclo[3.2.1]octane, **64**) was first isolated by Kinzer [151], and is a component of the aggregation pheromone of the southern pine beetle (*Dendroctonus frontalis*), and of the western pine beetle, *Dendroctonus brevicomis*. By means of bioassays with pure synthetic enantiomers, Mori [145, 152] has shown that the absolute configuration of natural **64** is (1*S*,5*R*). Chênevert and Caron [153] described an enantioselective synthesis of (1*S*,5*R*)-(-)-**64** in 90% e.e. via enzymatic desymmetrization of an achiral triol (Scheme 58).

A synthesis of racemic **64** was performed by Yang [154] *et al.* Diene **A** was subjected to a double dihydroxylation with catalytic osmium tetroxide and 4-methylmorpholine-*N*-oxide in MeCN–MeCOMe–H₂O (1:1:1), generating tetraol **B**. Subsequently, mono cleavage and acid-catalyzed intramolecular acetalation led to **64**. Use of AD-mix- α in the



Scheme 57.

Table 1.

	Solv.s and Temperature	Yield (%)	(1 <i>R</i> ,1' <i>R</i> ,5' <i>R</i> ,7' <i>R</i>)- 63	(1 <i>S</i> ,1' <i>R</i> ,5' <i>R</i> ,7' <i>R</i>)- 63
Li AlH ₄	THF, 0°C	86	32	68
NaBH ₄	MeOH, 0°C	92	36	64
Zn(BH ₄) ₂	THF, 0°C	84	25	75
K-Selectride	Toluene, -78°C	79	22	78
DIBAL-H	THF, 0°C	92	20	80

dihydroxylation step resulted in only poor enantioselectivity (16% e.e.) (Scheme 59).

9.5. 1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-ene (**65**)

In 2001, Nakashima [155] reported the identification of 1,3,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-ene (**65**) from the hexane extract of the brush organ located at the hind legs of male swift moths *Endoclyta excrescens*.

The absolute configuration was determined by synthesis in a preliminary communication by Marukawa and Mori [156]. The same authors reported the synthesis of the (1*R*,3*S*,5*S*)- and (1*S*,3*R*,5*R*)-isomers, starting from the pure enantiomers of ethyl 3-hydroxybutanoate [157] (Scheme 60).

9.6. (+)-Lineatin (**66**)

Lineatin [3,3,7-trimethyl-2,9-dioxatricyclo[3.3.1.0^{4,7}]nonane, **66**] is the most important constituent of the aggrega-

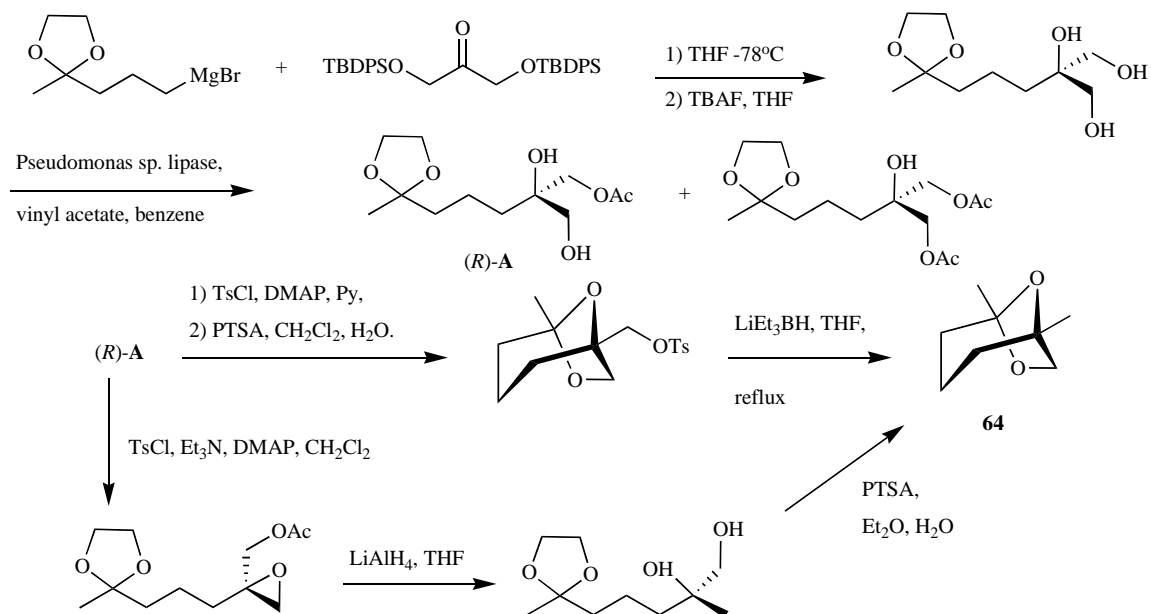
tion pheromone isolated from the frass of the female ambrosia beetle *Trypodendron lineatum*, which is a deleterious pest to coniferous forests in Europe and North America [158].

