SYNTHESIS OF MONOENIC ALIPHATIC PHEROMONES OF INSECT PESTS OF THE COTTON PLANT*

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Advances in the last decade in the field of the synthesis of monoenic aliphatic pheromones of insect pests of the cotton plant are generalized.

Among modern directions, harmless for the biosphere, for the biological protection of plants from pests great attention has been devoted recently to pheromones, since they do not pollute the environment and are harmless for Man and animals.

Modern integrated systems of plant protection are based on accurate information concerning the size of the populations of insect pests. Pheromones can be used for recording the seasonal dynamics of the populations and predicting optimum times of attack, and also for annihilating pests by the mass trapping of the males or by disorientation methods. They are also widely used for revealing foci of quarantine pests.

The number of investigations devoted to insect pheromones is constantly increasing. They consume approximately 14% of the world funds devoted to scientific programs on entomology [1].

Experimental results on questions connected with the identification, synthesis, and use of pheromones for combating various insect pests have been generalized in a series of review and monographs [2-7].

In the present review an attempt is made to generalize literature information predominantly from the last ten years on the sex pheromones of insect pests of the cotton plant belonging to the order Lepidoptera.

Dangerous pests of the cotton plant include the turnip moth, moths of the genus Heliothis, the pink bollworm, the beet armyworm, the beet webworm, and the Asian and Egyptian corn earworms, and great damage may be caused by the heart-and-dart, the silver Y, the wild,† and alfalfa moths and some other pests.

The sex pheromones of the majority of cotton-plant pests have already been identified, which has enabled methods to be developed for their synthesis. Synthetic sex pheromones are finding ever increasing practical use thanks to the development of methods for the isolation and purification of the pheromones and the identification of their structure, advances in the field of fine organic synthesis, the creation of preparative forms of synthetic pheromones, the development of various types of pheromone traps, etc.

The majority of sex pheromones produced by Lepidoptera that have been identified are unsaturated aliphatic alcohols, acetates, or aldehydes [2-7].

The composition of the sex pheromone of the turnip moth has been studied in detail. It is a multicomponent substance [8], and the populations of insects living in different countries are attracted to different components of mixtures of them. Thus, the population of the turnip moths found in France was attracted only to a single component – (Z)-dec-5-en-1-yl acetate (Z5DA), those in Denmark (Z)-dodec-7-en-1-yl acetate (Z7DDA), and in Switzerland to the three-component mixture Z5DA, Z7DDA, and (Z)-dodec-9-en-1-yl acetate (Z9DDA) [6]. In Bulgaria, it has been established by field screening that the males of the turnip moths are actively attracted both by (Z)-tetradec-9-en-1-yl acetate (Z9TDA) and by a mixture of Z9TDA

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†Literal translation; not identified entomotically – Translator.

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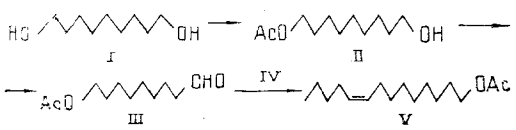
with (Z)-tetradec-11-en-1-yl acetate (Z11TDA), but the binary mixture has a considerably longer period of attractive action [9]. Thus, it is necessary to know the component composition of the sex pheromones and the exact ratio of the active components in geographically distinct populations. The study of the composition of the active fraction of the sex pheromone of the turnip moth found in the south-western region of the USSR has shown that the pheromone consists of three main components, Z5DA, Z7DDA, and Z9TDA. Compositions containing these comonents have shown the greatest attractiveness for the males of the pest in field trials [10].

Since the main components of the sex pheromone of the turnip moth are acetates of (Z)-monoenic alcohols, a whole series of syntheses has been based on the construction of a (Z)-alkenic carbon skeleton. The Wittig reaction, for example, is used for this purpose, permitting olefins to be obtained in the form of mixtures of (Z)- and (E)-isomers. The stereodirectivity of this reaction can be regulated by various factors. The performance of the interaction of alkylidenephosphoranes with aliphatic aldehydes in nonpolar solvents in the absence of lithium salts or in such dipolar aprotic solvents as DMFA, DMSO, and HMPT leads to the production mainly of the (Z)-monoenes containing the corresponding (E)-isomers as impurities [3, 6, 7].

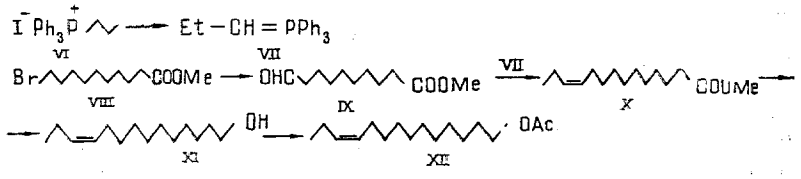
The demands on the stereoisomeric purity of the attractants are very high (frequently the presence of even a small amount of the opposite isomer causes an inhibition of the biological activity of the active agent), and therefore the inadequately high stereospecificity of the Wittig reaction requires great efforts for the subsequent separation of the geometric isomers [3, 6].

Thus, (Z)-tetradec-9-en-1-yl acetate (V) was obtained in the following way:



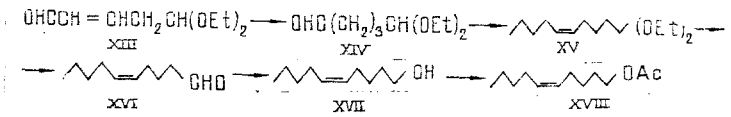
The acetylation of nonane-1,9-diol (I) gave 9-acetoxynonan-1-ol (II), which was oxidized to 9-acetyoxynonal (III), the condensation of which with amyltriphenylphosphonium bromide (IV) in the presence of MeONa in DMFA led to a mixture of the (Z)- and (E)-isomers (92:8), which was separated on silica gel impregnated with silver nitrate.

