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Synthesis of insect pheromones belonging to the group of (*Z*)-trisubstituted alkenes

N Ya Grigorieva, P G Tsiklauri

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Abstract. Stereo- and regiocontrolled methods for the construction of a (*Z*)-trisubstituted C=C bond and for the regiospecific introduction of a chiral fragment are exemplified in total syntheses of insect pheromones belonging to (*Z*)-trisubstituted alkenes. The bibliography includes 113 references.

I. Introduction

In the last two decades, it was found that the biological activities of a series of important natural compounds, such as low-molecular-weight bioregulators, *viz*., polyprenols, dolichols, antibiotics of a strobilurin family and pheromones of different species of insects, are associated with the presence of a (*Z*)-trisubstituted alkene fragment in these molecules. In this connection, the problem of the regio- and stereocontrolled synthesis of (*Z*)-trisubstituted alkenes is of substantial methodological and practical interest. A rather small group of insect pheromones containing this structural fragment represents a 'proving ground' for the elucidation of the synthetic potential of methods developed for the formation of (*Z*)-trisubstituted C=C bonds. In the total syntheses of these pheromones, all known procedures for the stereoselective construction of (*Z*)-trisubstituted alkenes were employed. These methods can find use in the preparation of other biologically active compounds. In addition, the approaches developed for the formation of chiral centres are also of obvious interest.

In the present review, methods for the regio- and stereocontrolled construction of (*Z*)-trisubstituted C=C bonds and the regiospecific introduction of a chiral centre, which are of importance for organic synthesis, are exemplified in total syntheses of pheromones of the above-mentioned group.

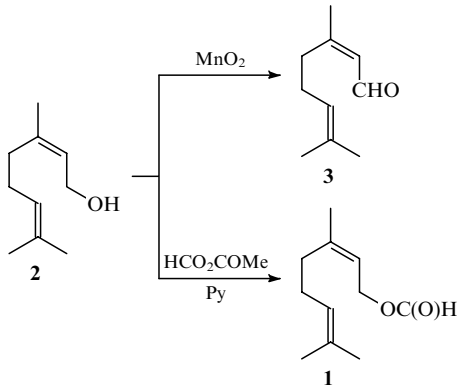
We believe that the solution of this problem calls for systematisation of the available data on the syntheses of the target structures, which are ranked in the order of increasing difficulty. Attention will be focussed on procedures for the construction of (*Z*)-trisubstituted alkene fragments and methods for the formation of chiral centres.

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II. Synthesis of the alarm pheromones of the mold mite *Tyrophagus putrescentiae*, the astigmatid mite *Glycyphagus domesticus* and the ant *Oecophylla longinoda*

In the late 1970s, Kuwahara *et al.*[1,2] demonstrated that neryl formate (**1**) is the alarm pheromone of one of the major pests of cereal crops, *viz*., the mold mite *Tyrophagus putrescentiae*. Later,[3] this conclusion was confirmed by bioassays of synthetic neryl formate (**1**) prepared from nerol (**2**).

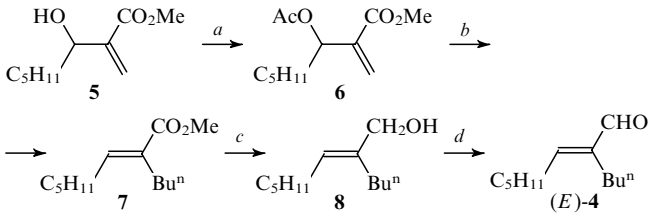


Later, Kuwahara and Koshii[4] have found that neral (**3**), which can also be readily prepared from nerol (**2**), is the alarm pheromone of the astigmatid mite *Glycyphagus domesticus*.

α,β-Unsaturated aldehyde **4**, which is a hexanal dimerisation product, was isolated by Baker and coworkers in 1975.[5] This is the alarm pheromone of the African weaver ant *Oecophylla longinoda*. Although, in strict accordance with the IUPAC nomenclature, aldehyde **4** is the (*E*)-isomer, the carbon substituents at the C=C bond are in *cis* positions with respect to each other. Disubstituted α,β-unsaturated aldehydes of this type are precursors of (*Z*)-methylalkenes. Hence, we believe that it is reasonable to consider the synthesis of the aldehyde **4** in the present review. In 1966, Basavaian and Hyma[6] synthesised the aldehyde **4** with the use of the Baylis – Hillman reaction[7] for the regio- and stereoselective construction of its trisubstituted alkene fragment.

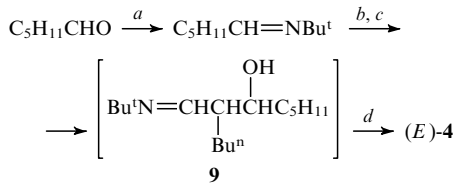
Hydroxy ester **5**, which was prepared by the condensation of hexanal with methyl acrylate under conditions proposed by Baylis and Hillman,[7] was converted into acetate **6**. The reaction of the latter with PrMgBr afforded ester **7** as the only product. Reduction of the ester group and oxidation of the resulting alcohol **8**

with pyridinium chlorochromate gave rise to the aldehyde **4** (the overall yield was 20.5%).



(*a*) AcCl, Py; (*b*) Pr^nMgBr; (*c*) Bu^i_2AlH; (*d*) PCC (pyridinium chlorochromate), CH_2Cl_2.

A simpler yet highly stereoselective procedure for the synthesis of the aldehyde **4**[8] involves condensation of *N-tert*-butylhexanimine with hexanal yielding β-hydroxy imine **9**. Acid scission of the latter afforded thermodynamically more favourable[9] aldehyde (*E*)-**4** in 70% yield (the stereoselectivity was ~ 98%). The aldehyde (*E*)-**4** was also identified by Baker *et al.*[10] as a component of the alarm pheromone of the beetle *Amblypelta nitida*.



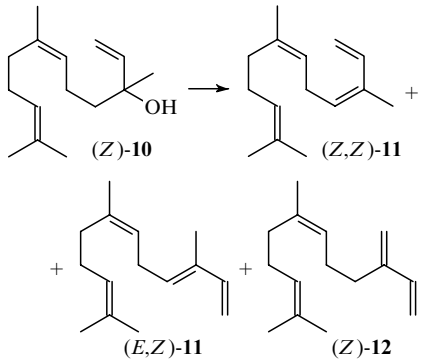
(*a*) Bu^tNH_2; (*b*) LDA (lithium diisopropylamide); (*c*) $C_5H_{11}CHO$; (*d*) H_3O^+.

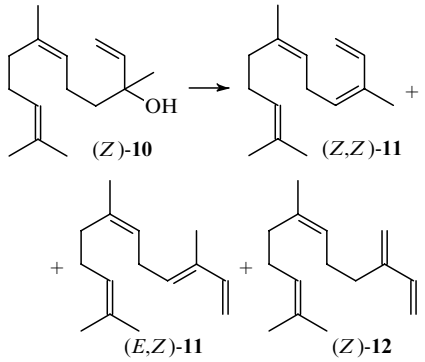
III. Syntheses of ant trail pheromones

1. Trail pheromones of the fire ant *Solenopsis invicta*

As early as 1959, Wilson[11] demonstrated that fire ants produce a special trail pheromone, which allows members of the community to find routes to sources of food, new areas, *etc*.

Van der Meer and coworkers[12] isolated this pheromone, established that it represents a mixture of at least five closely related compounds and separated these compounds by preparative GLC. Based on the results of studies of the physicochemical properties of individual components of this mixture, two compounds were assigned to the α-farnesene series and one compound was assigned to the allofarnesene series. The configurations of the pheromone components were established by comparing the spectral data (UV, ^{1}H NMR and mass spectra) of natural and authentic samples of α- and allofarnesenes synthesised in an unequivocal way. Thus dehydration of (*Z*)-nerolidol **10** in a $POCl_3$–Py system at 160 °C afforded a mixture of isomeric α-farnesenes, (*Z*,*Z*)- and (*E*,*Z*)-**11**, and (*Z*)-β-farnesene, (*Z*)-**12**. Dehydration of the isomer (*E*)-**10** under the same conditions gave rise to a mixture of (*E*,*E*)- and (*Z*,*E*)-α-farnesenes (**11**) and (*E*)-β-farnesene [(*E*)-**12**].[12]



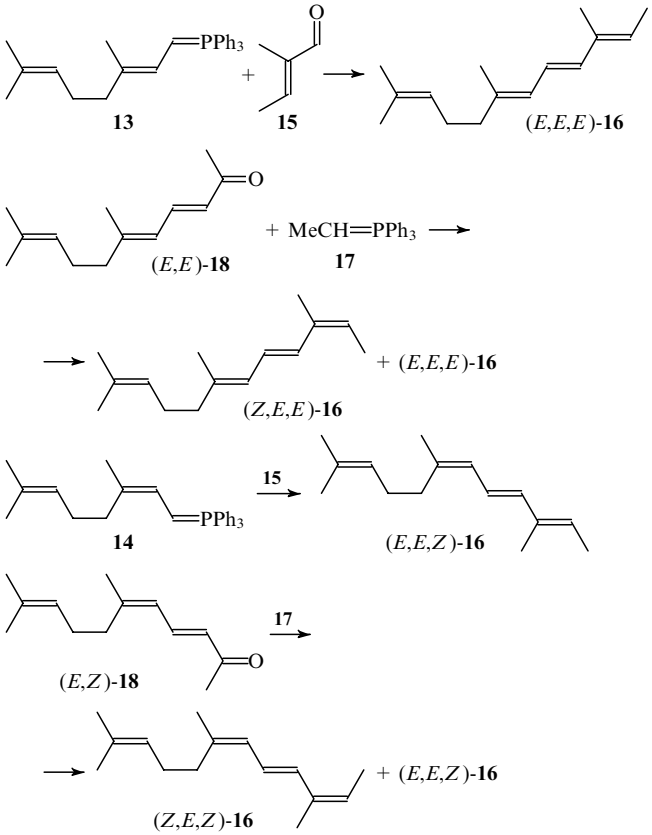


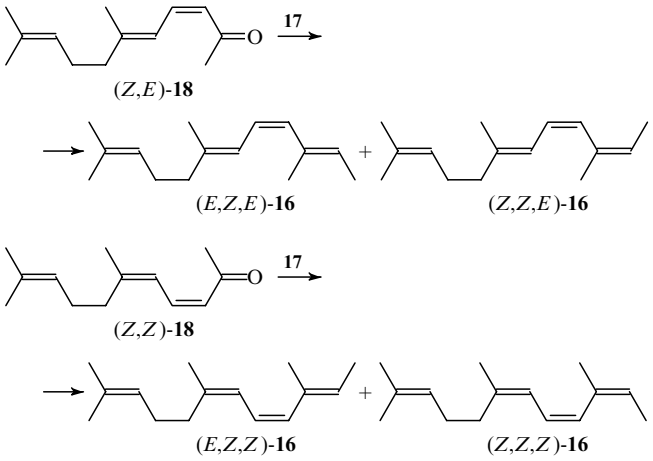
Based on comparison of the physicochemical characteristics of farnesenes **11** and the components of the fire ant trail pheromone, it was reliably established that the major component of this pheromone has the structure (*Z*,*E*)-**11** and one of the minor components has the structure (*E*,*E*)-**11**. It should be noted that α-farnesene (*Z*,*E*)-**11** was identified as a component of trail pheromones also of other ant species.[13]

With the aim of establishing the stereochemistry of the components of the fire ant trail pheromone belonging to the allofarnesene series, all eight possible isomeric allofarnesenes were synthesised using the Wittig reaction.[14]

It appeared that the condensation of ylides **13** and **14** generated from geranyl- and nerylphosphonium bromides, respectively, with tiglic aldehyde (**15**) proceeded stereoselectively to form allofarnesenes (*E*,*E*,*E*)-**16** and (*E*,*E*,*Z*)-**16**, respectively. To the contrary, the condensation of triphenylphosphonium ethylide **17** with isomeric pseudoionones (*E*,*E*)-**18** or (*E*,*Z*)-**18** was non-stereoselective.

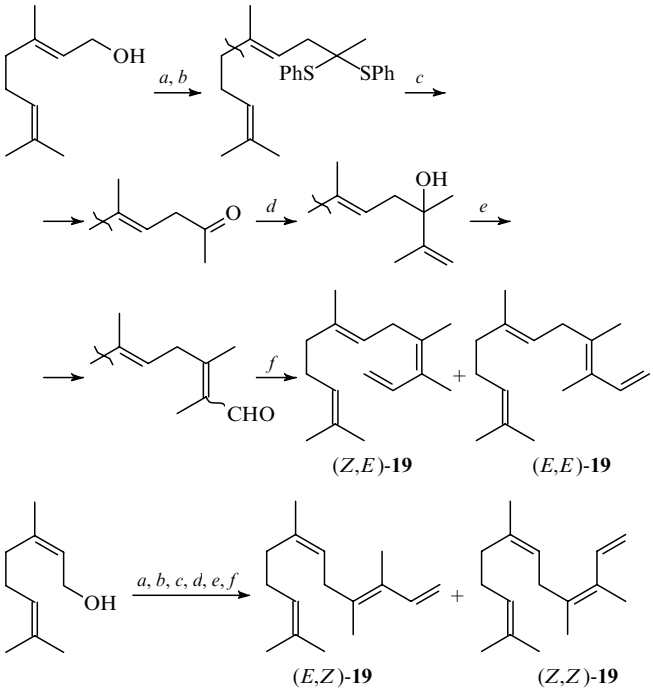
The reaction of the isomer (*E*,*E*)-**18** afforded a mixture of (*E*,*E*,*E*)- and (*Z*,*E*,*E*)-**16**, whereas the isomer (*E*,*Z*)-**18** gave a mixture of (*E*,*E*,*Z*)- and (*Z*,*E*,*Z*)-**16**. The condensation of the (*Z*,*E*)-pseudoionone, (*Z*,*E*)-**18**, with the ylide **17** yielded a mixture of (*E*,*Z*,*E*)-**16** and (*Z*,*Z*,*E*)-**16**, whereas the reaction of the





(*Z*,*Z*)-pseudoionone [(*Z*,*Z*)-**18**] with the ylide **17** afforded a mixture of (*E*,*Z*,*Z*)-**16** and (*Z*,*Z*,*Z*)-**16**. Comparison of the spectral properties (UV, ^{1}H NMR and mass spectra) of the individual allofarnesenes isolated by preparative GLC with those of the third component of the fire ant trail pheromone demonstrated that the latter is the stereoisomer (*Z*,*Z*,*Z*)-**16**. Bioassays of the allofarnesene isomers demonstrated that the compounds (*E*,*Z*,*E*)-, (*Z*,*Z*,*E*)- and (*E*,*Z*,*Z*)-**16** with the (*Z*)-configuration of the C(4) = C(5) bond exhibit the trail pheromone activity.

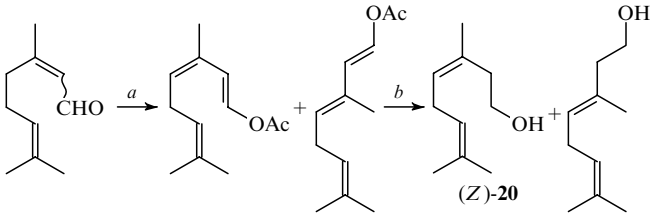
The fourth and fifth components of the trail pheromone of *S.invicta* were identified [15] as (*Z*,*E*)- and (*E*,*E*)-homofarnesenes **19** by comparing the physicochemical characteristics of these pheromone components with those of the compounds (*Z*,*E*)-, (*E*,*E*)-, (*E*,*Z*)- and (*Z*,*Z*)-**19**, which have been specially synthesised from nerol or geraniol.



