Stereodirectional Synthesis of the Main Component of Pheromone (9Z,12E)-Tetradeca-9,12-dienyl Acetate by Cross-coupling

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Abstract—By cross-coupling of alkynyl cuprate with crotyl halides was synthesized (9Z,12E)-tetradeca-9,12-dienyl acetate, the main component of pheromones of several insect species Lepidoptera. The assignment of the chemical shifts of diene system was performed by $^1$H and $^{13}$C NMR spectroscopy.

The (9Z,12E)-tetradeca-9,12-dienyl acetate (I), the main component of pheromone of insects Ephestia Kuehniella and Plodia Interpunctella, cereal pests, are synthesized by several methods [1-3].

$$\text{H}_3\text{C} \equiv \text{C} \equiv \text{C} \equiv \text{C} \equiv \text{C} \equiv \text{C} \equiv \text{C} \equiv \text{C} \equiv \text{C} \equiv \text{C} \equiv \text{C} \equiv \text{C} \equiv \text{CH}_2\text{OH} \quad \text{O} \equiv \text{Ac}$$

$$\text{I}$$

We described in [1] a successful stereospecific synthesis of this pheromone using as key stage saltless version of Wittig reaction: The attained stereospecific purity of the diene was 98%. The target of this study was the synthesis of pheromone I by cross-coupling of lithium homocuprate with crotyl chloride and crotyl bromide.

We studied formerly the cross-coupling of various primary and secondary allyl halides with lithium dialkynyl cuprates as a model reactions of regioselective 1,4-enyne synthesis [4]. We found the conditions affording 96-97% of regioselective cross-coupling.

For the multistage stereodirectional synthesis of pheromone I was chosen as starting compound dec-2-yn-1-ol (II) that was prepared by alkylation of dilithium salt of propargyl alcohol with heptyl bromide in liquid ammonia.

Preparation of the terminal decinol (III) without impurities of allenes, dienes, and nonterminal alkyne resulted from treating dec-2-yn-1-ol (II) with lithium 2-aminoethylamide in ethylenediamine at 60-70°C [5]. The terminal decynol was obtained in 82% yield in chromatographically pure state and was characterized by $^{13}$C NMR spectra.

The next stage of the synthesis required tetrahydropyranyl protection of the hydroxy group, and the corresponding tetrahydropyranyl decynyl ether was obtained in 95% yield and 97% purity and was used without further purification.

The second components in cross-coupling were crotyl halides. E-isomer of crotyl chloride of 99% purity was prepared by procedure developed by us previously consisting in replacement of hydroxy group in crotyl alcohol with chlorine by treating with triphenylphosphine complex with ethyl trichloro-

Table 1. Isomeric composition of coupling products of 9-decyn-1-ol homocuprate with crotyl halides

<table>
<thead>
<tr>
<th>Halide</th>
<th>Overall yield, %</th>
<th>Isomeric composition, %</th>
<th>Yield of pure isomer IV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IV</td>
<td>V</td>
</tr>
<tr>
<td>Crotol bromide</td>
<td>88</td>
<td>83</td>
<td>9</td>
</tr>
<tr>
<td>Crotol chloride</td>
<td>85</td>
<td>89</td>
<td>5</td>
</tr>
<tr>
<td>(E)-1-Chlorobut-2-ene</td>
<td>82</td>
<td>95</td>
<td>1</td>
</tr>
</tbody>
</table>

* A mixture of isomers was used.
acetate [6]. Besides we used in coupling a mixture of E- and Z-1-chlorobut-2-enes obtained in reaction of crotyl alcohol with hydrochloric acid. Crotyl bromide disregarding the method of its preparation always contains three isomeric bromides: E- and Z-1-bromo- but-2-enes, and 3-bromo-1-ene.

\[
\begin{align*}
\text{H}_3\text{C} & \text{OH} \xrightarrow{HX} \text{H}_3\text{C} \text{X} \\
+ \text{CH}_3 & \text{X} + \text{H}_2\text{C} \text{CH}_3 \\
\text{X} & = \text{Cl}, \text{Br}
\end{align*}
\]

The products of cross-coupling between terminal alkynyl cuprate and crotyl halides were studied and the yields of reaction products were evaluated after elimination of tetrahydropyranyl protective group by treating with p-toluenesulfonic acid in methanol. The structure and isomer ratio was estimated from GLC, \(^1\)H and \(^{13}\)C NMR data.