For the synthesis of (Z)-tetradec-11-en-1-yl acetate (XII), a scheme was proposed [12] the key stage of which was condensation between triphenylpropylidenephosphorane (VII) and 10-methoxycarbonyldecanal (IX) under the same conditions



The phosphorane (VII) was formed by the action of sodium methanolate in DMFA on triphenylpropylphosphonium iodide (VI). The (Z)-tetradec-11-enoate (X) obtained as the result of the condensation was reduced with $LiAlH_4$ to the corresponding alcohol (XI), and acetylation of the latter gave the pheromone component (XII). The product obtained in this way contained 95% of the (Z)-isomer and 5% of the (E)-isomer.

Bestmann succeeded in considerably increasing the stereospecificity of the Wittig reaction by generating phosphorus ylides from the corresponding phosphonium salts with sodium bis(trimethylsilyl) amide and performing the condensation at −78°C. In this case 98% of the (Z)-isomer and only 2% of the (E)-isomer was formed [13]. A number of (Z)-monoenic alcohols and their acetates have been obtained by this method – (Z)-dodec-7-en-1-yl acetate [14], (Z)-dec-5-en-1-yl acetate [15], and others. Kovalev et al. [16] synthesized (Z)-dec-5-en-1-yl acetate (XVIII) from the readily available monoacetal of glutaconic aldehyde (XIII):



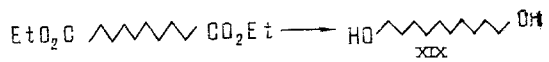
The hydrogenation (XIII) in the presence of 5% palladium on carbon gave the monoacetal of glutaraldehyde (XIV), which, on interaction with amyltriphenylphosphonium bromide under conditions described in [13] gave the key synthon – the acetal of (Z)-dec-5-enal (XV) – in 63% yield. Hydrolysis of the latter gave (Z)-dec-5-enal (XVI) which was reduced with lithium tetrahydroaluminate to (Z)-dec-5-enol (XVII). When the alcohol (XVII) was acetylated with acetyl chloride, the required acetate (XVIII) was obtained. The final product contained 4% of the (E)-isomer.

One of the most widely used method for synthesizing pheromones is the so-called acetylene route, where use is made of the capacity of monosubstituted acetylenes for undergoing metallation and alkylation with the formation of the key compounds – disubstituted acetylenes which are transformed stereodirectedly into the required (Z)- or (E)-alkenic compounds. This synthetic direction has been discussed fairly fully in a number of publications [3-7], and therefore we shall dwell only on some results reported recently.

The development and improvement of convenient methods for synthesizing monosubstituted acetylenes is continuing. Thus, the process of obtaining hex-1-yne under the conditions of the liquid-phase dehydrohalogenation of 1,2-dibromohexane in ethylcellosolve with caustic potash has been optimized [17]. Dehmlow [18] has obtained a number of alkenes under the conditions of phase-transfer catalysis (PTC) from vicinal dibromides by the action of solid KOH in petroleum ether. The catalysts were tetraoctylammonium bromide, Aliquat 336 (tricaprylammonium chloride), and 18-crown-6. The yields were high – 79-98%. The preparation of alkenes and dienes from 1,2-dihalogenoalkanes and halogenoalkenes under PTC conditions has been described [19]. Aromatic or alkylaromatic hydrocarbons or ethers were used as solvents, and as phase-transfer catalysts dibenzo-18-crown-6 or 18-crown-6 in an amount of 0.5-2% (molar) on the alkali used.

Other crown ethers with a smaller number of oxygen atoms in the ring or with a lipophilic branching of the polyether chain were less effective. The yield of desired products amounted to 80- 98%.

Some of the intermediate products are α, ω-diols, which are obtained by the reduction of diesters of the corresponding acids. Thus, the reduction of ester groups by lithium tetrahydroaluminate in toluene with the addition of ethers has been studied for the case of diethyl sebacate, as an example. When a mixture of toluene with 10-20% of diglyme was used, a 96% yield of decane-1,10-diol (XIX) was achieved [20].



ω-Halogenalkan-1-ols are widely used as alkylating agents for obtaining acetylenic alcohols from monosubstituted acetylenes. They are usually obtained from the corresponding diols by the action of aqueous solutions of HCl or HBr with heating under the conditions of continuous extraction by toluene, petroleum ether, heptane, and other solvents [3, 6, 7]. Unfortunately, in addition to the desired product, the dihalogeno derivative is formed as an impurity and great efforts are required for purification. Thus, when the diol (XIX) was heated with 48% HBr to 110°C with constant extraction by petroleum ether, a mixture of the initial (XIX), 10-bromodecan-1-ol, and 1,10-dibromodecane in a ratio of 2:85:13 was formed [21]. An effective method of converting α, ω-diols (XX) into ω-bromoalkan-1-ols (XXI) by boiling the diol, a 48% aqueous solution of HBr, and benzene with a head for eliminating water has been proposed. This method enables ω-bromoalkan-1-ols (XXI) to be obtained with a purity of 99% in satisfactory yields [21]:

$$HO(CH_2)_n OH \longrightarrow Br-(CH_2)_n-OH$$
$$XX \quad n=2-12 \quad XXI$$

The alkylation of a 1-alkynide ion, formed by the action of sodium or lithium amide, with primary alkyl halides can be carried out under various conditions. The best results are

achieved by the use of aprotic dipolar solvents such as DMFA, HMPT (hexamethylphosphorotriamide), and DMSO. The metallation of alk-1-ynes with a solution of n-butyllithium in hexane followed by alkylation in HMPT or THF-HMPT is also widely used [22-25]. A complex of lithium acetylenide with ethylenediamine is being used ever more widely for introducing a terminal acetylene group, the reaction being carried out in DMSO [26].