(*a*) PBr_3, Py; (*b*) $MeCH(SPh)_2$; (*c*) $HgCl_2$; (*d*) $H_2C=C(Me)MgBr$; (*e*) PCC, CH_2Cl_2; (*f*) $Ph_3P=CH_2$.

2. Trail pheromone of the ant *Leptogenys diminuta*

In 1991, Attygalle *et al.*[16] isolated the trail pheromone of the ants *Leptogenys diminuta*. Based on the results of physicochemical studies, the authors assigned the structure of (*Z*)-isogeraniol (**20**) to this pheromone. To decide between the (*Z*)- and (*E*)-configurations of compound **20**, the retention times (GLC) of the natural pheromone and the samples of (*Z*)- and (*E*)-**20** synthesised from citral enol acetates were compared.

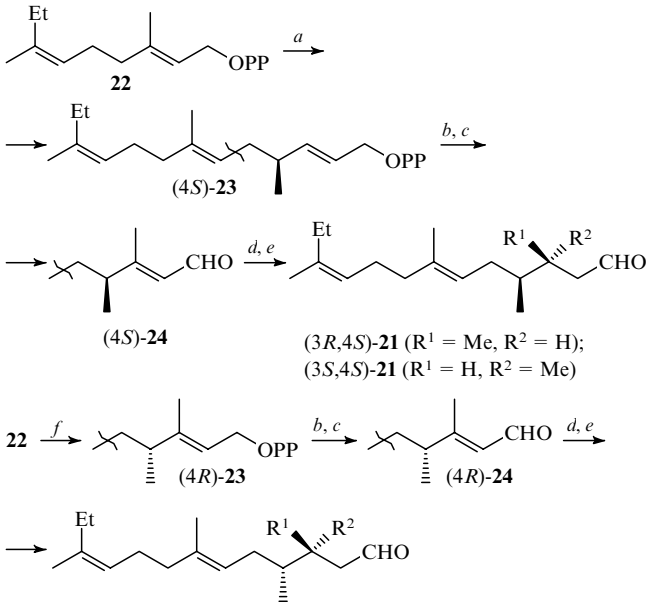


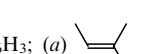
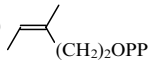
(*a*) Ac_2O, NaOAc; (*b*) $NaBH_4$.

3. Trail pheromone of Pharaoh's ant *Monomorium pharaonis* (faranal)

In 1977, Ritter *et al.*[17] isolated the trail pheromone of Pharaoh's ant *Monomorium pharaonis*, which is a pest of food and a dangerous carrier of wound infections. Based on the results of physicochemical studies, the structure of 3,4,7,11-tetramethyldeca-(6*E*,10*Z*)-dienal was assigned to this pheromone named faranal. However, the absolute configurations of the C(3) and C(4) centres in the molecule remained an open question up to 1980 when Kobayashi and coworkers [18] synthesised isomeric aldehydes **21** and demonstrated that only the compound (3*S*,4*R*)-**21** exhibited biological activity and, hence, the natural faranal had this configuration.

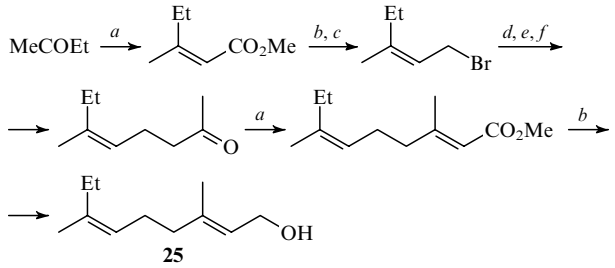
The key step of the synthesis involved condensation of (2*E*,6*Z*)-homogeraniol pyrophosphate **22** with (3*E*)- or (3*Z*)-3-methylpent-3-enyl pyrophosphate catalysed by farnesyl-pyrophosphate synthetase leading to chiral pyrophosphates (4*S*)- and (4*R*)-**23**, which was in accord with the results obtained previously.[19, 20] These compounds were converted into aldehydes (4*S*)- and (4*R*)-**24**, respectively. Selective reduction of the C(2) = C(3) double bond in the aldehydes (4*S*)-**24** and (4*R*)-**24** afforded a mixture of the diastereomeric aldehydes (3*R*,4*S*)- and (3*S*,4*S*)-**21**



PP is $P_2O_6H_3$; (*a*) , farnesyl-pyrophosphate synthetase; (*b*) alkaline phosphatase; (*c*) MnO_2; (*d*) Et_3SiH, $(Ph_3P)_3RhCl$; (*e*) H_3O^+; (*f*) , farnesyl-pyrophosphate synthetase

and a mixture of the diastereomers (3*R*,4*R*)- and (3*S*,4*R*)-**21**, respectively. The individual compounds were isolated by HPLC.

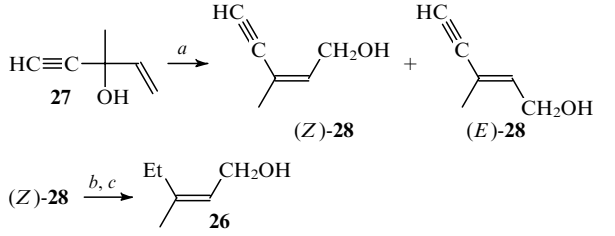
Homogeraniol **25** required for the preparation of the pyrophosphate **22** was synthesised [21] using a reaction sequence in which the key step of chain elongation (*a*) was non-stereoselective and, hence, it was necessary to separate isomers by rectification or chromatography.



(*a*) $(EtO)_2P(O)CH_2CO_2Me$, MeONa; (*b*) $LiAlH_4$; (*c*) PBr_3, Py; (*d*) Mg, $MeCOCH_2CO_2Me$; (*e*) NaOH; (*f*) H_3O^+.

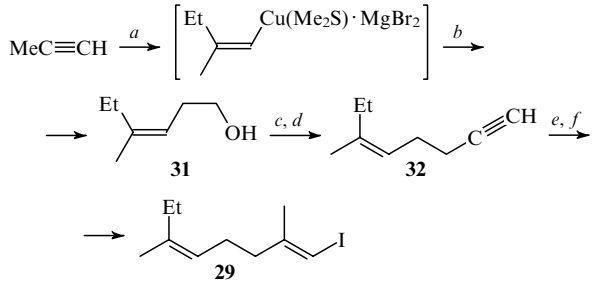
Generally, the synthesis of farnal [(3*S*,4*R*)-**21**] involves coupling of two building blocks. One of these blocks contains either only (*Z*)-trisubstituted alkene fragments or simultaneously (*Z*)- and (*E*)-trisubstituted fragments, while the second block contains the chiral portion of the molecule. The construction of the blocks of both types and their coupling to form the target faranal molecule [(3*S*,4*R*)-**21**] are considered below.

Mori and Ueda [22, 23] used an allylic alcohol **26** as the (*Z*)-trisubstituted alkene synthon. Its synthesis involved isomerisation of 3-methylpent-1-en-4-yn-3-ol (**27**) under the action of lithium acetylide and reduction of the triple bond in the alcohol (*Z*)-**28** isolated from its mixture with (*E*)-**28** (the ratio 85 : 15).



(*a*) HC≡CLi, (*b*) $NH_2NH_2 \cdot H_2O$; (*c*) H_2O_2, EtOH.

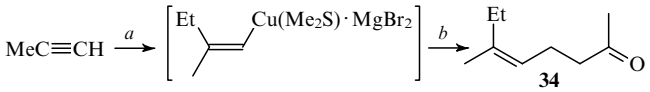
Baker *et al.*[24] performed a highly stereoselective synthesis of the alkene synthon **29** based on the *cis*-addition of organocopper compounds to terminal alkynes (this reaction had been discovered by Corey and Katzenellenbogen [25]). The reagent **30** was added to the starting propyne to give (*Z*)-homoallylic alcohol **31**. The alcohol **31** was converted into enyne **32** *via* tosylate. Successive treatment of compound **32** with a cuprate complex **33** [26] and iodine gave the target iodide **29** in 33.7% overall yield with a stereoselectivity exceeding 96%.



(*a*) $EtCu(Me_2S) \cdot MgBr_2$ (**30**); (*b*) PrC≡CLi,  ; (*c*) TsCl, Py; (*d*) HC≡CLi; (*e*) $MeCu(Me_2S) \cdot MgBr_2$ (**33**); (*f*) I_2.

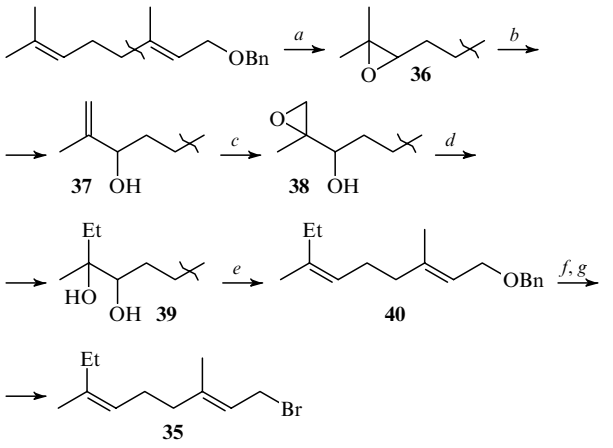
An analogous scheme was used in the synthesis of faranal performed by Mori and coworkers.[27] They succeeded in increasing substantially the yield in the step of conversion of the enyne **32** into the iodide **29** by applying Wipf's modification [28] of carboalumination.

The synthon **34** was prepared employing the cuprate procedure for the construction of the (*Z*)-alkene fragment of faranal.[29]



(*a*) **30**; (*b*) BuC≡CLi, $H_2C{=}CHCOMe$.

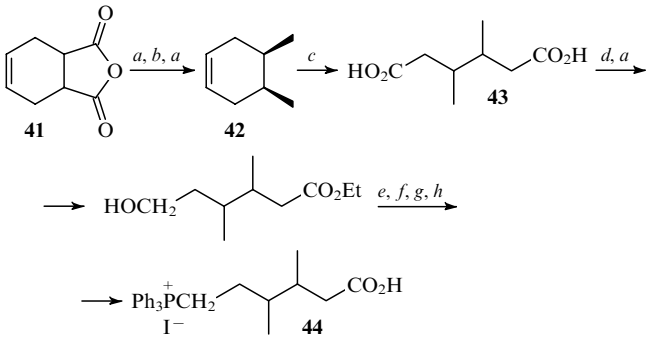
An alternative procedure for the construction of the (*Z*)-trisubstituted alkene fragment was used in the synthesis of bromide **35**, which is a key intermediate in the synthesis of faranal.[30, 31] Epoxide **36**, which can readily be prepared from benzyl ether of geraniol, was converted into allylic alcohol **37** in high yield. Sharpless's epoxidation of the latter, scission of the epoxy group in the resulting epoxide **38** with lithium dimethyl cuprate and, finally, elimination of the hydroxy groups from diol **39** according to a procedure proposed by Tanaka *et al.*[32] afforded benzyl ether **40**. The latter was converted into the bromide **35** according to standard procedures in a yield of 24% with respect to geraniol.



(*a*) *m*-Chloroperbenzoic acid (MCPBA); (*b*) $(Pr^iO)_3Al$, PhMe; (*c*) Bu^tO_2H, $VO(acac)_2$; (*d*) Me_2CuLi; (*e*) $HC(OMe)_2NMe_2$, Ac_2O; (*f*) Li/NH_3; (*g*) PBr_3, Py.

Conversions of the above-described alkene synthon blocks **26**, **29**, **34** and **35** into faranal [(3*S*,4*R*)-**21**] involved their coupling with blocks containing the 3,4-dimethylbutanal fragment. In many cases, an adduct of butadiene with maleic anhydride **41**, which was smoothly converted into *cis*-dimethylcyclohexene (**42**), was used as the starting compound for the preparation of these blocks. The ring-opening in the compound **42** and the transformation of dicarboxylic acid **43** giving rise to the target synthons have been performed in two ways. The path *I* [29] involved

Path *I*

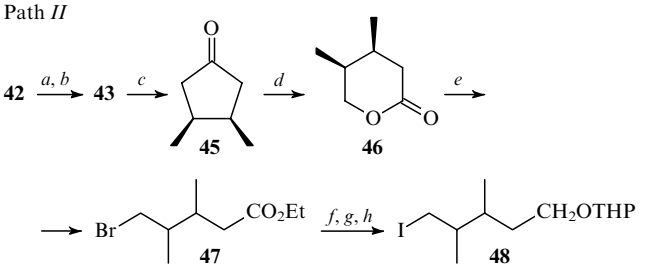


(*a*) $LiAlH_4$; (*b*) $MeSO_2Cl$, Py; (*c*) $KMnO_4$, Bu_4NHSO_4, H_2O–PhH; (*d*) EtOH, H_2SO_4, H_2O; (*e*) TsCl, Py; (*f*) LiI, MeCN; (*g*) NaOH; (*h*) Ph_3P, PhH.

oxidation of dimethylcyclohexene **42** with potassium permanganate under conditions of phase transfer catalysis followed by the transformation of the carboxy groups in the dicarboxylic acid **43** to form phosphonium salt **44**.

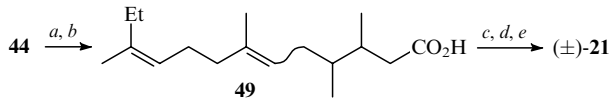
The path *II* [24] involved ozonation of dimethylcyclohexene **42** to form the acid **43**. Its pyrolysis afforded ketone **45** whose Baeyer – Villiger oxidation gave rise to lactone **46** (the total yield was 42.8% with respect to the adduct **41**). Treatment of the lactone **46** with anhydrous HBr in EtOH afforded bromo ester **47**, which was converted into iodide **48** according to standard procedures. The iodide **48** is a synthon for the construction of (±)-faranal.†

Path *II*



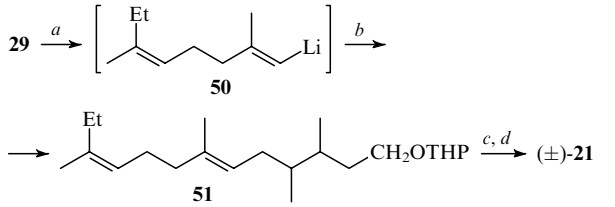
THP is tetrahydropyran-2-yl; (*a*) O_3; (*b*) CrO_3; (*c*) $Ba(OH)_2$, Δ; (*d*) MCPBA; (*e*) HBr, EtOH; (*f*) $LiAlH_4$; (*g*) 3,4-dihydro-2*H*-pyran (DHP), TsOH; (*h*) LiI, MeCN.

The target racemic faranal [(±)-**21**] was synthesised [29] by condensation of the ylide generated from the phosphonium salt **44** with the ketone **34**. The resulting 54 : 46 mixture of isomeric acids (6*E*)- and (6*Z*)-**49** was converted into a mixture of the racemic faranal [(±)-**21**] and its (6*Z*)-isomer through the corresponding ethyl esters and alcohols. The isomer (±)-**21** was isolated from the latter mixture by preparative GLC in 9.1% total yield.



(*a*) NaH, DMSO; (*b*) **34**; (*c*) CH_2N_2; (*d*) $LiAlH_4$; (*e*) PCC, CH_2Cl_2.

