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10-UNDECENOIC ACID IN THE SYNTHESIS OF INSECT PHEROMONES

G. Yu. Ishmuratov, M. P. Yakovleva,
and G. A. Tolstikov

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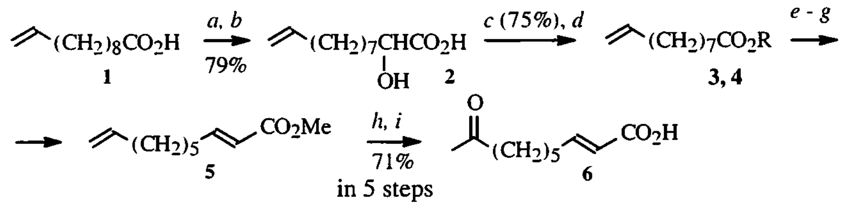
The literature on the use of 10-undecenoic acid in the synthesis of insect pheromones is reviewed.

Key words: insect pheromones, 10-undecenoic acid, synthesis, literature review.

Destructive distillation of castor-bean oil yields 10-undecenoic (undecylenoic) acid (**1**), which possesses two functional groups and is used in the food and perfume industries [1]. The acid is widely used in the synthesis of insect pheromones.

Preparation from 10-undecenoic acid of 9-oxo-2E-decenoic acid (**6**), a multifunctional pheromone of honeybee queens (*Apis mellifera* L.), has been described [2]. The carbon chain of **1** was shortened using successive α-hydroxylation and oxidative cleavage of the intermediate 2-hydroxy-10-undecenoic acid (**2**). A conjugated double bond with the E-configuration was introduced into the ester (**4**) via *syn*-elimination of the corresponding α-selenoxide; a keto group, via oxidation of the dienic ester (**5**) under Walker—Tsuji conditions.

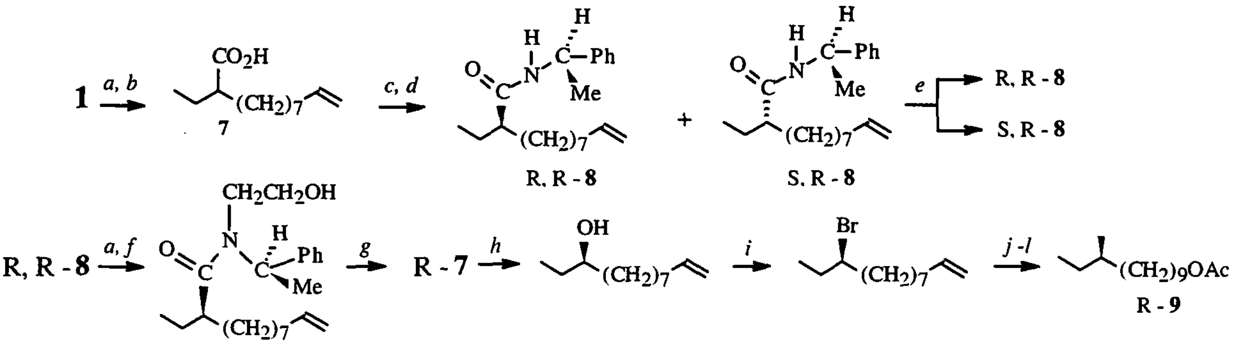


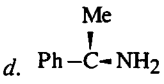
R = H (**3**), Me (**4**)

a. *i*-Pr_2NLi; *b*. O_2; *c*. CrO_3, $NaIO_4$; *d*. CH_2N_2;
e. LiH; *f*. PhSeCl; *g*. H_2O_2; *h*. $O_2/PdCl_2$-CuCl; *i*. OH^-

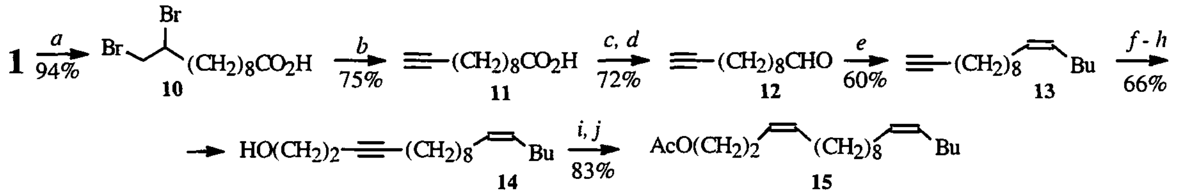
The R-enantiomer of 10-methyldodec-1-ylacetate (**9**), the sex pheromone of the lesser tea leaf roller (*Adoxophyes fasciata*), was synthesized using selective transformations of the product from α-alkylation of **1**, 2-ethyl-10-undecenoic acid (**7**), after separating it into the optically active isomers using the diastereomeric amides of R-α-phenylethylamine [3]. The N atom of the R,R-(**8**) amide, which was isolated by crystallization, was first hydroxyethylated in order to preserve the asymmetric center during acid hydrolysis.

Institute of Organic Chemistry, Ufa Scientific Center, Russian Academy of Sciences, 450054, Ufa, prospekt Oktyabrya 71, fax (3472) 35 60 66. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 87-96, March-April, 2000. Original article submitted March 6, 2000.



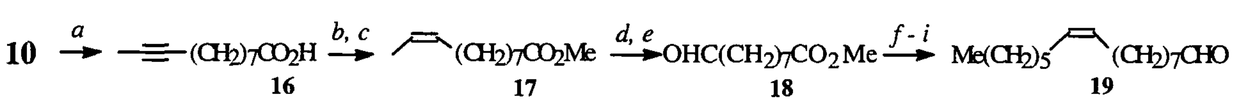
a. *i*-Pr_2NLi; *b.* EtBr; *c.* $SOCl_2$; *d.*  $Ph-\overset{Me}{C}-NH_2$; *e.* recrystallization; *f.*  ; *g.* $HClO_4$;
h. $LiAlH_4$; *i.* Br_2/PPh_3; *j.* $(Sia)_2BH$ (disiamylborane) / $LiEt_3BH$; *k.* $H_2O_2/NaOH$; *l.* Ac_2O/Py

Phase-transfer catalytic dehydrobromination of the dibromide **10**, which is prepared from **1**, produces 10-undecynoic acid (**11**), which has been used [4-6] to synthesize 3Z,13Z-octadecadien-1-ylacetate (**15**), a component of the sex pheromone of several Lepidoptera (*Synanthedon pictipes*, *S. myopaeformis*, *S. typuliformis*, and *S. hector*). The Z,Z-unsaturated carbon framework of **15** was constructed by stereospecific Wittig Z-olefination of the aldehyde **12** and catalytic hydrogenation of the enyne alcohol **14**, the product of hydroxyethylation of the terminal alkyne **13**.



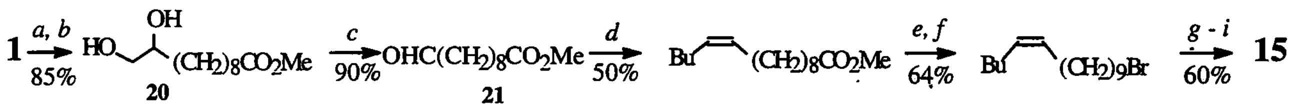
a. Br_2; *b.* KOH/Adogen 464 (methyltrialkyl (C8-C10)ammonium chloride) or Aliquat 336 (tricaprylmethylammonium chloride ($CH_3N[(CH_2)_7CH_3]_3Cl$/*c*-C_6H_{12}; *c.* $LiAlH_4$; *d.* PCC/AcONa; *e.* $Me(CH_2)_4P^+Ph_3Br^-$ / *t*-BuOK; *f.* *n*-BuLi;
g. $THPO(CH_2)_2Br$; *h.* TsOH/MeOH-H_2O; *i.* H_2/Pd-$BaSO_4$/quinoline; *j.* Ac_2O/Py

Increasing the temperature during dehydrohalogenation of **10** enables 9-undecynoic acid (**16**), which is isomeric with **11**, to be synthesized highly selectively. Reductive ozonolysis of the olefinic analog (**17**) of **16** gives the aldehydoester **18**, a key intermediate for 9Z-hexadecenal (**19**), a minor component of the sex pheromone of the cotton cutworm (*Heliothis armigera*) [7].



a. KOH, PEG (polyethyleneglycol), 150°C; *b.* MeOH/TsOH; *c.* H_2/Pd - $CaCO_3$-PbO;
d. O_3; *e.* Me_2S; *f.* $Me(CH_2)_6P^+Ph_3Br^-$ / $NaNH_2$ / THF; *g.* $LiAlH_4$; *i.* PCC

The usual method of cleaving a terminal double bond includes epoxidation using a peracid, acid opening of the epoxide to the vicinal diol (**20**), and its oxidative destruction, for example, by lead tetraacetate. This method makes it possible to produce from **1** the bifunctional synthon **21**, a versatile intermediate in the synthesis of several insect pheromones. Thus, the Z,Z-diene of pheromone **15** was built from **21** using two successive Wittig condensations [8-10].



