# Insect Sex Attractants; XII[1]. An Efficient Procedure for the Preparation of Unsaturated Alcohols and Acetates

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Nearly all sex attractants of lepidopterous insect species identified thus far have been proved to be long-chain unsaturated alcohols or their acetates[2]. The synthesis of these materials is usually accomplished via a key acetylenic intermediate **1**, which is obtained by the coupling reaction of an acetylenide with the appropriate alkyl halide.

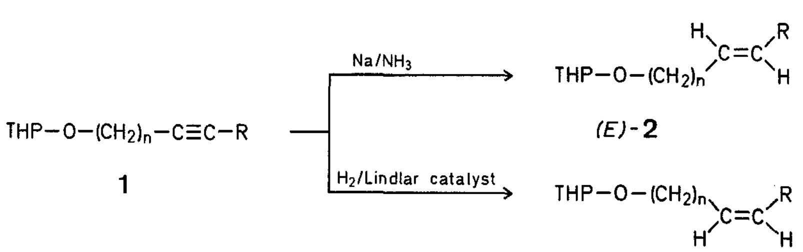
*(1)*

$$\text{THP-O-(CH}_2)_n\text{-C}\equiv\text{C}^{\ominus}\ \text{M}^{\oplus} + \text{R-X} \longrightarrow \text{THP-O-(CH}_2)_n\text{-C}\equiv\text{C-R} + \text{M-X}$$

**1**

*(2)*

*(3)*



THP = tetrahydropyran-2-yl

Reaction product **1** may then be readily reduced, either by chemical means, e.g. sodium/liquid ammonia to yield (*E*)-compound **2** (Reaction *2*), or catalytically, using Lindlar catalyst[3] to yield (*Z*)-compound **2** (Reaction *3*). The desired long-chain alcohol or acetate, respectively, is then obtained by the hydrolytic cleavage or the acetolysis of the THP-O bond.

This communication deals with an improved method of preparing intermediate **1**. The classical preparation of **1** is carried out according to Reaction *(1)*, using sodamide suspended in the reaction medium of liquid ammonia to form the acetylenide, which is then alkylated with the appropriate alkyl halide. This procedure suffers from rather variable yields due to low solubilities of some of the acetylenides in liquid ammonia and the concomitant reaction of the alkyl halide with the solvent. An improved procedure for carrying out the alkylation reaction is available using dioxane as the solvent and lithium as the counter ion[4]. Either lithium amide or butyllithium may be used as the metallating agent, the latter being preferable because of the far shorter reaction times needed to form the acetylenide. We have found that this reaction proceeds in excellent yields (70% average), but reflux times of 18–24 hr are needed to drive the reaction to completion. Another disadvantage is that low-boiling alkyl halides cannot be readily used.

Reaction *(1)* may be carried out in practically quantitative yields by using a mixture of hexamethylphosphortriamide (HMPT) and tetrahydrofuran as suggested by Normant[5]. The reaction proceeds extremely rapidly at or slightly below room temperature, so that there is no limitation to the normal alkyl halides that may be used. In a typical procedure, the acetylenic compound is dissolved in tetrahydrofuran and one equivalent of butyllithium in hexane is added at 25°. When the addition is complete, a solution of the alkyl halide in HMPT is added, being careful to keep the temperature of the reaction mixture below 25° (Method A).

$$\text{THP-O-(CH}_2)_n\text{-C}\equiv\text{CH} \xrightarrow[\text{2. X-(CH}_2)_m\text{-CH}_3]{\text{1. }n\text{-C}_4\text{H}_9\text{Li}} \text{THP-O-(CH}_2)_n\text{-C}\equiv\text{C-(CH}_2)_m\text{-CH}_3$$

**2**

Alternatively, the tetrahydrofuran/hexane solution of an acetylenide may be added to a solution of an ω-chloroalkyl tetrahydropyran-2-yl ether in HMPT (Method B).

$$\text{H}_3\text{C-(CH}_2)_m\text{-C}\equiv\text{CH} \xrightarrow[\text{2. Cl-(CH}_2)_n\text{-O-THP}]{\text{1. }n\text{-C}_4\text{H}_9\text{Li}} \text{THP-O-(CH}_2)_n\text{-C}\equiv\text{C-(CH}_2)_m\text{-CH}_3$$

**2**

The reaction is complete within a few minutes; the mixture is then poured into a large volume of ice water and extracted with hexane. The crude reaction product obtained may be reduced to the *trans* olefinic compound and then converted to the alcohol or the acetate without further purification. To prepare the *cis* compounds, the crude reaction product is hydrolyzed or acetolyzed and then purified prior to catalytic reduction.

