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SOME SOLID-PHASE SYNTHESES OF THE SEX ATTRACTANT OF THE SPRUCE BUDWORM—*trans*-11-TETRADECENAL[1]

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Abstract—The sex attractant of the spruce budworm, *Choristoneura fumiferana*, *trans*-11-tetradecenal (I), was synthesized on solid phases by three different routes from inexpensive 1,10-decanediol. The preparation of the *trans*-alkene I directly on the polymer support was not completely stereoselective.

Key Words—solid-phase synthesis, *trans*-11-tetradecenal, spruce budworm, *Choristoneura fumiferana*, *trans*-11-tetradecenol and acetate, 11-tetradecyne-1,10-diol.

It has been demonstrated that insoluble polymer supports can be used as monoprotecting agents of symmetrical diols (Wong and Leznoff, 1973; Fyles and Leznoff, 1976; Fréchet and Nuyens, 1976). Inexpensive symmetrical diols were then used as precursors in the solid phase syntheses of cis insect sex attractants via an alkyne-coupling route, a Wittig route, a "reverse" Wittig route (Leznoff and Fyles, 1976; Leznoff, Fyles, and Weatherston, 1977), and a two-step alkyne-coupling route (Fyles, Leznoff, and Weatherston 1977).

The synthesis of an isomerically pure trans insect attractant on solid phases presents a particularly difficult problem, as shown herein. Although the sex attractant, *trans*-11-tetradecenal (I), of the spruce budworm, *Choristo-*

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[1] The Use of Polymer Supports in Organic Synthesis, XIII.

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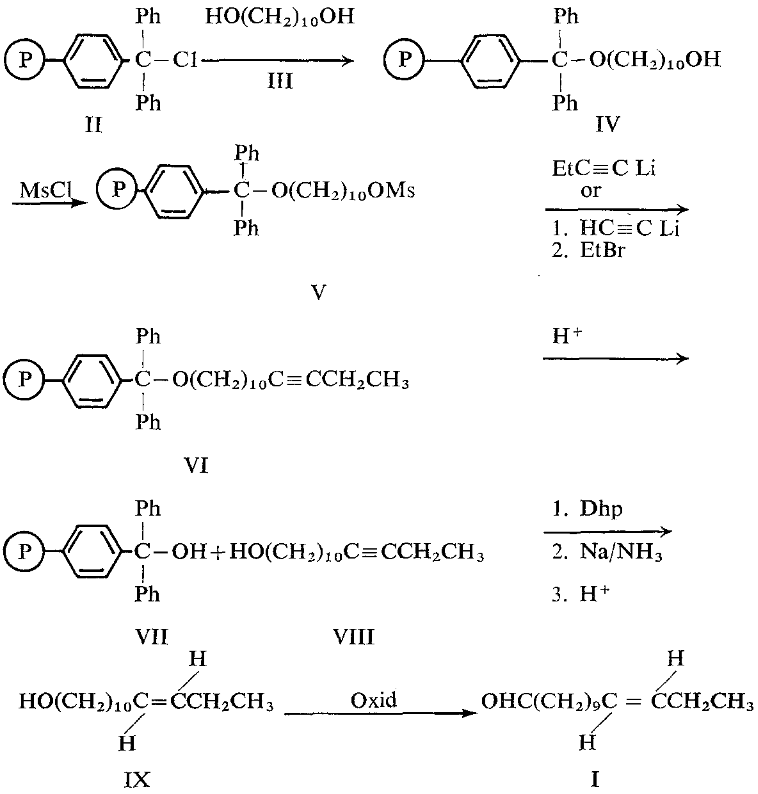
neura fumiferana, was isolated, characterized, and synthesized some time ago (Weatherston and Percy, 1970; Weatherston et al., 1971) and is even commercially available (Chemical Samples Co.), details of its synthesis and its spectroscopic characteristics have never been published.