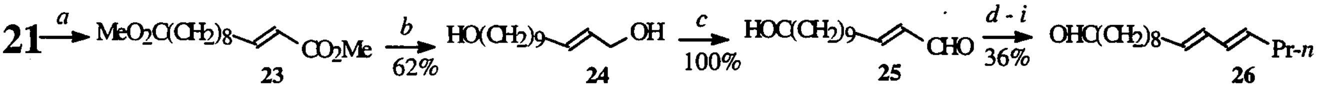
a. $HCOOH/H_2O_2$; *b.* Me_2SO_4/MeOH; *c.* $Pb(OAc)_4$; *d.* $Me(CH_2)_4P^+Ph_3Br^-/(Me_3Si)_2NNa$;
e. $LiAlH_4$; *f.* PBr_3; g. PPh_3; *h.* $(Me_3Si)_2NNa$; *i.* 

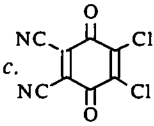
The monoene pheromone of *Dichocrocis punctiferalis*, a destructive pest of ginger and cardamon, was synthesized from **21** using the same olefination reaction [11].

$$\mathbf{21} \xrightarrow[26\%]{a-c} Me(CH_2)_4CH{=}CH(CH_2)_8CHO \quad \mathbf{22}$$

a. *n*-BuLi / $Me(CH_2)_5P^+Ph_3Br^-$; *b.* $LiAlH_4$; *c.* PCC

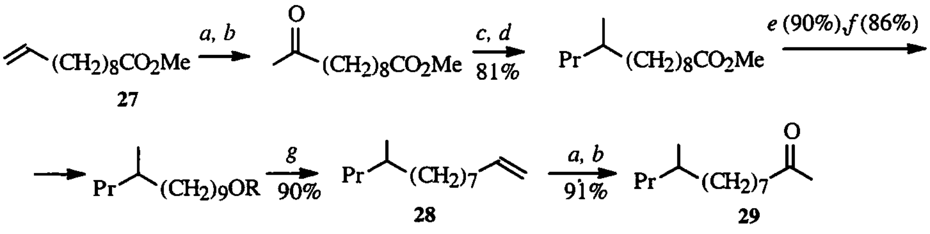
The first step toward 10E,12E-hexadecadienal (**26**), the basic component of the sex pheromone of the spiny moth (*Earias insulana*), utilizes the phosphonate modification of the Wittig reaction on aldehydoester **21** [12]. Further transformation of diester **23** included the chemoselective conversion through diol **24** to the α,β-unsaturated hydroxyaldehyde **25**, which was converted via olefination with *n*-butylidenetriphenylphosphonium and oxidation of the alcohol into **26**.



a. $(MeO)_2P(O)CH_2CO_2Me$ / *t*-BuOK; *b.* *i*-Bu_2AlH; *c.*  (DDQ); *d.* DHP/TsOH;

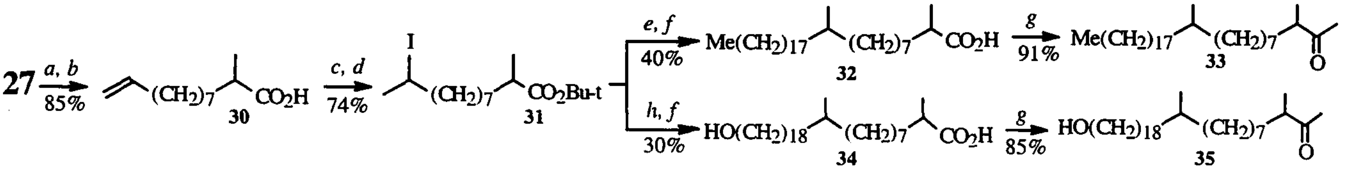
e. *n*-$BuP^+Ph_3Br^-$/*n*-BuLi; *f.* TsOH/MeOH-H_2O; *g.* I_2/*c*-C_6H_{12}; *h.* recrystallization; *i.* PCC

The sex pheromone of the southern corn rootworm (*Diabrotica undecimpunctata*), 10-methyltridecan-2-one (**29**), was prepared from the methyl ester of 10-undecenoic acid (**27**) using successive hydroxymercuration and demercuration of the terminal alkenes **27** and **28** in the first and last steps and Jones oxidation of the intermediate secondary alcohols [13].



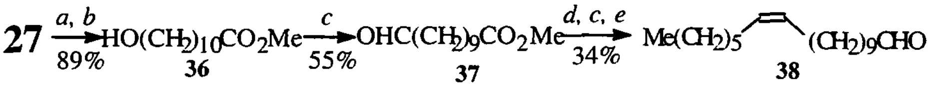
a. $Hg(OAc)_2$, then $NaBH_4$; *b.* CrO_3/H_2SO_4; *c.* *n*-$PrP^+Ph_3Br^-/(Me_3Si)_2NNa$;
d. H_2/Pd-C; *e.* $LiAlH_4$; *f.* TsCl/Py; *g.* *t*-BuOK/DMSO

Components of the sex pheromone of female German cockroaches (*Blatella germanica*), 3,11-dimethylnonacosan-2-one (**33**) and its 29-hydroxy analog (**35**), were synthesized via Wurtz coupling of the *t*-butyl ester of 10-iodo-2-methylundecanoic acid (**31**) and *n*-octadecyl- or 18-(2-tetrahydropyranyloxy)octadecylmagnesium bromides. The iodide **31** was prepared from the unsaturated ester **27** by successive α-methylation and Markovnikov hydroiodination of the 2-methyl-10-undecenoic acid **30**. Alkylation of the iodoester **31** by the appropriate Gringard reagents and deprotection gives the acid **32** or the hydroxyacid **34**. Treatment of these with methyllithium completes the synthesis of the target compounds **33** and **35** [14].



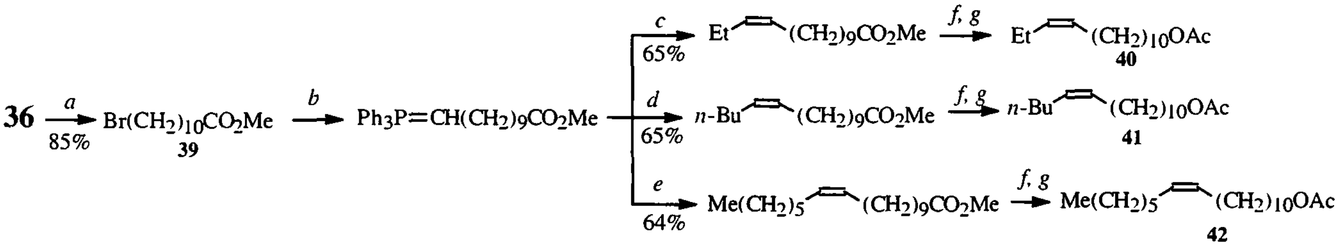
a. i-Pr_2NLi; b. MeI; c. KI/P_2O_5 / H_3PO_4; d.  $/H_2SO_4$; e. $Me(CH_2)_{17}MgBr/Li_2CuCl_4$;
f. $TsOH/H_2O$; g. MeLi; h. $THPO(CH_2)_{18}MgBr/Li_2CuCl_4$

Anti-Markovnikov hydrogenation of 27 via an organoboron intermediate gives the hydroxyester 36, which is transformed into the formyl derivative 37, which is then converted via the Wittig reaction into 11Z-octadecenal (38), the sex pheromone of the wax moth (*Achroia grisella*) and a minor component of the pheromone of *Earias vittella* [15].