In Table 1 are presented the data on isomeric composition of the coupling products for crotyl bromide, crotyl chloride, and individual E-1-chloro- but-2-ene.

\[
\begin{align*}
\text{H}_3\text{C} & \text{X} \\
(1) \text{[THPO-(CH}_2)_8\text{]} \xrightarrow{\text{CuLi}} & \text{H}_3\text{C} \text{R} \\
(2) \text{TsOH/MeOH} & \text{IV} \\
+ \text{H}_3\text{C} & \text{R} + \text{H}_2\text{C} \text{R} \\
\text{V} & \text{VI} \\
\text{R} & = -(\text{CH}_2)_8\text{OH}
\end{align*}
\]

At the use in reaction of mixtures of isomeric chlorides and bromides the regio and stereoselectivity of the reaction are relatively low (83–90%). As was expected the purest cross-coupling product (95%), E-tetradec-12-en-9-yn-1-ol (IV), was obtained from the pure E-1-chlorobut-2-ene. Further purification of enynol IV was carried out by low temperature crystallization from hexane at -30±50°C. Two recrystallizations with more homogeneous product and tree-four with less pure compound resulted in isomeric purity of compound attaining 98–99%.

In the \(^1\)H NMR spectrum of E-tetradec-12-en-9-yn-1-ol appear signals of protons at the double bond, those from methyl and methylene groups characteristic of hex-4-en-1-yn-1-yl fragment in the carbon backbone. The vicinal coupling constant of the olefinic protons amounting to 15 Hz evidences trans-configuration of the double bond. A characteristic feature of the \(^1\)H NMR spectrum of the coupling product, alcohol IV, is the appearance of a coupling constant \(^J\) 2.5 Hz in the signals of methylene groups at the triple bond corresponding to the long-range spin-spin coupling through the triple bond and unambiguously confirming the enyne system formation.

Enynol IV obtained was reduced with hydrogen over P-2Ni catalyst in the presence of ethylenediamine [7]. The reaction was monitored with GLC, since the initial E-tetradec-12-en-9-yn-1-ol and (9Z,12E)-tetradeca-9,12-dien-1-ol (VII) notably differ in retention times.

\[
\begin{align*}
\text{OH} & \text{C} \equiv \text{C} \equiv \text{CH}_3 \\
\text{IV} & \text{H}_2/\text{Ni} \\
25\,^\circ\text{C, EtOH} & \text{VII, 85%}
\end{align*}
\]

The reduction proceeds with a high yield (85%), and the reaction product VII according to GLC is of 98% purity and contains no more than 1% of isomeric dienes and less than 1% of alkenol.

Acylation of (9Z, 12E)-tetradeca-9,12-diene-1-ol (VII) with acetic anhydride in tetrahydrofuran in the presence of pyridine afforded the corresponding acetate I in 93% yield. The completion of acylation was checked by GLC. It is important since according to published data the attractive activity of pheromone for some insect species is suppressed in the presence of unacylated (9Z, 12E)-tetradeca-9,12-diene-1-ol. The isomer (9Z, 12E-I) obtained according to GLC, \(^1\)H and \(^{13}\)C NMR data is of 99% isomeric purity (impurity 1% of Z,Z-isomer) and of 98% general purity.

The isolated data on \(^1\)H NMR spectrum of this compound cannot serve as reliable confirmation of the double bonds configuration in the diene system. However, since both \(^1\)H and \(^{13}\)C NMR spectra and also retention time of the compound obtained by cross-coupling and that previously prepared by Wittig reaction coincide, we can conclude on formation of pheromone I.