In this paper, we describe the preparation of I on solid phases by three different routes. The synthesis of I was accomplished according to Scheme A. This method produces 11-tetradecyn-1-ol (VIII), previously prepared on solid phases (Leznoff and Fyles, 1976) by a conversion of 58% from III. Attempts to reduce the polymer-bound alkyne VI directly to a *trans*-alkene by the standard procedure (Campbell and Eby, 1941; Warthen and Jacobson, 1973) of using sodium in liquid ammonia predictably failed, as liquid ammonia is a notoriously bad solvent for performing chemical reactions on cross-linked polystyrene beads because of the inability of ammonia to swell the polymer beads. Hence, VIII, prepared on solid phases, was stereoselectively reduced in solution (Warthen and Jacobson, 1973) with sodium in liquid ammonia to give *trans*-11-tetradecen-1-ol (IX), which was analyzed by high-pressure

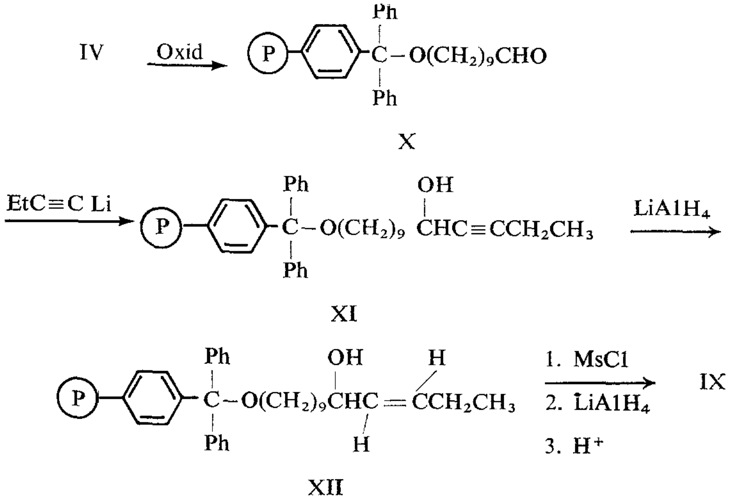
Scheme A



liquid chromatography (HPLC) and vapor-phase chromatography (VPC) as its acetate (Warthen, 1975). Oxidation of IX with a mixture of chromyl chloride, *tert*-butanol, and pyridine in CH_2Cl_2 (Sharpless and Akashi, 1975) gave I in 76% overall yield from VIII.

Although the synthesis of I was thus achieved partly on solid phases and partly in solution, we wished to accomplish the *total* synthesis of I on solid phases for adaptation to automation (Merrifield et al., 1966). An attempt to achieve this goal is outlined in Scheme B. It is known that propargylic alcohols can be reduced stereoselectively to *trans*-allylic alcohols (Bharucha and Weedon, 1953; Raphael, 1955), and we hoped that this procedure could be applied to the synthesis of a polymer-bound *trans*-alkene required for the synthesis of I. The polymer-bound diol IV was oxidized to the polymer-bound aldehyde X (Sharpless and Akashi, 1975; Leznoff et al., 1977). Treatment of X with 1-lithio-1-butyne gave the polymer-bound alkynol XI, which, on acid cleavage, yielded 11-tetradecyne-1,10-diol. Reduction of XI with $LiAlH_4$ or $NaAlH_2(OCH_2CH_2OCH_3)_2$ and subsequent elaboration according to Scheme B gave only VIII and IX in 28% and 15% conversions, respectively. The isolation of VIII can be readily rationalized if one assumes that the reduction of XI was incomplete. This sequence was particularly discouraging because I was contaminated by VIII and did not exhibit a sufficiently high cis–trans ratio (1:9 in the best instance) to warrant further development.

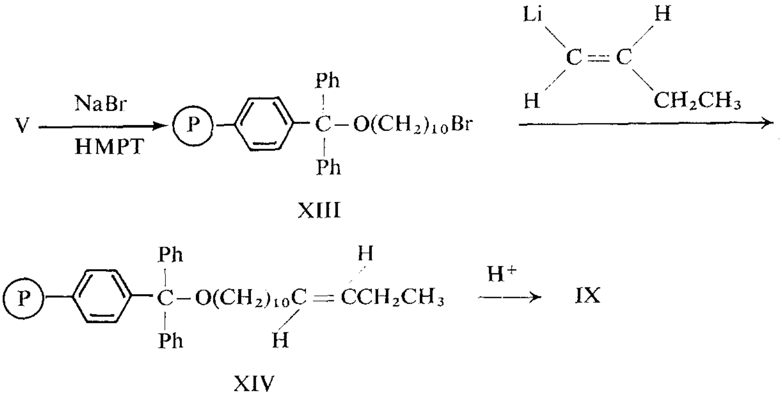
Scheme B



A third route to I is shown in Scheme C. In this approach, a polymer-bound bromide XIII, prepared from V, reacted with the preformed *trans*-1-