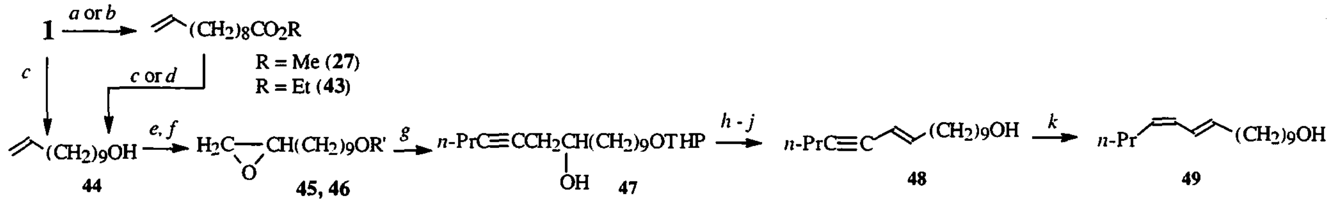
a. $Pr_4B_2H_2$; b. $H_2O_2/NaOH$; c. PCC; d. $Me(CH_2)_5CH{=}PPh_3$; e. $LiAlH_4$

A general method for synthesizing 11Z-unsaturated insect pheromones is based on Wittig olefination of various aldehydes (propanal, *n*-pentanal, and *n*-heptanal) by the phosphonium ion prepared from the methyl ester of 11-bromoundecanoic acid (39), which is readily available from 36. The products from reduction and acylation are converted into 11Z-tetradecen- (40), 11Z-hexadecen- (41), and 11Z-octadecen- (42) -1-ylacetates, attractants of the moths *Argyrotaenia velutinana*, *Mamestra configurata*, and *Lycorea ceres ceres*, respectively [16].



a. PBr_3; b. PPh_3, then t-BuOK; c. EtCHO; d. n-BuCHO; e. $Me(CH_2)_5CHO$; f. $LiAlH_4$; g. Ac_2O

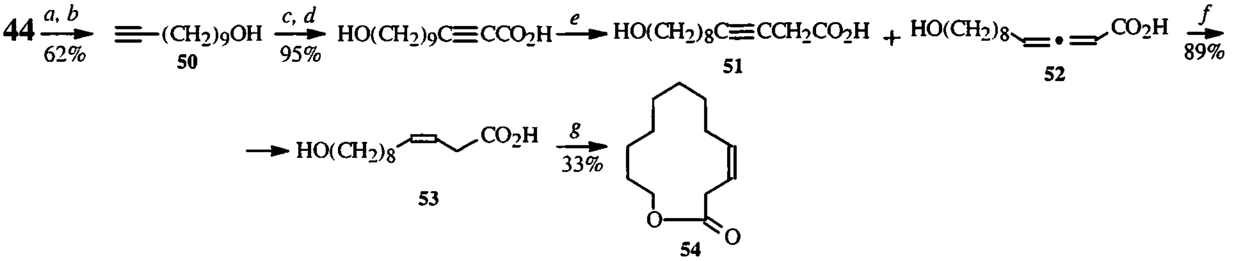
Hydridic reduction of 1 and its esters 27 and 43 produces 10-undecen-1-ol (44), which is used to synthesize 10E,12Z-hexadecadien-1-ol (49, bombykol), the sex pheromone of the mulberry silk worm (*Bombyx mori*). Oxidation of the double bond of 44 gives the epoxide 45, the oxiran ring of which is opened using the lithium derivative of 1-pentyne. The resulting acetylenic alcohol 47 is dehydrated via the corresponding tosylate to give an equimolar mixture of the 10E- and 10Z-enyne alcohols 48, which can be enriched in the E-isomer by recrystallization. Stereoselective hydrogenation of the triple bond in 48 gives the desired alcohol 49 [17].



R' = H (45), OTHP (46)

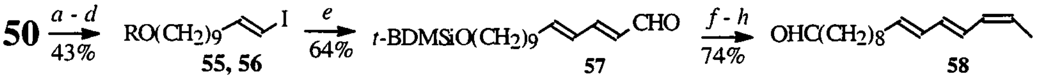
a. MeOH/TsOH; b. EtOH/TsOH; c. $LiAlH_4$; d. i-Bu_2AlH_4; e. MPPA(monoperphthalic acid); f. DHP/TsOH;
g. n-PrC≡CLi; h. TsCl/Py; i. KOH; j. H_3O^+; k. H_2/Pd-$CaCO_3$-PbO

Bromination of the double bond in the unsaturated alcohol **44** and subsequent dehydrobromination under phase-transfer catalytic conditions produces 10-undecyn-1-ol (**50**), which is used to prepare 3Z-dodecen-12-olide **54**, the principal component of the aggregation pheromone of the lesser red grain beetle (*Oryptolestes pusillus*). The synthesis of the macrolide **54** includes cyclization of 12-hydroxy-3Z-dodecenoic acid (**53**), which is prepared by successive carboxylation of the lithium derivative of the acetylenic alcohol **50**, basic migration of the triple bond from its position conjugated to the carboxylic acid, and Z-selective hydrogenation of the resulting mixture of acetylenic (**51**) and allenic (**52**) acids over a deactivated nickel catalyst [18].

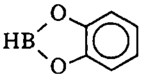


a. Br_2; *b.* KOH/18-Crown-12; *c.* *n*-BuLi; *d.* CO_2; *e.* $LiNH_2/NH_3/THF$; *f.* H_2/Ni-P2; *g.* $(PyS)_2/PPh_3$/MeCN, xylene

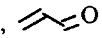
The sex pheromone of the Sphingidae butterfly *Manduca sexta*, 10E,12E,14Z-hexadecatrienal (**58**), contains a 10E-double bond that is introduced via selective iodination of an intermediate organoboron alkynol (**50**); and a 12E-bond, via addition of acrolein to the iodoester (**56**). The olefine of the aldehyde **57** is introduced using ethyltriphenylphosphonium to complete the synthesis of the carbon framework of the product (**58**) [19].



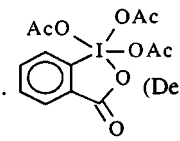
R = H (**55**), *t*-BDMSi (*t*-butyldimethylsilyl) (**56**)

a.