When ω-halogenoalkan-1-ols are used as alkylating agents, the hydroxy group is usually protected by the action of dihydropyran [27], chlorotrimethylsilane [28], isobutylene [28, 29] ethyl vinyl ether [30], or butyl vinyl ether [31].

In some cases, ω-halogenoalkan-1-ols are used without preliminary protection of the hydroxy group, and then an excess of sodium or lithium amide is necessary in the reaction in order to decrease the formation of the product of O-alkylation through the formation of the metal alcoholate (XXII) [25].

$$R-C\equiv CH + 2MNH_2 + X(CH_2)_nOH \longrightarrow$$
$$\longrightarrow R-C\equiv CM + X(CH_2)_nOM \longrightarrow$$
$$\longrightarrow \underset{\text{XXII}}{R-C\equiv C-(CH_2)_nOM} + MX$$
$$\downarrow H_3O^+$$
$$R-C\equiv C-(CH_2)_n-OH$$
$$M = Li, Na;\quad X = Cl, Br$$

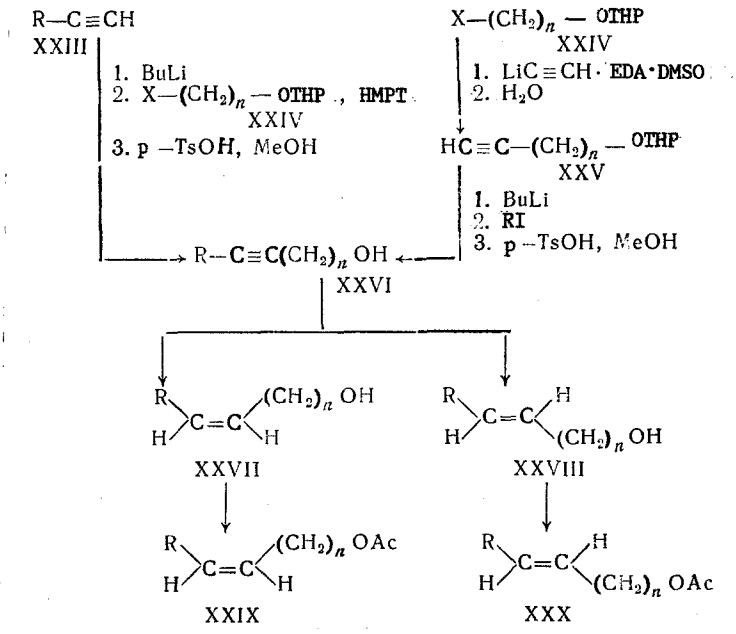
New prospects for obtaining terminal alkynes and alkynols were opened up after Brown and Yamashita [32] found that the Favorskii isomerization with migration of the triple bond to the end of the chain readily takes place in the potassium 3-aminopropylamide-1,3-diaminopropane system.

$$H(CH_2)_mC\equiv C(CH_2)_nH \longrightarrow H(CH_2)_{m+n}C\equiv C^-K^+ \xrightarrow[H_2O]{} H(CH_2)_{m+n}C\equiv CH$$

According to [33], systems consisting of lithium 2-aminoethylamide or 3-aminopropylamide and potassium tert-butoxide possess even greater activity.

The required monoenic alcohols have been obtained by the stereospecific transformation [25, 28, 30, 34, 35] of a triple bond into a (Z)- or (E)-double bond. The acetylation of these alcohols leads to their acetates, which are components of the attractants of many insects.

Rossi's work [36] may serve as an illustration of the approach to the synthesis of a number of components of sex pheromones through acetylenic intermediates:

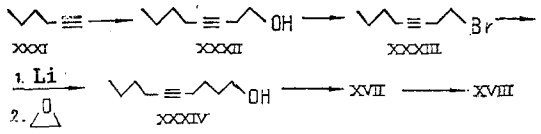


The alkynes (XXIII) were converted into the corresponding 1-alkynides by the action of a solution of BuLi in hexane at 0°C. Alkylation of the lithium alkynides with the 1-halogeno-ω-tetrahydropyranyloxyalkanes (XXIV) led to 1-tetrahydropyranyloxyalkynes, which, after the removal of the pyranyl protection, gave the alkyn-1-ols (XXVI). The alkynols (XXVI) can also be obtained from (XXIV) by the introduction of an ethynyl group with the aid of the lithium acetylide–EDA complex in DMSO at 0°C. The ω-tetrahydropyranyloxyalk-1-ynes (XXV) were alkylated (BuLi/HMPT) with the appropriate alkyl iodides, and then the protective group was eliminated by acid hydrolysis.

Selective hydrogenation over Lindlar catalyst poisoned with quinoline in pentane at −10°C gave the (Z)-isomers (XXVII) [containing less than 1.5% of the corresponding (E)-isomers].

The (E)-alkenols (XXVIII) were obtained by reducing the alkynols (XXVI) with an excess of $LiAlH_4$ in diglyme at 140°C. In this case, the amount of the corresponding (Z)-isomer was less than 1%. Acetylation with acetyl chloride in pyridine gave the desired (Z)- and (E)-acetates. Among the compounds obtained by this method have been (Z)-dodec-7-enyl acetate (R = C_4H_9, n = 6), and (Z)-tetradec-9-enyl acetate (R = C_4H_9, n = 8).