Alibés [159] *et al.* described a highly stereoselective formal synthesis of (+)-lineatin in 14 steps and 14% overall yield from the homochiral furanone **A** (Scheme 61). Key steps of this synthetic approach feature the diastereoselective construction of the cyclobutene derivative **B** by a photochemical cycloaddition, and a regiocontrolled oxymercuration reaction to form the dihydroxy compound **C**.

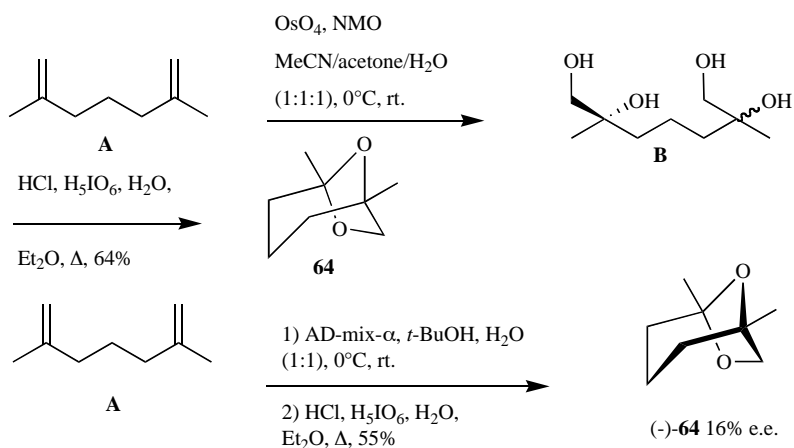
10. SYNTHESIS OF AN AMIDE AS PHEROMONE

10.1. (1'*S*,2*R*,2'*S*,3'*R*)-*N*-(1'-(Hydroxymethyl)-2',3'-dihydroxytetradecyl)-2-hydroxy-21-methyldocosanamide (**67**)

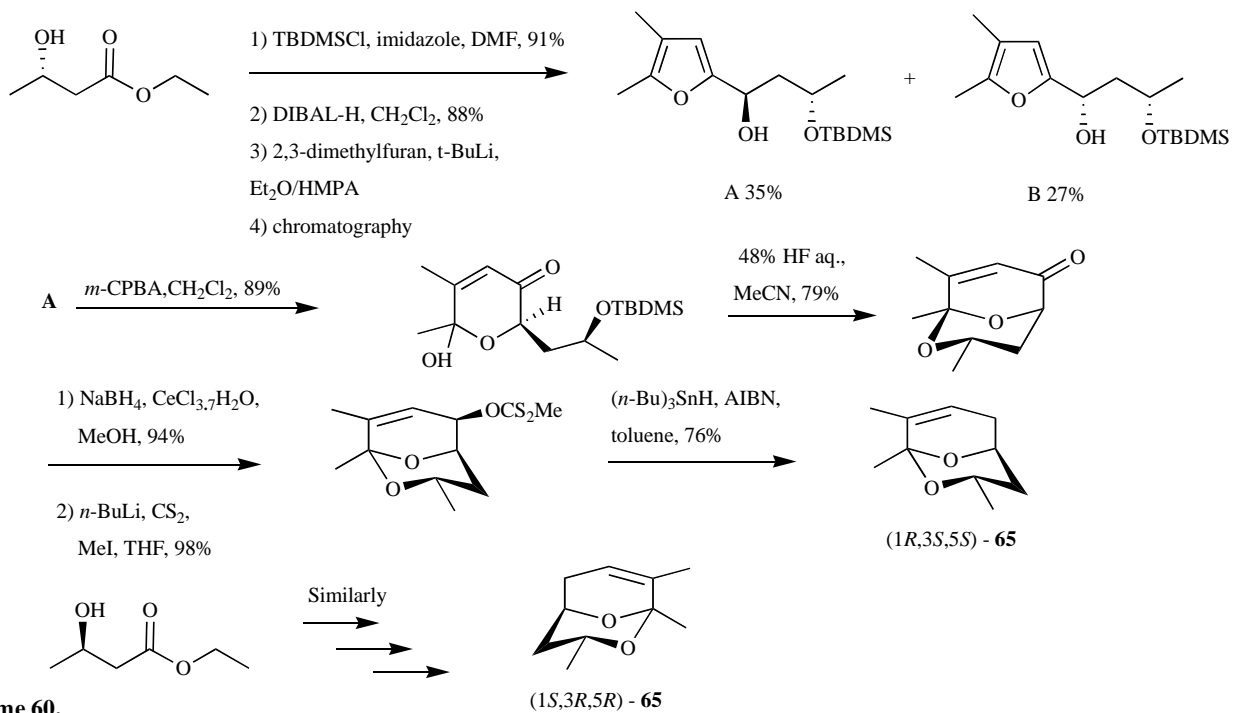
Asai *et al.* [162] reported in 2000 the ceramide (1'*S*,2*R*,2'*S*,3'*R*)-*N*-(1'-(hydroxymethyl)-2',3'-dihydroxytetradecyl)-2-hydroxy-21-methyldocosanamide (**67**) to be the sex phero-