(Catecholborane); *b.* H_2O; *c.* I_2/NaOH; *d.* *t*-BDMSiCl / imidazole / DMF;

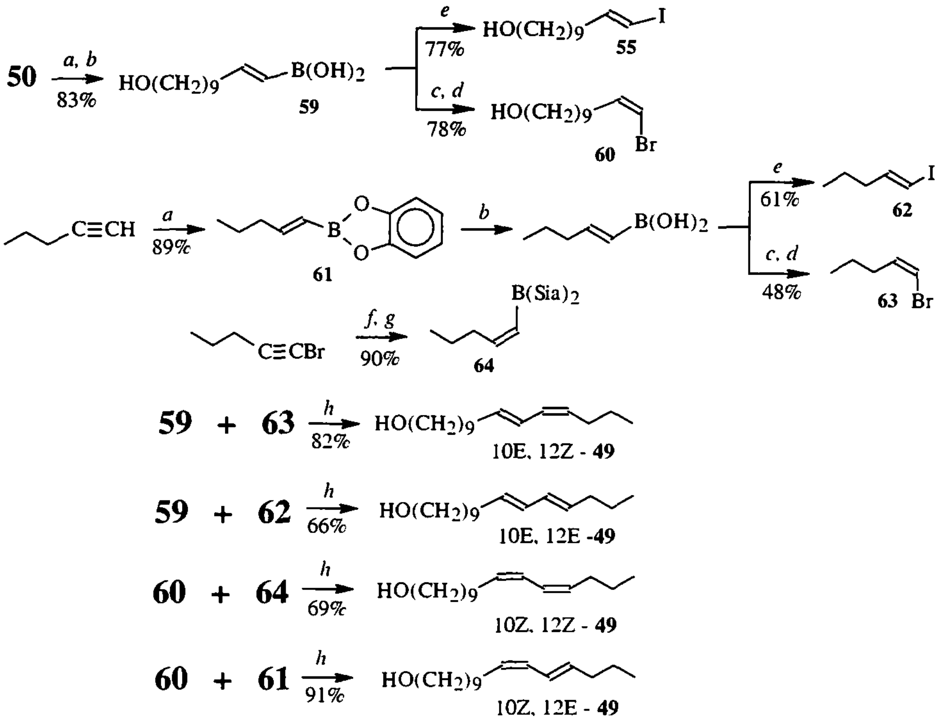
e. $Pd(OAc)_2$,


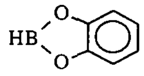
,K_2CO_3, *n*-$Bu_4N^+Cl^-$/DMF; *f.* $EtP^+Ph_3Br^-/(Me_3Si)_2NNa$; *g.* *n*-$Bu_4N^+F^-/H_2O$;

h.


(Dess-Martin periodinate)

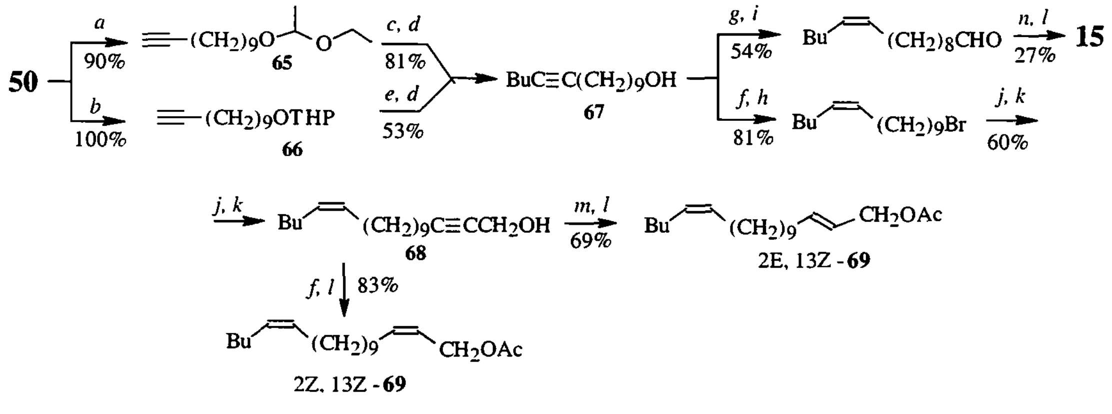
Bombykol (10E,12Z-hexadecadien-1-ol; 10E,12Z-**49**) and its 10Z,12Z-, 10Z,12E-, and 10E,12E- isomers are also synthesized via selective transformations of 10-undecyn-1-ol (**50**). Hydroboration of **50** followed by hydrolysis gives exclusively the alkenylboric acid **59** of the E-configuration. Successive treatment with bromine and sodium ethoxide gives the Z-unsaturated bromide **60** whereas reaction with iodine in the presence of base gives the E-olefinic iodide **55**.



a.  ; b. H_2O; c. Br_2; d. NaOMe; e. NaOH / I_2; f. $(Sia)_2BH$; g. *t*-BuLi; h. $Pd(PPh_3)_4$/NaOEt

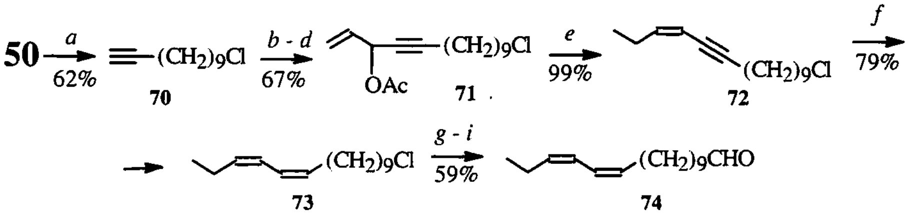
Compounds **59** and **60** are used to introduce a double bond in the 10-position of the desired products **49**. Analogous transformations of 1-pentyne via the intermediate E-unsaturated borate **61** produce the unsaturated E-iodide **62** and the Z-bromide **63**. Treatment of 1-bromo-1-pentyne with disiamylborane produces Z-alkenylborane **64**. The various combinations of **59-64** give all four stereoisomers of **49** [20, 21].

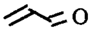
The ethoxyethyl (**65**) and tetrahydropyranyl (THP) (**66**) esters of the readily available alkynol **50** have been used to synthesize 2Z,13Z-**69**-, 2E,13Z-**69**-, and 3Z,13Z-**15**-octadien-1-ylacetates, components of the pheromones of many *Synanthedon* species. The *cis*-double bond in the 13-position and the Z- and E-allyl alcohols are introduced through the acetylenic (**67**) or propargyl (**68**) derivatives, respectively. The Z-homoallyl alcohol is introduced into **15** via Wittig olefination [22, 23].



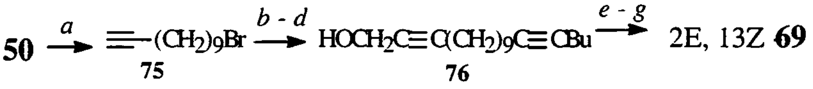
a. $EtOCH{=}CH_2$ / TsOH; b. DHP/TsOH; c. $LiNH_2$, then *n*-BuBr; d. TsOH/H_2O-MeOH; e. *n*-BuLi, then *n*-BuBr;
f. H_2/Ni-P2; g. H_2/Pd - $BaSO_4$/quinoline; h. CBr_4/PPh_3; i. PCC; j. $LiC{\equiv}CCH_2OTHP$; k. Dowex W-50; l. Ac_2O/Py ;
m. $LiAlH_4$; n. $Br^{-}Ph_3\overset{+}{P}$ OH /*n*-BuLi

A series of regio- and stereoselective transformations is used to synthesize 11Z,13Z-hexadecadienal (**74**), a pheromone of the orange caterpillar (*Pamyelois transitella*). This includes condensation of its chloro derivative **70** with acrolein catalyzed by dilithium tetrachlorocuprate; an S_N2' reaction of methylmagnesium bromide with the secondary allylic acetate **71**, and extension of the carbon framework of the diene chloride **73** by formylation of its magnesium derivative [24].