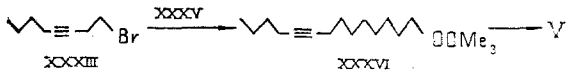
(Z)-Dec-5-en-1-yl acetate (XVIII) has also been synthesized via an acetylenic intermediate by the following scheme [37]:



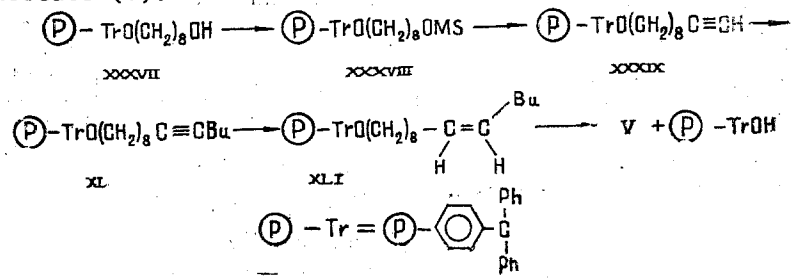
The initial compound was hex-1-yne (XXXI), the lithium derivative of which, under the action of 2-chloroethyl ether, gave oct-3-yn-1-ol (XXXII), which was converted via the tosylate into 1-bromooct-3-yne (XXXIII). The oxyethylation of the lithium derivative from the bromide (XXXIII) gave dec-5-yn-1-ol (XXXIV), which was reduced stereoselectively with borabicyclo[3.3.1]nonane(9-BBN) to (Z)-dec-5-en-1-ol (XVII). Acetylation of the latter led to the required (Z)-acetate (XVIII).

The preparation via acetylenic derivatives of (Z)-dec-5-en-1-yl acetate and (Z)-tetradec-9-en-1-yl acetate, starting from tetrahydrofuran and hex-1-ene has also been described [31].

Vig et al. [38] have developed a synthesis of (Z)-tetradec-9-en-1-yl acetate starting from propargyl alcohol. The growth of the carbon chain was carried out by two-stage malonation with ethyl monosodium malonate. The same compound has been obtained with the use as the key stage of the condensation of 1-bromooct-3-ene(XXXIII) with the Grignard reagent formed from 1-bromo-6-tert-butoxyhexane (XXXV) at −20°C in the presence of Li_2CuCl_4. The subsequent conversion of the tert-butyl ether (XXXVI) into the corresponding acetate with a mixture of acetic acid and acetyl chloride and partial hydrogenation over P-2Ni catalyst led to (Z)-tetradec-9-enyl acetate (V) [39]:

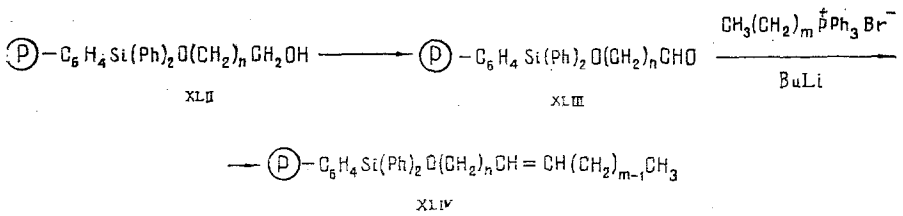


The synthesis of sex attractants on polymeric supports has been studied in detail [40]. In the majority of cases, the initial stage for such syntheses is the addition of symmetrical diols to polymer-bound trityl chloride. An example of such an approach is the synthesis of (Z)-tetradec-9-enyl acetate (V):



The free hydroxy group of octane-1,8-diol bound to the polymer (XXXVII) was treated with methanesulfonyl chloride, and the mesylate obtained (XXXVIII) was treated with lithium acetylenide. This gave the polymer-bound alkyne (XXXIX), which was metallated with butyllithium and was then alkylated with butyl bromide. The resulting polymer (XL) was hydrogenated selectively with diisoamylborane to the (Z)-alkene (XLI), and, after acid hydrolysis, the hydroxy group was deblocked and the (Z)-alkenol was isolated and was converted into the acetate (V). The overall yield of pheromone was 40%. The polymeric support was readily regenerated and could then be used repeatedly.

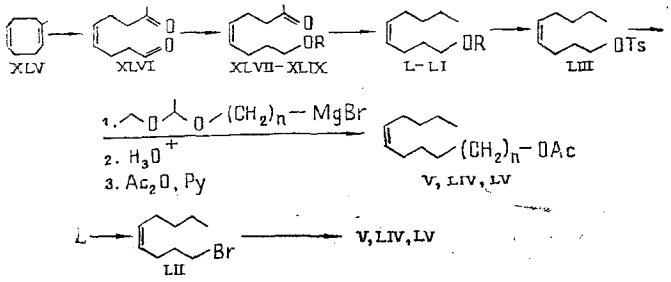
The use of polymer-bound chlorotriphenylsilane in the solid-phase synthesis of the sex pheromones of insects has been described [41]:



The polymer-bound diol (XLII) was oxidized to the corresponding aldehyde (XLIII), which was then treated with the ylide generated from an alkyltriphenylphosphonium bromide, giving the polymer-bound alkyne (XLIV). After detachment and acetylation, the final product consisted of a mixture (Z)- and (E)-isomers in a ratio of 81:19.

Recently, a number of new approaches to the synthesis of monoenic aliphatic alcohols and their acetates and aldehydes has been proposed.