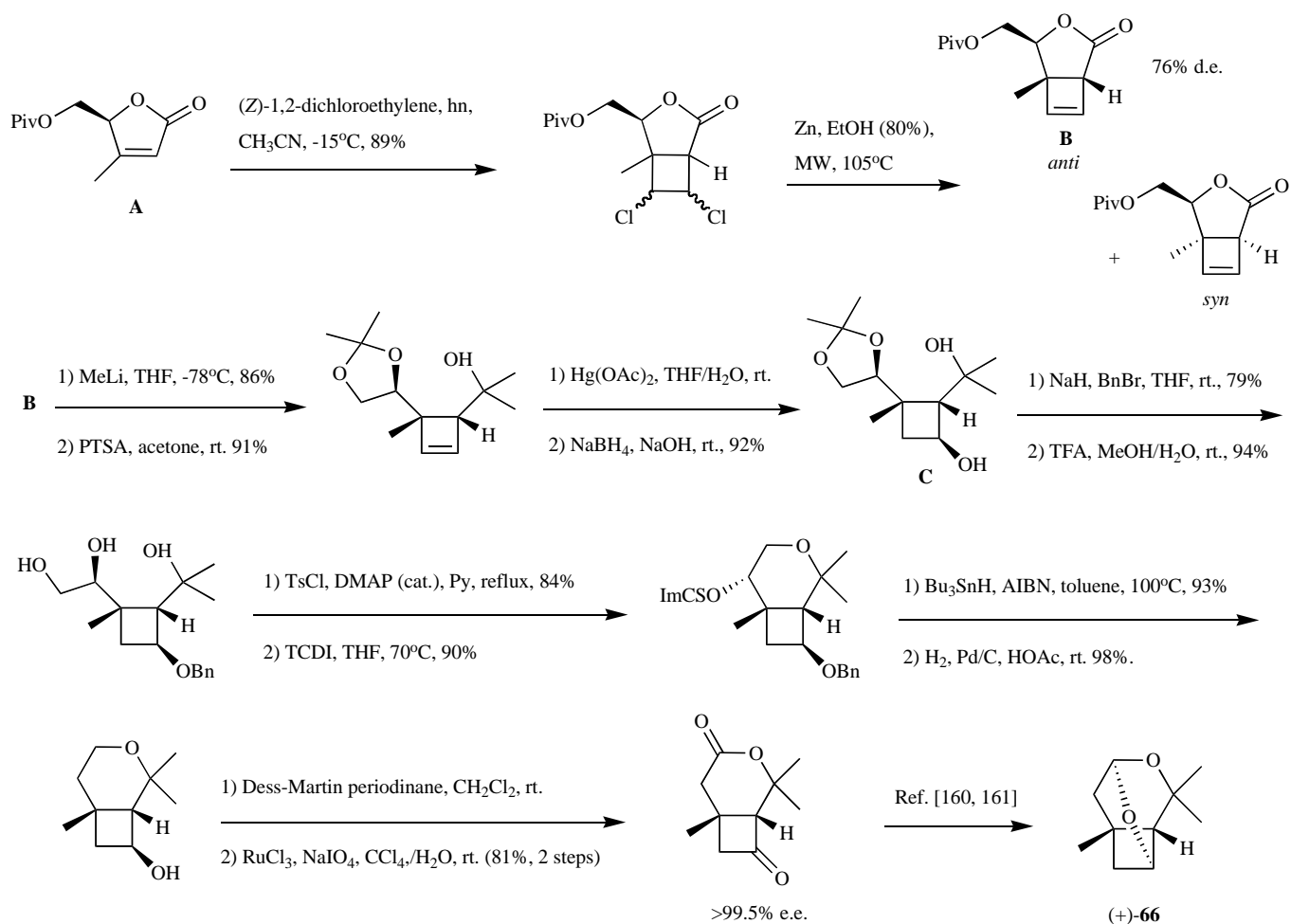
Scheme 58.