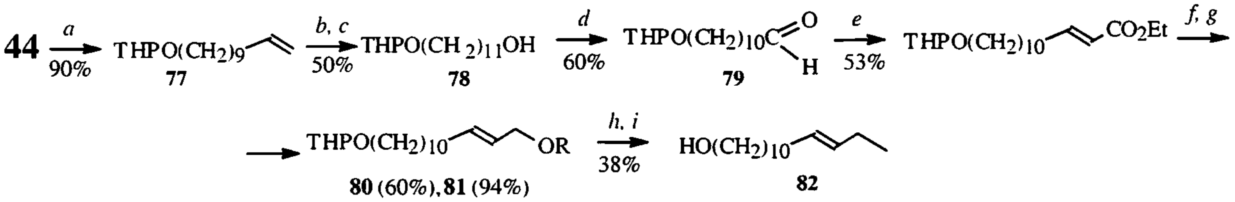
a. MsCl / Py; *b*. EtMgBr; *c*.  ; *d*. Ac_2O/Py; *e*. $MeMgBr/Li_2CuCl_4$;
f. $(C_6H_{11})_2BH$, then AcOH; *g*. Mg; *h*. $HC(OEt)_3$; *i*. HCOOH

The diyne precursor **76** of the 2E,13Z-diene pheromone **69** is prepared from the same alcohol (**50**) by successive alkylation of its bromo derivative **75** with the THP derivative of propargyl alcohol and *n*-butylbromide [25].



a. PBr_3/Br_2; *b*. $THPOCH_2C{\equiv}CH/NaNH_2$; *c*. $NaNH_2$/n-BuBr; *d*. $TsOH/MeOH\text{-}H_2O$;
e. $LiAlH_4$; *f*. $H_2/Pd\text{-}CaCO_3\text{-}PbO$; *g*. $Ac_2O/AcONa$

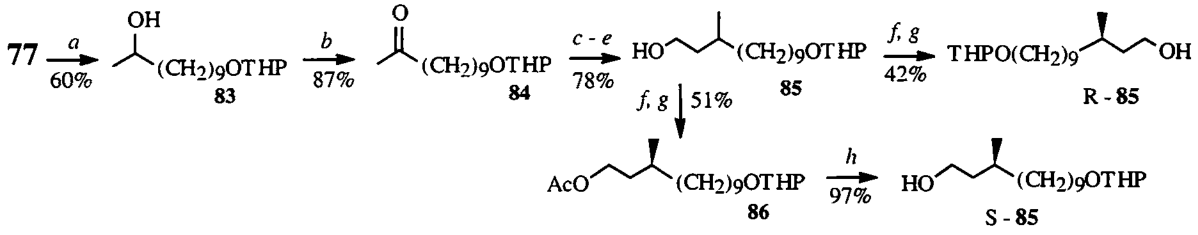
The THP ester of 10-undecen-1-ol (**77**) is also widely used to synthesize low-molecular-weight insect bioregulators. For example, anti-Markovnikov hydrogenation of an organoboron intermediate gives the monosubstituted diol **78**. Oxidation of **78** to aldehyde **79**, Horner olefination, and further usual transformations give 11E-tetradecen-1-ol (**82**), the sex pheromone of the leaf rollers *Archips argyropilus* and *Platynota stultana* [26].



R = H (**80**), Ms (**81**)

a. DHP/TsOH; *b*. $NaBH_4/BF_3 \cdot EtO$; *c*. $H_2O_2/NaOH$; *d*. PCC/AcONa; *e*. $(EtO)_2P(O)CH_2CO_2Et/NaH$;
f. $LiAlH_4/L\text{-}NaO_2CCH(OH)CH(OH)CO_2K$; *g*. $MsCl/Et_3N$; *h*. Me_2CuLi; *i*. HCl

The R- and S-enantiomers of 12-(2-tetrahydropyranyloxy)-3-methyldodecan-1-ol (**85**), key synthons for several optically active insect pheromones, are obtained from the same THP ester (**77**) by successive Markovnikov hydrogenation and olefination of ketone **84** prepared from the corresponding alcohol **83**.

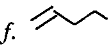


a. $Hg(OAc)_2$, then $NaBH_4$; *b*. PCC; *c*. $(EtO)_2P(O)CH_2CO_2Et/NaH$; *d*. H_2 / cat;
e. $LiAlH_4$; *f*. $CH_2{=}CHOAc$ / lipase from *Candida rugosa*; *g*. SiO_2; *h*. OH^-

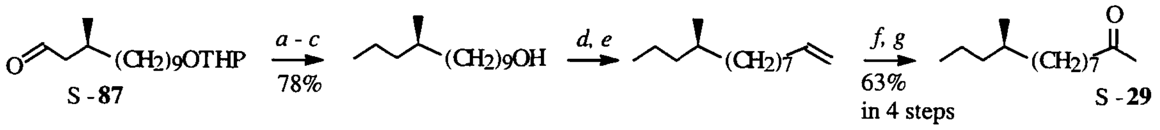
Enzymatic *trans*-acetylation of racemic alcohol **85** by *Candida rugosa* lipase produces a mixture of the optically pure S-acetate **86** and alcohol of R-(**85**), which are separated by chromatography [27].

Wittig olefination of the aldehyde R-(**87**) derived from the R-enantiomer of **85** gives after removal of the protecting group and hydrogenation to 10-methyltetradecan-1-ol (**88**), which is converted by alkylation of its tosylate **89** to 14S-methyl-1-octadecene (S-**90**), the sex pheromone of the peach leaf miner (*Lyonetia clerkella* L.) [27].

R = H (**88**), Ts (**89**)

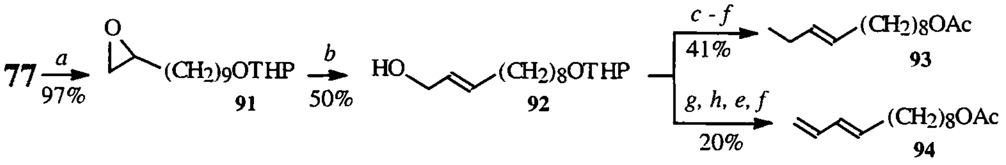
a. PCC; *b*. MeCH=PPh$_3$; *c*. TsOH/MeOH-H$_2$O; *d*.H$_2$/Pd-C; *e*. TsCl/Py; *f*.  MgBr /CuI

Similar transformations of the S-enantiomer of aldehyde **87** provide a basis for synthesizing the natural pheromone S-(**29**) [27].



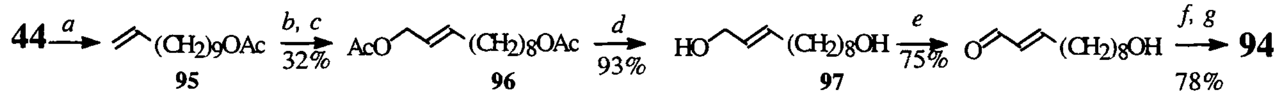
a. CH=PPh$_3$; *b*. TsOH/MeOH-H$_2$O; *c*. H$_2$/Pd-C; *d*. TsCl/Py; *e*. *t*-BuOK/DMSO; *f*. Hg(OAc)$_2$, then NaBH$_4$; g. PCC

The synthesis of pheromone components of the red bollworm moth (*Diparopsis castanea* Hmps.), 9E-dodecen-(**93**) and 9E,11-dodecadien-(**94**)-1-yl acetates, utilizes an intramolecular rearrangement of epoxide **91**, which is available from unsaturated THP-ester **77**, into the allylic alcohol **92** [28].



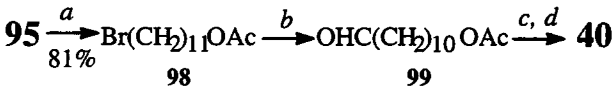
a. MCPBA (*m*-chloroperbenzoic acid)/NaOAc; *b*. *i*-Pr$_2$NLi; *c*. MsCl/Et$_3$N;
d. Me$_2$CuLi; *e*. TsOH/MeOH-H$_2$O; *f*. Ac$_2$O/Py; *g*. PCC; *h*. Me$^+$PPh$_3$I$^-$/NaH

The pheromone component **94** is also obtained from 10-undecen-1-ol (**95**) acetate by successive transformation into diacetate **96** and then diol **97** with nonequivalent hydroxyl groups. Selective oxidation of the allylic alcohol in **97** and subsequent olefination completes the synthesis [29].



a. Ac$_2$O/AcONa; *b*. NBS; *c*. AcONa; *d*. NaOH; *e*. MnO$_2$; *f*. CH$_2$=PPh$_3$; *g*. Ac$_2$O/Py

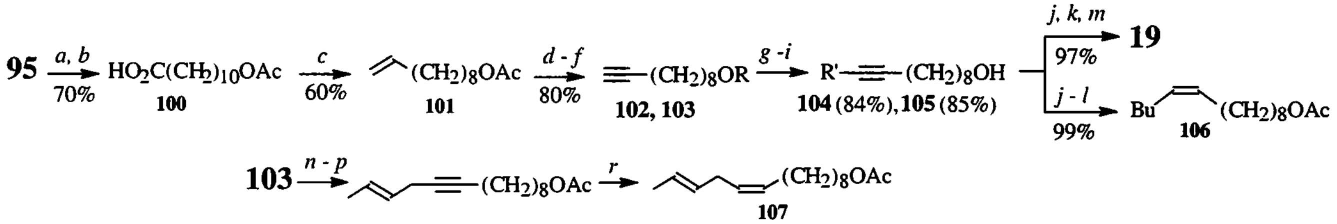
The synthesis of the sex pheromone of the moth *Ostrinia nubilalisc* **40** is based on the Z-olefination of aldehyde **99**, which is obtained from the unsaturated acetate **95** via successive radical hydrobromination and oxidative substitution of the bromine for oxygen in bromoacetate **98** [30].