The work of a group led by G. A. Tolstikov is interesting. They have synthesized pheromones of this class by the ozonolysis of readily available cyclic unsaturated compounds. Thus, the acetates of (Z)-tetradec-9-en-1-ol, of (Z)-dodec-7-en-1-ol, and of (Z)-hexadec-11-en-1-ol have been obtained from 1-methylcycloocta-1-cis,5-cis-diene (XLV) – a cyclic codimer of isoprene and butadiene [42]. The synthesis was performed by the following scheme:

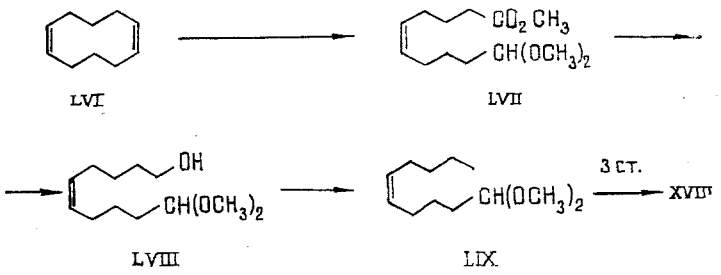


R = H (XLVII, L), Ac (XLVIII, LI), –CH(CH$_3$)OC$_2$H$_5$ (XLIX)
n = 3 (LIV), 5 (V), 7 (LV)

Ozonolysis of the diene (XLV) gave non-cis-4-ene-1,8-dione (XLVI), which was converted by the action of potassium triacetoxyhydroborate into 9-hydroxynon-5(Z)-en-2-one (XLVII) [(XLVIII) is the corresponding acetoxy derivative, and (XLIX) the 1-ethoxyethyl ether]. The selective reduction of the tosylhydrazone of the hydroxyketone (XLVIII) with sodium triacetoxyhydroborate gave the unsaturated alcohol (L), and its acetylation the corresponding acetate (LI). Bromination of the alcohol (L) by the action of phosphorus tribromide led to 1-bromonon-4(Z)-ene (LII), a key synthon for obtaining the pheromones of the (Z)-alken-1-ol series. The corresponding components of sex pheromones were synthesized by the action of the Grignard reagent obtained from the bromide (LII) on the 1-ethoxyethyl ethers of the corresponding ω-bromo alcohols followed by acid hydrolysis and acetylation.

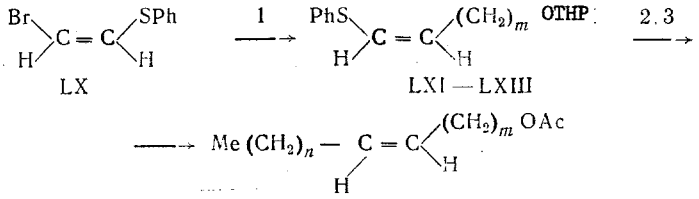
A new approach has been developed for the synthesis (Z)-dec-5-en-1-yl acetate (XVIII) which is based on the ozonolysis of (Z,Z)-cyclodeca-1,6-diene (LVI), leading to methyl 10, 10-dimethoxydec-5-enoate (LVII). The reduction of (LVII) with diisobutylaluminum hydride

(DIAH) led to 10-hydroxy-1,1-dimethoxydec-5(Z)-ene(LVIII), the deoxygenation of which via its tosylate gave 1,1-dimethoxydec-5(Z)-ene (LIX). The subsequent elimination of the acetyl protection and reduction of the aldehyde formed gave (Z)-dec-5-enol, the acetylation of which led to the desired pheromone (XVIII) [43]. The overall yield of decenyl acetate calculated on the initial diene (LVI) was 27%.



LVI LVII LVIII LIX

A general approach to the synthesis of monoolefinic sex pheromones of insects with the (Z)- or the (E)-configuration has been proposed in [44]. Thus, a series of acetates of (Z)-monoenic alcohols has been obtained by the following scheme, which includes two cross-coupling reactions with (Z)-1-bromo-2-phenylthioethene (LX) in the presence of Ni(II) or Pd(II) complexes:



LX LXI—LXIII

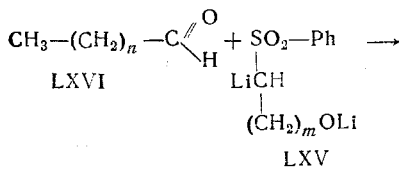
V, XII, LIV, LV, LXI, LXIV

(LXI) $m = 6$ (LIV) $m = 6$; $n = 3$ (XII) $m = 10$; $n = 1$
(LXII) $m = 8$ (LXIV) $m = 8$; $n = 1$ (LV) $m = 10$; $n = 3$
(LXIII) $m = 10$ (V) $m = 8$; $n = 3$

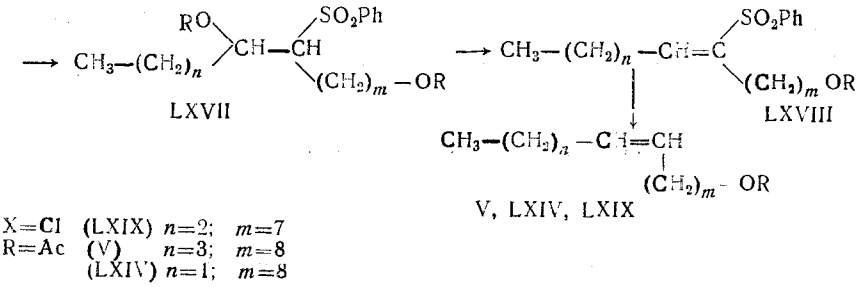
Reagents: 1 — THPO $-(CH_2)_m MgX$ — $[PdCl_2(PPh_3)_2]$; 2 — $Me(CH_2)_n MgBr$ — $[NiCl_2(dppe)]$; 3 — Ac_2O.