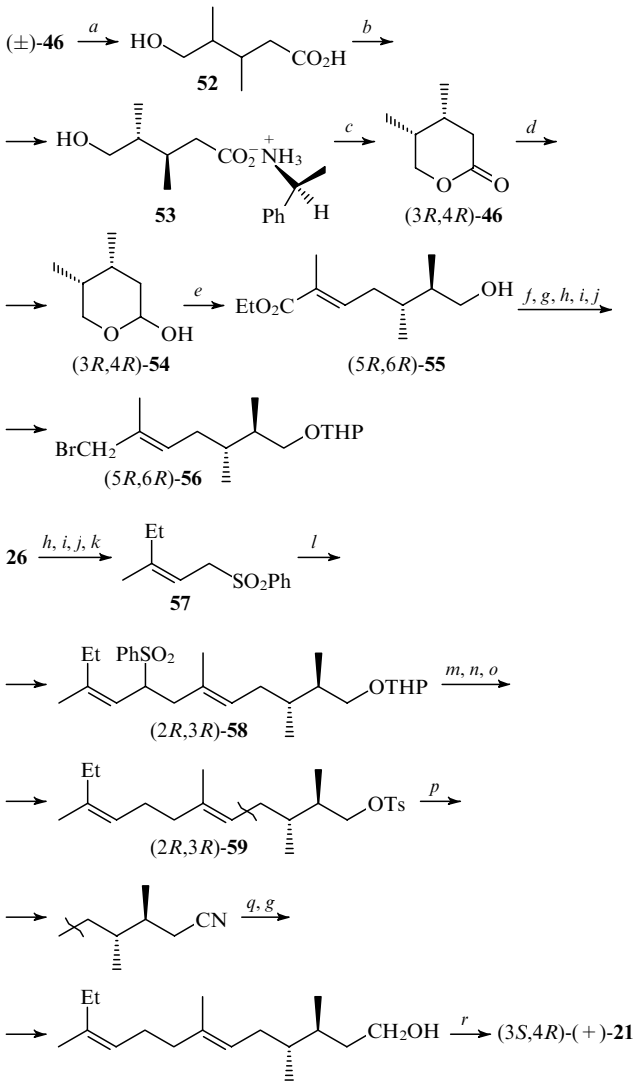
To reach the same goal, Baker *et al.*[24] used condensation of a lithium derivative **50**, which was prepared from the iodide **29**, with the iodide **48**. This condensation is highly stereoselective. The resulting tetrahydropyranyl ether **51** was converted into the (±)-faranal [(±)-**21**] in a total yield of 18% with respect to the iodide **48**.



(*a*) Bu^tLi, Et_2O, −90 °C; (*b*) **48**, Et_2O – THF (1 : 3); (*c*) H_3O^+; (*d*) PCC, CH_2Cl_2.

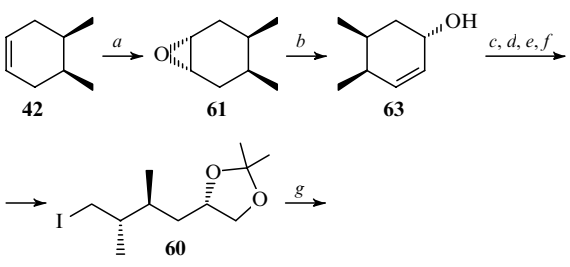
Mori and Ueda [22,23] were the first to synthesise natural (3*S*,4*R*)-(+)-**21**. The key step of this scheme involved asymmetric resolution of hydroxy acid (±)-**52**, which was prepared from the lactone (±)-**46**, using treatment with (*S*)-(−)-α-phenylethylamine. Acidification of the resulting salt **53** afforded the lactone (+)-**46** whose (3*R*,4*R*)-configuration was confirmed by conversion into (*R*)-citronellic acid.

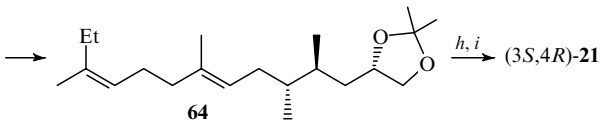
† Recently, Tolstikov and coworkers [33] have reported an efficient synthesis of methoxymethyl analogues of the compound **48**.

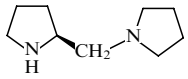
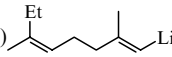


(*a*) NaOH; (*b*) (*S*)-(−)-α-phenylethylamine; (*c*) HCl; (*d*) Bu^i_2AlH; (*e*) $(EtO)_2P(O)CH(Me)CO_2Et$, NaOEt; (*f*) DHP, TsOH; (*g*) $LiAlH_4$; (*h*) BuLi; (*i*) TsCl; (*j*) LiBr, Et_2O – HMPA (hexamethylphosphoric triamide); (*k*) $PhSO_2Na$, DMF; (*l*) BuLi, THF – HMPA, (5*R*,6*R*)-**56**; (*m*) Li/NH_3; (*n*) H_3O^+; (*o*) TsCl, Py; (*p*) NaCN, DMSO; (*q*) NaOH, EtOH; (*r*) PCC, CH_2Cl_2.

Reduction of (3*R*,4*R*)-**46** into chiral lactol **54** followed by the Horner – Emmons reaction of the latter with triethyl 2-methyl-2-phosphonoacetate afforded hydroxy ester (5*R*,6*R*)-**55**, which was converted into bromide (5*R*,6*R*)-**56** using a sequence of standard reactions. The chiral bromide (5*R*,6*R*)-**56** was condensed with sulfone **57** prepared from the alcohol **26**. Desulfation of the resulting sulfone **58** followed by the replacement of the protective group afforded tosylate (2*R*,3*R*)-**59**, which was the starting product in the final steps of the synthesis of faranal [(3*S*,4*R*)-(+)-**21**] identical with the natural specimen.



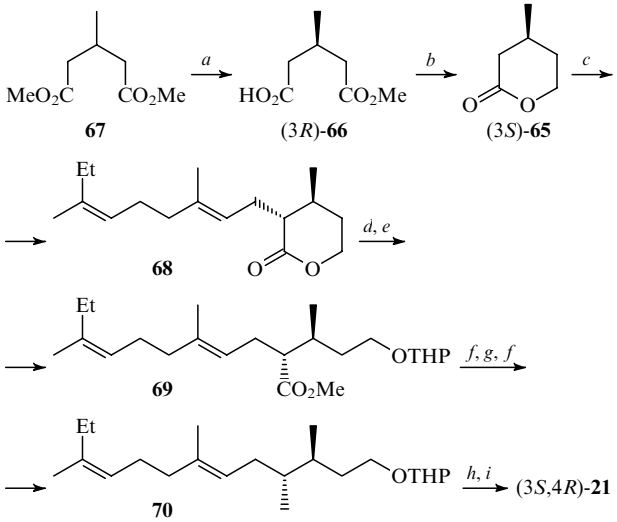


(*a*) MCPBA; (*b*)  (**62**); (*c*) O_3, CH_2Cl_2; (*d*) $NaBH_4$; (*e*) MeCOMe, TsOH; (*f*) I_2, Ph_3P, imidazole; (*g*)  Li (**50**); (*h*) H_3O^+; (*i*) $NaIO_4$.

Later, Mori and Murata [27] developed a shorter synthetic route to faranal [(3*S*,4*R*)-(+)-**21**]. The key chiral synthon for this compound, *viz*., iodide **60**, was prepared in five steps starting from dimethylcyclohexene **42**. The asymmetric resolution of *meso*-epoxide **61** using the lithium derivative of (*S*)-pyrrolidin-2-ylmethyl)pyrrolidine (**62**) afforded allylic alcohol **63**, which was purified by recrystallisation of the corresponding 3,5-dinitrobenzoate to *ee* ~ 100%. Ozonation of the compound **63**, reduction and protection of the hydroxy groups at C(1) and C(2) in the resulting triol followed by substitution of the hydroxy group at C(6) gave rise to the iodide **60**. Condensation of **60** with 6-ethyl-2-methylhepta-1,5-dienyllithium (**50**) resulted in enantiomerically pure acetal **64**. Hydrolysis of **64** followed by periodate oxidation of the resulting diol gave rise to (3*S*,4*R*)-**21** (in a total yield of 12.5% with respect to propyne), which was used for the preparation of the lithium derivative **50**.

The chiral fragment of faranal was constructed also with the use of lactone (3*S*)-**65** formed from methyl hydrogen (3*R*)-3-methylglutarate [(3*R*)-**66**].[30,31] Enzymic hydrolysis of the dimethyl ester **67** using pig liver esterase (PLE) afforded the ester **66** with an optical purity of 85%. This ester was purified by recrystallisation of 1-cinchonidinium salt to *ee* 100%.

Alkylation of the enolate prepared from lactone **65** with the bromide **35** gave rise to lactone (2*R*,3*S*)-**68** containing ~ 6% of the (2*S*,3*S*)-isomer. Transesterification of the lactone **68** followed by protection of the hydroxy group in the resulting hydroxy ester afforded ester **69** whose methoxycarbonyl group was converted into the methyl group in three standard steps. The resulting tetrahydropyranyl ether **70** was converted into (3*S*,4*R*)-**21** in a total yield of ~ 2% with respect to geraniol, which was the starting compound for the preparation of the bromide **35**.



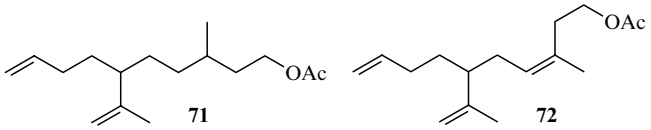
(*a*) PLE; (*b*) Na/NH_3, EtOH; (*c*) Et_2NLi, **35**; (*d*) MeOH, Et_3N; (*e*) DHP, Py·TsOH; (*f*) $LiAlH_4$; (*g*) $MeSO_2Cl$, Py; (*h*) H_3O^+; (*i*) PDC (pyridinium dichromate), CH_2Cl_2.

IV. Syntheses of insect sex pheromones

1. Synthesis of sex pheromones of scales

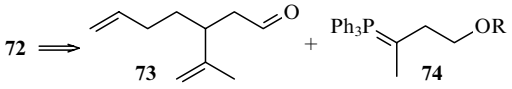
a. Sex pheromone of the California red scale

Roelofs *et al*.[34,35] isolated the female-produced sex pheromone of the California red scale *Aonidiella auranti*, which is the major pest of citrus crops distributed throughout the tropical and subtropical regions. This pheromone was found to consist of two components. Based on the data of physicochemical studies, it was proposed that these components have structures **71** and **72**.

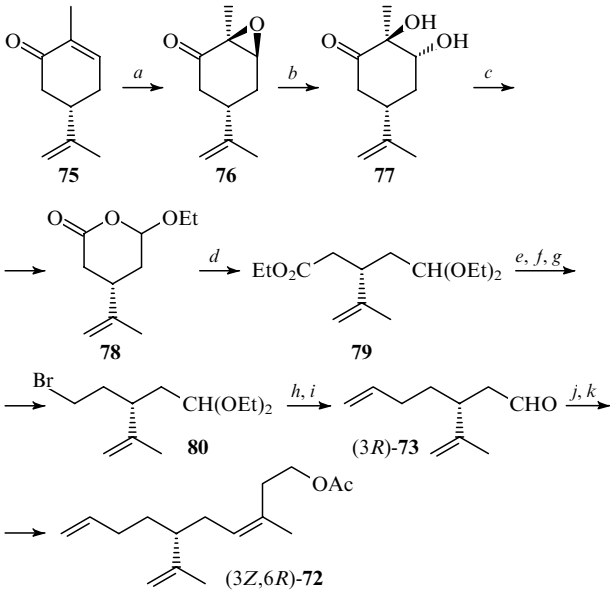


Due to the deficiency of the isolated natural substance, the absolute configurations of these compounds were established only by comparing the physicochemical characteristics of the pheromone components with those of all possible isomers synthesised starting from (*S*)- and (*R*)-carvone. It was found that only the (3*S*,6*R*)-acetate **71** and the (3*Z*,6*R*)-acetate **72** exhibit the pheromone activity.

The retrosynthetic analysis of the molecule **72** shows that the simplest approach to its construction involves the Wittig reaction between synthon blocks **73** and **74**. This approach was used in the first synthesis of the compound **72**.[36]



The aldehyde (3*R*)-**73** was prepared by oxidative scission of (*S*)-carvone (**75**) *via* epoxide **76** and diol **77**. Ethoxy lactone **78** prepared from the diol **77** was converted into compound **79** and then into bromide **80** in three standard steps. Treatment of the bromide **80** with vinyllithium followed by hydrolysis afforded the aldehyde **73**.

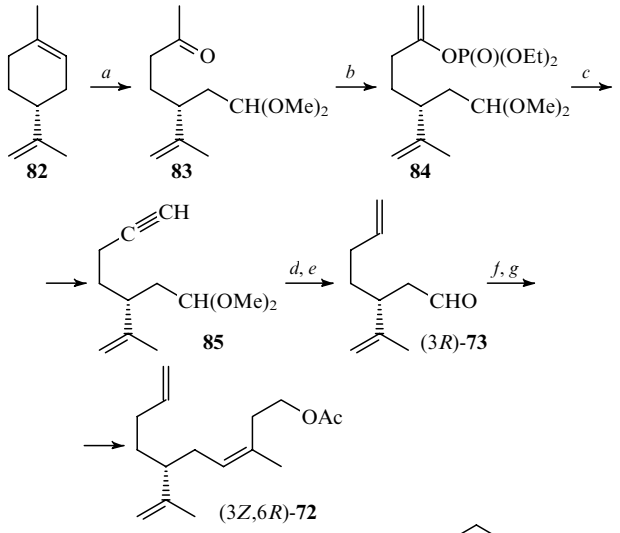


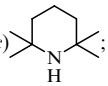
(*a*) H_2O_2, NaOH; (*b*) $HClO_4$, H_2O, THF; (*c*) $Pb(OAc)_4$, EtOH; (*d*) $HC(OEt)_3$, TsOH, EtOH; (*e*) $LiAlH_4$; (*f*) TsCl, Py; (*g*) NaBr, HMPA; (*h*) $CH_2=CHLi$; (*i*) H_3O^+; (*j*) $Ph_3P^+CH(Me)(CH_2)_2OH\ Br^-$ (**81**), 2 equiv. of BuLi; (*k*) Ac_2O, Py.

The reaction of the aldehyde **73** with ylide obtained from phosphonium salt **81** gave rise to a 52 : 48 mixture of isomeric alcohols. Separation of a mixture of (3*Z*)- and (3*E*)-acetates **72**

obtained from these alcohols by preparative GLC afforded compound (3*Z*,6*R*)-**72** in 2.53% total yield.‡

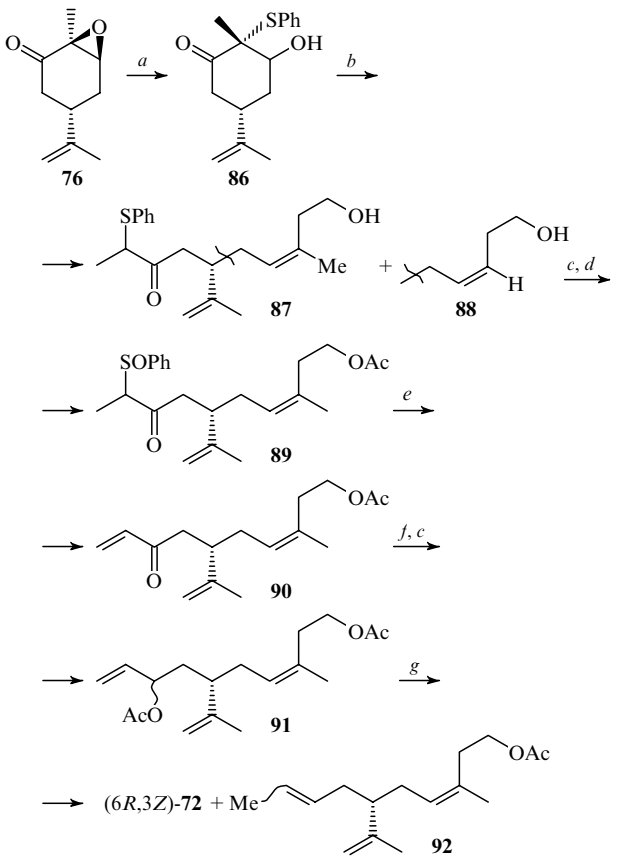
The acetate (3*Z*,6*R*)-**72** was also synthesised [37] starting from (*R*)-limonene **82** according to a similar strategy, but using a more efficient procedure. Ozonolysis of limonene **82** yielded oxo acetal **83**, which was converted into enyne acetal **85** through hydroxy acetal phosphate **84** according to Negishi.[38] Hydrolysis of the latter yielded aldehyde, which was subjected to hydrogenation to form the diene aldehyde (3*R*)-**73**. Condensation of the latter with ylide generated by the reaction of $(Me_3Si)_2NLi$ with the phosphonium salt **81** afforded a 2 : 1 mixture of isomeric alcohols, which were separated by chromatography. Acetylation of the (3*Z*)-isomer produced (3*Z*,6*R*)-**72** in 37% total yield.