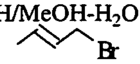
$$\mathbf{95} \xrightarrow[81\%]{a} \underset{\mathbf{98}}{\mathrm{Br(CH_2)_{11}OAc}} \xrightarrow{b} \underset{\mathbf{99}}{\mathrm{OHC(CH_2)_{10}OAc}} \xrightarrow{c,\,d} \mathbf{40}$$

a. HBr/Bz_2O_2; *b*. $C_5H_5N\to O/NaHCO_3$; c. Ⓟ– $[n\text{-}PrPh_2P^+]Br^-$ (Phosphonium salt on a polymeric support)/NaH; *d*. Ac_2O/Py

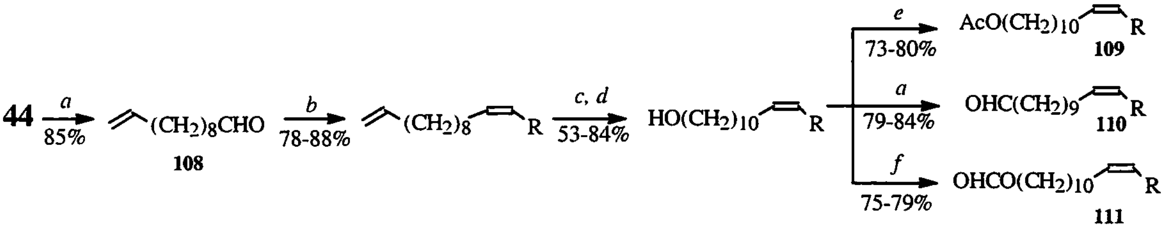
Several 9Z-unsaturated acyclic pheromones of the *Lepidoptera* family have been synthesized. These include 9Z-tetradecen-(**106**)- and 9Z,12E-tetradecadien-(**107**)-1-ylacetates and 9Z-hexadecenal (**19**), pheromone components of the pine cutworm (*Panolis flammea*), the grinder (*Ephestia kuchniella*), and the southern (*Plodia interpunctella*) pyrelid and cotton cutworm (*Heliothis armigera*), respectively. The synthesis consists of a two-step homologation of 10-undecen-1-ylacetate (**95**) into 9-decen-1-ylacetate (**101**) through the intermediate acetoxyacid **100**. The key 9-decyn-1-ol (**102**) is obtained in high yield from **101** via successive phase-transfer catalytic bromination and dehydrobromination. The acetylenic precursors **104** and **105** are transformed into the Z-unsaturated analogs **19** and **106** in high (98%) stereochemical purity by using a Cp_2TiCl_2 catalyst for the Grignard reaction with *iso*-butylmagnesium bromide [31].



R = H (**102**), THP (**103**); R' = *n* - Bu (**104**), $Me(CH_2)_5$ (**105**)

a. $BF_3\cdot Et_2O/NaBH_4$; *b*. H_2CrO_4; *c*. $Pb(OAc)_4/Cu(OAc)_2\ H_2O$; *d*. Br_2; *e*. *t*-BuOK/DB[18]6 (dibenzo-18-crown-6); *f*. DHP/TsOH; *g*. $LiNH_2$; *h*. *n*-BuBr or $Me(CH_2)_5Br$; *i*. $TsOH/MeOH\text{-}H_2O$; *j*. *i*-$BuMgBr/Cp_2TiCl_2$; *k*. HCl; *l*. Ac_2O/Py; *m*. PCC; *n*. EtMgBr; *o*. CuI; *p*.  ; *r*. $H_2/Ni\text{-}P2$

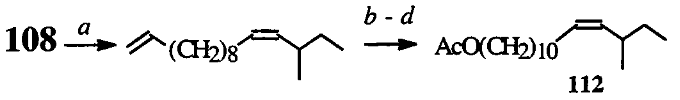
A general approach to the synthesis of a whole series of insect pheromones (**109**, **110**) and their analogs (**111**) with the 11Z-alkenyl structure includes a stereospecific Wittig reaction in which the carbonyl compound is 10-undecenal (**108**) [32, 33].

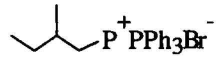


R = Et, *n*-Bu, $Me(CH_2)_4$, $Me(CH_2)_5$, $Me_2CH(CH_2)_2$, Et_2CHCH_2

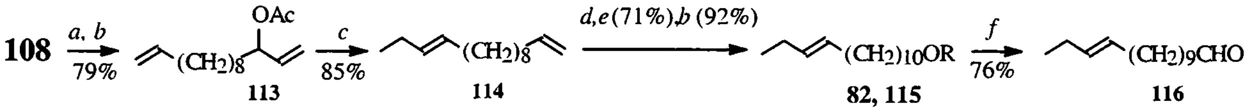
a. PCC; *b*. $RCH_2P^+Ph_3Br^-/(Me_3Si)_2NNa$; *c*. 9-BBN (9-borabicyclo[3,3 1]nonane); *d*. $H_2O_2/NaOH$; *e*. Ac_2O/Py; *f*. N-formylimidazole

Analogous conversions of aldehyde **108** are used to prepare 13-methyl-11Z-pentadecen-1-ylacetate (**112**), an analog of the sex pheromone of *Ostrinia nubilalis* [34].



a.  $/(Me_3Si)_2NNa$; *b*. 9-BBN; *c*. $H_2O_2/NaOH$; *d*. Ac_2O/Py

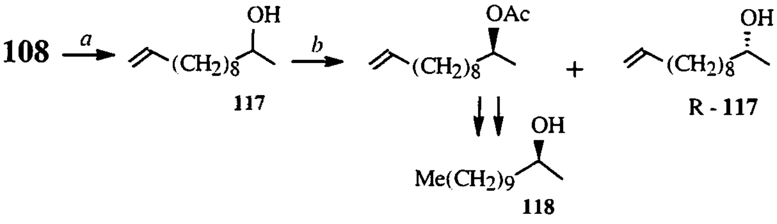
A key step in the assembly of the carbon framework of 11E-tetradecenal (**116**) and the corresponding alcohol **82** and acetate **115**, which are found in the pheromones of many insects of the Lepidoptera family, for example, the destructive agricultural pest meadow moth *Loxostege sticticalis*, is the regio- and stereospecific S_N2' reaction of methylmagnesium cuprate with the secondary allyl acetate **113**. The latter is prepared via condensation of vinylmagnesium bromide with 10-undecenal (**108**). Chemo- and regioselective anti-Markovnikov hydrogenation of the addition product, 1,11E-tetradecadiene (**114**), is performed using an organoboron intermediate [35].