The Grignard reagents obtained from 1-halogen-ω-(tetrahydropyranyloxy)alkanes were mixed with compound (LX), and in the presence of the catalyst $[PdCl_2(PPh_3)_2]$ gave the 1-phenylthio-ω-(tetrahydropyranyloxy)alk-1-ens (LXI-LXIII). A second cross-coupling reaction with the corresponding Grignard reagent in the presence of catalytic amounts of $[NiCl_2(dppe)]$ led to tetrahydropyranyloxy-substituted alkynols which were acetylated with acetic anhydride to form (Z)-dodec-7-en-1-yl(LIV), (Z)-dodec-9-en-1-yl(LXIV), (Z)-tetradec-9-en-1-yl (V), (Z)-tetradec-11-en-1-yl-(XII), and (Z)-hexadec-11-en-1-yl (LV) acetates. The overall yields of the pheromones amounted to 52-60%, and their isomeric purity was more than 97%.

M. Julia [45] has performed the synthesis of the (Z)-dodec-8-en-1-yl (LXIX), (Z)-dodec-9-en-1-yl and (Z)-tetradec-9-en-1-yl acetates with the aid of sulfones in the following way. A reaction mixture consisting of metallated ω-hydroxy sulfones (LXV) and the corresponding aldehydes (LXVI) was converted by the action of acetic anhydride into a diastereoisomeric mixture of β-acetoxysulfones (LXVII). Elimination with powdered NaOH led to the (E)-vinyl sulfones (LVIII). The stereospecific hydrolysis of the sulfonyl group with a mixture of $Na_2S_2O_4$ and $NaHCO_3$ led to the corresponding unsaturated alcohols, the acetylation of which gave the sex pheromones. The stereoisomeric purity of the compounds obtained exceeded 99%.

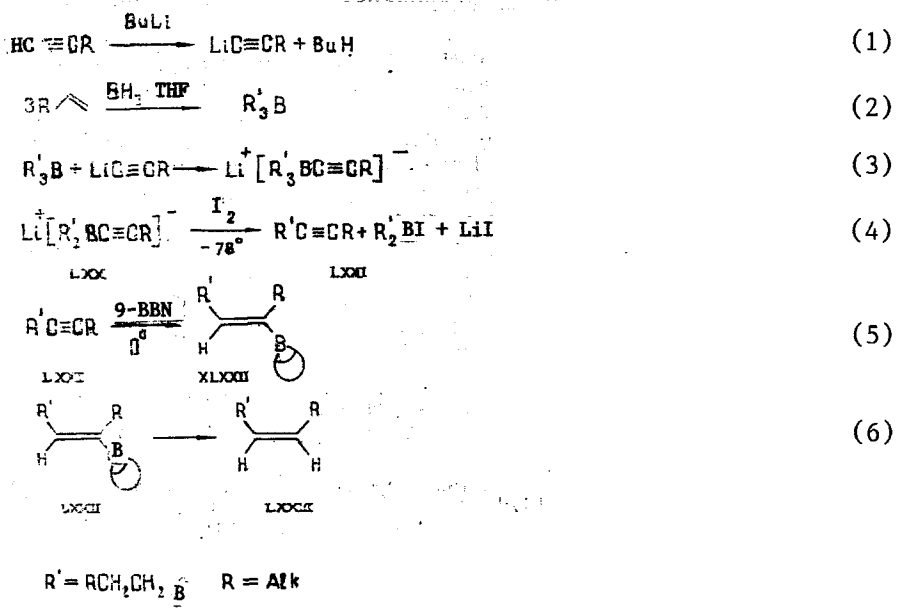


LXVI LXV



X=Cl (LXIX) $n=2$; $m=7$
R=Ac (V) $n=3$; $m=8$
(LXIV) $n=1$; $m=8$

A stereospecific synthesis of straight-chain (Z)-monoolefinic pheromones via lithium trialkyl(alkyn-1-yl)borates has been proposed by Brown [46]:

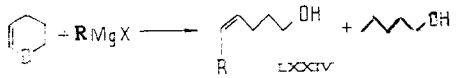


The unsymmetrical alkynes (LXXI) are readily obtained by the reaction of iodine with trialkyl(alkyn-1-yl)borates (LXX), essentially in quantitative yield (Eqs. 1-4).

The monohydroboration of the alkynes (LXXI) with 9-borabicyclo[3.3.1]nonane (9-BBN) led to the corresponding B-vinyl-9-BBN (LXXII), the protonolysis of which gave the corresponding (Z)-olefins (LXXIII).

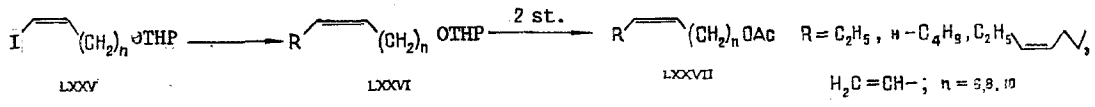
Wenkert et al. [47] have developed a new method for obtaining (Z)-olefins (LXXIV) by the interaction of (2H)-3,4-dihydropyran with Grignard reagents catalyzed by [1,3-bis-(diphenylphosphino)propane]nickel dichloride—dpppNiCl$_2$.

This reaction in suitable for the construction of a large number of (Z)-alkenic pheromones.