### Preparation of Ynyl Tetrahydropyranyl Ethers 1; General Procedure:

Method A: To a stirred solution of the ω-tetrahydropyranyloxy-1-alkyne (20 mmol) in absolute tetrahydrofuran (20 ml) was added butyllithium (22 mmol) in hexane (15 ml) while keeping the temperature below 10°. The alkyl halide (22 mmol) in HMPT (35 ml) was added dropwise while keeping the temperature below 25°. The reaction mixture was worked up within 30 min by pouring into a large volume of ice water and extracting twice with hexane.

The organic layer was washed once with water, once with brine, and dried. Evaporation of the solvent yielded the desired crude product in quantitative yield.

Method B: A slurry of 1-lithio-1-alkyne (22 mmol), prepared at −10° from a 1-alkyne (25 mmol) in absolute tetrahydrofuran (15 ml) and butyllithium (22 mmol) in hexane (15 ml), was added to a solution of an ω-chloroalkyl tetrahydropyran-2-yl ether (20 mmol) in HMPT (30 ml) keeping the temperature below 25°. The reaction mixture was worked up within 30 min as in Method A.

**Preparation of Ynyl Acetates:**

To the crude ynyl tetrahydropyranyl ether (20 mmol) as prepared above was added a 10:1 acetic acid/acetyl chloride (20 ml) mixture and left at 35°–40° overnight. The resultant dark mixture was decomposed by pouring on ice and extracted three times with hexane. The hexane layer was washed with 10% sodium hydrogen carbonate, water, and brine and then dried. Evaporation of the hexane afforded the desired acetate, which was purified by fractional distillation (see Table 1).

**Preparation of *trans*-Enyl Acetates (*Z*-2):**

To a stirred, refluxing solution of crude ynyl tetrahydropyranyl ether (20 mmol) in liquid ammonia (50 ml) and absolute tetrahydrofuran (50 ml), sodium (50 mg-atom) was added in two portions. Upon discharge of the blue color, the ammonia was allowed to evaporate and saturated aqueous ammonium chloride (20 ml) was added cautiously. The resultant two-phase mixture was poured into hexane and washed with water and brine and dried. Upon evaporation of the hexane, the crude enyl tetrahydropyranyl ether was converted to the acetate as described above. The *trans* enyl acetate was purified by fractional distillation (see Table 2).

Table 1. Preparation of Ynyl Acetates[a]

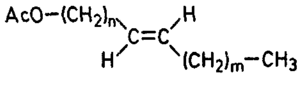
$AcO-(CH_2)_n-C{\equiv}C-(CH_2)_m-CH_3$

| Method | m | n | b.p./mm | $n_D^{25}$ | Yield %[b] |
|---|---|---|---|---|---|
| A | 0 | 12 | 110–112°/0.05 | 1.4528 | 85 |
| A | 6 | 5 | 109–111°/0.005 | 1.4482 | 92 |
| A and B | 1 | 5 | 73–73°/0.1 | 1.4460 | 88 |

[a] Satisfactory elemental and G.L.C. analyses and consistent spectra were obtained for all new compounds.

[b] Based on 1-alkynyl tetrahydropyran-2-yl ether or on ω-chloroalkyl tetrahydropyran-2-yl ether starting materials.

Table 2. Preparation of *trans*-Enyl Acetates (*Z*-2)[a]



| m | n | b.p./mm | $n_D^{25}$ | Yield %[b] |
|---|---|---|---|---|
| 0 | 12 | 106–108°/0.05 | 1.4462 | 80 |
| 6 | 5 | 104–105°/0.05 | 1.4446 | 81 |
| 1 | 5 | 58–60°/0.05 | 1.4386[c] | 85 |

[a] Satisfactory elemental and G.L.C. analyses and consistent spectra were obtained for all new compounds.

[b] Based on 1-alkynyl tetrahydropyran-2-yl ether or on ω-chloroalkyl tetrahydropyran-2-yl ether starting materials.

[c] Ref.[6], b.p. 65–70°/0.3 mm; $n_D^{25}$: 1.4343.

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