R = H (**82**), Ac (**115**)

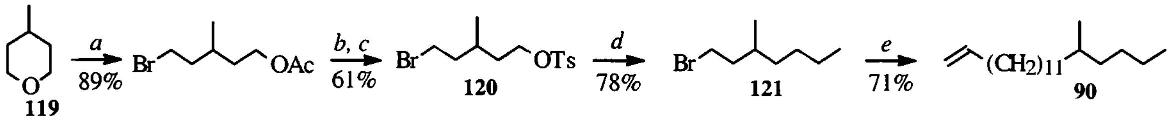
a. MgBr ; *b.* Ac_2O/Py; *c.* MeMgI/CuI; *d.* 9-BBN; *e.* H_2O_2/AcONa; *f.* PCC

A simple synthesis of dodecan-2S-ol (**118**), an ant pheromone (*Crematogaster*), is based on the enantiomerically specific esterification of the racemic unsaturated precursor **117** using pig pancreatic lipase (PPL) as a catalyst [36].



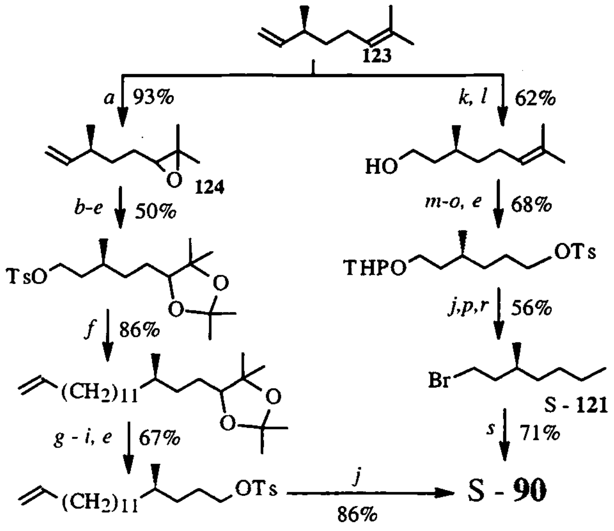
a. MeMgI; *b.* OAc /PPL

Halide derivatives of 10-undecen-1-ol (**44**) are also used in the chemistry of insect pheromones. Thus, the racemic analog of pheromone **90** is obtained by Wurtz coupling of 1-bromo-10-undecene (**122**) and the methyl-branched bromide **121**, which can be synthesized by chemoselective alkylation of the bromotosylate **120** that is readily available from 4-methyltetrahydropyran (**119**) [37].



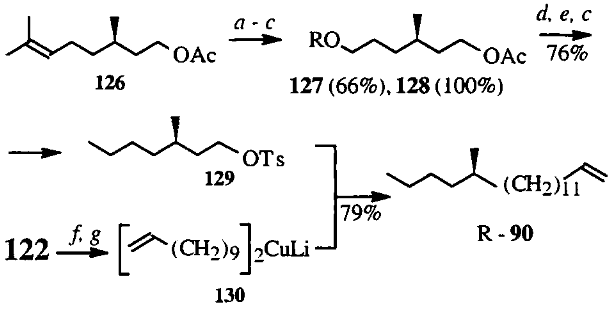
a. AcBr/$ZnCl_2$; *b.* TsOH/MeOH-H_2O; *c.* TsCl/Py; *d.* Et_2CuLi; *e.* $(CH_2)_9Br$ (**122**)/Mg/CuI-bipy (2,2'-bipyridyl)

Synthesis of the natural pheromone S-(**90**) from S-(+)-dihydromyrcene (**123**) utilizes the Grignard reagent from the same bromide **122**. The chiral center of the product is introduced using a series of selective transformations of the monoepoxide **124** and S-citronellol (**125**), products of the chemoselective epoxidation and hydration of the starting diene **123** according to the literature methods [38-42].



a. MPPA; *b*. $HClO_4$; *c*. $Me_2CO/TsOH$; *d*. B_2H_6, then $H_2O_2/NaOH$; *e*. TsCl/Py ; *f*. **122**/Mg/Li_2CuCl_4; *g*. $AcOH/H_2O$; *h*. HIO_4; *i*. $NaBH_4$; *j*. $MeMgI/Li_2CuCl_4$; *k*. i-Bu_3Al; *l*. O_2; *m*. DHP/TsOH; *n*-O_3; *o*. $NaBH_4$; *p*. HCl; *r*. PBr_3/Py; *s*. **122**/Mg/CuI-bipy

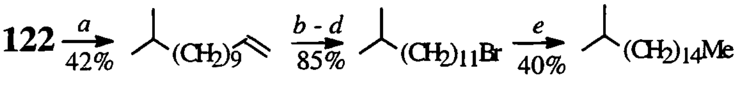
The optical isomer of the peach leaf miner pheromone R-(**90**) is prepared by successive extension of the carbon framework of the mono-protected diol **127** that is obtained via ozonolysis-reduction of R-citronelloate **126** and alkylations of its tosyl derivative **128** and then the intermediate **129** with di[methyl- and 10-undecenyl-(**130**)] lithium cuprate reagents, respectively [43].



R = H(**127**), Ts (**128**)

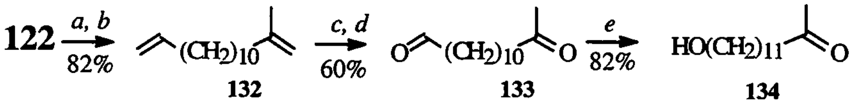
a. O_3; *b*. $NaBH_4$; *c*. TsCl/Py; *d*. Me_2CuLi; *e*. NaOH; *f*. Li; *g*. CuI

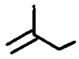
The synthesis of 2-methylheptadecane (**131**), the sex pheromone of tiger moths (Arctiidae), is performed in two steps by extending the carbon framework of 10-undecen-1-ylbromide (**122**) using isopropyl- and *n*-butylmagnesium bromides [44].



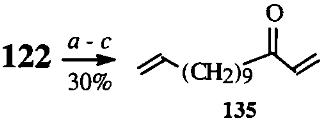
a. i-$PrMgBr/Li_2CuCl_4$; *b*. $NaBH_4/BF_3 \cdot OEt_2$; *c*. $H_2O_2/NaOH$; *d*. PBr_3/Py ; *e*. n-$BuMgBr/Li_2CuCl_4$

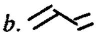
An original synthesis of 13-hydroxy-2-oxotridecane (**134**), a honeybee attractant isolated from the extract of fruit of *Evodia hupehensis* Dode, includes ozonolysis-reduction of the methyl-branched diene **132**, which is prepared by Wurtz coupling of the magnesium derivative of bromide **122** and methylallylchloride, and selective reduction of the formyl group in the intermediate ketoaldehyde **133** by sodium trisacetoxyborohydride [45, 46].



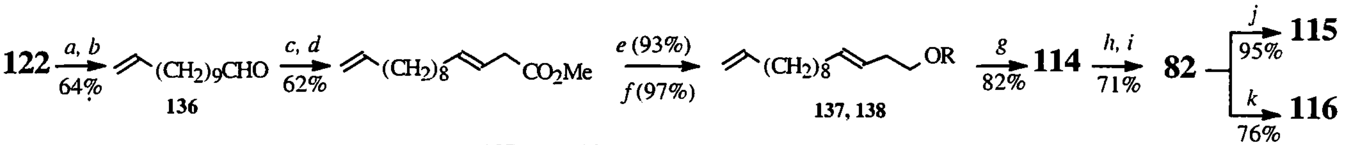
a. Mg; *b*. Cl/ CuI-bipy; *c*. O_3; *d*. Me_2S; *e*. $NaBH(OAc)_3$

The synthesis of 1,13-tetradecadien-3-one (**135**), a protective agent produced by the East-African termite (*Schedorhinotermes lamanianus* Sjostedt), is based on condensation of the Grignard reagent from 10-undecen-1-ylbromide (**122**) and acrolein [47].



a. Mg; *b*. O ; *c*. MnO_2

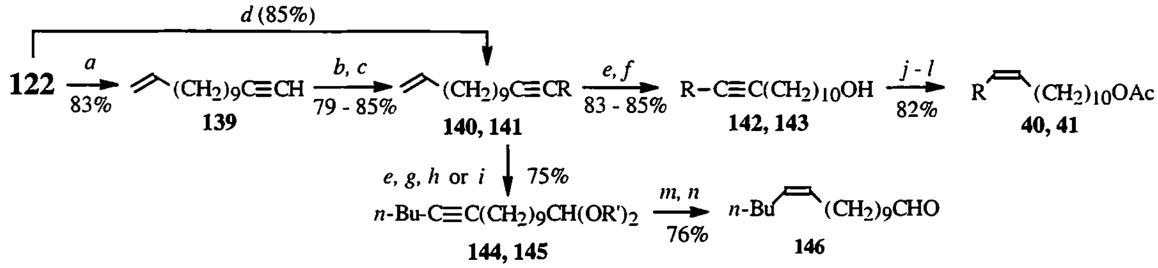
Pheromones **82**, **115**, and **116** are synthesized starting from the unsaturated bromide **122**. Successive lengthening of the carbon backbone by formylation of its magnesium derivative and a modified Knoevenagel reaction of intermediate 11-dodecenal (**136**) is used.