(*a*) O_3, MeOH, −70 °C; (*b*) LDA, $ClP(O)(OEt)_2$; (*c*) ; (*d*) H_3O^+; (*e*) H_2, Lindlar catalyst; (*f*) **81**, $(Me_3Si)_2NLi$; (*g*) Ac_2O, Py.

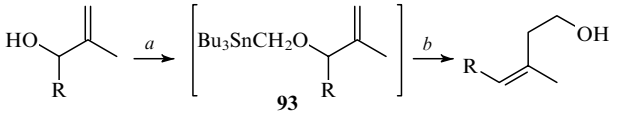
A substantial drawback of the above-considered syntheses of the acetate **72** is the non-stereoselectivity of the key step of the construction of the (*Z*)-trisubstituted C=C bond by the Wittig reaction. Caine and Crews [39] have overcome this drawback using another synthetic scheme. It appeared that when treated with the ylide, which was generated from the salt **81** under the action of BuLi in a mixture of THF and HMPA, β-hydroxy α-phenylthio ketone **86** prepared from the oxirane **76** [40] underwent the retro-aldol reaction followed by the Wittig olefination to form alcohol (3*Z*)-**87**. This compound did not contain an admixture of the (3*E*)-isomer but was contaminated with desmethyl analogue **88** (∼ 15%). The resulting mixture was converted into a mixture of the corresponding acetoxy sulfoxides from which sulfoxide **89** was isolated by chromatography. Thermal desulfinylation of the sulfoxide **89** afforded trienone **90**, which was converted into a mixture of diacetates **91**. Hydrogenolysis of the acetates **91** yielded a 89 : 11 mixture of the pheromone (3*Z*,6*R*)-**72** and its regioisomer **92**. Separation of this mixture was a very tedious procedure. Thus, in spite of the stereoselectivity of the construction of the (*Z*)-trisubstituted C=C bond, this scheme has no advantages over the scheme proposed by Becker and Sahali [37] as regards both the number of steps and the yield of the target compound **72**.

Still and Mitra [41] developed a more efficient procedure for the stereoselective construction of the (*Z*)-trisubstituted alkene fragment in the compound **72**. It was found that the reactions of BuLi with allylic trialkylstannylmethyl ethers of the type **93** were



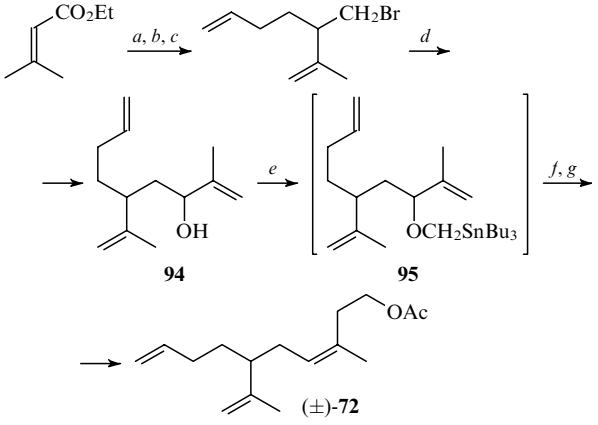
(*a*) PhSH, Et_3N, MeCN; (*b*) **81**, 2 equiv. of BuLi, THF, HMPA; (*c*) Ac_2O, Py; (*d*) MCPBA; (*e*) 135 °C, 0.15 mm Hg; (*f*) $LiAlH_4$; (*g*) HCO_2NH_4, $PdCl_2(PPh_3)_2$, dioxane.

accompanied by a [2,3]-sigmatropic rearrangement yielding (*Z*)-trisubstituted homoallyl alcohols.



R = Alk; (*a*) KH, Bu_3SnCH_2I; (*b*) BuLi.

This finding has been used in the synthesis of the racemic acetate **72**. The key intermediate, *viz*., alcohol **94**, was prepared in four steps starting from ethyl 3-methylcrotonate. The transforma-

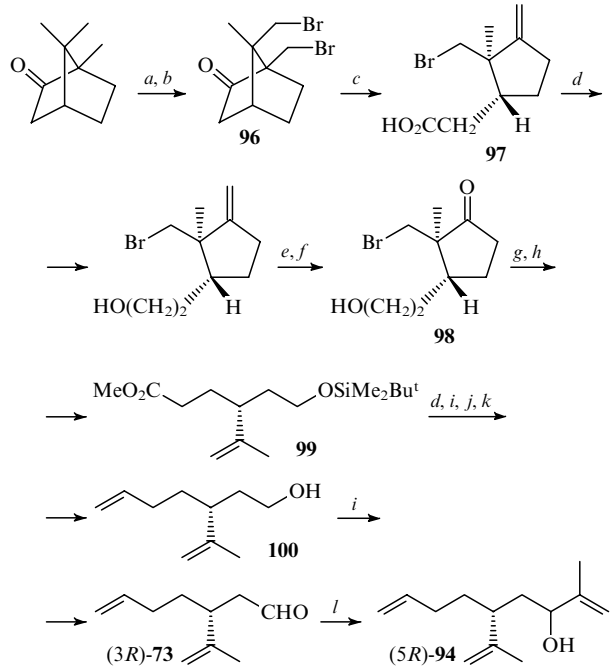


(*a*) LDA, $CH_2=CH(CH_2)_2Br$; (*b*) $LiAlH_4$; (*c*) *N*-bromosuccinimide (NBS), PPh_3; (*d*) Mg, $H_2C=C(Me)CHO$; (*e*) KH, Bu_3SnCH_2I; (*f*) BuLi; (*g*) Ac_2O, Py.

‡ Simultaneously, the isomer (3*E*,6*R*)-**72** was isolated; the isomers (3*Z*,6*S*)-**72** and (3*E*,6*S*)-**72** were prepared analogously starting from (*R*)-carvone.

tion of the skeleton of the alcohol **94** through organotin compound **95** followed by acetylation afforded (±)-**72** in 32% total yield with the stereoselectivity exceeding 95%.

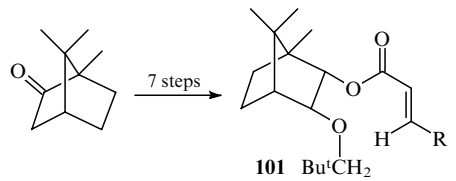
The acetate (3*Z*,6*R*)-**72** was also synthesised [42,43] using the Still rearrangement. The required alcohol (5*R*)-**94** was prepared [42] from (+)-camphor. An efficient enantiospecific procedure developed previously [44–46] for the cleavage of 9,10-dibromocamphor **96** yielding bromoacid **97** has been employed.

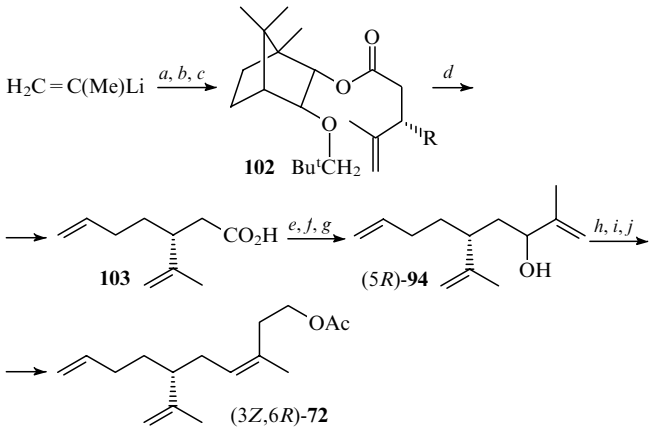


(*a*) Br_2, $ClSO_3H$; (*b*) Zn, AcOH; (*c*) KOH, DMSO, H_2O; (*d*) $LiAlH_4$; (*e*) O_3, MeOH; (*f*) Me_2S; (*g*) Bu^tMe_2SiCl, 4-$Me_2NC_5H_4N$; (*h*) NaOMe, MeOH; (*i*) PDC, CH_2Cl_2; (*j*) $H_2C=PPh_3$; (*k*) Bu_4NF; (*l*) $H_2C=C(Me)MgBr$.

Substituted cyclopentanone **98**, which was synthesised from compound **97** according to standard procedures, is (like compound **96**) a β-bromo ketone and underwent smooth ring-opening following protection of the hydroxy group to form acyclic ester **99**. The latter was transformed into dienol **100** and then into the aldehyde (3*R*)-**73** according to standard procedures. The reaction of the aldehyde (3*R*)-**73** with isopropenylmagnesium bromide afforded the alcohol (5*R*)-**94** in 8% total yield. Since the conversion of the alcohol (±)-**94** to the acetate (±)-**72** had been already performed by Still and Mitra,[41] the above-described procedure for the preparation of (5*R*)-**94** can be formally considered as the first total stereoselective synthesis of (3*Z*,6*R*)-**72**.

Oppolzer and Stevenson [43] synthesised the acetate (3*Z*,6*R*)-**72** also with the use of (+)-camphor, but this was used as a chiral matrix rather than as a synthon. This approach was based on the known fact [47] that alkenyl cuprates stabilised by Bu_3P add with high stereoselectivity to enoates of the type **101** prepared from camphor. In this case, the induced chirality is completely retained after removal of the matrix.



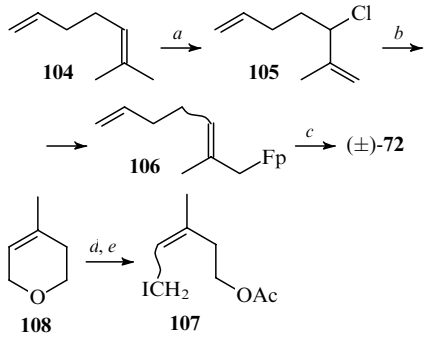


R = $(CH_2)_2CH=CH_2$; (*a*) Bu_3P, CuI, −70 °C; (*b*) $BF_3 \cdot Et_2O$; (*c*) **101**; (*d*) NaOH, EtOH, H_2O; (*e*) $LiAlH_4$; (*f*) $(COCl)_2$, DMSO, Et_3N; (*g*) $H_2C=C(Me)Li$; (*h*) KH, Bu_3SnCH_2I; (*i*) BuLi; (*j*) Ac_2O, Py.

Thus enoate **101** [prepared from (+)-camphor in seven steps] added the complex of diisopropenyl cuprate with Bu_3P to form ester **102** with an enantioselectivity of ~ 95%. Saponification of the ester **102** afforded chiral acid **103**. This acid was converted into the alcohol (5*R*)-**94** according to standard procedures. The latter was transformed into (3*Z*,6*R*)-**72** using the Still rearrangement in 20% total yield.

The synthesis of the triene **72** still attracts interest. This pheromone serves as a test substance for examining every new method proposed for the construction of (*Z*)-trisubstituted C=C bonds.

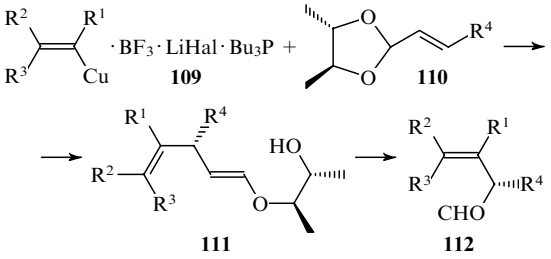
Thus the compound **72** was chosen [48] as one of the subjects for the comparison of the reactivities of allylic organoiron nucleophiles with those of allylsilanes and allylstannanes. The synthesis of (±)-**72** involved the conversion of the commercially available diene **104** into a mixture (~ 1 : 1) of organoiron compounds (2*Z*)- and (2*E*)-**106** *via* allylic chloride **105**. The second synthon required for the construction of the triene **72**, *viz*., iodide **107** (a ~ 1 : 1 mixture of the isomers), was prepared from 4-methyl-5,6-dihydro-2*H*-pyran **108** according to standard procedures.



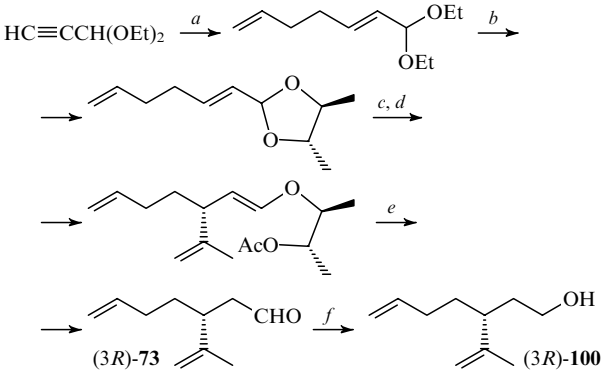
Fp = $C_5H_5Fe(CO)_2$; (*a*) $Ca(OCl)_2$; (*b*) NaFp; (*c*) **107**, $MeNO_2$; (*d*) AcCl, $K[PtCl_3(C_2H_4)]$; (*e*) NaI, Me_2CO.

In spite of the geometric inhomogeneity of the iodide **107**, its condensation with organoiron derivatives **106** at ~ 20 °C afforded (±)-**72** (the yield was 42%) containing < 1% of an admixture of the (3*E*)-isomer. The selectivity of the reaction was attributed to the high reactivity of the (3*Z*)-iodide **107** due to the anchimeric assistance to ionisation provided by the acetoxy group. This scheme is attractive because it involves a small number of steps and does not require the introduction and removal of protective groups.

The syntheses of the aldehyde (3*R*)-**73** and the alcohol (3*R*)-**100**,[49] which are the key intermediates in the synthesis of (3*Z*,6*R*)-**72**, were carried out with the use of a previously discovered 1,4-addition of complex organocopper compounds of the type **109** to acetals **110** prepared from α,β-enals and (*R*,*R*)-butane-2,3-diol. Dienol ethers **111** prepared by the highly regio- and diastereoselective reaction were subjected to hydrolysis to form aldehydes **112** in quantitative yields.



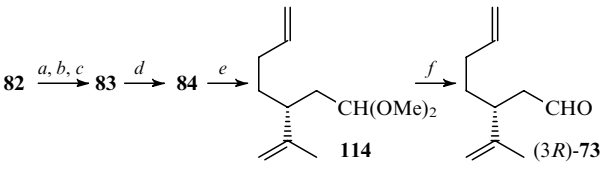
This scheme was tried out in the synthesis of the aldehyde (3*R*)-**73** starting from propargylaldehyde diethyl acetal (the yield was 50%, *ee* 85%). The aldehyde (3*R*)-**73** was reduced to the alcohol (3*R*)-**100** in quantitative yield.