lithio-1-butene (Neumann and Seebach, 1976) to give a polymer-bound alkene XIV, which, on acid treatment and oxidation as described before, gave IX in 37% yield and 67% conversion from starting diol III. The synthesis of I according to Scheme C proceeded well, but the cis–trans ratio (1:3) was not as high as the analogous reaction in solution (Neumann and Seebach, 1976). Perhaps the necessity of using slightly higher temperatures and hexamethylphosphoric triamide (HMPT) as solvent in the coupling step contributed to the diminished selectivity on the solid phase.

Scheme C



The synthesis of a trans insect sex attractant, *trans*-11-tetradecenal (I), has been achieved partially on solid phases using inexpensive symmetrical diols. The synthesis of I totally on solid phases has been accomplished, but further work must be done to give I having a cis–trans ratio of 4:96, comparable to that of the natural attractant (Sanders and Weatherston, 1976).

METHODS AND MATERIALS

Instruments and Standard Procedures

A Bausch and Lomb Abbé 3L refractometer was used to record the refractive indices (n_D). Infrared spectra (IR) were recorded on a Unicam SP1000 IR spectrophotometer as neat films between NaCl disks unless otherwise specified. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian EM360 spectrometer, with deuteriochloroform as solvent and tetramethylsilane as internal standard. Mass spectra (MS) were recorded on a Perkin-Elmer-Hitachi RMU6E mass spectrometer. Silica gel was used for all thin and preparative layer chromatography. Fractions were extracted with ether in a Soxhlet extractor. Filtration was done under vacuum through sintered glass Büchner funnels. Filtration under an inert atmosphere was done as previously described (Fyles and Leznoff, 1976). Microanalyses were performed by G. Gygli of Toronto.

Vapor-phase chromatograms were run with a Perkin-Elmer 990 instrument using a 17 ft × 1/8 in. column of 10% Silar 10C on Gaschrom Q(60/80) at a temperature of 175° and a nitrogen flow rate of 15 ml/min. High-pressure liquid chromatograms were run with a Waters Associates Model 440 instrument, with an R-400 refractive index detector. A 30 × 0.4 cm reverse phase μ Bondapak C-18 column with 30% water in acetonitrile was used at a flow rate of 0.8–1.0 ml/min. Spectral and analytical data are given for all new compounds and for known compounds where data are unreported.

trans-11-Tetradecen-1-ol(IX) and Its Acetate

Compound IX was prepared from VIII by the method of Warthen and Jacobson (1973) in 90% yield.

n_D: 1.4597.
IR: γ 3350, -OH; 3020 and 960 *trans*-CH=CH.
NMR: δ 5.4 (m, 2H); 3.6 (t, 2H, J = 8 Hz); 3.0 (s, broad, 1H); 2.3–1.9 (m, 4H); 1.8–1.2 (m, 16H); 0.95 (t, 3H, J = 7 Hz).
Anal. calc. for $C_{14}H_{28}O$: C 79.18, H 13.29; found: C 79.20, H 13.18.

The acetate of IX was prepared by treatment of IX with acetic anhydride in pyridine. Analysis of the acetate by HPLC revealed less than 0.5% contamination by the cis isomer.

n_D: 1.4531.
IR: γ 1740, $CH_3C=O$; 1240; C–O; 960, *trans* CH=CH.
NMR: δ 5.4 (m, 2H); 4.2 (t, 2H, J = 8 Hz); 2.3–1.9 (m, 7H); 1.8–1.2 (m, 16H); 0.95 (t, 3H).
MS: m/e (16 eV) 254 (0.6) (M); 194 (100) (M–HOAc).
Anal. calc. for $C_{16}H_{30}O_2$: C 75.54, H 11.89; found: C 75.41, H 11.80.

trans-11-Tetradecenal (I)

Oxidation of IX by the method of Sharpless and Akashi (1975) and subsequent purification by preparative TLC (eluant, benzene) yielded I in 85% isolated yield. Analysis of I by HPLC and VPC showed more than 98% of I was in the trans form.

n_D: 1.4495.
IR: 2720, O=C–H; 1720, C=O; 960, trans CH=CH.