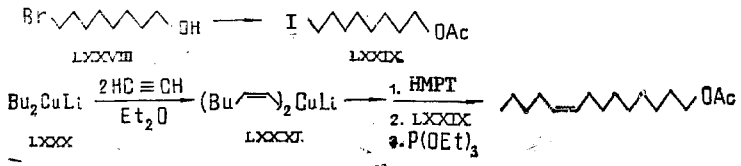


$$R = CH_3 - C_6H_{13}, C_8H_{17}$$

For the synthesis of (Z)-tetradec-9-en-yl and (Z)-dodec-9-en-1-yl acetates, Michelot [48] has used the coupling of the cis-iodoalkene element (LXXV) with the corresponding Grignard reagents in the presence of catalytic amounts of tetrakis(triphenylphosphine)palladium. The required pheromones (LXXVII) were obtained by eliminating the tetrahydropyranyl protective group in compounds (LXXVI), followed by acetylation. The isomeric purity of the substances obtained was 99%.



Of great of value for the synthesis of pheromones with the (Z)-configuration is the carbocupration reaction of acetylene [49], which enables (Z)-alkenes with a very high stereoisomeric purity (99.5%) to be obtained. For some insect sex pheromones, such a high degree of purity of the geometric isomers is extremely important. Thus, for example, (Z,Z)-octadeca-3,13-dien-1-yl acetate – the main component of the sex pheromone of the females of Synanthedon pictipes – attracts the males only if the 3,4-double bond has the Z-configuration to the extent of at least 99.5%. Other methods – reduction with Lindlar catalyst, P-2Ni or 9-borabicyclo[3.3.1]nonane – do not give such a high stereochemical purity [3, 6, 7]. By using the carbocupration action, French scientists under the leadership of Normant [51-53] have obtained a number of pheromones with very high (Z)-isomeric purity. As an example we can give the preparation of (Z)-tetradec-9-en-1-yl acetate with an isomeric purity of 99.5% [53].

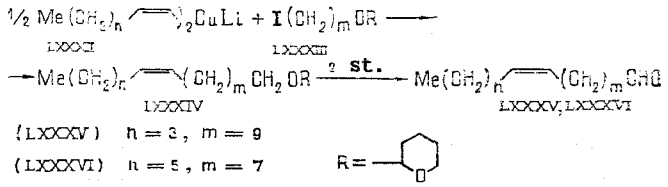


8-Iodooct-1-yl acetate (LXXIX) was obtained from 8-bromooctan-1-ol (LXXVIII). The interaction of lithium dibutylcuprate (LXXX) with acetylene gave the (Z)-hex-1-enylcuprate (LXXXI). The latter was caused to react with HMPT, the iodide (LXXIX), and triethyl phosphite, and gave an 80% yield of the required pheromone (V).

A very common and dangerous pest of the cotton plant is the corn earworm, or bollworm, Heliothis armigera Hbn. It has been established that the main components of its sex pheromone are (Z)-hexadec-11-enal, (Z)-tetradec-11-enal, and (Z)-hexadec-9-enal [54-56], a mixture of (Z)-hexadec-11-enal and (Z)-hexadec-9-enal in a ratio of 9:1 possessing a high attractiveness [57]. According to Kovalev [58], a mixture of (Z)-hexadec-11-enal and (Z)-tetradec-11-enal in a ratio of 3:1 is also attractive. The sex attractant of the American species Heliothis zea is a mixture of (Z)-hexadec-11-enal and (Z)-hexadec-9-enal in a ratio of 60:1, although each of these compounds taken separately does not attract the males of this pest [59, 60]. The same compounds are components of the sex pheromone of the American species of moth Heliothis virescens [61].

Components of the sex pheromone of the corn earworm are usually obtained by the Wittig olefination of carbonyl compounds [3, 6, 7, 62, 63] or by the acetylene route [3, 6, 7, 64-67] with the oxidation of the corresponding (Z)-alkenols by various oxidizing agents [3, 6, 7], the pyridinium chlorochromate proposed by Corey [68] being used fairly frequently. Oxidation by this reagent in dichloromethane enables the required aldehydes to be obtained without a double bond being affected and with no more far-reaching oxidation of the aldeyde group.

Other methods for the synthesis of these compounds have been developed. Thus, (Z)-hexadec-11-enal (LXXXV) and (Z)-hexadec-9-enal (LXXXVI) have been obtained by the application of the carbocupration reaction to acetylene [69].

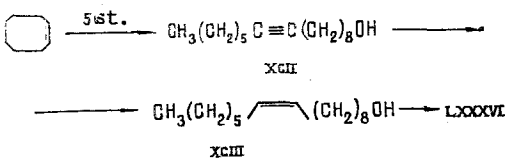


The alkylation of the (Z)-alk-1-enylcuprate (LXXXII) with the iodine derivative (LXXXIII) led to the (Z)-alkenolic compound (LXXXIV), which, after hydrolysis and oxidation, gave the required components of the sex pheromone with good yield and a (Z)-isomeric purity of 99.5%.

In the same paper, the preparation of the pheromone (LXXXV) in 80% yield and 98% purity by the alkylation of propargyl alcohol (LXXXVII) with nonyl bromide (LXXXVIII) followed by isomerization of the triple bond in the alkynol (LXXXIX) into the terminal position is described. The dodec-11-yn-1-ol (XC) obtained was then converted, by alkylation with butyl bromide, stereoselective hydrogenation of the alkenol (XCI), and oxidation, into the required (Z)-hexadec-11-enal.