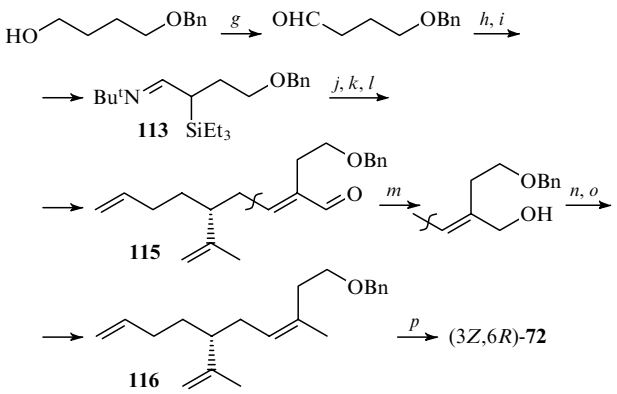


(*a*) $[H_2C=CH(CH_2)_2]_2CuLi$; (*b*) (2*R*,3*R*)-HOCH(Me)CH(Me)OH, TsOH; (*c*) $H_2C=C(Me)Cu\cdot LiBr\cdot BF_3\cdot PBu_3$; (*d*) Ac_2O, Py; (*e*) HCO_2H; (*f*) $NaBH_4$.

The aldehyde (3*Z*,6*R*)-**72** was also synthesised[50] using a highly stereoselective procedure developed by one of the authors[51–53] of the present review for the construction of (*Z*)-trisubstituted alkenes based on the facts that (*E*)-isomers of α,β-disubstituted acroleins are thermodynamically favourable and that they are stereospecifically converted into (*Z*)-trisubstituted alkenes.

According to this methodology, Baudouy and Prince[50] chose the aldehyde (3*R*)-**73** and α-(triethylsilyl)imine **113** as synthons for the construction of (3*Z*,6*R*)-**72**. The aldehyde (3*R*)-**73** was prepared from limonene according to a scheme reported previously.[37] However, Baudouy and Prince[50] developed a direct procedure for the conversion of the hydroxy acetal phosphate **84** into diene acetal **114**, which made it possible to reduce the scheme by two steps. The aldehyde (3*R*)-**73** was formed upon hydrolysis of the acetal **114** in quantitative yield. The second synthon, *viz*., silylated imine **113**, was prepared in three standard steps starting from the monobenzyl ether of butane-1,4-diol.

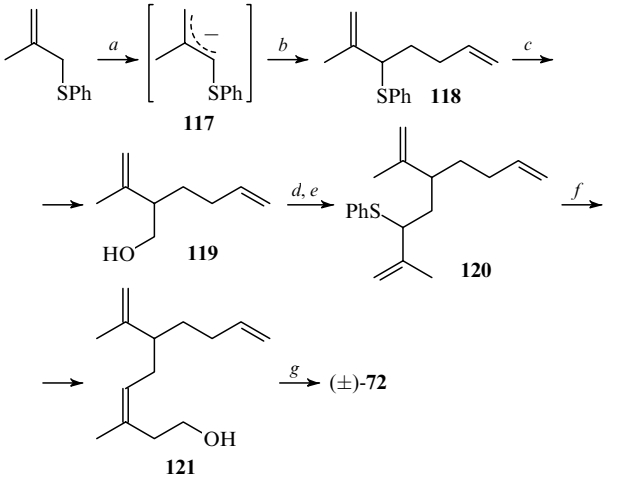




(*a*) O_3, MeOH; (*b*) $(H_2N)_2CS$; (*c*) $HC(OMe)_3$, $CeCl_3\cdot 6H_2O$; (*d*) LDA, $ClP(O)(OEt)_2$, THF; (*e*) Li/NH_3, THF; (*f*) $HClO_4$, THF, H_2O; (*g*) $(COCl)_2$, DMSO, Et_3N; (*h*) Bu^tNH_2, 4 Å molecular sieves; (*i*) LDA, Et_3SiCl; (*j*) Bu^sLi, (3*R*)-**73**; (*k*) H_3O^+; (*l*) $C_5H_5N\cdot HCl$, CH_2Cl_2; (*m*) $LiAlH_4$, Et_2O; (*n*) $C_5H_5N\cdot SO_3$, THF; (*o*) $LiAlH_4$, THF; (*p*) Ac_2O, $HClO_4$.

Condensation of the imine **113** deprotonated under the action of Bu^sLi with the aldehyde (3*R*)-**73** afforded acrolein **115**. The mixture formed initially was kept in a CH_2Cl_2 solution containing pyridinium chloride for 4 h after which the content of the (*Z*)-isomer was no higher than 1%. The carbonyl group in compound **115** was reduced to the methyl group in three standard steps. The replacement of the protective benzyl group in the resulting ether **116** by the acetate group gave rise to (3*Z*,6*R*)-**72** in 30% total yield.

The construction of the pheromone (±)-**72**[54] based on a method for the generation of allyllithium compounds by reductive lithiation of readily available allyl phenyl sulfides with aromatic radical anions[55–57] has proved the utility of this procedure. The regiocontrolled addition of unsymmetrical alkyllithium derivatives to carbonyl compounds (which had been developed by the authors previously) employed in this synthesis is of particular interest. Thus treatment of the allyllithium intermediate with $Ti(OPr)_4$ allows one to perform the subsequent reaction with an aldehyde at the more substituted position of the allylic system, whereas treatment with $CeCl_3$, on the contrary, makes it possible to perform this reaction at the less substituted position.

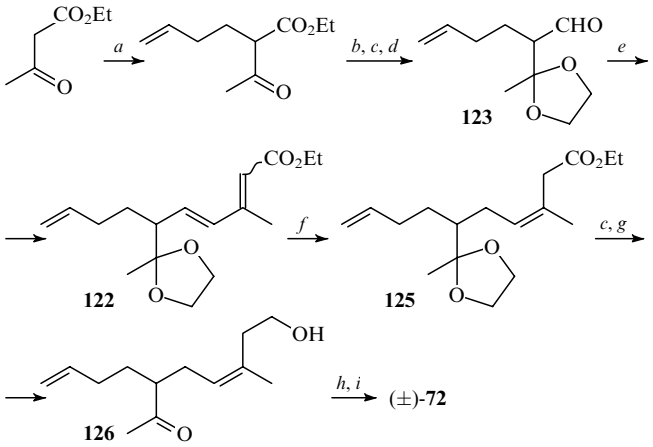


(*a*) Bu^sLi; (*b*) $H_2C=CH(CH_2)_2Br$; (*c*) lithium 4,4′-di(*tert*-butyl)biphenylide (LDBB), −78 °C, $Ti(OPr)_4$, CH_2O; (*d*) CBr_4, Ph_3P; (*e*) **117**; (*f*) LDBB, −78 °C, $CeCl_3$, CH_2O; (*g*) Ac_2O, Py.

Thus alkylation of the anion **117** generated from isobutenyl phenyl sulfide under the action of Bu^sLi with but-3-enyl bromide occurred exclusively at the α position to form sulfide **118**. Reductive lithiation of the latter with lithium 4,4′-di(*tert*-butyl)-

biphenylide followed by *in situ* treatment of the reaction product with $Ti(OPr)_4$ and the reaction of the resulting organotitanium compound with formaldehyde afforded alcohol **119**, which was converted into allyl sulfide **120**. The sulfide **120** was subjected to reductive lithiation. The successive treatment of the resulting alkyllithium intermediate with $CeCl_3$ and formaldehyde gave rise to alcohol (3*Z*)-**121** from which the acetate (±)-**72** was obtained in 22.4% total yield.

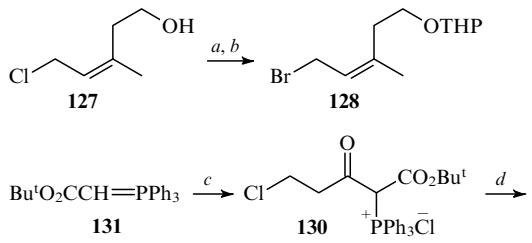
In 1995, Serebryakov and coworkers [58] synthesised the acetate (±)-**72** using the highly selective 1,4-*cis*-hydrogenation of conjugated dienes in the presence of carbonyl chromium complexes [59] for the construction of the (*Z*)-trisubstituted C=C bond. This method had been employed previously [60,61] in the synthesis of natural compounds. The triene **122** required for this synthesis was prepared in five steps from ethyl acetoacetate.

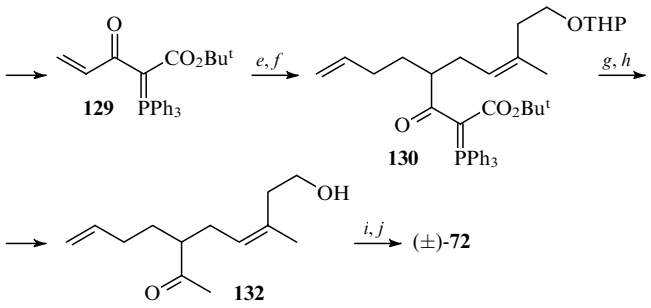


(*a*) EtONa, EtOH, $H_2C=CH(CH_2)_2Br$; (*b*) $HO(CH_2)_2OH$, TsOH; (*c*) $LiAlH_4$; (*d*) PCC, CH_2Cl_2; (*e*) $(EtO)_2P(O)CH_2CH(Me)=CHCO_2Et$ (**124**), KOH, PhH, 18-crown-6 (18-C-6); (*f*) H_2, $(PhCO_2Me)Cr(CO)_3$, Me_2CO, 120 °C; (*g*) H_3O^+; (*h*) $Ph_3P=CH_2$; (*i*) Ac_2O, Na_2CO_3, 100 °C.

Alkylation of ethyl acetoacetate with but-3-enyl bromide, the conversion of the resulting oxo ester (after protection of the carbonyl group) into hydroxy ketal and oxidation of the latter afforded aldehyde **123**. Condensation of **123** with triethyl 3-methyl-4-phosphonocrotonate (**124**) under conditions of phase transfer catalysis according to a procedure developed previously [62] gave rise to a 2:1 mixture of the trienes (2*E*)- and (2*Z*)-**122**. Hydrogenation of the conjugated diene system in the presence of a chromium complex afforded (3*Z*)-ester **125**, which virtually did not contain an admixture of the (3*E*)-isomer. The ester **125** was converted into hydroxy ketone **126** by standard procedures. The reaction of the ketone **126** with methylidenetriphenylphosphorane followed by acetylation of the resulting alcohol completed the synthesis of (±)-**72** (the total yield was 4.3%).

In the synthesis of the compound **72**, Cooke and Burman [63] did not develop a new approach to the construction of the (*Z*)-trisubstituted C=C bond but used the available (*Z*)-alkene fragment in chlorohydrin **127** (*Z* > 98%), which had been described previously [64] and which was converted into bromide **128** in two steps.



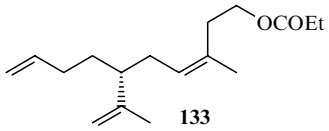


(*a*) DHP, HCl; (*b*) NaBr, *N*-methylpyrrolidone; (*c*) $Cl(CH_2)_2COCl$; (*d*) MeONa; (*e*) $H_2C=CHCH_2Li$; (*f*) **128**; (*g*) AcOH, 90 °C; (*h*) NaOH; (*i*) Ac_2O, Py; (*j*) $Ph_3P=CH_2$.

In the study cited (Ref. 63), an ingenious method for the assembly of the molecule (±)-**72** was used. Phosphorane **129** was used as the key compound in this synthetic scheme. The compound **129** was generated from phosphonium salt **130**, which was prepared by acylation of *tert*-butoxycarbonylmethylidenetriphenylphosphorane **131** with β-chloropropionyl chloride. Successive treatment of the phosphorane **129** with prop-2-enyllithium and the bromide **128** afforded the phosphorane **130** containing the major structural fragments of the pheromone (±)-**72**. The phosphorane **130** was converted into hydroxy ketone **132** by a procedure developed previously.[65] Acetylation of the latter followed by the reaction of the resulting acetate with methylidenetriphenylphosphorane gave rise to (±)-**72** in 8.5% total yield.

b. Sex pheromone of the white peach scale

Subsequent to the pheromone of the California red scale **72**, a structurally similar female-produced sex pheromone of the white peach scale *Pseudaulascaspis pentagona*, *viz*., propionate **133**, was isolated.[66]

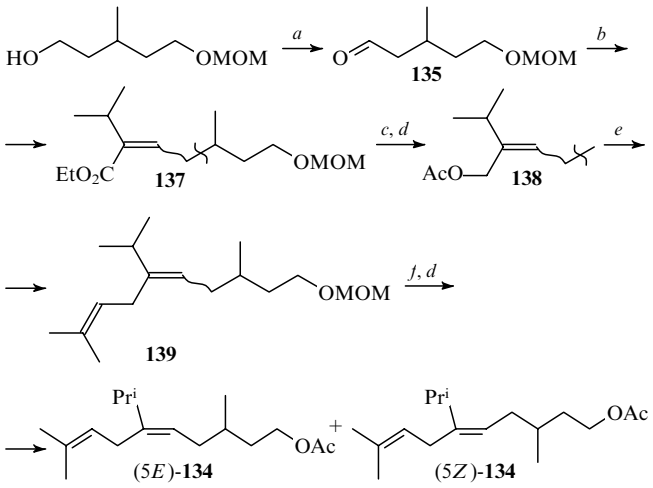


The structure of compound **133** was established by physicochemical methods and the absolute configuration of the C(6) centre was determined based on the results of bioassays of both enantiomers, which have been synthesised starting from (+)- and (−)-limonenes according to a scheme analogous to that used in the synthesis of the acetate **72** (see Section IV.1.a). Only the (3*Z*,6*R*)-propionate **133** appeared to be the active attractant.[67]

Serebryakov and coworkers [58] performed a highly stereoselective synthesis of the compound **133** according to a procedure analogous to that developed by them for the pheromone **72**.

c. Sex pheromone of the yellow scale

Gieselmann *et al*.[68] isolated the female-produced sex pheromone of the yellow scale *Aonidiella citrina*, a species morphologically very similar to *A.auranti*, and established its structure. Although the pheromone of the yellow scale (3*R*,5*E*)-**134** is formally the (5*E*)-isomer, we consider this compound in the present review because the branches of its major hydrocarbon chain, like those in the pheromones of the California red scale and the white peach scale, are in the *cis* positions with respect to each other. Because of this, (3*R*,5*E*)-**134** was synthesised according to procedures analogous to those used for the preparation of pheromones containing the (*Z*)-trisubstituted C=C bond. Based on the results of physicochemical studies,[68] the structure (5*E*)-**134** was assigned to this pheromone [with the accuracy of the absolute configuration of the C(3) centre]. This structure was confirmed by two independent syntheses. One of these syntheses [69] involved the Horner–Emmons reaction of aldehyde **135** with an anion generated from phosphonate **136**.



MOM is methoxymethyl; (*a*) PCC, AcONa, CH_2Cl_2; (*b*) $(EtO)_2P(O)CH(Pr^i)CO_2Et$ (**136**), EtONa; (*c*) Bu^i_2AlH; (*d*) Ac_2O, Py; (*e*) $(Me_2C{=}CH)_2CuLi$; (*f*) Cl_3CCO_2H.

The resulting mixture (4 : 1) of the esters (*Z*)- and (*E*)-**137** was converted into a mixture of acetates **138** through the corresponding alcohols. Treatment of the compounds **138** with diisobutenyllithium cuprate afforded a mixture of isomers **139**, which was converted into a mixture of acetates (5*E*)-**134** and (5*Z*)-**134** in two standard steps also in a ratio of 1 : 4. Bioassays of the isomers separated by preparative GLC demonstrated that only the compound (5*E*)-**134** exhibited the attractant activity.

Suguro *et al.*[70] reached the same conclusion when performing the stereoselective synthesis of the isomeric acetates **134** from the common precursor, *viz.*, ester (5*E*)-**140**. This ester was prepared with a stereoselectivity of 92% by the *in situ* Claisen – Johnson [3,3]-sigmatropic rearrangement of orthoester **141** (Scheme 1).