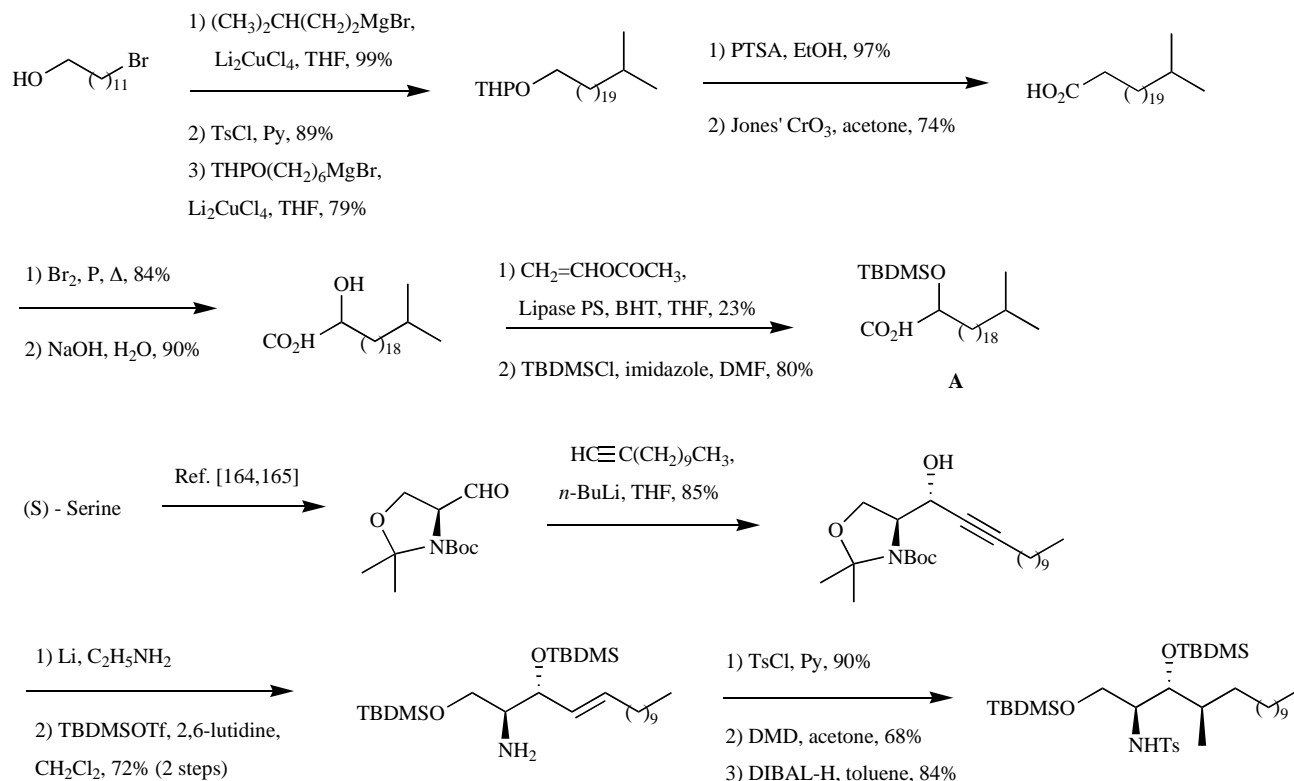
Scheme 59.