NMR: δ 9.7 (t, 1H, $J = 0.5$ Hz); 5.4 (m, 2H); 2.4 (m, 2H); 2.1–1.8 (m, 4H); 1.8–1.2 (m, 14H).
MS: m/e 210 (4.3) (M); 192 (16.2); 44 (100).
Anal: calc. for $C_{14}H_{26}O$: C 79.94, H 12.46; found; C 80.09, H 12.31.

Polymer-Bound Propargylic Alcohol XI)

To a solution of 50 mmol of 1-lithio-1-butyne in 80 ml of tetrahydrofuran (THF) was added 10 g of polymer-bound aldehyde X, derived from IV containing 0.60 mmol/g of III, and 80 ml of hexamethylphosphoric triamide (HMPT). The mixture was stirred under an argon atmosphere overnight, hydrolyzed with water, filtered, washed, and dried as previously described (Leznoff et al., 1977). The IR spectrum of XI did not exhibit an absorption band at 1720 cm^{-1} caused by unreacted X.

11-Tetradecyne-1,10-diol

Acid hydrolysis (Leznoff et al., 1977) of 1.0 g of XI and purification of the product by preparative TLC (eluant, ether–benzene, 1:1) gave 54 mg (0.31 mmol) of 1,10-decanediol (III) (R_f, 0.25) and 30 mg (0.13 mmol) of 11-tetradecyne-1,10-diol (R_f, 0.70) in 21% yield, or 44% conversion from III.

nD: 1.4450.
IR: γ 3400, –OH; 2320, C$\equiv$C.
NMR: δ 4.2 (m, 1H); 3.6 (t, 2H, $J = 8$ Hz); 3.0 (s, broad, 2H); 2.4–1.9 (m, 4H); 1.8–1.2 (m, 14H); 0.95 (t, 3H, $J = 8$ Hz).
MS: m/e 226 (1) (M); 225 (4); 224 (5); 208 (14) (M-H_2O); 43 (100).
Anal: calc. for $C_{14}H_{26}O_2$; C 74.29, H 11.58; found C 74.36, H 11.46.

Polymer-Bound trans-Allylic Alcohol XII

In a typical experiment, 2 g of XI was added to a solution of 25 mmol of $LiAlH_4$ or $NaAlH_2(OCH_2CH_2OCH_3)_2$ in 40 ml of THF or benzene, respectively. The mixture was heated under reflux under an argon atmosphere overnight, cooled, filtered under anhydrous conditions (Fyles and Leznoff, 1976), and washed with three 25-ml portions of dry solvent. Polymer XII was transferred to a Büchner funnel, washed, and dried (Leznoff et al., 1977). The IR spectrum of XII was uninformative.

Since acidic cleavage of XII yielded a complex mixture of products, XII was directly converted to a mesylate (Leznoff et al., 1977), reduced to polymer-bound *trans*-alkene as described for the formation of XII, and cleaved with acid to yield, upon purification by TLC, some recovered III, alkynol VIII in 28% yield, and the desired IX in 15% yield. Analysis of IX as its acetate by HPLC and VPC, revealed a cis–trans ratio of only 1:9 in the best instance.

Polymer-Bound trans-Alkene XIV

To a solution of 5 mmol of *trans*-1-lithio-1-butene at −80° was added 1.2 g of XIII (Leznoff et al., 1977), containing 0.3 mmol/g of Br, and 30 ml of HMPT. The resulting slurry was allowed to warm to room temperature over 1 h, then warmed to 60° and stirred overnight. The polymer was filtered, washed (Leznoff et al., 1977), and air dried. The IR spectrum of XIV was uninformative.

Acid cleavage of XIV yielded IX, as before (Leznoff et al., 1977). Analysis of IX, as its acetate, by HPLC and VPC revealed a cis–trans ratio of 1:3.

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