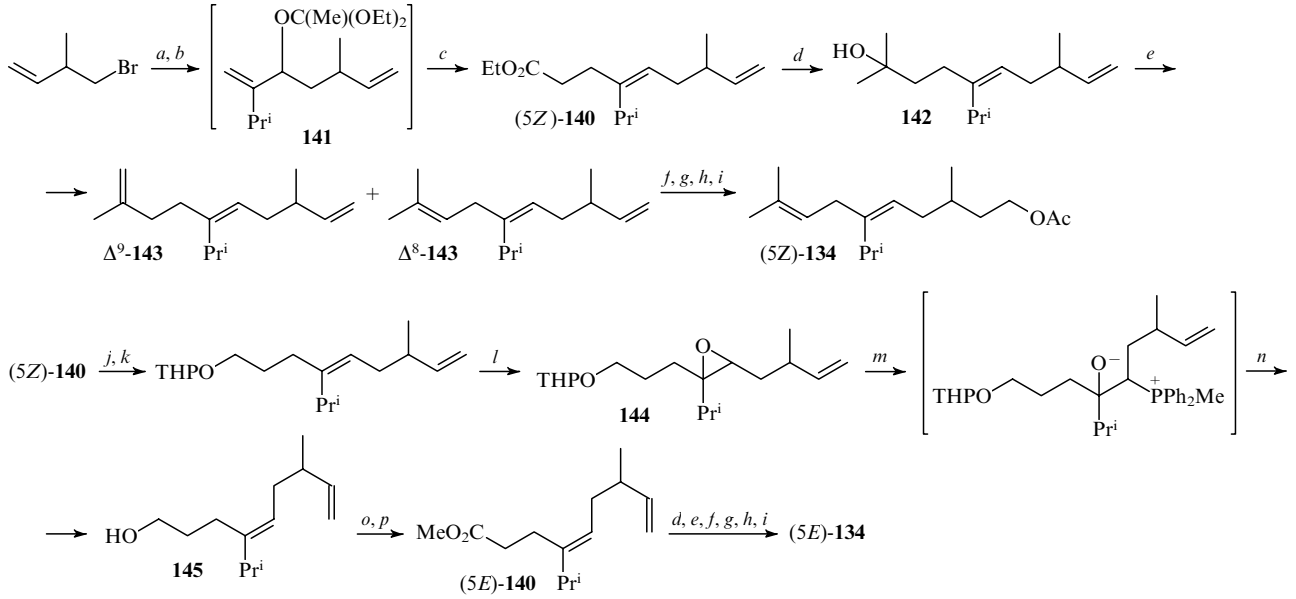
Treatment of the ester **140** with MeMgI afforded alcohol **142**, which was dehydrated to form a mixture of regioisomeric trienes **143**. Hydroboration of this mixture under standard conditions gave rise to a mixture of the corresponding alcohols from which the (5*Z*)-isomer was isolated by chromatography. Acetylation of the latter afforded the acetate (5*Z*)-**134** in ~ 1% total yield.

The ester (5*E*)-**140** required for the preparation of the acetate (5*E*)-**134** was synthesised *via* epoxide **144** by the Vedejs method.[71] Successive treatment of the epoxide **144** with lithium diphenylphosphide and methyl iodide afforded the corresponding tetrahydropyranyl derivative, which was converted into alcohol **145**. Oxidation of the hydroxy group in the alcohol **145** and methylation of the resulting carboxylic acid gave rise to the ester (5*E*)-**140**, which was converted into (5*E*)-**134** in 0.5% total yield by an analogous procedure.

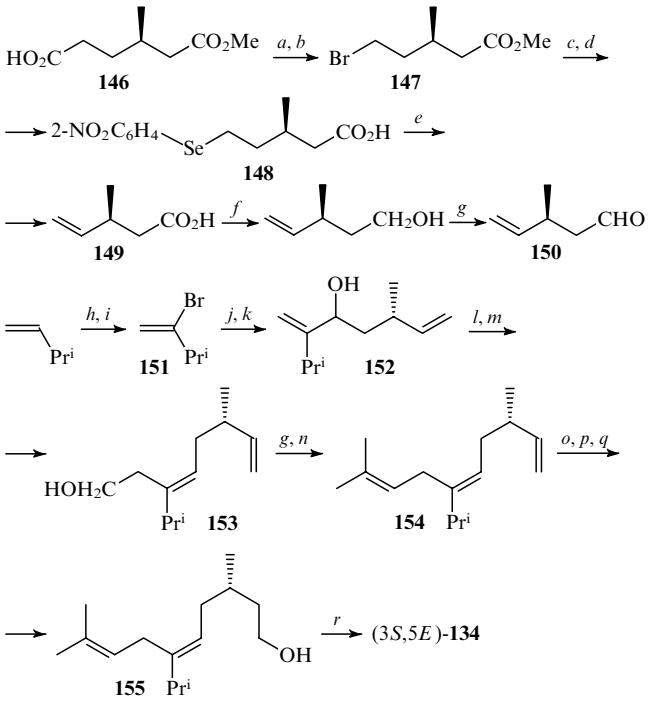
Mori and coworkers [72] established the absolute configuration of the C(3) centre in the acetate **134** and performed the synthesis of (3*S*,5*E*)-**134** exhibiting the high attractant activity. For this purpose, chiral monoester (*R*)-**146**, which was synthesised from (*R*)-citronellic acid, was used as the starting compound. The Hunsdiecker reaction of the monoester (*R*)-**146** afforded bromide **147**, which was transformed into acid **149** *via* selenide **148**. The acid **149** was smoothly converted into aldehyde **150**. The reaction of the aldehyde **150** with an organomagnesium compound prepared from bromide **151** gave rise to alcohol **152**, which was subjected to the Still rearrangement. The alcohol **153** containing the trisubstituted alkene fragment was obtained with a stereoselectivity of > 95%. The reaction of an aldehyde prepared from **153** with isopropylidenetriphenylphosphorane afforded triene **154**. Hydroboration – oxidation of the terminal double bond in the triene **154** followed by acetylation of the resulting alcohol **155** completed the synthesis of (3*S*,5*E*)-**134** (the total yield was 0.2%).

Later, Mori and Kuwahara [73] performed a more efficient synthesis of (3*S*,5*E*)-**134**. According to this scheme, the trisubstituted alkene fragment was also constructed by the Still rearrangement. The key intermediate, *viz.*, benzyloxy alcohol **156**, was prepared by the reaction of the organomagnesium derivative of the bromide **151** with aldehyde **157**. The latter was synthesised by the seven-step transformation of methyl (*R*)-citronellate [(*R*)-**158**]. The conversion of the benzyloxy alcohol **156** according to Still giving rise to benzyloxy alcohol **159**, oxidation of the latter and treatment of the resulting aldehyde with isopropylidenetriphenylphosphorane afforded benzyl ether **160**. The target acetate (3*S*,5*E*)-**134** was prepared from **160** in 7% total yield.

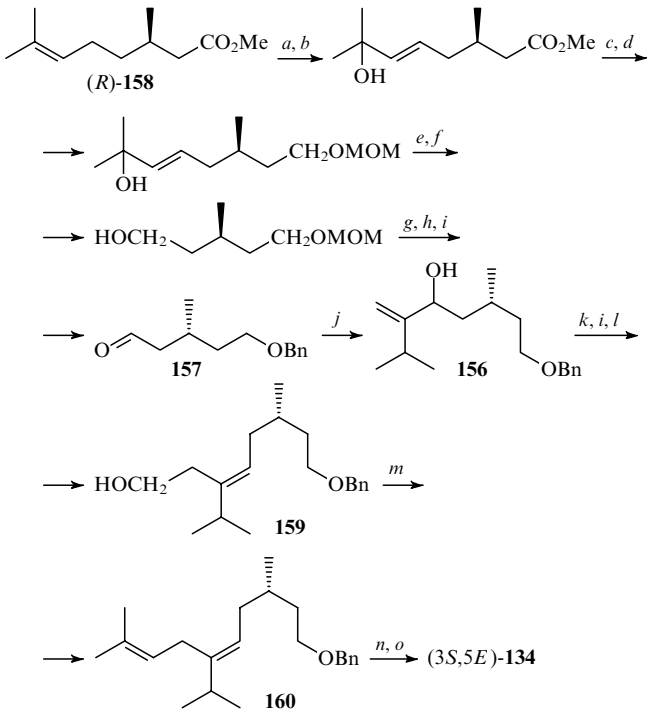
Scheme 1



(*a*) Mg, $H_2C{=}CH(Pr^i)CHO$; (*b*) $MeC(OEt)_3$; (*c*) $EtCO_2H$, 135 °C; (*d*) MeMgI; (*e*) $POCl_3$, Py; (*f*) 9-borabicyclo[3.3.1]nonane (9-BBN); (*g*) NaOH; (*h*) H_2O_2; (*i*) Ac_2O, Py; (*j*) $LiAlH_4$; (*k*) DHP, TsOH; (*l*) MCPBA; (*m*) Ph_2PLi, MeI; (*n*) H_3O^+; (*o*) PDC, DMF; (*p*) CH_2N_2.



(*a*) Ag_2O; (*b*) Br_2; (*c*) 2-$NO_2C_6H_4SeCN$, $NaBH_4$; (*d*) NaOH, Δ; (*e*) H_2O_2; (*f*) $LiAlH_4$; (*g*) PDC, CH_2Cl_2; (*h*) Br_2; (*i*) 2,5-$Me_2C_6H_3OH$, NaH; (*j*) Mg; (*k*) **150**, THF; (*l*) KH, Bu_3SnCH_2I; (*m*) BuLi; *n*) $Ph_3P{=}CMe_2$; (*o*) 9-BBN; (*p*) NaOH; (*q*) H_2O_2; (*r*) Ac_2O, Py.

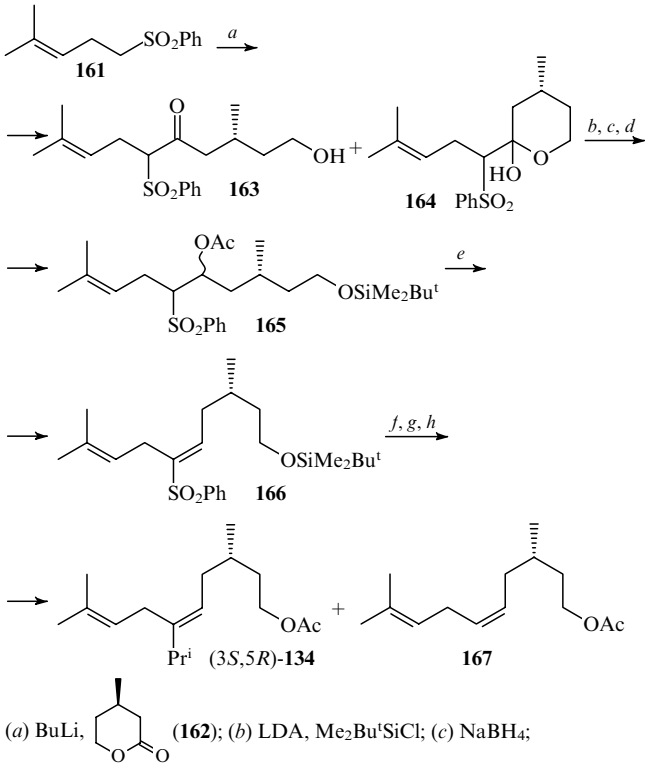


(*a*) $(PhSe)_2$, H_2O_2; (*b*) $Bu^t_2O_2$; (*c*) $LiAlH_4$; (*d*) NaH, $MeOCH_2Cl$ (MOMCl); (*e*) O_3, $NaHCO_3$, MeOH; (*f*) $LiAlH_4$; (*g*) NaH, BnCl; (*h*) TsOH, MeOH; (*i*) PDC, CH_2Cl_2; (*j*) $H_2C{=}C(Pr^i)MgBr$; (*k*) KH, $Bu^n_3SnCH_2I$; (*l*) BuLi; (*m*) $Ph_3P{=}C(Me)_2$; (*n*) Li/NH_3; (*o*) Ac_2O, Py.

Simultaneously, Mori and Kuwahara [73] prepared (3*R*,5*E*)-**134** in 10% total yield. Bioassays demonstrated that only the (3*S*)-enantiomer exhibited the attractant activity.[73, 74]

Although Mori and coworkers [70, 72, 73] succeeded in performing stereoselective synthesis of (3*S*,5*E*)-**134**, the synthetic schemes involved many steps and, as a result, the target compound was prepared in low yield. Later, more efficient syntheses of the acetate (5*E*)-**134** were performed.[75–77]

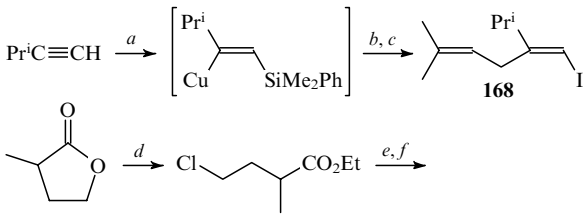
Julia and coworkers [75] constructed the chiral fragment in the acetate (5*E*)-**134** by the reaction of an anion generated from sulfone **161** with (3*R*)-methylvalerolactone (**162**). When treated with *tert*-butyldimethylchlorosilane, the resulting mixture of hydroxy oxo sulfone **163** and hemiketal **164** was quantitatively converted into the silyl derivative of hydroxy oxo sulfone **163**. Reduction of the carbonyl group in **163** followed by acetylation of a mixture of the resulting alcohols afforded a mixture of acetates **165**. Elimination of AcOH from the acetates **165** resulted in sulfone **166** containing an admixture (< 2%) of the (5*Z*)-isomer.

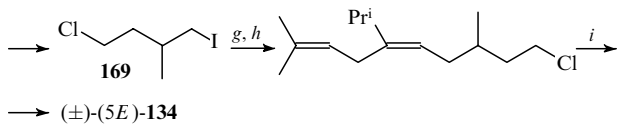


(*a*) BuLi, (**162**); (*b*) LDA, Me_2Bu^tSiCl; (*c*) $NaBH_4$; (*d*) Ac_2O, dimethylaminopyridine (DMAP), Py; (*e*) NaOH; (*f*) Pr^iMgBr, $FeCl_3$; (*g*) Bu_4NF; (*h*) Ac_2O, Py.

The reaction of the sulfone **166** with Pr^iMgBr in the presence of $FeCl_3$ afforded, like other analogous reactions studied previously,[78] a 1 : 1 mixture of products of replacement and elimination of the sulfonyl group. After removal of the silyl protection, acetylation and chromatographic separation of the resulting mixture of the acetates (3*S*,5*E*)-**134** and **167**, (3*S*,5*E*)-**134** was isolated in 17.2% total yield.