R= H (**137**), Ts (**138**)

a. Mg; *b*. DMF; *c*. $CH_2(COOH)_2$/Pyp ·AcOH; *d*. MeOH/TsOH; *e*. *i*-Bu_2AlH;
f. TsCl/Py; *g*. $LiAlH_4$; *h*. *i*-$Bu_2AlH/ZrCl_4$; *i*. O_2; *j*. Ac_2O/Py; *k*. PCC

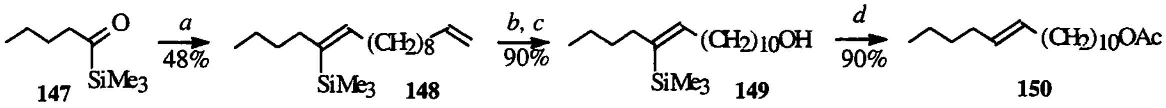
The low reactivity of ozone toward acetylene compared with vinyl groups suggested an effective route for synthesizing several 11Z-monoene insect pheromones (**40**, **41**, and **146**). 11Z-hexadecenal (**146**) is a pheromone component of the cotton moth (*Heliothis armigera*) and the rice-stem borer (*Chilo suppressalis*). The key compounds **140** and **141** are obtained from the bromide **122** either successively (through the α,ω-enyne **139**) or in one step (*d*). Reduction of the products from selective ozonolysis of the alkenynes **140** and **141** gives the acetylenic alcohols **142** and **143** and the acetals **144** and **145**, which are precursors of the Z-unsaturated acetates **40** and **41** and the aldehyde **146**, respectively [51-54].



R = Et (**40**, **140**, **142**), *n* - Bu (**41**, **141**, **143**); (OR') = $(OMe)_2$ (**144**), OCH_2CH_2O (**145**)

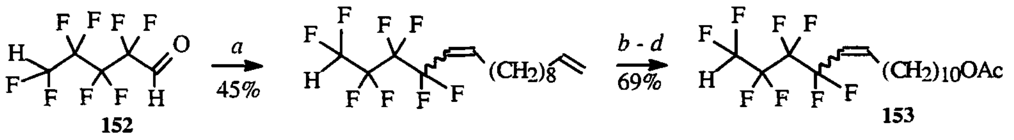
a. HC≡CLi; *b*. $LiNH_2$; *c*. EtBr or n-BuBr; *d*. n-BuC≡CLi; *e*. O_3; *f*. $NaBH_4$; *g*. Me_2S; *h*. MeOH/TsOH;
i. $(CH_2OH)_2$/TsOH; *j*. 9-BBN; *k*. AcOH; *l*. Ac_2O/Py; *m*. H_2/Pd; *m*. $H_2/Pd\text{-}CaCO_3\text{-}PbO$; *n*. Py ·TsOH/$H_2O$

The acetate of 11E-hexadecen-1-ol (**150**), the sex pheromone of the sweet potato pyrelid (*Brachmia macroscopa*), is synthesized in high stereoisomeric purity (>99%) from the unstable ylide **151**, which is prepared from 10-undecenyl-1-bromide (**122**), and the aliphatic acylsilane **147** using a lithium-salt catalyst. Hydroboration of the diene intermediate **148** with a bicyclic borane occurs regiospecifically, giving after oxidation the E-unsaturated alcohol **149**. Reduction of the trimethylsilyl group in **149** is carried out under acylating conditions [55].



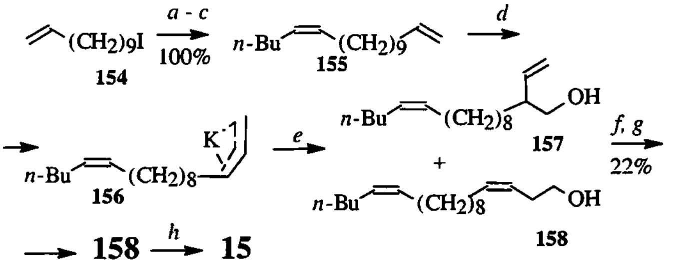
a. $(CH_2)_8CH{=}PPh_3$ (**151**)/LiI; *b.* 9-BBN; *c.* H_2O_2/NaOH; *d.* AcCl/MeCN

The fluorinated analog **153** of the cabbage moth (*Mamestra brassicae*) sex pheromone is synthesized using Wittig olefination with the same phosphorane **151**. The carbonyl compound is 2,2,3,3,4,4,5,5-octafluoropentanal (**152**) [56].



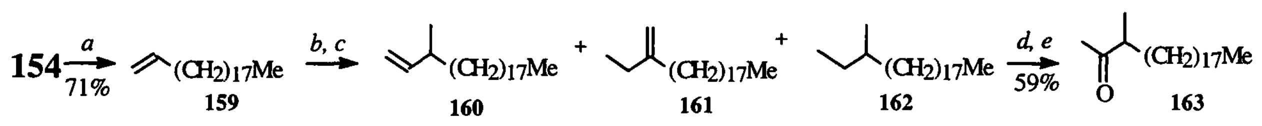
a. **151**; *b.* 9-BBN; *c.* H_2O_2 / NaOH; *d.* Ac_2O/Py

Metallation by trimethylsilylpotassium of Z-5,16-heptadecadiene (**155**), which is prepared by reaction of the unstable ylide from 1-iodo-10-undecene (**154**) and pentanal, gives the intermediate **156**, treatment of which with paraformaldehyde gives a mixture (2:3) of regioisomers of the homoallyl alcohols **157** and **158**. The latter is readily converted after isolation from the mixture into the sex pheromone of the peach clear-winged moth (*Sanninoidea exitiosa*) (**15**) [57].



a. PPh_3; *b.* KNH_2; *c.* *n*-BuCHO; *d.* Me_3SiK/ MgCl ;
e. $(CH_2O)_n$; *f.* distillation; *g.* recrystallization; *h.* Ac_2O/Py

A rational approach to the synthesis of 3-methylheneicosan-2-one (**163**), an analog of the sex pheromone of the German cockroach (*Blatella germanica*), is based on reductive β-vinylation of the key α-olefine **159**, which in turn is obtained by Wurtz coupling of the iodide **154** and nonylmagnesium bromide. The vinylation product **160** contains a total of up to 25% of its isomer **161** and the saturated analog **162** as an impurities. Transformation of **160** into the corresponding ketone **163** by the Walker—Tsuji reaction enables it to be easily purified by chromatography [58, 59].



a. Me(CH$_2$)$_8$MgBr/CuI-bipy; *b*. AlEt$_3$/Cp$_2$ZrCl$_2$; c.  /Ni(acac)$_2$/PPh$_3$/*i*-Bu$_2$AlH; *d*. O$_2$/PdCl$_2$-CuCl; *e*. SiO$_2$

Thus, the literature review clearly demonstrates the synthetic potential and promise of using 10-undecenoic acid to synthesize low-molecular-weight bioregulators, in particular, insect pheromones.

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