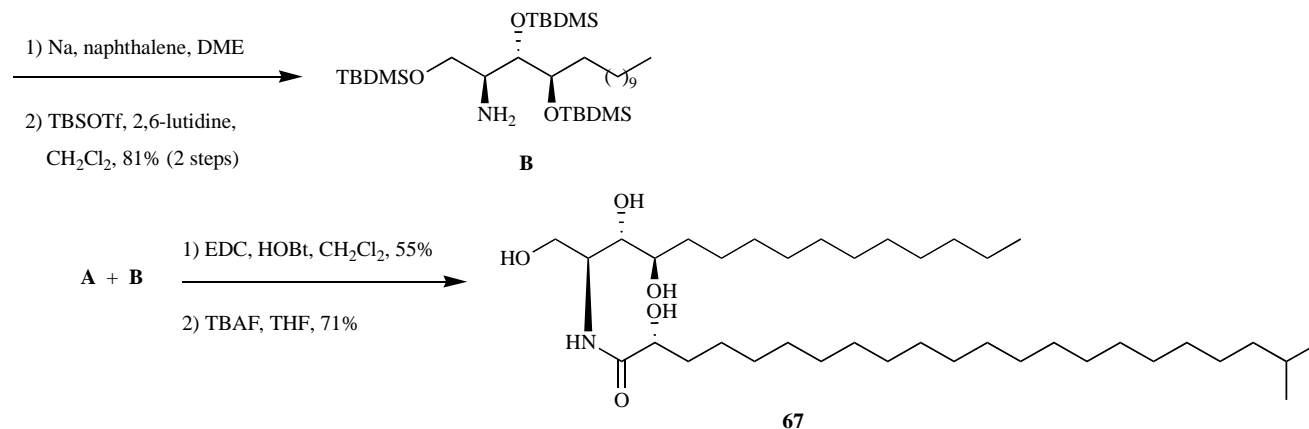


Scheme 60.



Scheme 61.



**Scheme 62.**

none of the female hair crab, *Erimacrus isenbeckii*. Masuda *et al.* [163] described an enantiodivergent synthesis, employing 12-bromododecan-1-ol for the synthesis of the acid moiety **A** with a lipase-catalyzed resolution of hydroxy-acid in the key step, and (*S*)-serine for the construction of the amine moiety **B**, which were reacted to give the amide **67** (Scheme 62).

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ABBREVIATIONS

Ac	=	acetyl	HONO	=	gaseous nitrous acid
AIBN	=	azobisisobutyronitrile	KIPBH	=	potassium <i>tri</i> -isopropoxyborohydride
BnBr	=	benzyl bromide	LDA	=	lithium diisopropylamide
CAN	=	ceric ammonium nitrate	LiHMDS	=	lithium hexamethyldisilazide
CSA	=	camphorsulfonic acid	<i>m</i> -CPBA	=	<i>m</i> -chloroperbenzoic acid
DABCO	=	1,4-diazabicyclo[2.2.2]octane	MeCBS	=	methyl oxazaborolidine
DEAD	=	diethyl azodicarboxylate	MsCl	=	methanesulfonyl chloride (mesyl chloride)
DET	=	diethyl tartrate	NaHMDS	=	sodium hexamethyldisilazide
DHP	=	3,4-dihydro-2 <i>H</i> -pyran	NIS	=	<i>N</i> -iodosuccinimide
(DHQ) ₂ -PHAL	=	hydroquinine 1,4-phthalazinediyl diether	NMO	=	<i>N</i> -methylmorpholine- <i>N</i> -oxide
DIBAL-H	=	diisobutylaluminium hydride	PCC	=	pyridinium chlorochromate
DIPEA	=	ethyl-diisopropylamine	PDC	=	pyridinium dichromate
DMAP	=	4-dimethylaminopyridine	PPh ₃	=	triphenyl phosphine
DME	=	dimethoxyethane	PPL	=	porcine pancreatic lipase
2,2-DMP	=	2,2-dimethoxypropane	PPTS	=	pyridinium <i>p</i> -toluenesulfonate
DMF	=	<i>N,N</i> -dimethylformamide	PTSA	=	<i>p</i> -toluenesulfonic acid
DMPU	=	1,3-dimethyltetrahydropyrimidin-2(1 <i>H</i>)-one	Py	=	pyridine
DMSO	=	dimethylsulfoxide	SOCl ₂	=	thionyl chloride
HMPA	=	hexamethylphosphoramide	TBAF	=	tetra- <i>n</i> -butylammonium fluoride
HOBt	=	1-hydroxybenzotriazole	TBDMSCl	=	<i>tert</i> -butyldimethylsilyl chloride
			TBDPSCl	=	<i>tert</i> -butyldiphenylchlorosilane
			TCDI	=	1,1'-thiocarbonyldiimidazole
			TDA-1	=	tris-(3,6-dioxahexyl)amine
			TFA	=	trifluoroacetic acid
			THF	=	tetrahydrofuran
			THP	=	tetrahydropyran
			TMEDA	=	tetramethylethylenediamine
			TMPDA	=	tetramethylpropylenediamine
			TMSCl	=	trimethylsilyl chloride
			TMSOTf	=	trimethylsilyl trifluoromethanesulfonate
			TPAP	=	tetrapropylammonium perruthenate

TsCl = *p*-toluenesulfonyl chloride (tosyl chloride)
 TsNHNH₂ = *p*-toluenesulfonyl hydrazine

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