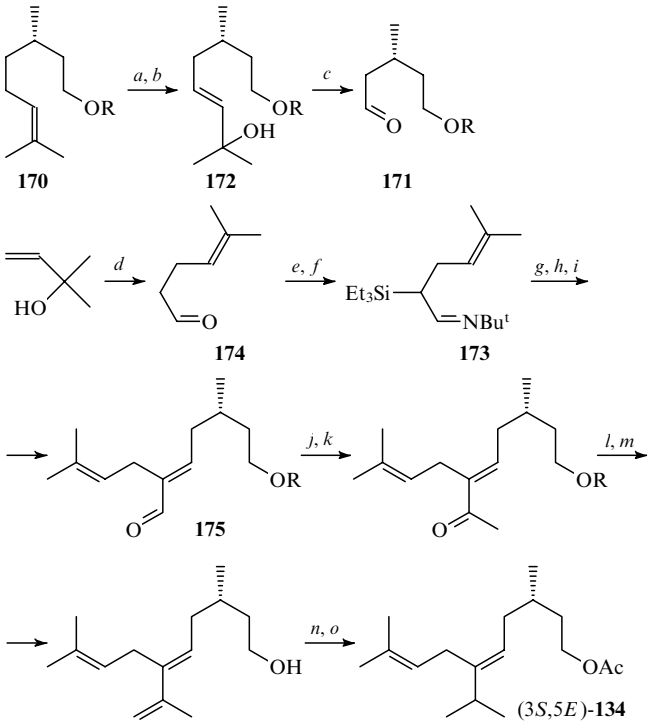
Millar [76] constructed the trisubstituted alkene fragment in the compound (5*E*)-**134** based on the above-mentioned highly stereoselective addition of cuprates to alkynes. Thus successive treatment of 3-methylbut-1-yne with $(PhMe_2Si)_2CuLi$ (Ref. 79) and 3-methylbut-2-enyl bromide gave rise to vinylsilane containing 16% of the S_N2'-addition product. This mixture was converted into the corresponding iodides. Flash chromatography of the latter afforded iodide **168** in 39% total yield. This iodide was transformed into the target acetate (±)-(5*E*)-**134** by cross-coupling with an organozinc reagent synthesised from iodide **169**. The reaction product was converted into the target acetate (±)-(5*E*)-**134** (the total yield was ~ 16%).





(*a*) 2 equiv. of $PhMe_2SiLi$, CuCN, THF; (*b*) $BrCH_2CH=CMe_2$; (*c*) I_2; (*d*) HCl, EtOH; (*e*) $LiAlH_4$; (*f*) $I_2 \cdot Ph_3P$, imidazole; (*g*) Zn, THF; (*h*) **168**, $(Ph_3P)_4Pd$; (*i*) NaOAc, HMPA.

The pheromone (3*S*,5*E*)-**134** was also synthesised [77] starting from (*S*)-citronellyl pivalate (**170**). The highly stereoselective construction of the trisubstituted alkene fragment took advantage of thermodynamic predominance of the (*E*)-isomers of α,β-disubstituted acroleins,[53] *i.e.*, it is based on the approach used previously [50] in the synthesis of the pheromone of the California red scale **72**. The first synthon, *viz.*, aldehyde **171**, was prepared from the ester **170** by oxidation of its phenylselenenyl derivative with di-*tert*-butyl peroxide.

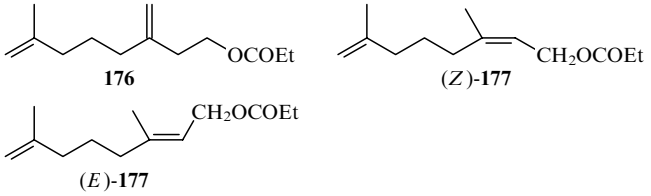


R = $COBu^t$; (*a*) $(PhSe)_2$, H_2O_2; (*b*) $Bu^t_2O_2$; (*c*) O_3, −78 °C; (*d*) $EtOCH=CH_2$, H_3PO_4, 150 °C; (*e*) Bu^tNH_2, 4 Å molecular sieves; (*f*) LDA, Et_3SiCl; (*g*) Bu^sLi, **171**; (*h*) CF_3CO_2H, H_2O; (*i*) $C_5H_5N \cdot HCl$; (*j*) MeMgI; (*k*) $(COCl)_2$, DMSO, Et_3N; (*l*) $Ph_3P=CH_2$; (*m*) Bu^i_2AlH; (*n*) H_2, $(Ph_3P)_3RhCl$; (*o*) Ac_2O, Et_3N.

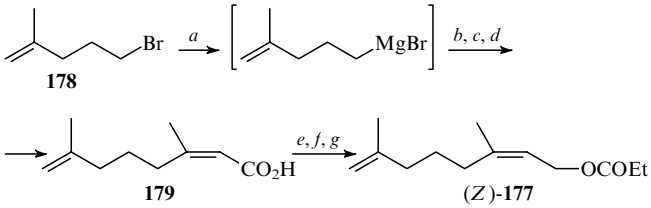
Subsequent ozonolysis of the resulting tertiary alcohol **172** afforded the aldehyde **171**. The second synthon, *viz.*, silylated imine **173**, was prepared by condensation of 2-methylbut-3-en-2-ol with ethyl vinyl ether followed by successive treatment of the resulting aldehyde **174** with Bu^tNH_2 and Et_3SiCl. Condensation of the imine **173** with the aldehyde **171** under conditions used previously [50] in the synthesis of the pheromone **72** yielded acrolein **175**, which virtually did not contain the (*Z*)-isomer. The carbonyl group in the aldehyde **175** was converted into the isopropyl fragment in six steps. The target acetate (3*S*,5*E*)-**134** was prepared in 25% total yield. This is the best result obtained in the synthesis of the sex pheromone of the yellow scale.

d. Sex pheromone of the San Jose scale

Almost simultaneously with the pheromone of the yellow scale, the female-produced sex pheromone of the San Jose scale *Quadraspidiotus perniciosus*, which is a widespread polyphagous pest of fruit and decorative trees, was isolated.[80] Two major components of this pheromone, *viz.*, esters **176** and (*Z*)-**177**, were identified by physicochemical methods. More recently,[81] the ester (*E*)-**177** was also found. It was demonstrated that the pheromone contains these components in a ratio of 47.55 : 47.75 : 4.70.[81] Each of these components exhibits approximately the same biological activity.



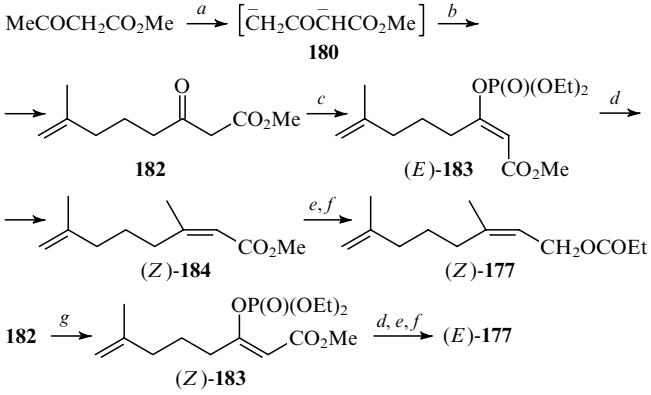
The ester (*Z*)-**177** was synthesised for the first time [82] with the use of the above-mentioned highly stereoselective addition of dialkyl cuprates to alkynes in the key step of the construction of the (*Z*)-trisubstituted alkene fragment.



(*a*) Mg; (*b*) $CuBr \cdot Me_2S$; (*c*) $HC{\equiv}CMe$; (*d*) CO_2, $(EtO)_3P$, HMPA; (*e*) CH_2N_2; (*f*) Bu^i_2AlH; (*g*) $(EtCO)_2O$, Py.

The reaction of cuprate obtained from the magnesium derivative of bromide **178** with propyne proceeded as *cis*-addition. Treatment of the reaction mixture with CO_2 afforded (2*Z*)-acid **179**. The latter was converted into the target pheromone (*Z*)-**177** in 29% total yield using standard procedures.

Alderdice *et al.*[83] synthesised the ester (*Z*)-**177** using the stereoselective conversion of enol phosphates of β-oxo esters into (*Z*)-trisubstituted α,β-unsaturated esters.[84]

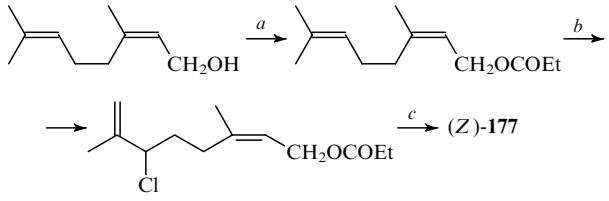


(*a*) NaH, BuLi; (*b*) $H_2C=CH(Me)CH_2CH_2OTs$ (**181**); (*c*) $(EtO)_2P(O)Cl$, Et_3N; (*d*) MeMgCl, MeCu; (*e*) Bu^i_2AlH; (*f*) $(EtCO)_2O$, Py; (*g*) $(EtO)_2P(O)Cl$, NaH.

Thus dianion **180** generated from methyl acetoacetate underwent smooth alkylation under the action of tosylate **181** to form β-oxo acid ester **182**. The latter was converted into enol phosphate (*E*)-**183**. Treatment of (*E*)-**183** with MeMgCl in the presence of a catalytic amount of MeCu afforded ester (*Z*)-**184**, which was transformed into the target pheromone (*Z*)-**177** through the corresponding alcohol in ~ 40% total yield. Deprotonation of the oxo ester **182** with NaH instead of Et_3N afforded the (*Z*)-enol phosphate **183**. The latter was converted into the component of the pheromone of the San Jose scale, *viz.*, the propionate (*E*)-**177**, in three steps.

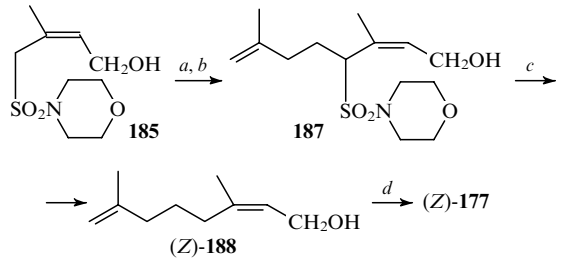
Nerol is a convenient starting compound for the synthesis of the ester (*Z*)-**177**. However, isomerisation of the C(6)=C(7) double bond appeared to be a difficult problem. Only after several

unsuccessful attempts,[85] an efficient reagent for this isomerisation, *viz*., *tert*-butyl hypochlorite, was found.[86,87] The propionate (*Z*)-**177** was synthesised according to this scheme in three steps in 40% total yield.



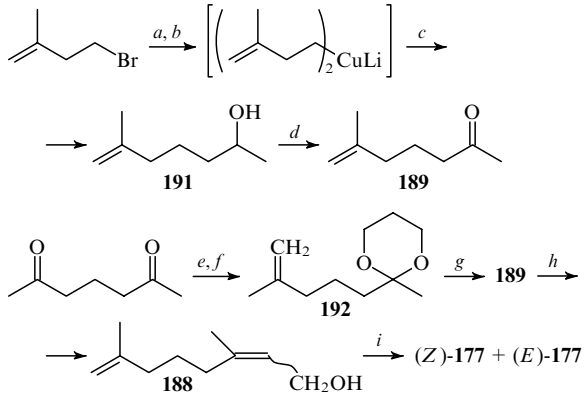
(*a*) $(EtCO)_2O$, Py; (*b*) Bu^tOCl, SiO_2; (*c*) $NaBH_4$, LiI.

Moiseenkov *et al*.[88] synthesised the propionate (*Z*)-**177** starting from isoprenoid (*Z*)-hydroxy sulfonamide **185**.[89] The synthetic scheme involved alkylation of the sulfonamide **185** with 3-methylbut-3-enyl iodide **186** to form sulfonamide **187** and reductive desulfation of the latter in the presence of dibenzo-18-crown-6 (DB-18-C-6). The reaction proceeded virtually without migration of the C=C bond to form alcohol (*Z*)-**188**, which was converted into the propionate (*Z*)-**177** in 51% total yield.



(*a*) BuLi, THF; (*b*) $H_2C=C(Me)(CH_2)_2I$ (**186**); (*c*) Na/NH_3, C_6H_{14}, DB-18-C-6; (*d*) $(EtCO)_2O$, Py.

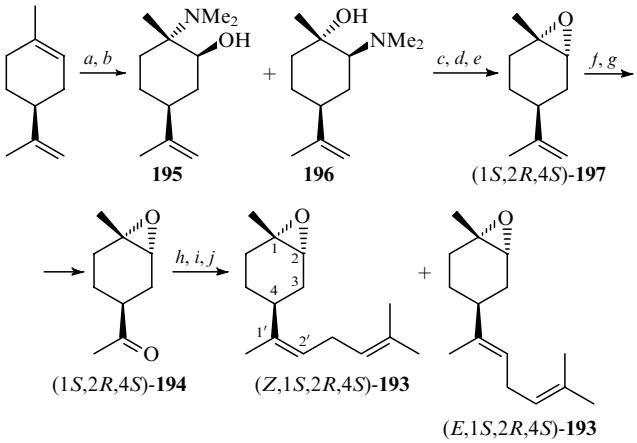
A mixture of propionates (*Z*)- and (*E*)-**177** was synthesised by Chinese chemists.[90–92] The synthesis involved the Wittig reaction of ketone **189** with ylide generated from phosphonium salt **190** followed by the conversion of the resulting mixture of alcohols **188** into a mixture of propionates (*Z*)- and (*E*)-**177**. The key intermediate, *viz*., the ketone **189**, was prepared in two ways. The first route[90,91] involved oxidation of alcohol **191** formed in the reaction of diisopentenyl cuprate with propylene oxide. The second route[92] involved the conversion of heptane-2,6-dione monoketal into the ketone **189** *via* ketal **192**.

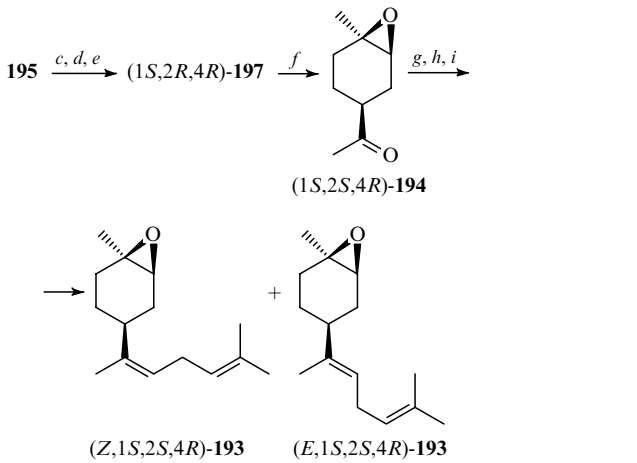


(*a*) Li; (*b*) CuI; (*c*) ; (*d*) PCC, CH_2Cl_2; *e*) $BnO(CH_2)_3OH$ on a polymeric support; (*f*) $Ph_3P=CH_2$; (*g*) H_3O^+; (*h*) $(Ph_3P^+CH_2CH_2OH)Cl^-$ (**190**), B^-; (*i*) $(EtCO)_2O$, Py.

2. Synthesis of the male-produced sex pheromone of the southern green stinkbug *Nezara viridula*

The southern green stinkbug *Nezara viridula* is a pest of cotton, citrus, cereal and vegetable crops, which is widely distributed in tropical and subtropical regions. The first data on the structure of the male-produced sex pheromone of *N.viridula* were published in 1971.[93] However, its major component was isolated only in 1987.[94] Based on the results of physicochemical studies, the structure of epoxybisabolene (**193**) was assigned to this component. With the aim of establishing the stereochemistry of the natural pheromone, eight of its isomers were synthesised [94] starting from (*R*)- and (*S*)-limonenes using the modified Julia procedure [75] in the step of construction of the trisubstituted alkene fragment.[95] The approach used in the cited study [94] is exemplified in the syntheses of the (*Z*)- and (*E*)-isomers of (1*S*,2*R*,4*S*)-**193** considered below. The necessary key intermediate, *viz*., epoxy ketone **194**, was prepared in the individual state with the use of a reaction sequence involving epoxidation of (*S*)-limonene and conversion of the resulting mixture of α- and β-epoxides into a mixture of amino alcohols **195** and **196**. The latter compounds were converted into the corresponding tosylates and separated by chromatography.