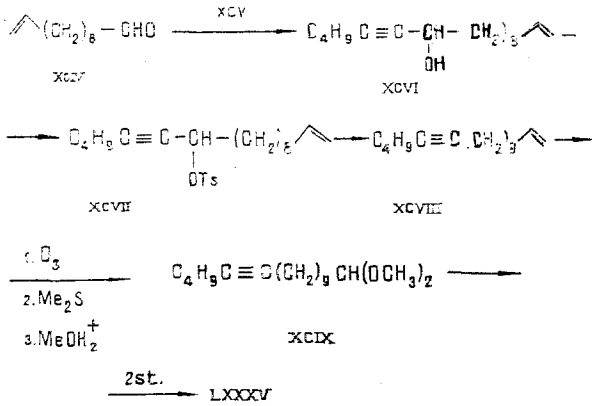
$$HC \equiv C - CH_2OH + CH_3(CH_2)_8Br \longrightarrow CH_3(CH_2)_8 - C \equiv$$
LXXXVII LXXXVIII LXXXIX
$$\equiv C - CH_2OH \longrightarrow HC \equiv C(CH_2)_{10}OH \longrightarrow C_4H_9C \equiv$$
XC XCI
$$\equiv C(CH_2)_{10}OH \longrightarrow LXXXV$$

A convenient synthesis of (Z)-hexadec-9-enal (LXXXVI) from the readily available cyclooctene has recently been developed [70], the conversion of the alkynol (CXII) into (Z)-hexadec-9-en-1-ol (CXIII) being performed with the aid of siobutylmagnesium bromide in the presence of dicyclopentadienyltitanium dichloride (Cp_2TiCl_2).



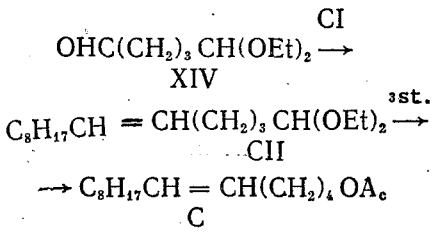
Oxidation of the alkynol (CXIII) with pyridinium chlorochromate gave the desired product containing not less than 95% of the (Z)-isomer.

The synthesis of (Z)-hexadec-11-enal based on the interaction of the readily available undec-10-enal (XCIV) with hex-1-ynylmagnesium bromide (XCV) has been carried out in the same laboratory [71]. The stereopurity of the aldehyde obtained was not less than 95%.



The deoxygenation of the 11-hydroxyheptadec-1-en-12-yne (XCVI) formed, via the corresponding tosylate (XCVII), gave the key synthon heptadec-1-en-12-yne (XCVIII). The enzyme (XCVIII) was converted by ozonolysis into 1,1-dimethoxyhexadec-11-yne (XCIV), which was hydrogenated stereoselectively over Lindlar catalyst in the presence of quinoline and was then converted by elimination of the acetal protection in an acid medium into the desired (Z)-alkenal (LXXXV).

The sex pheromone of the heart-and-dart moth consists of two monoenic acetates – (Z)-tetradec-5-en-1-yl acetate (C) and (Z)-tetradec-9-en-1-yl acetate [72]. The synthesis of the acetate (C) has recently been achieved from the monoacetal of glutaraldehyde (XIV) [73]. The interaction of the aldehyde (XIV) with the n-octylmethylenephosphorane generated by the action of sodium bis(trimethylsilyl)amide on onyltriphenylphosphonium bromide (CI) at −78°C, gave the diacetal of tetradec-cis-5-enal (CII), which, after acid hydrolysis, reduction, and acetylation yielded the cis-acetate (C):



The sex pheromone of the gamma moth Autographa gamma L. contains (Z)-dodec-7-en-1-ol and its acetate]74, 75]. The sex pheromone of the beet webworm Loxostege sticticalis L. is (Z)-tetradec-11-en-1-yl acetate [76.

Thus, a number of stereoselective syntheses of monoenic aliphatic pheromones of insect pests of the cotton plant have been considered and advances in this field have been generalized.

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IMMUNOMODULATING ACTIVITY OF GOSSYPOL DERIVATIVES

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L. Biktimirov, A. I. Ismailov, and K. G. Urazmetov

UDC 547.554:615.37

Information is given on the immunosuppressive activity of a number of gossypol derivatives, and it is shown that practically all the compounds studied are immunotropic. The structural-functional relationship and the dose-dependent nature of the action of the substances obtained are shown.

The search for methods of stimulating and depressing the immune system as a whole and individual cell populations of it is regarded as the main task of immunocorrection [1]. The search for effective immunomodulators is being carried out in the most diverse directions, but hitherto these investigations have mainly borne an empirical nature. This is due to the complexity of the organism and of the functioning of the immune system, which consists of various populations of cells interacting with one another and various substances secreted by these cells [1]. The final effect (immunostimulating or immunodepressive) depends on the integral action of a given modulator on the functional activity of the immunocompetent cells.

Both substances of protein nature and also physiologically active compounds of synthetic [2] and plant [3] origin may be immunocorrecting. At the present time, reports have appeared of the existence of immunostimulating properties in plant polyphenols [4, 5].

In the present paper we give information on the immunomodulating activity of gossypol derivatives. The basis for the study of this type of activity of gossypol was its possession of antitumoral [6] and antiviral [7] activities.

It has been found that gossypol possesses some immunosuppressive activity, and to enhance this effect it was desirable to modify its structure, which would permit the influences of various functional groups of the gossypol molecule and of the nature of substituents on its activity to be determined simultaneously.

Because of the structure of gossypol, it is possible to obtain ethers and esters, azomethines, and condensation products with compounds containing active methylene groups [8].

A consideration of the comopunds obtained in relation to their immunosuppressive action showed that the ethers (II)-(IV), although they possessed activity, did so to a smaller degree than the initial gossypol (I). Substitution of the hydroxy groups led to a fall in the activity that was almost proportional to the degree of substitution (Fig. 1).

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