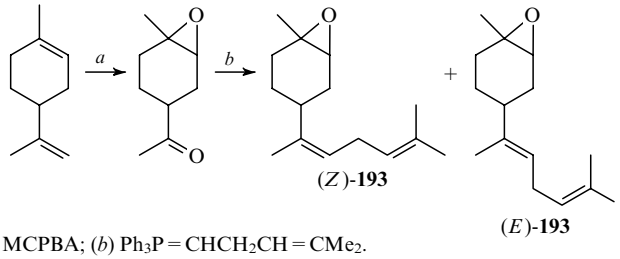


(*a*) MCPBA; (*b*) Me_2NH, H_2O; (*c*) TsCl, Py; (*d*) MeI; (*e*) KOH; (*f*) O_3, CH_2Cl_2; (*g*) Ph_3P; (*h*) $Me_2C=CH(CH_2)_2SO_2Ph$ (**198**), BuLi; (*i*) PhCOCl, Py; (*j*) Na/Hg, THF, MeOH.

Amino tosylate corresponding to the amino alcohol **196** was transformed into the quaternary ammonium salt and then into individual epoxide (1*S*,2*R*,4*S*)-**197**. Ozonation of the double bond in (1*S*,2*R*,4*S*)-**197** followed by the reaction of the resulting epoxy ketone (1*S*,2*R*,4*S*)-**194** with deprotonated sulfone **198** afforded β-hydroxy sulfone. The latter was converted into benzoate. Subequent reductive elimination gave rise to a 1:1 mixture of the (*Z*)- and (*E*)-isomers of epoxybisabolene (1*S*,2*R*,4*S*)-**193**. The individual isomers were isolated by HPLC. The (*Z*)- and (*E*)-iso-

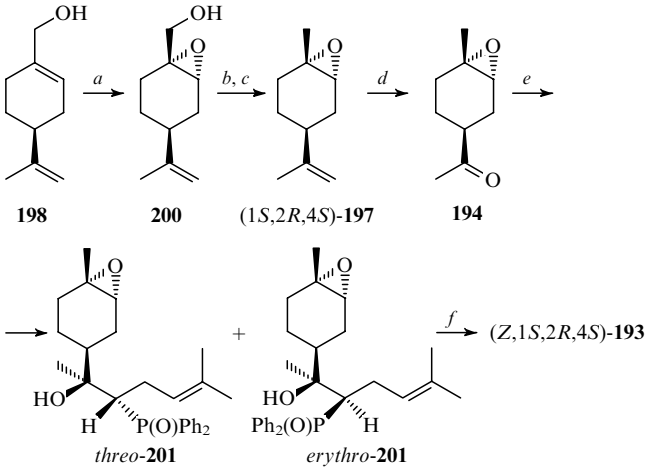
mers of epoxybisabolene (1*S*,2*S*,4*R*)-**193** were prepared analogously from epoxy ketone (1*S*,3*S*,4*R*)-**194**. Four other isomeric epoxybisabolenes were prepared starting from (*R*)-limonene. Based on comparison of the physicochemical characteristics of the isomers synthesised with those of the male-produced pheromone of stinkbugs of the Brazilian population, it was reliably established that the pheromone is epoxybisabolene (*Z*,1*S*,3*R*,4*S*)-**193**. Bioassays demonstrated that only this isomer was attractive to *N.viridula* females.

Later, it was shown [96–99] that other isomers of epoxybisabolene **193** with the (*Z*)-configuration of the C(5)=C(6) double bond as well as (*Z*)-bisabolene are sex pheromones of stinkbugs from other regions. The ratio between the components in the pheromone mixture varies depending on the habitat. In this connection, synthesis of racemic epoxybisabolene (*Z*)-**193** starting from racemic limonene (patented by Mori *et al.*[100]) is of interest. The individual epoxybisabolene (*Z*)-**193** was isolated from a mixture with the (*E*)-isomer by chromatography.



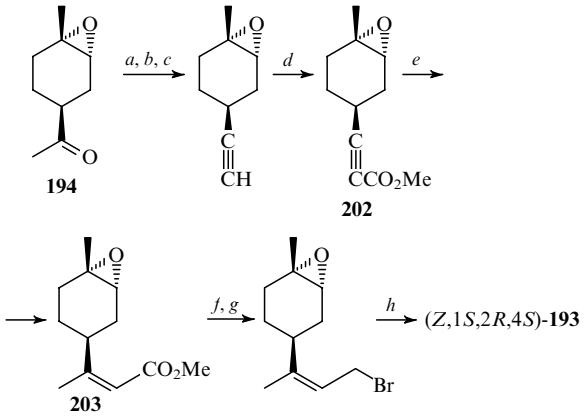
(*a*) MCPBA; (*b*) $Ph_3P=CHCH_2CH=CMe_2$.

The major component of all pheromone mixtures of the southern green stinkbug, *viz*., epoxybisabolene (*Z*,1*S*,2*R*,4*S*)-**193**, was synthesised [101] from commercially available perillyl alcohol **198**. The key step of this scheme involved the Horner–Emmons reaction of the ketone **194** with phosphine oxide **199**. Epoxidation of perillyl alcohol **198** according to Sharpless afforded hydroxy epoxide **200**. The hydroxymethyl group of **200** was reduced to the methyl group through the corresponding mesylate. The resulting epoxide **197** was converted into the corresponding epoxy ketone **194** (the total yield was 47%). The reaction of the latter with an anion generated from the phosphine oxide **199** gave rise to a mixture of *erythro*- and *threo*-phosphine oxides **201**. The former was isolated by chromatography from a mixture with (*E*)-epoxybisabolene, which was formed due to decomposition of the unstable *threo*-**201**, and was converted into the epoxybisabolene (*Z*,1*S*,2*R*,4*S*)-**193** (the total yield was 18%).



(*a*) (D)-(−)-tartaric acid, $Ti(OPr^i)_4$, Bu^tO_2H; (*b*) $MeSO_2Cl$, Py;
(*c*) $LiAlH_4$; (*d*) $KMnO_4$, DB-18-C-6, CH_2Cl_2;
(*e*) $Me_2C=CH(CH_2)_2P(O)Ph_2$ (**199**), BuLi; (*f*) NaH, DMF.

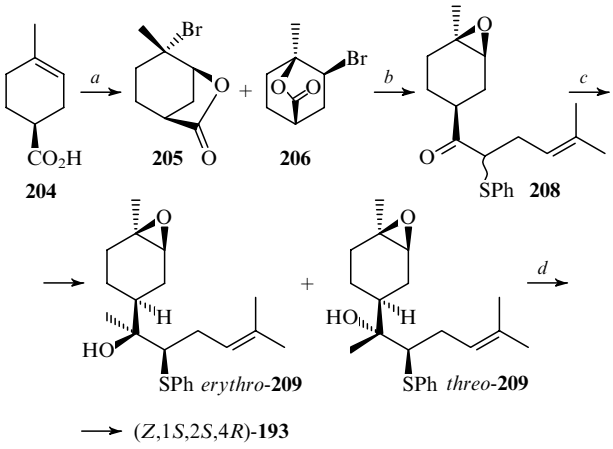
Efficient syntheses of the isomers (*Z*,1*S*,2*R*,4*S*)-, (*Z*,1*S*,2*S*,4*R*)-, (*Z*,1*R*,2*S*,4*R*)- and (*Z*,1*R*,2*R*,4*S*)-**193** were carried out[102] starting from the commercially available mixture of α- and β-epoxides of (*S*)- and (*R*)-limonenes. The (*Z*)-trisubstituted alkene fragment was constructed using the highly stereoselective *cis*-addition of dialkyllithium cuprates to acetylenecarboxylic esters. The scheme of the synthesis is exemplified below in the preparation of the isomer (*Z*,1*S*,2*R*,4*S*)-**193**.



(*a*) LDA; (*b*) $(EtO)_2P(O)Cl$; (*c*) 2.5 equiv. of LDA; (*d*) BuLi, $ClCO_2Me$; (*e*) Me_2CuLi; (*f*) Bu^i_2AlH; (*g*) CBr_4, PPh_3; (*h*) Bu^tLi, $Me_2C=CHBr$.

Substituted acetylenecarboxylic ester **202** was prepared from the epoxy ketone (1*S*,2*R*,4*S*)-**194** in four steps. The addition of dimethyllithium cuprate to the ester **202** afforded ester (2*Z*)-**203**. The latter was transformed into (*Z*,1*S*,2*R*,4*S*)-**193** in 24% total yield according to standard procedures. Analogously, the isomer (*Z*,1*S*,2*S*,4*R*)-**193** was prepared from the ketone (1*S*,2*S*,4*R*)-**194** and the isomers (*Z*,1*R*,2*R*,4*R*)- and (*Z*,1*R*,2*R*,4*S*)-**193** were prepared from α- and β-epoxides of (*R*)-limonene, respectively.

(*Z*,1*S*,2*S*,4*R*)-Epoxybisabolene was also synthesised [103] starting from acid **204**, which was prepared by the asymmetric Diels–Alder reaction.[104] Bromolactonisation of the acid **204** gave rise to a mixture of bromo lactones **205** and **206**. Treatment of this mixture with 4-methyl-1-phenylthiopent-3-enyllithium (**207**) afforded phenylthio ketone **208** in high yield. The reaction of the compound **208** with MeLi gave rise to a mixture of *threo*- and *erythro*-hydroxy sulfides (**209**) separated by flash chromatography. Treatment of *threo*-**209** with P_2I_4 in the presence of Et_3N produced the target epoxybisabolene **193** in a total yield of 18% with respect to the acid **204**.



(*a*) NBS, Na_2CO_3; (*b*) $Me_2C=CHCH_2CH(Li)SPh$ (**207**); (*c*) MeLi;
(*d*) P_2I_4, Et_3N, CH_2Cl_2.

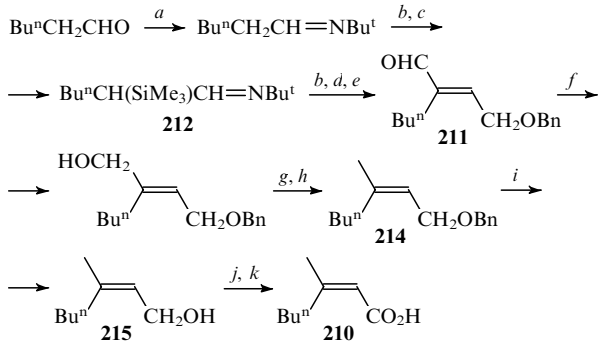
3. Synthesis of the sex pheromones of the dry bean beetles *Callosobruchus analis* and *C.maculatus*

The female-produced sex pheromone of the dry bean beetle *Callosobruchus analis* was isolated in 1991.[105] Based on the data

of GLC-mass spectrometry, the structure of 3-methylheptenoic acid containing a double bond at position 2 or 3 was assigned to this pheromone. Comparison of the physicochemical properties of the pheromone isolated with those of authentic 3-methylheptenoic acids containing a double bond at different positions (which were synthesised by the Reformatsky, Wittig or Horner–Emmons reactions) demonstrated that the pheromone of *C.analis* females is 3-methylhept-(2*Z*)-enoic acid (**210**). Bioassays of isomeric 3-methylheptenoic acids demonstrated that 3-methylhept-(3*Z*)-enoic acid is also the attractant for males of the dry bean beetle *C.analis*. This acid was identified as the major component of the sex pheromone of the dry bean beetle *C.maculatus*.[105, 106]

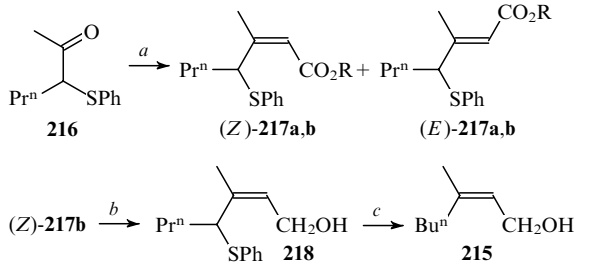
A highly stereoselective synthesis of 3-methylhept-(2*Z*)-enoic acid (**210**) was carried out according to two procedure. The first procedure[107] was based on the fact that the (*E*)-isomers of α,β-disubstituted acroleins are thermodynamically favourable.

In this scheme, the key intermediate was the (*E*)-isomer of substituted acrolein **211**, which was formed with a stereoselectivity of > 95% upon condensation of the trimethylsilyl derivative of *N*-*tert*-butylhexanimine (**212**) with glycolaldehyde benzyl ether (**213**).[107] Stereospecific reduction of the carbonyl group in the aldehyde **211** to the hydroxymethyl group and then to the methyl group *via* sulfate afforded benzyl ether **214**. Deprotection followed by oxidation of the resulting alcohol **215** gave rise to the acid **210** (the total yield was 12%).



(*a*) Bu^tNH_2; (*b*) LDA; (*c*) Me_3SiCl; (*d*) $OHCCH_2OBn$ (**213**); (*e*) H_3O^+; (*f*) $NaBH_4$; (*g*) $Py\cdot SO_3$; (*h*) $LiAlH_4$; (*i*) Li/NH_3; (*j*) MnO_2; (*k*) Ag_2O.

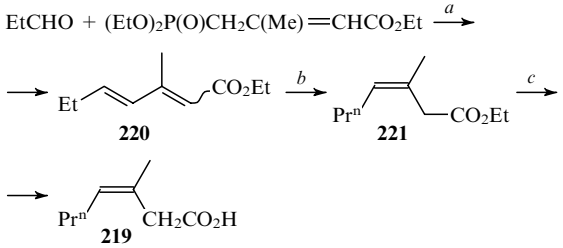
The second procedure[108] was based on our version of the highly stereoselective Peterson olefination[109, 110] of methyl ketones. The method involves the introduction of a bulky phenylthio substituent at the C(3) atom. This substituent can be readily removed from the reaction product.



R = Me (**a**), Bu^t (**b**); (*a*) $Me_3SiCH_2CO_2R$, LDA; (*b*) $[AlH_3]$; (*c*) Na/NH_3, C_6H_{12}, DB-18-C-6.

Olefination of α-phenylthio ketone **216**, which was prepared according to Warren's method,[111] with alkyl trimethylsilylacetates afforded a mixture of 4-phenylthio esters (2*Z*)- and (2*E*)-**217a**,**b** (the ratios of the isomers were 92 : 8 and 85 : 15 for **217a** and **217b**, respectively). Reduction of the (Z)-ester **217b** isolated by chromatography with AlH_3 *in situ* gave rise to 4-phenylthio alcohol (2*Z*)-**218** desulfation of which afforded the alcohol **215** in 10.3% total yield. It should be noted that the yield of the alcohol **215** prepared according to the first procedure reached 26%.

3-Methylhept-(3*Z*)-enoic acid **219** was synthesised by Serebryakov and coworkers.[112, 113] The key step of this scheme involved 1,4-*cis*-hydrogenation of conjugated dienes proposed by Frankel *et al*.[59]



(*a*) KOH, 18-C-6, PhH; (*b*) H_2, $Cr(CO)_6$, C_6H_{14}; (*c*) KOH, HCl.

Condensation of propanal with triethyl 3-methyl-4-phosphonocrotonate under conditions of phase transfer catalysis afforded a mixture of esters (2*E*,4*E*)- and (2*Z*,4*E*)-**220**. Hydrogenation of this mixture over $Cr(CO)_6$ gave rise to ester (3*Z*)-**221** with 99% purity. Saponification of the ester **221** under mild conditions produced the acid **219** in 11.4% total yield.

* * *

In conclusion, note that the synthesis of insect pheromones is a good 'proving ground' for new methods of organic chemistry. All the aforesaid refer in full measure both to stereoselective procedures for the construction of (*Z*)-trisubstituted C=C bonds and to procedures for the construction of chiral synthons required for the preparation of pheromones of the group under consideration.

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